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EDITORIAL

Plagiarism : Time For Introspection

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Plagiarism is becoming a serious problem in schools, colleges, institutes and universities. Presence of a number of websites and an easy access to them through internet gives everyone availability to a wide range of materials. It is aggravated by "cut and paste "strategy in computers.

Plagiarius—is a Latin word meaning kidnapper, derived from Greek word plagium meaning kidnapping.[1] To plagiarize is to steal and pass off [the ideas or words of another] as one's own without crediting the source or to commit literary theft and present it as new and original idea or product derived from existing source.[2]Plagiarism is the" wrongful appropriation" and "stealing and publication of another author's language, thoughts, ideas or expressions" and representation of them as one's own original work.[3] It is a practice of taking someone else's work or ideas and passing them off as one's own.[3] Plagiarism is considered an academic theft or dishonesty. It is considered as disciplinary offence and one who commits such offence is liable to disciplinary action.

Cases of Plagiarism are increasing due to changes in government resolutions about number of publications by a teacher in Medical colleges required for increments in salary, promotions to higher posts and MCI requirements. If we refer to "**Uniform requirements for biomedical** journal" [4] it clearly mentions the rules and regulations for publication of a research paper. When a paper is sent for publication an undertaking is needed by all authors stating that this paper is not sent for publication to other journal .The sequence of authors is given indicating contribution of each author for that paper. Now a tug of war has started in sequencing the names as only first two authors or an author and corresponding author is taken into consideration for real publication. If it is a dissertation only post graduate guide and student can be accommodated. If head of department is a guide both are safe. But it may so happen that even though student has done most of the work the guide and head of department may insist on putting their name first. If a guide is transferred someone else may omit his or her name for publishing. When a student leaves the institute after passing , post graduation guide may omit his or her name. This is the beginning of kidnapping each other's work.

Plagiarism may be unintentional or intentional.[5]

Unintentional Plagiarism

- Paraphrasing poorly: changing a few words without changing the sentence structure of the original or changing the sentence structure but not the words
- Quoting poorly: putting quotation marks around part of a quotation but not around all of it or putting quotation marks around a passage that is partly paraphrased and partly quoted.
- Citing poorly: omitting an occasional citation or citing inaccurately.

Intentional Plagiarism

- Passing off as one's own pre-written papers from the Internet or other sources.
- Copying an essay or article from the Internet, on-line source, or electronic database without quoting or giving credit.
- Cutting and pasting from more than one source to create a paper without quoting or giving citation.
- Borrowing words or ideas from other students or sources without giving credit.

Types of Plagiarism: depend on the degree to which copying is done. [5]

Direct Plagiarism (Ghost writer): Plagiarism of Words

The use of another's exact words without citing the author. A significant portion of the text from a single source is copied by the writer without doing any alteration. When a word to word transcription of a section of someone else's work is done without attribution and without quotation marks it is direct plagiarism. We can call it as a Ghost writer. This deliberate plagiarism of someone else's work is

unethical and academically dishonest. It can lead to disciplinary actions including expulsion.

Recently a case of stolen thesis came to the notice in the institute. Dissertation was sent to an external examiner outside state for evaluation , by the University. Using this data, even without changing values, the examiner prepared a paper on this dissertation and published it in an indexed journal. The candidate was not aware of the stolen things and came to know about it while searching on internet.

Plagiarism of Structure

When a person uses someone else's ideas in his own words it is restatement or paraphrase. In a paraphrasing a person has to change both words and sentence structure without changing the content. If keeping the content proper citation is not given it is plagiarism of structure.

It is advantageous to highlight the fact that other sources support your own ideas. Good paraphrasing makes the ideas of original source fit smoothly into the paper.

Plagiarism of Ideas

Presenting another's ideas as your own without giving credit to the person.

Submitting a paper without citing or incorrectly citing another's idea.

Plagiarism of Self

When a person submits his or her own previous work by changing the title, to maybe two or more different journals or mixes parts of previous work without permission from all others involved in that project ,it is self plagiarism.

Plagiarism of authorship

When replication of another's work is done, when one submits a paper that is downloaded from internet or from a friend and is presented as his own.

An author is someone who had made substantial intellectual contribution to the study. [4] Authorship should be based on:

1. Substantial contribution to concept, design, acquisition of data, analysis and interpretation of data.

2. Drafting the article or revising it critically for important intellectual content.

3. Final approval of the version to be published When a large group has concluded the work, the group should identify the individual who accepts direct responsibility for the manuscript.

Corresponding author should clearly indicate preferred citation and should clearly identify all authors.

Name other members in acknowledgements. All contributors who don't meet criteria for authorship should be in acknowledgement section. e.g. pure technical work, writing assistance ,departmental head who provided only general support ,financial support. A written permission is needed for acknowledgment.

How much plagiarism is plagiarism?[6]

This question is similar to asking how much I steal would constitute theft? Even lifting a sentence without acknowledgement constitutes plagiarism. In July2002, vice chancellor of a leading University in Australia resigned because it was revealed that he lifted several passages from other academics without acknowledgement in his book.

Legal aspects of plagiarism in India[7]

Section 57 of Indian copyright Act 1957, gives authors the right to claim “authorship” of their works among other things. Section 63 of Indian Copyright Act considers infringement as criminal offence and awards some punishment for both i.e. violation of section 57 and copyright infringement. Plagiarism is an offence under section 63 of Indian copyright act and the culprit can be put behind bars. a person can be imprisoned from six months up to three years. The issue was raised in the governing body chaired by Union minister of health and family welfare.J.P.Nadda on October 13 last year. A report of institute's ethics committee was cited to probe the allegations.

Shimna Kanwar from timesgroup.com has reported recently: 3 senior doctors have been chargesheeted for plagiarism and data manipulation in PGMIER Chandigarh. This comes at a time when the prestigious medical –cum –research institute framed its guidelines on plagiarism.

PLAGIARISM LAW

Colleges, universities, professional entities certainly have the authority to punish plagiarists in various ways. For example- a marking –giving zero, fail in exam, suspension from work, expulsion from college,

extending the term, giving a letter of warning , all these come under legal issue.

PLAGIARISM LAW in USA[8]

Copyright law: the owner of copyright (true author) could sue a plagiarist in federal court for violation.

SOPA (STOP ONLINE POLICY ACT) PIPA (PROTECT INTELLECTUAL PROPERTY ACT)

In USA SOPA is to fight online trafficking in copyrighted intellectual property. Provisions include requesting of court orders to bar advertising networks and payment facilities from conducting business with infringing websites and search engines from linking to the sites and court orders requiring internet service provider to block access to the sites. The law could expand existing criminal laws to include unauthorized streaming of copyright material imposing a maximum penalty of 5 years prison.

How to avoid Plagiarism?[9,10]

1. When you plan to write a research paper, prepare an outline of your paper. Do not copy at all.

2. Try to learn what is written, digest it and explain in your own words

3. When you are unsure always ask your guide. He or she is more than happy to answer your questions.

4. Focus on difference between different authors on the same topic; evaluate the strengths and weaknesses of their arguments.

5. Take through notes from all sources, organize the information that is collected and avoid doing writing of your research at the last minute

6. Writing, rewriting takes a longer time for good research.

7. Identify the quote, provide the source

8. Copied passages must not form substantial portion of your work.

9. Proper acknowledgement is required if you borrow idea from others

10. Get in the habit of marking page numbers and make sure you record bibliographic information or web addresses for every source right away.

Prevention of plagiarism [5]

1. Develop a topic based on previously written material but write something new and original.

2. Rely on opinion of experts on a topic but improve upon their opinions

3. Give credit to researchers while making your own contribution

4. Follow a standard documentation method e.g. MLA, APA format

Deteriorating condition of the educational system occurs due to plagiarism. The exclusive rights to reproduce .adapt, translate and publish their work or allow others to do so are collectively called copyright. It grants the authors "special right" to be attributed to their work. It is a moral right. Self plagiarism is not considered as an offence in Indian copyright Act 1957 as the author who is the owner of copyright has all the rights for reproduction of the words.[7]

Internet makes plagiarism easier but it also makes detection of plagiarism easier. Softwares are available free of cost to check plagiarism online[11,12]. You can feed the paper and check plagiarism. It is not difficult to detect it by an experienced teacher. You cannot deceive yourself. It involves a matter of honesty, integrity. Stay away from it.

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Review Article 1

Management Of Chronic Pancreatitis: A Concise Review

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Chronic pancreatitis (CP) is a progressive and a usually symptomatic fibrosis of the pancreas with consequent exocrine and endocrine dysfunction due to loss of pancreatic glandular tissue. Once the process of CP becomes advanced in there is little that can be done to arrest disease progression irrespective of the initial pathology, however treatment of its causative factors may slow disease progression in a subset of patients. Progressive destruction of pancreatic acinar tissue, the islets of Langerhans and inflammation and fibrosis collectively account for almost all the major symptoms of CP namely malabsorption and malnutrition, diabetes mellitus and pain respectively.

Almost half the patients of CP will be labeled as idiopathic despite exhaustive investigations and greater that a third will be due to chronic alcohol intake. The relative proportion of these etiologies may differ in different centers however these two causes account for almost 80 percent of all patients of CP [1]. Other causes of CP include hypertriglyceridemia, hyperparathyroidism, autoimmune pancreatitis and pancreas divisum a ductal anomaly of the pancreatic duct. Genetic mutations are now being increasingly recognized as a cause of CP and may soon replace a large segment of the so-called idiopathic variety of pancreatitis. Several dominant genetic mutations namely SPINK1, CPA1, CTRC, CEL, CFTR and PRSS1 and their variations have been identified as a cause of CP [2].

The diagnosis of CP in symptomatic patients can be made in over 95 percent of patients using a combination of imaging techniques like MRI pancreatography, CT scan and an endoscopic ultrasound, all of which will reveal specific changes representing gland destruction, inflammation and changes in ductal anatomy. Tests of pancreatic secretory function viz. estimation of fecal fat, fecal chymotrypsin and fecal elastase 1 are also helpful in patients with advanced disease.

Despite the advances in diagnostic techniques and a better understanding of its pathophysiology, CP still remains a challenging disease to treat.

Presentation and symptoms

CP usually presents with pain, which is its primary symptom, found in over 90 percent of patients. Less commonly the patients will first present either with steatorrhea or diabetes. Pain is often severe and lasts for several hours to days and may be continuous or episodic and is dull and boring in nature, often radiating to the back. The variation in the quality and intensity of pain often makes it difficult to assess the benefit of therapies aimed at relief of pain in CP. Contrary to popular belief the pain of pancreatitis may not disappear as the disease progresses, as the pain is not an outcome of acinar destruction but a result of stromal inflammation and fibrosis with consequent irritation and entrapment of nerve endings. Exocrine insufficiency manifests as diarrhea, bloating and steatorrhea with associated weight loss, malnutrition and deficiency of fat-soluble vitamins. As a rule malabsorption does not occur until over ninety percent of the gland is destroyed, a process which may take several years after the onset of the CP. Hence, at the time of initial diagnosis one may not expect more than a quarter of the patients to have evidence of malabsorption, which in itself an indication that disease progresses is a highly variable manner in different patients. Diabetes mellitus is usually detected in between 30 to 50 percent patients with CP at the time of initial presentation; conversely a small percent of diabetics between 3-5 percent will have evidence of CP during evaluation [3,4,5]. Rarely patients with CP will present with large pancreatic pseudocysts, pancreatic ascites or gastrointestinal bleeding the latter due to segmental portal hypertension associated with splenic vein thrombosis.

Management of Chronic Pancreatitis

The management of CP primarily encompasses the

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management of pain, and the symptoms related to exocrine and endocrine insufficiency. Identification and treatment of the cause of CP, management of associated malnutrition, psychiatric counseling for concomitant depression and addictions, and the management of local complications of CP like pseudocyst, pancreatic ascites, bleeding and secondary neoplasms are other important aspects of management.

Management of pain

Analgesics

Pain management in pancreatitis requires a multimodal approach. The step up approach used to treat pain in cancer patients is often used to manage pain in patients with CP. Paracetamol is safe and is the preferred drug for pain relief and can be administered orally in a dose of 1.5 to 3.0 grams per day. It is advisable not to exceed this dose of paracetamol especially in alcoholics who may have varying degrees of underlying liver dysfunction, which can induce paracetamol toxicity at lower doses. Non-steroidal anti-inflammatory agents can be used if paracetamol is ineffective. Addition of (NSAIDs) to paracetamol will have a cumulative effect. Short duration treatment schedules with NSAIDs are preferred especially in view of their gastrointestinal side effects. In high risk groups it is better to start a proton pump inhibitor along with NSAIDs to prevent gastroduodenal ulcers and erosions.

When both paracetamol and NSAIDs fail to control the pain of CP, tramadol should be used in a dose of 50 to 150 mg per day. It has an efficacy comparable to opioids in some patients with a low addicting potential during short-term use. Side effects are insignificant compared to the benefit of pain relief offered by tramadol.

Fentanyl 50 microgram/hour transdermal patches offer excellent relief from pain, with a single patch able to provide relief for up to 72 hours. Fentanyl patches should be used as a substitute for injectable opioids whenever possible.[6] Buprenorphine tables administered by the sublingually in a dose of 4 to 24 mg/day is another effective treatment option [7].

Some patients however will continue to have refractory pain and will require injectable pentazocine 30 mg with phenergan. Others may need strong opioids viz. injectable pethidine 100 mg or morphine 10 mg, however these agents should be used for a short duration because of their addicting potential. Morphine sulfate tablets 15 mg two to three times a day can be tried before using injectable opioids [6]. Since the peak intensity of pain is often of a short duration it is advisable to rapidly shift to a less potent agent once pain decreases.

Abstinence from alcohol decreases pain episodes and slows disease progression in patients with alcoholic CP and hence such abstinence must be rigorously followed [8,9]. Tobacco use is an independent risk factor for CP and there is now strong evidence that smoking accelerates disease progression [10].

Pain management: Analgesic failure and opioid use

For patients who have inadequate pain relief with analgesics, for those who require long-term medication and also for those patients who frequently need opioids for pain relief in CP the following treatment options are available.

1. Addition of a non analgesic co-medication
2. Endoscopic treatment for pain
3. Surgery for pain
4. Experimental therapies for pain

1 Addition of a non-analgesic co-medication

Pancreatic enzyme therapy has been tried in patients with pain due to CP. A meta-analysis however found no beneficial effect of enzymes on pain relief in CP [11] Nevertheless pancreatic enzymes may may have beneficial effects on abdominal discomfort related to PEI (e.g. gas and bloating) besides a placebo effect on pain itself. Present treatment guidelines do not recommend enzyme supplements for relief of pain in CP.

Antidepressants are used by many clinicians despite the limited data and conflicting evidence of their benefit for pain relief in CP. Selective serotonin reuptake (SSRIs) inhibitors and serotonin–noradrenaline reuptake inhibitors (SNRIs) have been tried as pain relieving adjuvants in management of chronic pain with variable results [12]. Their use is best reserved for patients of CP with evidence of concomitant depression

Gabapentinoids have been used for managing pain in CP, with encouraging results. Pregabalin 50 to 100 mg per oral twice or thrice daily when used for short periods of time as a supplement to milder analgesic agents may offer moderate pain relief [13].

2 Endoscopic interventions for pain relief.

In the last two decades endoscopic therapy of pancreatic disease has largely replaced surgery as the first option for management of refractory pancreatic pain. The relatively low morbidity of endoscopic treatment and its more than modest efficacy favour its use in those patients with CP who frequently resort to analgesics. The endoscopic procedure changes according to the cause of pain in CP, and hence the cause of pain has to be carefully evaluated before undertaking endoscopic therapy. For example parenchymal pain in CP will not respond to pancreatic stenting while endoscopic dilatation and stenting of a stricture in the pancreatic duct will give remarkable relief from pain.

Assessment of pain in CP will include a search for one of the following causes listed below.

a) Pain due to pancreatic stricture causing pancreatic ductal hypertension

b) Obstructing pancreatic calculi.

c) Pancreas divism

d) Pancreatic Pseudocysts

e) Pain due to parenchymal inflammation

f) Inflammatory pancreatic mass

g) Development of neoplasm due to CP

a) Pain due to pancreatic stricture and resultant increased pressure in the pancreatic duct responds very well to dilatation of the pancreatic stricture and stenting. High success rates of around 88 percent for both immediate and long-term pain relief have been reported after pancreatic stenting for strictures in patients with CP in large series [14,15]. Patients with a single stricture are the best candidates for stenting and patients will multiple strictures may not get adequate pain relief unless simultaneous multiple stents or self-expanding metal stents are used[16].

b) Pancreatic calculi can be treated with extracorporeal shockwave lithotripsy (ESWL). Treatment with ESWL is recommended for radiopaque stones larger than 5 mm and for those obstructing the main pancreatic duct (MPD). After fragmentation the stone fragments are usually mechanically removed from the pancreatic duct. A meta-analysis, which analysed 491 patients, showed that ESWL is useful for clearing (MPD) stones and for decreasing CP-related pain [17]. A review of 11 large studies in the 1149 patients reported a successful fragmentation rate of 89 percent by ESWL [18].

c) Pancreas divism is a condition in which the main pancreatic duct drains into the duodenum via the minor papilla instead of the major papilla. The resultant pancreatic ductal hypertension results in recurrent episodes of pain, associated with gland destruction and progression to chronic pancreatitis. Endoscopic papillotomy of the minor papilla and pancreatic duct stenting can give excellent relief especially, if performed early in recurrent pancreatitis. The role of endoscopic intervention in established CP however is less certain [19].

d) Pancreatic pseudocyst may or may not be the cause of pain in CP. However pseudocyst with infection, intracystic hemorrhage and those associated with severe pain and tenderness over the cyst are indications for drainage. Pseudocyst can be drained by the use of endoscopic ultrasound using either the gastric trans mural route or the duodenal transpapillary route. A success rate of 79.2% was reported in a large series, with more recent studies reporting success rates of over 85% [20]. The success rates are likely to improve further with the introduction of newer cyst drainage systems and transgastric drainage stents. Results for endoscopic drainage are comparable to surgery and are associated with a lower mortality of around 0.2 percent. Recurrence of pseudocyst is uncommon after endoscopic drainage occurring in about 7.6 percent of cases [20].

e) Refractory pain due to parenchymal inflammation responds poorly to pancreatic ductal stenting. Blocking the celiac plexus using an endoscopic ultrasound guided technique can offer relief from pain. After a test block using lignocaine a radiofrequency ablation of the celiac plexus is performed using a trans-mural route. Results are however disappointing and the use of EUS-guided coeliac plexus blocks cannot be recommended as routine therapy for pain in CP. Only one-half of the patients experience pain reduction after celiac plexus block and only 10 percent of patients will have durable pain relief beyond 6 months [21]. Aggravation of pain and postural drop in blood pressure are important adverse effects, which have limited the use of this treatment [22]. A percutaneous approach that was formerly used to block the celiac plexus has been given up because of the risk of

pneumothorax and paraplegia.

f and g) Pain of inflammatory pancreatic masses and neoplasia does not respond well to endoscopic therapy. Surgery may offer pain relief in these patients. Other novel and experimental therapies may be tried if surgery is not feasible or fails to alleviate pain.

3. Surgical intervention for pain in CP

Three types of surgical options are possible for pain in CP.

1. Decompression of the MPD to alleviate pancreatic ductal hypertension

2. Resection of inflammatory masses

3. Combination of both techniques.

Decompression techniques are recommended in patients with a dilated MPD (> 7–8 mm) in the absence of an inflammatory mass [23]. They provide pain relief in 66%–91% of patients with a low risk of postoperative complications. Exocrine and endocrine insufficiency does not result from de-compressive surgery and the procedure related mortality is less than 2% [24] However 50% of patients experience a recurrence of pain on the long term follow up[25].

Resection offers the best results in patients with an inflammatory pancreatic mass or post-obstructive pain due to benign or malignant ampullary or pancreatic head tumors, and in CP affecting the pancreatic body or tail [26] Pancreatico-duodenectomy gives long-term pain relief in about 75% of patients [27]. Long-term postoperative morbidity (20 %) is however significant[28].

The more conservative mixed techniques with resection and drainage procedures are perhaps the most widely practiced technique for alleviating pain in CP. Essentially the mixed techniques are based on the removal of the inflammatory mass in the pancreatic head and drainage of the obstructed pancreatic region (body and tail). The two mixed techniques frequently used are the duodenal preserving resection or Beger technique and the Frey method. The Freys method involves the coring out of the pancreatic head followed by a longitudinal pancreaticojejunostomy [29]. Since the duodenum and the intrapancreatic bile duct remain preserved, there is improvement in the post-operative nutritional status, correction of delayed gastric emptying and an improved quality of life in treated patients. In several randomised controlled clinical trials, mixed interventions have shown short-term and long term pain relief in pain relief in 70–100% and 82–100%. of patients respectively [30,31]. The improvement in pancreatic exocrine and endocrine function after surgery however remains a matter of debate.

4. Experimental and novel therapies

In refractory cases Intrathecal morphine using controlled continuous infusion pumps has given good pain relief[32].

High dose radiation to the pancreas has been used as a treatment for pain in CP. In one study a single dose of 8Gy resulted in a complete pain relief in 13 out of 15 patients [33,34]. However the risk associated with radiation exposure and the limited number of patents studied will prevent widespread use of radiation unless pain relief and its safety are replicated in a controlled trials.

Spinal cord stimulation via epidural lead placement mid thoracic vertebral level has been shown to alleviate pain in CP in a small group of patients[35].

Management of pancreatic exocrine insufficiency (PEI)

Mild pancreatic exocrine insufficiency is common in both CP and in insulin dependent diabetes mellitus. Mild PEI however needs no treatment, Severe PEI occurs when over 90 percent of the gland is destroyed. Steatorrhea, gas, bloating weight loss and malnutrition are the inevitable consequences of advanced CP. The coefficient of fat absorption (CFA) is generally accepted as the gold standard for the diagnosis of PEI in CP. The CFA requires patients to maintain a strict diet containing 100 g of fat per day over five days, and to collect the total amount of feces excreted over the last three days of this five-day period. A CFA< 93% is considered pathological [36]. Fecal Elastase 1 estimation is the most frequently used indirect test for PEI but has only 54–75% sensitivity in mild to moderate PEI [37,38]. Monoclonal fecal Elastase 1 estimation is more sensitive for making a diagnosis of PEI but is not widely available.

PEI has been demonstrated in approximately 26 to 50% of patients with insulin-dependent diabetes mellitus (IDDM), and in about 12 to 50% of patients with non-insulin-dependent diabetes (NIDDM), [39,40]. Steatorrhea and azotorrhoea in severe PEI result when exocrine pancreatic function is reduced by > 90%[41].

Clinical symptoms and signs of micronutrient deficiencies due to impaired absorption of lipid soluble vitamins include: vitamin K deficiency (ecchymosis); vitamin E deficiency (ataxia and peripheral neuropathy); vitamin A deficiency (impaired night vision and xerophthalmia) and vitamin D deficiency (tetany, osteomalacia and osteoporosis). PEI leads to hyperoxaluria resulting in formation of urinary oxalate stones.

The mainstay of treatment of PEI is pancreatic enzyme replacement therapy (PERT). High Lipase content of the preparation and a pH sensitive delivery system are critical to the efficacy of the preparation used. The enteric-coated microspheres or mini- microspheres of < 2mm in size are the preparations of choice for PEI. Clinical trials comparing different enzyme preparations for managing PEI are unavailable and the effect of different enzyme preparations on the coefficient of fat absorption is the best yardstick of its efficacy. The efficacy of pH-sensitive, enteric-coated, mini-microspheres in patients with CP has been demonstrated in several recent studies including our own [42,43]. Enteric-coated preparations have been demonstrated to be more effective than conventional uncoated preparations. The most recent and well-designed RCTs have shown the efficacy of PERT with enteric-coated minimicrospheres for doses ranging from 40,000–80,000 PhU of lipase per main meal, and half that dose per snack [42,43],

The aim of PERT is the normalisation of nutritional parameters (both anthropometric as well as biochemical) and an improved quality of life (QoL) as assessed by the QoL questionnaire.

In cases with unsatisfactory clinical response, the enzyme dose should be increased

(doubled or tripled). Addition of or a proton pump inhibitor (PPI) may increase the efficacy of PERT and should always be tried before dose escalation. Small intestinal bacterial overgrowth (SIBO) is a frequent problem associated with PEI in CP and may contribute to malabsorption [44]. Treatment with antibacterial agents may alleviate symptoms and may enhance the efficacy of PERT in cases where SIBO is suspected.

Management of malnutrition

Malnutrition is frequent in CP patients. Its incidence varies between 8 to 39 percent in various series, with a higher prevalence rate are reported from India [45,46]. Weight loss among patients with CP appears to be common and has been observed in about 20% to 49% of patients [45,46]. Nutritional screening can be quickly assessed using the Malnutrition Universal Screening Tool (MUST), which has been recommended in CP [47]. This useful nutritional assessment tool can be effectively used for follow up of patients on PERT to assess its nutritional benefit.

Dietary counseling for a balanced diet is cheaper and is as effective as the use of expensive commercial food supplements. Maintaining a diary of daily dietary intake further aids dietary management in malnourished patients [48]. However, malnutrition exists in many forms and sarcopaenia with or without specific nutrients deficiencies may occur without weight loss or a low BMI. Specific dietary recommendations in CP include a daily diet of 2000- 3000 calories, consisting of 1.5 to 2 g/kg body weight of protein, 5 g/kg of carbohydrates, and 20-25% of total calories consumed as fat per day.

Osteoporosis due to deficiency of Vitamin D is present in over a quarter of patents with PEI and malnutrition with the corresponding osteoporosis rate for controls at 8.6 to10 percent[49].

Diabetes Mellitus in CP

Diabetes mellitus secondary to pancreatic diseases (such as CP) is classified as pancreatogenic diabetes or Type IIIc diabetes mellitus (T3cDM) according to the current classification of diabetes mellitus [50]. Metformin and Insulin in combination with other anti diabetic agents are preferred for managing diabetes in CP [51]. The diabetes of CP is highly labile partly due to reduced levels of glucagon, which stimulates gluconeogenesis and prevents a sudden drop in blood sugar levels.

Identification and treatment of systemic causes of pancreatitis

Hypertriglyceredemia, hyperparathyroidism and autoimmune pancreatitis are frequently encountered in clinical practice. Early diagnosis and treatment of these conditions can prove immensely beneficial in slowing the progress of CP in select patients.

Psychiatric counseling in CP

Psychiatric counseling in CP is advised in cases where depression interferes with therapy and the patient's

quality of life. De-addiction counseling is required in patients with alcohol dependence. Patients with pain may also benefit by the use of antidepressants. No clear-cut guidelines however exist on psychological counseling and drug therapy in CP.

Pancreatic transplantation and stem cell therapy

Pancreatic transplantation and stem cell therapy are directed at correcting the extremely labile diabetes found in patients with CP. Such therapies are not directed at correcting PEI, which can be otherwise well controlled by PERT. Several stem cell techniques have been developed however none has been used in routine clinical practice due to lack of controlled data. Similarly pancreatic transplantation for diabetes mellitus, which is being widely used, is rapidly being replaced by more efficient and physiological insulin delivery systems. These therapies should hence be performed only in centers that have exhaustive experience with their use.

In conclusion management of CP is a challenging with combination of problems requiring treatment facing the treating physician. Treatment goals are difficult to achieve and many patients may give up treated in frustration and choose less scientific remedies. Hence the need to counsel the patients on the need to adhere to treatment in order to prevent long term morbidity and mortality from complications of CP cannot be overemphasized.

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Anaesthesia For Laryngeal Laser Surgery

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ABSTRACT

Laser surgery offers several advantages to the surgeon and patient; i.e. microscopic precision, a bloodless operative field & early recovery. We have reviewed selected aspects of anaesthetic management of patient undergoing laser surgery of larynx & outlined the principles of laser technology. We also emphasized on currently available measures to prevent problems of laser surgery.

Key words - anaesthesia for laser surgery, airway fire, laser tubes

Introduction

Laser – Light Amplification by Stimulated Emission of Radiation. The discovery of laser is a Noble prize winning achievement of 20th century. Though it is path breaking discovery, it is associated with inherent rate of complications. Lasers have been used in laryngeal surgeries since 1972, when Strong and Jako first reported the use of carbon dioxide laser (CO2) in the human larynx [(1)].

Airway surgery is unique in that it involves the anaesthesiologist and surgeon working in the same anatomic field. Even without the use of a laser in a shared airway, procedures are challenging when the airway is compromised. The addition of a laser beam (i.e., ignition source) into a shared airway can cause a catastrophic fire.

Role of Anaesthetist

Maintain Oxygenation

Keep patient anaesthetised

Provide adequate space for surgeon in operating field.

Reduce incidence of airway fire by special approaches

To deal with crisis

Reduce postoperative complications

Principles of Laser Technology

History

In 1960, Theodore Maiman produced light amplification by the stimulated emission of radiation (LASER) using a ruby crystal and red light [(2)]. Throughout the 1960s and 1970s, many substrates and ions were tried as the laser medium.

Physics

In 1917, Einstein postulated that if a photon released from an excited atom collided with another atom already in the excited state, the second atom would release two photons with the same wavelength, phase, and direction (i.e., identical photons). If these two photons stimulated more excited atoms, more identical photons would be released. Einstein called this process stimulated emission of radiation, and it is the basic principle of laser physics.

The critical features of laser light are the following:

1. Collimation—precisely aligned beam that can be seen on the moon

2. Coherence—light in phase

3. High-power density

4. Narrow spectrum of frequency

5. Can be pulsed for less than 10−11 seconds (femto second range)

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Types

Type of Laser	Laser Wavelength (nm)	Color	Fiberoptic Transmission
Gas			
Helium-neon	633	Red	Yes
Argon	500	Blue-green	Yes
Carbon dioxide	10,600	Invisible	No
Solid			
Ruby	695	Red	Yes
Nd:YAG	1,060	Invisible	Yes
KTP	532	Green	Yes

KTP, Potassium titanyl phosphate; *Nd:YAG*, neodymium:yttrium-aluminum-garnet.
Adapted from Sosis MB: *Probl Anesth* 7:160, 1993.

Specific laser hazards

(1) Atmospheric contamination,

(2) gas embolism

(3) inappropriate energy transfer.

Atmospheric contamination: laser plume

Tissue destruction during surgical laser procedures produces a complex particulate aerosol as polyaromatic hydrocarbons, hydrogen cyanide, formaldehyde, benzene, and cellular material (dead and alive) and smoke plume[3].

Fine particulates (mean size 0.31 μm; range 0.1 to 0.8 μm) can lead to reduced mucociliary function, airway inflammation, interstitial pneumonia, bronchiolitis and emphysema[4].

The mutagenic potential of the plume from a CO2 laser on 1 g of tissue is equivalent to inhaling the smoke from three unfiltered cigarettes. Viral DNA has been detected in plume from human papilloma virus (HPV).

Smoke evacuators are 99% effective at eliminating the plume when situated within 1 centimetre of the target site their use in the Operation Room is strongly advised and supported by OSHA(Occupational Safety & Health Administration). High-filtration masks that filter plume particulates down to 0.3 to 0.1 μm is essential.

Embolism

The Nd:YAG laser system has been associated with venous gas embolism. Continuous airway CO2 monitoring may help with the detection of embolization.

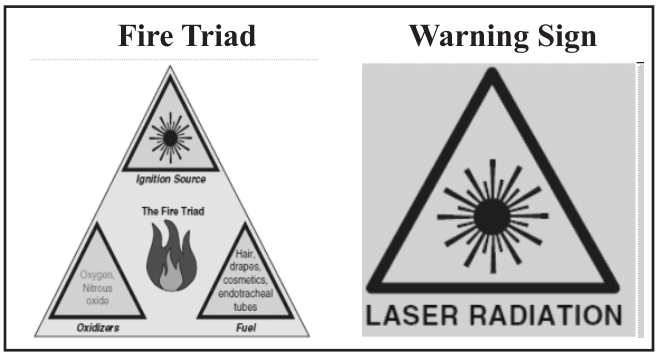
Energy transfer to an inappropriate location

Laser activation can result in injury to patients and OR personnel or damage to property. Laser ignition of any combustible fuel (e.g., surgical drapes, plastic endotracheal tubes [ETTs], ointment on the skin) may also occur either by unintentional direct beam strike or by reflectance and scatter of the beam off specular surfaces.

Eye injury and protection

The blink reflex is too slow to guard against laser injury. Visible and near infrared light (400 to 1400 nm) can damage the retina. Argon, KTP, Nd : YAG, or ruby lasers are likely to cause rapid permanent damage to the retina. Ultraviolet and far-infrared light is absorbed by the anterior structures. Infrared energy from a CO2 laser causes corneal and lens injury[5]. Proper protective eyewear with side shields and appropriate filtering capabilities and optical density (specific for the type of laser to be used) are safety essentials for all present in the OR. The eyes of patients should be taped, closed and covered with saline-soaked opaque material or a metal shield. The Nd : YAG and argon lasers can penetrate glass, and any windows in the operating room should have an opaque covering to prevent penetration by laser radiation.

A warning sign should be placed on the operating room.



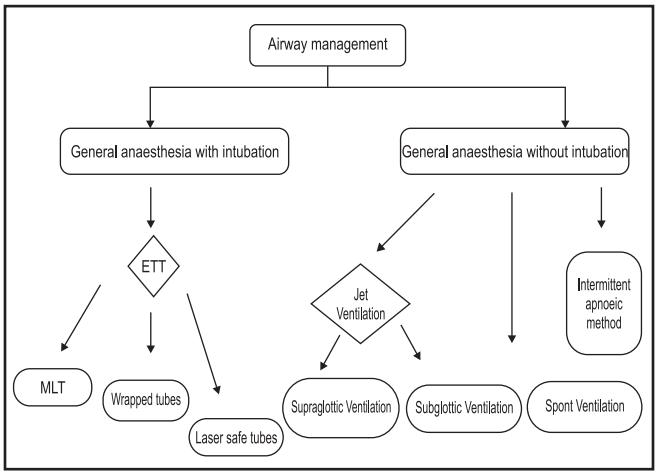
OPERATING ROOM FIRE

Oxygenation and ventilation:

In an updated 2013 ASA Practice Advisory for the Prevention and Management of Operating Room Fires, the majority of the ASA taskforce members "…strongly agree that the use of nitrous oxide (N_2O) should be avoided in settings that are considered high risk for

fire[6]. A 2013 analysis of the ASA Closed Claims database, which dates back to 1985, found that laser fires during general anaesthesia occurred with inspired oxygen concentrations greater than 30% and states that it should be "kept as low as clinically feasible…" to "…avoid hypoxia.

Modes of ventilation [7]



Technique	Advantages	Disadvantages
Spontaneous ventilation	Ideal surgical access	No airway protection $EtCO_2$ values inaccurate Difficult to control depth of anesthesia Vocal cords move expectedly Risk of laryngospasm and aspiration
Intermittent apnea	Unobstructed view of larynx No need of jet ventilation No movement of vocal cords	Trauma from repeated intubation Interrupted ventilation and surgery
Positive pressure ventilation via micro laryngeal tubes	Familiar to all Control of ventilation Protection against aspiration Reliable $EtCO_2$ value Less OR pollution	Hindered surgical access Risk of airway fire Obscure posterior glottis lesion
Supra glottic jet ventilation	Maximal access to surgical field Least risk of ignition	Gastric distension Malalignment of rigid suspension laryngoscope with poor ventilation Vibration of cords Debris and blood blown into distal airway Difficult to monitor $EtCO_2$ value
Subglottic jet ventilation	Minimal vocal cord movement and more efficient than supra glottic ventilation	Risk of barotraumas Need of TIVA
Trans tracheal jet ventilation	Assists in management of difficult airway if placed prior to induction	Catheter may kink, block or dislodge Bleeding, barotraumas Tumor seeding
High frequency jet ventilation	Less peak airway pressure Less hemodynamic compromise Minimal movement of vocal cords and excellent operative field Laser compatible	Requires special ventilators Risk of gas trapping and barotrauma

Jet ventilation: It is a type ventilation system in which a gas tight separation of respiratory system from the environment does not exist. High pressure O_2 (50 psi) is delivered to the airway at high velocities, through a jet injection cannula creating a negative pressure and causing a venturi effect.

Special endotracheal tubes - LASER-RESISTANT ENDOTRACHEAL TUBES

Tube	Special features	Recommend laser	Not recommended	disadvantages
Laser flex	Stainless steel airtight spiral with PVC tip and double cuff.	CO_2, KTP, Nd : YAG at low power	Nd : YAG at high power	Cuff is inflammable Reflect laser beam
Bivona Laser Endotracheal Tube	Aluminum spiral with silicon coat and self inflating foam cuff	CO_2	KTP, Nd : YAG	Cuff difficult to deflate if punctured
Norton tube	Spiral wounded stainless steel without cuff	CO_2, KTP, Nd : YAG		Rough exterior Reflect laser beam Difficult surgical exposure
Xomed Laser-Shield II Tube	Aluminum silicon layer extends over cuff	CO_2, KTP	Nd : YAG	Silicon is inflammable Cuff is not laser proof
Wrapped Standard tubes	Wrapped with Aluminum or copper foil tape with adhesive back. Merocel laser guard (merocel wrap) Cheap.	CO_2, KTP, Nd : YAG		Risk of fire is high Rough edges Thickness is high No cuff protection
Laser tubes	White rubber tube with merocel sponge Double cuff within cuff	CO_2, KTP, Nd : YAG		Thick walled tube Unprotected cuff

Conventional tubes are at risk of AIRWAY FIRE

Other considerations - Vagal hyperactivity often occurs during instrumentation of the trachea and during suspension laryngoscopy, in particular. Intense (deep) neuromuscular blockade is often a surgical need during

laser on minute targeted areas in the airway. Vaccination against human papilloma virus and Protection of operating room people against viral infection by special masks.

Management of airway fires [8]

Prevention and Preparedness

1. Keep the O2 concentration at approximately 30%, or less if possible. Use an O2/air mixture. Avoid N2O.

2. Use a "laser-safe" endotracheal tube.

3. Inflate the endotracheal tube cuff with dyed normal saline to provide an early indicator of cuff rupture.

4. Use a pre-prepared 50-mL syringe of saline to extinguish any fire, and flood the surgical field if a fire occurs.

5. Have an extra endotracheal tube available for reintubation in case a fire occurs.

6. Inform the surgical team working on the airway of any situation in which high concentrations of O2 are being used.

In the Case of an Airway Fire

1. Stop Lasering. Stop ventilation. Turn O2 off (as well as N2O if it was mistakenly in use).

2. Inform the surgical team, and assign someone to call the control desk for help.

3. Remove the burning endotracheal tube and drop it in the bucket of water, if available.

4. Put out the fire with your improvised fire extinguisher.

5. The area should be flushed with saline.

When the Fire Is Extinguished

1. Ventilate the patient with 100% O2 by facemask (or supra-glottic airway if appropriate).

2. When the patient is stable, assess the extent of airway damage. Consider using a ventilating rigid bronchoscope; debris and foreign bodies should be removed.

3. Reintubate the patient if significant airway damage is found.

4. When appropriate, arrange for admission to an ICU.

5. Provide supportive therapy, including ventilation and antibiotics, and extubate when appropriate.

6. Tracheotomy may be needed.

About 10 cases of laryngeal laser surgery were done in our hospital in past 2 months.

Vocal cord Papillomatosis – 4

Vocal cord nodule – 3

Vocal cord carcinoma – 3

Here we are discussing about the details of anaesthesia technique used for all the patients. For convenience anaesthesia procedure of a single patient is explained in detail.

Case –laryngeal papilloma for laser (diode) excision

45 y female ASA 2. Known case of hypertension since one year with h/o change in voice since 4 months - progressive associated with fatigability. O/E patient is obese, BMI 33 & short neck. Vitals stable, investigations - WNL. VDL –b/l vocal cord papilloma.

A meticulous preoperative history, physical examination with particular attention to potential airway problems are taken into consideration.

Anaesthesia goals include profound muscle paralysis to provide masseter muscle relaxation for introduction of scope, immobile surgical field, adequate oxygenation, ventilation and cardiovascular stability during period of surgical stimulation. Profound relaxation is required until the end of surgery and rapid recovery is essential.

Pre op preparation :

Potential risks of laser surgery and post op complications like airway oedema was explained to the patient and relatives and due consent was taken. Anxiolytics – Tab.diazepam 10mg hs was given one day prior to surgery. Morning dose of antihypertensive – tab amlodipine 5mg + atenolol 50mg was taken by patient. Vitals, ECG, SPO2,ETCO were monitored.

Induction - Inj. Glycopyrrolate 5mcg per kg i.m. 20 minutes prior to procedure, Inj. ondansetron 0.08mg per kg i.v.,Inj. dexamethasone 8mg i.v.,Inj. midazolam 1mg i.v.,Inj. Fentanyl 50mcg i.v.Pre oxygenation done with 100% O2 for 3 minutes. Inj.propofol 2 mg/kg i.v. followed by inj.lignocaine 60mg i.v.BMV checked. Inj. Succinyl scoline 100mg i.v. given. Under direct laryngoscope, Intubation done with portex cuffed endotracheal tube no 6 wrapped with aluminium foil

using tincture benzoin as adhesive. Cuff was inflated with air.

Maintenance- 33% O2 given (because we don't have facility of medical air).Sevoflurane as inhalational agent Controlled ventilation done with BAIN'S circuit. Inj. Vecuronium used as muscle relaxant.Saline soaked gauze kept below vocal cord .i.e. between vocal cord and ETT cuff(diode laser precisely used with pointer through rigid laryngoscope over the lesion)

Extubation- Inj.esmolol 0.5mg per kg iv given prior to extubation .Inj. glycopyrrolate 0.04mg i.v + inj. neostigmine 0.05 mg i.v and for Post operative analgesia – Inj. diclofenac 75mg i.v slowly given.Post operatively After extubation patient was observed for any complication like laryngeal edema and laryngeal spasm.

NO COMPLICATIONS NOTED DURING INTRA OPERATIVELY AND POST OPERATIVELY AND PATIENTS DISCHARGED TO HOME ON POST OPERATIVE DAY 3-5 WITHOUT ANY COMPLICATIONS

Conclusion

Use of laser in surgery is increased in past decade. Though, it is a boom for surgeons and patients, its associated with multiple complications. So better understanding of physics behind laser and good knowledge of tackling associated problem will result in smooth conduct of anaesthesia and surgery. Smooth and safe general anaesthesia in compromised airway with abnormal anatomy, sharing of airway with surgeons, avoidance of potential laser hazards, prevention of awareness, wide awake patient after surgery with least postoperative complication are main challenges for anaesthesia for laryngeal laser surgery. With use of safety measures and special techniques for anaesthesia, the problems of laryngeal laser surgery are minimized.

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ORIGINAL ARTICLE

A Clinico-Epidemiological Study Of Acne Vulgaris In A Tertiary Care Centre

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ABSTRACT

INTRODUCTION : Acne vulgaris is a common dermatological disorder of the pilosebaceous unit usually presenting at puberty. The major factors involved in pathogenesis are increased sebum production, abnormal microbial flora, cornification of pilosebaceous duct, inflammation and increased androgen levels. Aims and objectives: To evaluate etiological factors and correlate clinical and epidemiological parameters of acne vulgaris.

Methodology : This observational study was carried out in a tertiary care centre between February 2017 to June 2017 and included 100 patients. Detailed history taking and examination were performed which included parameters like age, gender, duration, site, associated symptoms and signs, personal history, family history, drug history, menstrual history, acne grade, body mass index (BMI), Fitzpatrick skin type, hormonal levels and ultrasonography findings.

RESULTS : We encountered higher prevalence of acne vulgaris in females and age group 20-35 years. Aggravating factors were stress (65%),cosmetics (48%), summer flare (32%),smoking (22%),menstrual irregularities (18%) and drug intake (6%).Most common grade of acne vulgaris was grade 2 (45%).Associated features observed were seborrhoeic dermatitis (56%), pseudoacanthosis nigricans (29%), higher BMI (21%), hirsuitism (6%), fever (1%),ultrasonography findings suggestive of polycystic ovarian syndrome(45%),elevated levels of serum prolactin (26%),testosterone (8%), dehydroepiandrostenedione (DHEAS)(4%) and lutenising hormone / follicular stimulating hormone level ratio (LH/FSH >2) (10%). Conclusion: Multiple etiological and aggravating factors are found to be associated with acne vulgaris. Hence, thorough evaluation of each patient is necessary for appropriate treatment.

KEY WORDS : Acne vulgaris, clinical presentation, epidemiology, tertiary care centre.

Introduction

Acne vulgaris is a multifactorial disease and occurs primarily at puberty.[1.] Acne vulgaris affects 85% of young adults.[2,3.] It is a chronic inflammatory disease of pilosebaceous units characterized by comedones, papules, pustules, nodules and cysts.[1] The major factors involved in pathogenesis are an increased sebum production, abnormality of microbial flora, cornification of pilosebaceous duct, production of inflammation and increased androgen level.[4,5]

Despite advances in understanding the pathophysiology of acne, much less appears to have been written about its epidemiology, which is strange considering that acne is almost universal in teen years. Epidemiology not only describes the burden of disease in terms of incidence, prevalence and variations according to age, sex, social class, ethnic group and geography, but also has the potential to identify specific risk factors for disease occurrence or progression, which may be amenable to manipulation. Discovery of risk factors or factors that exacerbate existing disease could lead to appropriate primary or secondary preventive measures and treatments, which in turn could lead to population benefits in terms of health and reduced expenditure on relatively ineffective treatments.[6.]

Face being the commonest site of affection, acne has a great psychological and social impact.[1,4.] There are a few

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studies on acne vulgaris in Indian literature which correlate clinical symptoms and their causative factors. It is necessary to explore the prevalence of acne vulgaris as well to study the association of acne vulgaris with various causative factors. Hence, this study aimed at evaluating the clinical and epidemiological profile of acne vulgaris in a tertiary care institute.

Methodology

It was an observational cross-sectional study conducted on 100 patients presenting to dermatology out-patient department of a tertiary care institute between February and June 2017. Institutional Ethics committee approval was taken. All patients were enrolled with a written informed consent (from legal guardians in case of minors).

Inclusion criteria:

• Males and females between 0 to 35 years of age with acne vulgaris.

• Patients willing to give consent for enrollment in study.

Exclusion criteria: Unwilling patients

A detailed history and examination were carried out for each patient which included age, gender, age of onset, duration, site involved, economic status, personal history, family history, drug history, menstrual history, grade and score of acne vulgaris [tables I & II], body mass index, Fitzpatrick skin type of patients, associated symptoms and signs, hormonal levels and ultrasonography findings. Data were entered in Microsoft Excel and tabulated. The frequency of causative factors associated with acne was expressed in terms of percentages.

Table I: Clinical grades of acne vulgaris.[4]

Grades of Acne	Findings
Grade 1	Predominantly comedones, occasional papules
Grade2	Predominantly papules, few comedones, few pustules
Grade3	Predominant pustules, nodules, abscesses.
Grade 4	Nodules and cysts

Table II: Global acne scoring system for acne vulgaris:[4,7]

Table II (a) :	
Location	Factor
Forehead	2
Right Cheek	2
Left Cheek	2
Nose	1
Chin	1
Chest and Upper Back	3

Table II (b) :	
TYPE OF LESION	GRADE OF LESION
No Lesions	0
Comedones	1
Papules	2
Pustules	3
Nodules	4

The score for each area (local score) was calculated using the formula: Local score = factor x Grade (0-4). The global score is the sum of local scores, and acne severity was graded using the global score.[2]

Table II(c):			
Mild	Moderate	Severe	Very Severe
0-18	19-30	30-38	>39

Results

Total 100 cases were enrolled in our study comprising 62 males and 38 females. 66% of cases belonged to age group of 20-35 years. Duration of acne ranged from 1-2 years in 45%.(Graph I) Aggravating factors (table III) included drugs like antitubercular therapy (1%), oral contraceptive pills (2%), antiretroviral drugs (1%) and unknown drugs (2%) in 6% of cases. 48% of cases had history of using cosmetics, 65% had history of psychological stress, 22% had history of smoking, 47% females had a history of premenstrual flare of acne, 32%

cases had exacerbation in summer season, 18% cases each had history of irregular menstrual cycles and similar history in family. 21% of cases had a high body mass index .(normal level ranges from 18.5 to 24.9 for both genders). On examination, 29% cases had pseudoacanthosis nigricans, 6% had hirsuitism and 56% cases had seborrhoeic dermatitis [Table III]. Majority of patients of acne vulgaris (39%) belonged to Fitzpatrick skin type 2 (table IV)

Table III-Aggravating factors of Acne vulgaris

Factors	Percentage of cases
FAMILY HISTORY	18%
COSMETIC	48%
STRESS	65%
ADDICTION(SMOKING)	22%
PREMENSTRUAL FLARES	47%
SUMMER FLARE	32%
IRREGULAR PERIODS	18%

Table IV- Distribution of patients according to type skin

Fitzpatrick Skin Type	No. of persons(%)
I	1%
II	39%
III	33%
IV	20%
V	7%
Total	100

Table V- Distribution of cases according to global acne score

Type Of Acne	No. of persons(%)
Mild (1-18)	1%
Moderate (19-30)	39%
Severe (30-38)	33%
V. Serve > 39	20%
Total	100

Out of all the 100 cases, 45% had grade 2 acne, 28% had grade 4 acne, 14% had grade 3 acne while remaining 13% had grade 1 acne. According to global acne score 47% of cases had moderate type,26% very severe,14% had mild type while 13% cases had severe type of acne vulgaris. 26% had features of polycystic ovarian disease on ultrasonography. Majority of patients (18%) who showed PCOS (polycystic ovarian syndrome) on ultrasonography had grade 2 acne vulgaris. 26% cases demonstrated raised serum prolactin levels, out of which 9% cases had grade 2 acne vulgaris. 2% of patients were found to have raised 17β- hydroxyprogesterone levels; 8% of cases showed raised free testosterone levels, 4% patients had raised dehydroepiandrostenedione (DHEAS) levels and 10% of total cases had elevated LH/FSH ratio.

Discussion

Acne begins in the early teens with the onset of facial sebum production and can persist in some cases into adulthood for unclear reasons. Majority (66%) of cases in our study belonged to the age group of 20-35 years. The higher mean age than in previous studies[1,7] could co-relate with the associated and aggravating factors encountered like cosmetic use and stress which are more rampant in older age group.

The female predilection observed in our study (62%) was similar to that reported by Patil M et al [1] (57%), but in contrast to the findings of Adityan B et al[7] (44.3 %). The effect of acne vulgaris on self-consciousness, anxiety in social interaction and overall impaired quality of life is well documented[6]. Previous studies have found female subjects to have an increased risk of depression and suicidal ideation and the impact was associated with longer acne duration[6].

Nearly half our patients had history of cosmetic use which compares well with Patil M, Bendigeri J [1] and might also explain the female preponderance and higher mean age of affected individuals. Specific sub-types of acne have been described in literature like acne cosmetica, pomade acne etc to illustrate the comedogenic potential of various hair and skin products. Pre-menstrual flare, noted in 47% of our females, is a well-recognised entity attributed to the reduced size of the pilosebaceous duct between days 15-20 of the menstrual cycle.

Psychological stress is perceived to be a major trigger factor for acne. A significant proportion of our patients believed that stressful circumstances exacerbated their acne which is similar to that observed by Patil M et al.[1] In our study, 22% were smokers. The exact association of smoking with acne is controversial. An earlier case series suggested an inverse relationship hinting at an anti-inflammatory effect of a component in cigarettes[3]. Later, a large cross-sectional analysis found a statistically significant correlation and dose-dependent relationship between number of cigarettes and acne severity.[3] Impaired vasoreactivity, ascorbic acid deficiency and impaired collagen synthesis may play a role in the pathogenesis.

32% of our patients had a summer flare, which is contrary to the conventional view that acne worsens in winter and improves in summer. 18% of females had irregular menstrual cycles and 6% females had hirsutism. There seems to be varied opinion regarding the association of acne with clinical markers of hyperandrogenism like hirsutism.[7] We encountered 56% patients with seborrhoeic dermatitis. The role of seborrhoea in the pathogenesis of acne and seborrhoeic dermatitis is well established with sebum in both these conditions demonstrating high triglyceride levels.

Nearly a quarter of our cases recorded an elevated body mass index with a mean much higher than that reported by Khunger N[8]. This could indicate a faulty diet and sedentary life-style in most of these individuals. The few studies that have explored this relationship concluded that a high-glycemic index diet and high BMI contributed to a higher prevalence and severity of acne.[6] Another feature encountered in our cohort was pseudoacanthosis nigricans, which is considered a marker of metabolic syndrome and insulin resistance[9].

In our study, the predominant grade of acne was grade 2 followed by grade 4 that means according to global acne severity score, moderate grade is predominant followed by very severe grade. This was consistent with the findings of Khunger N[8]. On the other hand, Adityan B and Thappa DM[7] observed grade 1 to be the foremost severity grade of acne vulgaris in their study on 186 patients.

A small sub-set of our patients presented with monomorphic papulo-pustular rash involving face and trunk characteristic of drug-induced acne. Topical steroid abuse is considered one of the commonest causes of this type of acne.[3] However, in our series, anti-tubercular drugs and oral contraceptives were the chief culprits.

Hormonal evaluation is usually recommended in females with recalcitrant acne or clinical evidence of hyperandrogenism. In the present study, 8% of cases with grade 2 acne were found to have polycystic ovaries on ultrasonography. Upon hormonal evaluation of suspected cases (74 cases), 9% patients had raised serum prolactin levels, 2% cases had raised 17β-hydroxyprogesterone levels; 8% cases were found to have elevated free testosterone levels while 4% cases had raised dehydroepiandrostenedione (DHEAS) levels. In our study 10% of total cases had elevated LH/FSH ratio. Elevation of LH/FSH ratio is considered pathognomonic but not diagnostic of PCOS.[5]

The strength of this study is that we analysed most of the clinical and biochemical factors thought to be associated with acne. However the limitation is that the statistical significance of this association with clinical severity could not be assessed.

Conclusion

We identified multiple modifiable aggravating factors for acne vulgaris. This knowledge can guide treatment strategies, particularly non-pharmacological interventions like stress management, appropriate diet, exercise and judicious use of cosmetics. Our study also underlines the relevance of clinical and biochemical evaluation for hormonal abnormalities and insulin resistance. There is paucity of studies in Indian literature elaborating this aspect of acne which deserves attention.

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ORIGINAL ARTICLE

Comparative Study Of IV Ketamine And IV Tramadol For Control Of Shivering In Cases Of Caesarean Section Under Spinal Anaesthesia

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ABSTRACT

INTRODUCTION : Post anaesthetic shivering is one of the most important problem of current clinical anaesthesiology practice seen both in patients receiving regional anaesthesia as well as general anaesthesia. It causes several undesirable physiologic consequences which may be detrimental to patients with low cardiopulmonary reserve.

Objective : objective of our study was to compare a small dose of **Ketamine**, NMDA receptor antagonist, with that of **Tramadol** an opioid analgesic for control of shivering during spinal anaesthesia and study the side effect profile

Methods: Total 80 cases undergoing emergency and elective caesarean section were included in the present study (randomized double blind) that developed shivering after spinal anesthesia. Subarachnoid block given with inj bupivacain 0.5% Heavy (1.5 to 2.5cc) at L3-L4 or L4-L5 space . Patients who developed grade 3 or 4 shivering were included in the study. Patients were randomly divided into two groups of 40 each and study drug administerd after delivery of the baby.

Group T n=40 patients .Received Tramadol 0.5mg per kg I.V. and

Group K n=40 patients. Received Ketamine 0.5 mg per kg I.V.

Results : Ketamine group showed control of shivering in 3.11 minutes as compared to Tramadol which controllled shivering in 4.90 minutes .Ketamine was more efficacious as the response rate of Ketamine was 95% as compared to the Tramadol where the response rate was 87.5%.

Conclusion

Both Tramadol and Ketamine were effective in controlling the shivering but Ketamine was more potent.Side effects were not seen except sedation in Ketamine group

KEY WORDS : Shivering , Spinal anaesthesia, Caesarean , Tramadol, Ketamine.

Introduction

Surgery and general anaesthesia impair the normal balance between heat production and loss. Anaesthetic agents, opioids and sedatives inhibit behavioural and autonomic responses, leaving patients essentially poikilothermic.

Considering clinical importance and frequency, post anaesthetic shivering was ranked as the 6th most important problem of current clinical anaesthesiology among 33 low morbidity clinical outcomes.[1] Shivering occurs in patients receiving regional anaesthesia as well as those patients receiving general anaesthesia. The main cause of shivering intra or post operative are temperature loss, decreased sympathetic tone and systemic release of pyrogens.[2]

Shivering causes several undesirable physiologic consequences including increase in oxygen consumption, carbon dioxide production and minute ventilation. It may induce arterial hypoxemia, lactic acidosis, increased intra ocular pressure (IOP), intra cranial pressure (ICP) and interference with patient monitoring like ECG, NIBP and SpO2 etc. It may negate orthopaedic procedures like fractures and dislocations and can be detrimental to patients with low cardiopulmonary reserve.[3]

Apart from the discomfort and aggravated pain, no link

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has been demonstrated between their occurrence and an increase in cardiac morbidity but it is preferable to avoid post anaesthetic shivering since it is oxygen draining.

Spinal anaesthesia causes core to periphery redistribution of heat due to spinal induced vasodilatation and shivering is preceded by core hypothermia following spinal anaesthesia .It may not trigger sensation of cold as the cutaneous vasodilatation resulting from sympathetic blockade increases skin temperature leading to a sensation of warmth although accompanied by thermoregulatory shivering.[4]

Non-pharmacological methods used for control of shivering are radiant warmer[5] , space blankets[6] warm fluids[7] etc.Various pharmacological treatments like i.v. opioids, Alfentanil, Pethidine[8] 5-HT3 antagonists; Ondansetron, Dolasetron[9] and cholinomimetic agent Physostigmine [10] have been used; however, side effects like hypotension, hypertension, sedation, respiratory depression, nausea and vomiting, limit their use.

Our study was designed to compare a small dose of **Ketamine**, NMDA receptor antagonist, with that of **Tramadol** an opioid analgesic for control of shivering during spinal anaesthesia.

Material and Methods

After approval from institutional ethical committee, total no of 80 cases undergoing emergency and elective caesarean section were included in the present study (randomized double blind) that developed shivering after spinal anesthesia. Patients were divided into two groups of 40 each. Randomization of the patients was done using computerized randomization charts. Pre anesthetic check up was done.

Inclusion Criteria

1.Age between18 to 40 years ,

2.ASA grade I & II and developing shivering intra operative or postoperative in emergency or elective caesarean section.

Exclusion Criteria

1.Patients with cardiopulmonary, renal, liver disorder

2.Known hypersensitivity to Tramadol and Ketamine,

3.Hypothyroidism or hyperthyroidism

4.Severe PIH or eclampsia,

5.Psychological disorder

6.Known case of alcohol or drug abuse

7.Receiving drug for labour analgesia or other medication likely to affect thermoregulation

A written informed consent was obtained in each case in their vernacular language. All emergency drugs & facilities were available in the operation theatre. Patients under study went through preoperative assessment including detailed case history, physical examination and all necessary investigations. Patients were kept NBM (nil by mouth) for at least 6 hours prior to procedure in planned surgery.

An IV cannula of 18G was secured and preloading with ringer lactate done in both group of patient and monitors attached . No premedication given. Subarachnoid block given with inj bupivacain 0.5%Heavy (1.5 to 2.5cc as per height of patient) at L3-L4 or L4-L5 space using 25G Quinckes needle and adequate level set. Operating room temperature kept between 21 to 23°C. Patients who developed grade 3 or 4 shivering as per Wrench criteria were included in the study.

Wrench criteria of shivering

Grade 1 No shivering.

Grade 2 One or more of following

Piloerection

peripheral vasoconstriction

peripheral cyanosis

visible muscle activity

Grade 3 Visible muscle activity confined to one muscle group.

Grade 4 Visible in more than one muscle group.

Grade 5 Gross muscle activity involving whole body

Drug therapy started as per patient group after delivery of baby. Patients were randomized in 2 groups

Group T n=40 patients .Received Tramadol 0.5mg per kg I.V.

Group K n=40 patients. Received Ketamine 0.5 mg per kg I.V.

Parameters studied

1. Time of appearance of shivering
2. Response rate (Percentage of patients in which shivering controlled within 15 minutes)
3. Side effects and complications
4. Failure to control the shivering.
5. Recurrence of shivering.

If shivering grade remained same 15 minutes after the administration of study drug, the treatment regarded as less effective and rescue treatment in the form of i.v dexamethasone 5mg was administered to control the shivering.

Patients were monitored intra operatively for pulse rate, blood pressure, oxygen saturation and body temperature (in axilla) recorded before commencement of surgery, every 5 min for one hour and every 15 min for rest of procedure.

Post operative vitals , oxygen saturation, sedation, extent of shivering and side effects monitored in all the patients.

Results

Table I

Parameter	Group T	Group K	P-value
Mean Age in Years (24.50)	40	40	0.542
Mean weight (kg)	59.83	59.93	0.871
ASA grade I	21	20	0.999
ASA grade II	19	20	0.999
Elective	21	19	0.823
Emergency	19	21	0.823

2 independent sample t-test, and chi square test p-value > 0.05.Both the groups were similar with respect to each other

Table II

Parameter	Group T	Group K	P-value
mean time for shivering after SA(min)	22.20	22.20	0.999
Grades of shivering III	34	26	0.069
Grades of shivering IV	6	14	0.069
Pre operative temp	37.00	37.00	0.811
Temp during shivering	36.29	36.31	0.508
Mean HR during shivering	80.95	78.25	0.082
Mean HR after control	77.40	77.05	0.082
Mean SBP during shivering	120.90	121.40	0.386
Mean SBP after control	117.45	117.85	0.410
Mean DBP during shivering	73.65	73.95	0.582
Mean DBP after control	71.90	71.80	0.816
Mean SpO2 during shivering	98.68	98.88	0.120
Mean SpO2 after control	98.83	98.85	0.829

By using 2 independent sample t-test, p-value > 0.05 no significant difference between the above parameters in group T and group K

Table III Time required for control of shivering

Group	Number of patients	Time required for control of shivering		P-value
		Mean	SD	
Group T	40	4.90	4.24	0.03
Group K	40	3.11	3.12	

2 independent sample t-test, P-value 0.03 (p-value < 0.05) there was significant difference between mean Time required for control of shivering in group T and group K.

Table IV

Response rate (Percentage of patients in which shivering controlled within 15 minutes) in Group T and Group K.

Time to control	Group		Total	P-value
	Group T	Group K		
> 15 min	5(12.5%)	2(95%)	9	0.154
< 15 min	35(87.5%)	38(5%)	71	
Total	40	40	80	

Chi-square test, p-value > 0.05 no significant association between the response rate in Group T and group K.

Table V-

Comparison of side effect (Sedation)

Side effect(Sedation)	Group		Total	P-value
	Group T	Group K		
Sedated	0	5	5	0.055
Not sedated	40	35	75	
Total	40	40	80	

By using Chi-square test, (p-value > 0.05) there was no significant association between the sedation with group T and group K.

DISCUSSION

Regional anaesthesia, either central neuraxial block or peripheral nerve block is a safe and very popular technique used for various surgeries. However, 19-33% of patients undergoing regional anaesthesia develop shivering, though it is also found to occur after general anaesthesia. The probable mechanisms could be decrease in core body temperature secondary to sympathetic block[2] peripheral vasodilatation; increased cutaneous blood flow, which leads to increased heat loss through skin; cold temperature of operation theatre; rapid infusion of cold IV fluids; and effect of cold anaesthetic drugs upon the thermo sensitive receptors in the spinal cord. It has been mentioned that hypothermia may cause post anaesthetic shivering by alteration of thermoregulatory mechanism. However, no relationship has been shown between axillary temperature and occurrence of shivering. Rigors occur commonly, as a protective response to core hypothermia, though it may occur in the presence of normothermia. In our study, there was no significant difference in axillary temperature among the groups. We had to resort to continuous measurement of axillary temperature by thermometer as we felt that a nasal, oesophageal or rectal probe would be uncomfortable for the patients. A number of factors including age, duration of surgery, temperature of the operating room and infusion solution, are risk factors for hypothermia and shivering. So in our study, patients over the age of 40 years were excluded. The temperature of operating room was maintained at 21° to 23° C and infusions of crystalloid solution were warmed. We also excluded the patients having history of acute infections, sepsis and fever to reduce their confounding effect.

Pharmacological intervention resets the shivering threshold to a lower level, thereby decreasing rigors and its episodes. Various pharmacological therapies have been tried including opioids (e.g. Pethidine[8], Ketanserin, Propofol, Ondansetron[9], Granisetron, Doxapram, Physostigmine[0], Nefopam and Ketamine etc., but debate for an 'ideal anti-shivering drug' still continues.

In the present study, we compared the efficacy of Tramadol and Ketamine for treatment of shivering after spinal anaesthesia in patients undergoing elective and emergency caesarean sections.

Tramadol's distinct features in the treatment of shivering are its weak sedative and smaller respiratory depressive properties than Morphine, particularly in parturient and patients with low cardiopulmonary reserve. Tramadol does not inhibit the neuronal reuptake of nor epinephrine and 5-hydroxytrytpamine, facilitate 5-hydroxytrytpamine release, and activates μ-opioid receptors. Each of these actions is likely to influence thermoregulatory control. However Tramadol had only slight thermoregulatory effects. Thus, it is unlikely to provoke hypothermia or to facilitate fever. The main opioid effect of tramadol is mediated via the μ receptor, with minimal effect at kappa or sigma binding sites. Tramadol may induce its antishivering effect via the additive or synergistic action of both kappa opioid receptor and 2 adrenergic mechanisms. The interaction of kappa opioid and 2 adrenoceptor mechanisms working in a complementary or synergistic manner to produce anti shivering effects seems a possible explanation.[11]

Pausawasdi S.et al[12] studied Tramadol in dosages of 1mg/kg intravenously and found that in all patients shivering gotcontrolled in 45 seconds to 6 minutes(in our study mean time 4.90 minutes)

De Witte J and colleagues[13] used Tramadol (0.5/1/2 mg per kg, i.v.) or normal saline on shivering . They observed that Tramadol in 0.5mg/kg was effective with minimal side effects. These results were in accordance with our study results.

Wason R and colleague[14] evaluated the effectiveness of prophylactic Ketamine, Clonidine and Tramadol and

concluded that the prophylactic use of Ketamine, Clonidine and Tramadol were effective in preventing shivering during neuraxial anaesthesia without major untoward side-effects. The result was consistent with our study where we used inj.Ketamine and inj.Tramadol in the same dosage.

Hidayah and colleagues[15]used IV Ketamine 0.5 mg/kg (Group K), IV Tramadol 0.5 mg/kg (Group T) or normal saline as control (Group P) supports our study Only, patients receiving ketamine were more sedated(table no V).

Ketamine, a competitive NMDA receptor antagonist, also inhibits postoperative shivering. It is likely that NMDA receptor antagonists modulate thermoregulation, modulate noradrenergic and serotoninergic neurones in the locus coeruleus. Ketamine has several other pharmacological properties; these include being a k opioid agonist, blocking amine uptake in the descending inhibitory monoaminergic pain pathways, having a local anaesthetic action and interacting with muscarinic receptors. Therefore it probably controls shivering by non-shivering thermogenesis either by action on the hypothalamus or by the b-adrenergic effect of nor epinephrine.[16]

Kose and colleagues[17] compared Meperidine 25 mg, Ketamine 0.5 mg/kg, or Ketamine 0.75 mg/kg IV for treatment of postoperative shivering. however, nystagmus and feeling like "walking in space" was experienced with both doses of ketamine. Ketamine 0.5-0.75 mg/kg was more rapid for the reduction of postoperative shivering , but with undesirable side effect profile. In our study Ketamine in the dose of 0.5mg/kg was effective and no other side effect seen except sedation (table no V)

We can say that group T and group K are comparable with respect to age, weight, ASA grades, Emergency and elective procedures, grades of shivering (Table I). There no significant difference in pre operative temperature, HR, SBP, DBP and SpO2 in both groups and even after the control of shivering(Table II).

Mean time required to control shivering in T group is 4.90 minutes which is in accordance with the studies of Pausaudi S.et al[12], Mean time required to control shivering in K group is 3.11 minutes. P-value is 0.03. By using 2 independent sample t-test p-value < 0.05 therefore there is significant difference between mean time required to control shivering in group T and Group K(Table III)

Table IV shows the comparison of response rate in K group it is 95% and in T group the response rate is 87.50. By using Chi-square test (P-value 0.154) this is not significant.

In group T, side effect (Sedation) are nil which is in accordance with the study of Wason R and colleague.[14] while in group K 5 patients had side effect in the form of sedation (Table 5).The finding that side effect of Ketamine is sedation which is in accordance with Kamal and colleagues[18] and Kose and colleagues. p-value is 0.055. By using Fish Chi-square test (p-value > 0.05),it was statistically insignificant.

Conclusion

Both Tramadol and Ketamine were effective in controlling the shivering without side effects except sedation in Ketamine group which can be advantageous in reducing anxiety and trauma of child birth. Ketamine was more potent in controlling shivering in 3.11 minutes as compared to Tramadol which controlled shivering in 4.90 minutes.Ketamine was more efficacious as the response rate of Ketamine was 95% as compared to the Tramadol where the response rate was 87.5%.

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ORIGINAL ARTICLE

Study Of Stress Levels Among Mothers Of Babies Admitted In Neonatal Intensive Care Unit (NICU) In A Tertiary Care Centre

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ABSTRACT

Objective : To determine the stress levels among mothers of babies admitted in Neonatal Intensive Care Unit (NICU) and to identify demographic characteristics that influence their stress levels.

Methods : A cross sectional study was carried out at a tertiary care centre over a period of six months. Stress levels were assessed using Parental Stressor Scale: Neonatal Intensive Care Unit (PSS: NICU) questionnaire. Stress was quantified using Likert scale. The statistical analysis was done using SPSS statistical software ver.18. Mean and standard deviations were calculated and t test was applied.

Results : The mean score for the subscales, sights and sounds was 2.74, looks and behaviour was 4.08, alteration in the parental role was 4.24. Increased maternal age, prematurity and longer hospital stay was associated with higher stress levels.

Conclusion : NICU mothers are under stress and appropriate counselling targeted towards specific stressors is required.

Keywords : Parenteral Stressor Scale: Neonatal intensive care unit (PSS: NICU)

Introduction

The admission of a baby in Neonatal Intensive Care Unit (NICU) have the potential to exacerbate stress for the parents. NICU mothers experience multiple stressors related to medical condition of the baby, complexity of NICU environment and perceived vulnerability of the infant.[1-2].The parents find difficulty in fulfilling their parental role as the baby is admitted in NICU[3-4]. Many factors influence the reaction of the parents towards their babies' NICU admission. Miles and Carter explained that as a result of the various factors that can influence the parents, each parent develops his or her own way of making judgments about the NICU experience[3]. For example, some parents, may view their situation as positive since their infant is getting the care he or she needs, others may see it as negative when the infant or staff is unable to correspond to their expectations or needs, some parents may cope by using the environmental resources available to them such as the support of the NICU staff, while others may use personal resources such as family, friends or financial assets.

The studies have been conducted to explore various factors which influence the stress levels in parents of NICU admitted babies[5-10]. It is important to identify factors associated with increased parental stress in order to develop effective interventions for reducing the stress of the NICU parents. With this background, the present study was conducted to determine the levels of stress experienced by mothers of babies admitted in NICU in a tertiary care centre in Maharashtra.

Methods

This cross sectional study was carried out at a tertiary care hospital. The study period was from 1st July 2016 to 31st December 2016. Institutional ethics committee approval was taken to conduct the study. Mothers of the babies admitted in the Neonatal Intensive Care Unit for various reasons such as prematurity, birth asphyxia, congenital malformations, jaundice etc. were included in the study. The mothers whose baby is admitted for more than 24 hours in NICU and given informed consent for the study were enrolled in the study. The mothers with previous history of psychiatric illness were excluded from the study. A convenient sample of 150 mothers was recruited during the study period. Demographic details of NICU mothers like age, education, occupation, and hospitalization details like type of the delivery, maturity of the baby, birth weight, mode of feeding etc. were collected.

Stress levels among the mothers were assessed using the Parental Stressor Scale: Neonatal Intensive Care Unit

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(PSS: NICU) a questionnaire in both English and Marathi language[1]. The scale consists of four subscales that measures stress related to a) the sights and sounds of the unit b) the appearance and behaviours of the infant c) the impact on the parents' role and their relationship with their baby and d) the staff behaviours and communications. The responses to the PSS: NICU were scored on a 5-point Likert scale ranging from 1 point for "not at all stressful", 2 points for "mild stress", 3 points for "fairly moderate stress", 4 points for "very stressful" and 5 points for "extreme / severe stress". Higher scores indicate more stress. The statistical analysis was carried out with the help of SPSS Software version 18. Mean and standard deviations were calculated and t test was applied.

Results

The mean age of the mothers participating in the study was 23.9 years with a range between 18 years to 30 years. 14.7 % of the mothers were illiterate, 19.3 % went to primary school, 50 % received high school education while 16 % had done their graduation. Among the participants, 61.3 % of the mothers were housewives whereas 38.7 % were employed.

The birth weight of babies ranged from 950 grams to 2800 grams with a mean of 1780 grams. The premature births among the babies were 57.3 % whereas remaining 42.7 % were full term births. 68.6 % of the participants had vaginal delivery and the rest 31.4 % had caesarean or instrumental delivery. The most common diagnosis for NICU admission was prematurity (57.3 %) followed by birth asphyxia (11 %), cardiovascular disorders (10 %), congenital abnormalities (7 %), metabolic abnormalities (6 %), jaundice (3 %) and other diseases (5.7 %).

The various components of Parenteral Stressor Scale: Neonatal intensive care unit (PSS: NICU) and their corresponding maternal stress scores are given in Table I.

Table I: Parental stress measured by PSS: NICU (n=150)

Subscales and components	Stress score	
	Mean	S.D.
a. Sights and sounds		
1. Presence of monitors and equipments	2.61	0.860
2. Constant noises of monitors and equipments	2 .32	0.822
3. Other sick babies in the room	2.29	0.848
4. Sudden noises of monitor alarms	3.36	0.06
5. Large number of staff in NICU	1.56	0.836
6. Having a ventilator to breathe	4.28	0.480
Mean score	2.74	0.646

Subscales and components	Stress score	
	Mean	S.D.
b. Looks and behaviour of the infant		
1. Tubes and equipments on or near baby	3.89	0.814
2. Seeing needles and tubes being put on baby	4.20	0.836
3. Baby fed by tube	4.30	0.867
4. Unusual colour of the baby	4.14	0.693
5. Limp and weak appearance of baby	4.01	0.666
6. Small Size of baby	3.98	0.634
7. Baby not crying like other babies	3.92	0.807
8. Jerky Movements of baby	4.20	0.836
9. Seeing my baby in pain	4.30	0.867
10. Seeing my baby looking sick	4.02	0.668
11. Wrinkled appearance of baby	4.00	0.547
Mean score	4.08	0.586

Subscales and components	Stress score	
	Mean	S.D.
c. Parental role alteration		
1. Being separated from baby	4.37	0.744
2. Not feeding my baby myself	4.14	0.626
3. Not being able to care for my baby myself	4.21	0.774
4. Not being able to hold my baby when I want	3.89	0.814
5. Feeling helpless and unable to protect baby	4.14	0.681
6. Feeling helpless about how to help baby	4.57	0.742
7. Not having time to be alone with baby	3.98	1.075
8. Sometimes forgetting what baby looks like	4.25	0.683
9. Not being able to share baby with other family members	4.30	0.676
10. Feeling that staff is closer to my baby than I am	4.57	0.545
Mean score	4.24	0.682

Table II: Stress levels in mothers (n= 150)

Subscales	High level (4.0-5.0)	Medium level (3.0-3.9)	Low level (1.0-2.9)
Sights and sounds	18	44	88
Looks and behaviours	86	45	19
Parental role	87	41	22

The highest level of stress in mothers was found in the areas of looks and behaviour and parental role alterations (Table II)

Table III: Maternal stress levels in relation to demographic characteristics

Characteristic	Groups	N	Mean subscale stress scores (S.D.)			
			Sights & sounds	Looks & behaviour	Parental role	*P* value
Age	18-25	94	2.85(0.43)	3.96(0.59)	4.09(0.60)	p<0.05
	26-30	56	2.64(0.62)	4.18(0.56)	4.35(0.42)	
Education	Illiterate	22	2.69(0.60)	4.01(0.58)	4.16(0.51)	p>0.05
	Primary	29	2.76(0.63)	3.96(0.59)	4.23(0.58)	
	High school	75	2.85(0.43)	4.16(0.51)	4.33(0.42)	
	Graduation	24	2.69(0.60)	4.18(0.56)	4.23(0.41)	
Occupation	Housewife	92	2.64(0.62)	3.98(0.58)	4.26(0.61)	p>0.05
	Employed	58	2.85(0.43)	4.17(0.63)	4.22(0.58)	
Type of delivery	Vaginal	103	2.69(0.56)	4.03(0.60)	4.17(0.67)	p<0.05
	Caesarean	47	2.77(0.45)	4.13(0.49)	4.28(0.54)	
Length of NICU stay	<7 days	63	2.55(0.67)	3.96(0.58)	4.13(0.49)	p<0.05
	>7 days	87	2.85(0.43)	4.18(0.63)	4.34(0.63)	
Maturity of the baby	Preterm	86	2.61(0.74)	4.28(0.54)	4.35(0.57)	p<0.05
	Term	64	2.85(0.43)	3.86(0.59)	4.12(0.56)	
Mode of Feeding	Direct feeding	53	2.69(0.60)	3.96(0.59)	4.18(0.59)	p>0.05
	Expressed	97	2.85(0.43)	4.18(0.56)	4.28(0.56)	

Increasing age of mothers, type of delivery and longer duration of stay in NICU were associated with higher stress levels among the mothers. The stress level was found to be significantly higher among the mothers with preterm babies than mothers with term babies. The characteristics like education of mother, occupation and mode of feeding did not significantly affect the stress levels among the mothers (Table III).

Discussion

It is necessary to explore the factors which aggravate the stress levels among the mothers having their babies with NICU admissions. Identification of such stressors helps to develop appropriate interventions to reduce the maternal stress and cope up them in NICU environment.

The sights and sounds of NICU caused lesser stress and few parents reported stress in the area of staff communication and relationship in a study carried out by Miles et al[1]. Another study carried out by Chourasia et al showed that stress score was highest for parental role alteration followed by looks and behaviour of the baby and sights and sounds of NICU[8]. Similar findings were observed in this study. However, the staff behaviours and communications were not studied.

According to studies by Chourasia N et al and Dudek-Shriber L., consistent predictors of stress were length of stay, extreme prematurity, increased maternal age and cardiovascular diagnosis[8 & 11]. In the study carried out by Ashwani et al parents' gender, staff communication and maturity of baby were significantly associated with higher parental stress[9]. In the present study increased maternal age, type of delivery, prematurity of baby and longer NICU stay were associated with higher maternal stress. The psychometric properties of the PSS: NICU have been evaluated and found to be consistently significant.[12-13]

A study by Jopek et al revealed that it is possible to decrease the stress level among NICU parents by explaining the background of the disease, the current clinical condition of the newborn, the necessity of diagnostic and treatment procedures and involving the parents in the basic care of the newborn[14]. There is need for appropriate counselling to reduce the maternal stress with respect to subscales of PSS: NICU.

Conclusion

The findings of the present study document stress experienced by the mothers of NICU babies. The mothers having their babies in NICU are under stress and appropriate counselling targeted towards specific stressors is required. This information can be used to design effective coping strategies for parents at different time points during their infant's hospitalization.

Conflict of Interest: None

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ORIGINAL ARTICLE

Comparison Of Sympathetic Autonomic Functions In Overweight And Normal Weight Normotensive Persons.

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ABSTRACT

BACKGROUND : Most of the Indian population is overweight (BMI=25-29.9kg/m^2).Overweight people are also at higher risk for cardiovascular diseases. But mechanism behind increased cardiovascular risk is not yet known. Most of the studies have shown that obesity induced hypertension is associated with autonomic dysfunction. Autonomic dysfunction could be a mechanism behind increased cardiovascular risk in overweight people. So this study was aimed to understand cardiovascular reactivity to sympathetic stress in overweight normotensive persons using two sympathoexcitatory maneuvers like sustained hand grip (SHG) and cold pressor test (CPT).

OBJECTIVES: To measure and compare sympathetic autonomic functions in overweight and normalweight normotensive persons**.**

METHODOLOGY: In 60 healthy, normotensive male volunteers from employees of BJGMC Pune, we measured blood pressure and heart rate response in overweight (BMI 25-29.9kg/metres^2) study group and compared with age and sex matched normalweight (BMI 18-24.9kg/metres^2) control group during two sympathoexcitatory maneuvers : CPT & SHG.

RESULTS: Blood pressure response (ΔSBP, ΔDBP) to sympathetic stress was increased statistically significantly in overweight group as compared to normalweight group during CPT and SGH maneuvers.(p-value <0.05) There was no significant difference in HR response between the two groups during either maneuver (p-value >0.05).

CONCLUSION: Overweight persons showed significant rise in sympathetic activity during sustained hand grip test as compared with normalweight persons. This indicates sympathetic over activity in response to sympathetic stress and greater future risk of hypertension in normotensive overweight persons.

KEY WORDS: BMI, autonomic dysfunction, overweight, normalweight, CPT, SHG.

Introduction

Major portion of Indian population is overweight (BMI=25-29.9kg/m^2).[1] Overweight people are also at higher risk for cardiovascular diseases.[2] But it is not yet understood about the mechanism associated with the increased cardiovascular risk and hypertension in overweight people.

Some studies have been shown that autonomic dysfunction could be a reason associated with obesity (BMI $\geqslant$ 30 kg/m^2) induced hypertension.[3] Sympathetic nervous system helps to control the reaction of the body to stress. Some previously done studies have suggested that increased cardiovascular reactivity to stress is risk factor for cardiovascular diseases and hypertension. [4]

Cardiovascular responses to sympathetic stress had been less studied in overweight normotensive individuals. The purpose of this study was to understand the cardiovascular reactivity to sympathetic stress in overweight normotensive subjects. The cardiovascular reactivity to sympathetic stress was studied by measuring and comparing blood pressure response and heart rate response during two sympathoexcitatory maneuvers like cold pressor test (CPT) and sustained hand grip test (SHG) in overweight and normalweight normotensive person.

Objective

To measure and compare sympathetic autonomic functions in overweight and normalweight normotensive persons**.**

Methods

The study was designed as analytical, cross-sectional, comparative study in the Department of Physiology of BJGMC medical college, Pune. The synopsis of study protocol was submitted to the institutional ethics committee and approval was obtained. Study was conducted from December 2013 to September 2015.

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Subjects were selected by using certain inclusion and exclusion criteria by simple random sampling.

Inclusion criteria:

Thirty overweight normotensive male subjects in the age group 35 to 50 years having BMI =25-29.9 kg/m^2 and sinus rhythm on ECG were selected for study group. Thirty age and gender matched healthy normotensive subjects having BMI =18-24.9 kg/m^2 were selected for control group.

Exclusion criteria for study group and control group:

Obese person having BMI $\geqslant$ 30 were excluded. Subjects with history of diabetes mellitus, cardiac diseases, bronchial asthma, Reynaud's disease, alcohol abuse and tobacco chewing or smoking, who regularly practice yoga were excluded.

Sample size:

For study group, 30 overweight normotensive male subjects were selected. For control group, 30 healthy age and gender matched, normalweight normotensive subjects were selected.

After explaining study and taking informed consent, both blood pressure and heart rate responses was measured and compared in overweight and normalweight groups during cold pressor test (CPT) and sustained hand grip (SHG).

1] Cold Pressor Test (CPT):[5]

Resting blood pressure was recorded with the subject sitting comfortably and immersing his hand in cold water upto wrist and the temperature was maintained at 4-6^0 C throughout the procedure. Blood pressure measurement was made from the other arm at 30 second intervals for a period of 2 minutes. After 2 minutes, the subject was asked to remove his hand. The maximum rise in the systolic and diastolic blood pressure and heart rate was recorded. Participants were instructed to maintain normal breathing patterns and avoid breath holding.

4] Sustained hand grip test (SHG):[6]

Maximum voluntary contraction (MVC) was recorded by asking the subjects to squeeze the bars of hand grip dynamometer by dominant hand to produce a maximum effort as much as possible and maintaining the maximal effort for 2-3 sec. Three trials were given with interval of 10 sec between each trial to avoid fatigue. Then blood pressure was recorded at 30% of MVC by asking the subject to apply pressure on a handgrip dynamometer for 1 minute at 30% of maximal voluntary contraction and simultaneously the blood pressure changes were observed by using automatic digital machine. The difference between the systolic, diastolic blood pressure records (DBP) and heart rate just before the release of contraction and just before starting handgrip maneuver was taken as a measure of the response.

Statistical Analysis:

The results were given as Mean ± Standard Deviation. Comparisons were performed using unpaired student's t-test in the two groups. A p-value of less than 0.05 was considered as statistically significant. Statistical software SPSS (Statistical Package for the Social Science) version 20 was used for the analysis of data. Microsoft word and Microsoft excel have been used to create text documents, graphs and tables etc.

RESULTS

Table no 1: Hemodynamic changes during sustained hand grip (SHG) test

Parameter	Overweight Normotensive		Normalweight Normotensive		p-value
	Mean	SD	Mean	SD	
ΔSBP (mm of Hg)	19	0.45	16	0.34	p<0.05*
ΔDBP (mm of Hg)	18	0.38	15	0.42	p<0.05*
ΔHR (beats/min)	13	0.53	12	0.71	p>0.05

Table no 2: Hemodynamic changes during cold pressor test (CPT).

Parameter	Overweight Normotensive		Normalweight Normotensive		p-value
	Mean	SD	Mean	SD	
ΔSBP (mm of Hg)	19	0.52	14	0.50	p<0.05*
ΔDBP (mm of Hg)	17	0.48	15	0.42	p<0.05*
ΔHR (beats/min)	12	0.50	11	0.61	p>0.05

Discussion

Most of the Indian population is overweight which is not yet included in obese group.[1]Overweight condition is also associated with increased cardiovascular risk and increased incidence of hypertension.[7]Mechanism underlying the increased risk with overweight is yet not clear. Autonomic dysfunction can be a reason for increased risk associated with overweight. So this study was aimed to measure and compare sympathetic autonomic function in overweight and normalweight persons. If autonomic dysfunction is diagnosed early it could prevent morbidity and mortality associated with overweight.

In the present study, it was observed that increase in blood pressure response (Δ SBP, Δ DBP) in overweight group was statistically significantly greater than normalweight group during sympathetic stress like CPT and SHG ($p<0.05$*).

Our results are comparable with the study done by Jeanie P [7]who got exaggerated MSNA (muscle sympathetic nerve activity) response to the CPT and concluded that increased sympathetic reactivity to cold stress contributes to increased risk of hypertension. Our results are also in accordance with Thorat KD[8,] Martini G[9], Grewal S[10].

Result of the present study can be explained as-

Stored fat acts as endocrine organ and releases peptides called adipokines like TNF-α, Leptin, IL-1 and IL-6. Leptinreleased from fat cells stimulatessome regions in the hypothalamus directly which may produce excitatory influence on the vasomotor center of the medulla.[11]

Leptin regulates energy homeostasis and food intake by binding to specific Leptin receptors in the hypothalamus and increasing sympathetic outflow.[12]Obese patients have less soluble form of Leptin receptors (sOB-R).[13]Leptin resistance is a very common state in obesity. Leptin may be cause of increased sympathetic nervous system activity by increasing the concentrations of circulating norepinephrine. [14,15]Leptin resistance decreases as the adiposity level decreases and this reduction improves cardiovascular function [16].

Conclusion

The present study showed significantly increased sympathetic activity in overweight group as compared to normalweight group. Sympathetic activity increases as the BMI increase. Even though normotensive, people are at higher risk of cardiovascular risk in future if they are overweight.

Limitations

Present study did not consider type of fat deposition i.e. peripheral or central.

Conflict of Interest: None

Funding source: None

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ORIGINAL ARTICLE

Corrected QT (QTc) Interval In Female Patients Of Subclinical Hypothyroidism And Overt Hypothyroidism.

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ABSTRACT

Introduction: The aim of present study was to evaluate the effect of altered thyroid status on ventricular repolarization of newly diagnosed patients with subclinical hypothyroidism and overt hypothyroidism. We also correlated QTc interval with serum TSH.

Study design: This study was a cross sectional comparative study.

Materials and Methods: QTc interval was recorded in 114 female subjects with age 30 to 45 years. According to thyroid function tests subjects were divided into three groups as subclinical hypothyroidism (n=38), overt hypothyroidism (n=38) and euthyroid subjects (n=38) as control.

Results: The QTc interval in patients of subclinical hypothyroidism and overt hypothyroidism was statistically significantly increased when compared with euthyroid subjects. Also QTc interval had positive correlation with serum thyroid stimulating hormone (TSH) level in all subjects.

Conclusion: The increased ventricular repolarization time in patients with subclinical hypothyroidism and overt hypothyroidism may predispose to the risk of ventricular arrhythmia, which might be prevented by early treatment.

Key words: Subclinical Hypothyroidism, Overt Hypothyroidism.

Introduction

Subclinical hypothyroidism is common disorder which is apparently asymptomatic and characterized by slightly increased thyroid stimulating hormone (TSH), normal tri-iodothyronine (T3) and thyroxine (T4) levels. But, overt hypothyroidism is characterized by decreased levels of T3, T4 hormones and increased levels of TSH hormone.[1,2] QT interval corrected for heart rate (QTc) is an index of the inhomogeneity of ventricular repolarization.[3] Many studies have shown correlation of increased QTc with increased risk of ventricular arrhythmias and sudden death.[4,5,6] Also previous studies observed association of increased QTc with overt hypothyroidism.[7,8,9] However, presence of QTc interval changes in subclinical hypothyroidism are not much known. We have studied the exact correlation of QTc with serum TSH in subclinical hypothyroid and overt hypothyroid groups.

Aims and Objectives

The aim of present study was to evaluate the effect of newly diagnosed patients of subclinical hypothyroidism and overt hypothyroidism on ventricular repolarization with gender, age and BMI matched apparently healthy controls.

Material and Methods

This study was a cross sectional comparative study. The synopsis of study protocol was submitted to the institutional ethics committee and it was approved. Total of 114 female volunteers were selected with age ranging from 30 to 45 years from the patients attending medicine OPD and their relatives. Newly diagnosed female patients of subclinical hypothyroidism (n=38) and overt hypothyroidism (n=38), those who were not taking any treatment or medicines for thyroid disorder were included. Also those patients having other diseases which could alter autonomic reactivity like diabetes, electrolyte imbalance cardiovascular disorders, arrhythmia, hypertension, hepatic or renal failure or consumption of any medication that might alter cardiac conductibility were excluded. Diagnosis of subclinical hypothyroidism and overt hypothyroidism was based on both clinical and biochemical criteria (Thyroid hormone profile).[2] Those patients having normal total T3, normal total T4 and elevated TSH hormones were included in subclinical hypothyroid group. Patients having low total T3, low total T4 and high TSH were grouped in overt hypothyroid. Age and sex matched healthy controls (n=38) were selected from the relatives of study group subjects.

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Table I: Thyroid Hormone profile, Laboratory reference range by ELISA test.

Tests (Parameters)	Expected normal Value
Total T3	56 to 188 ng/dl
Total T4	4.87-11.72 µg/dl
TSH	0.4-4.0µIU/ml

In the study all the participants were explained verbally in detail about the purpose and every step in the study. Adequate opportunity was given to discuss their queries. A written consent was obtained from all the participants. The detailed medical history was taken and clinical examination was done. Then all the participants were asked to come in the morning at 8 am. 5ml fasting blood sample was obtained under all aseptic precautions. Serum was separated and serum total T3, T4 and TSH was estimated by using Enzyme linked immunosorbent assay (ELISA) method. The subject were advised to avoid tea or coffee at breakfast and to attend the physiology department laboratory between 9:00 to 11:00 a.m. on the day of examination.

Then different parameters were recorded.

Height was measured to nearest centimetre and weight was measured in kilograms. Body Mass Index (BMI) / Quetelet's index was calculated using following formula.[10]

$$BMI = \frac{\text{weight in kg}}{(\text{height in meter})2}$$

Resting ECG (Electrocardiogram) was recorded in lead II after a 15 minutes rest in supine position and baseline heart rate of patients was measured. Patients having heart rate in between 60-90 beats/min were included. Blood pressure was measured in supine position with a standard mercury manometer. QT intervals were measured in lead II from onset of QRS complex to the end of T wave. Three consecutive QT intervals were measured and average was taken. QT interval was corrected (QTc) by Bazett's formula (QTc = QT/square root of R-R interval) for heart rate.[11]

Statistical analysis:

The data was presented as mean ± standard deviation. Comparisons were performed using one way ANOVA (Analysis Of Variance) for multiple groups and posthoc Bonferroni's multiple comparison Test was applied. Then Co-efficient of correlation in bivariate relationships was obtained using the Pearson's correlation test. A "p" value of less than 0.05 was considered as statistically significant and “p” value of less than 0.001 as statistically highly significant. Statistical software namely Graphpad Prism for windows, version 5.01 was used.

Results

Table II: Showing comparison of clinical and biochemical parameters between euthyroid, subclinical hypothyroid and overt hypothyroid groups.

Groups / Parameters (Mean±SD) (normal range)	Euthyroid (n=38)	Subclinical hypothyroid (n=38)	Overt Hypothyroid (n=38)	Anova p value
Age (years)	37.18 ± 5.41	37.00 ± 4.46	36.52 ± 4.84	p>0.05 NS
BMI	22.74 ± 2.04	23.10 ± 1.22	23.48 ± 1.24	p>0.05 NS
Total T3 (56 to 188 ng/dl)	104.37 ± 22.66	93.48 ± 27.34	39.76 ± 9.00	<0.001
Total T4 (4.87 to 11.72 µg/dl)	7.70 ± 2.04	7.00 ± 1.69	2.65 ± 0.91	<0.001
TSH (0.4 to 4.0 µIU/ml)	2.19 ± 1.01	11.07 ± 3.42	59.08 ± 25.40	<0.001
QTc (seconds)	0.39 ± 0.02	0.41 ± 0.04	0.42 ± 0.04	< 0.001

p<0.05 = statistically significant, p<0.001 = statistically highly significant, **NS = statistically non-significant, SD= standard deviation.**

Table III: Showing Bonferroni's multiple comparison test in between two individual groups.

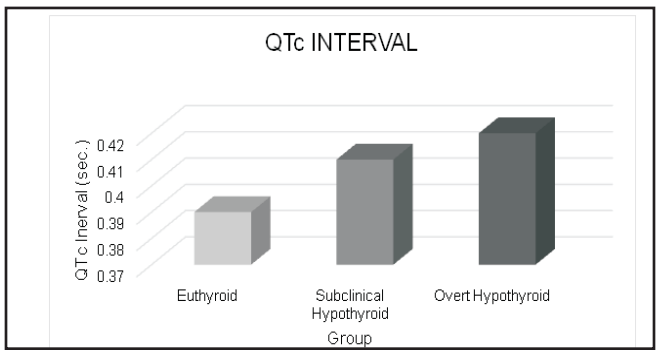
Groups / Parameters	Euthyroid VS Subclinical hypothyroid	Euthyroid VS Overt Hypothyroid	Subclinical hypothyroid VS Overt Hypothyroid
Total T3	P > 0.05 NS (t=2.24)	P < 0.001 (t=13.31)	P < 0.001 (t=11.07)
Total T4	P > 0.05 NS (t=1.88)	P < 0.001 (t=13.59)	P < 0.001 (t=11.70)
TSH	P < 0.05 (t=2.61)	P < 0.001 (t=16.75)	P < 0.001 (t=14.13)
QTc interval	P < 0.05 (t=2.43)	P < 0.001 (t=3.86)	P > 0.05 NS (t=1.43)

p<0.05 = statistically significant, p<0.001 = statistically highly significant, NS = statistically non-significant.

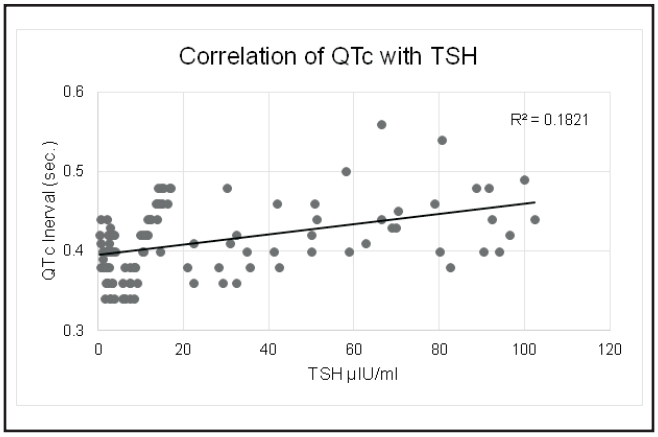
Table II shows comparison between the mean values of Age, BMI, total T3 (Tri-iodothyronine), total T4 (thyroxine), TSH (thyroid stimulating hormone) levels and QTc interval in euthyroid, subclinical hypothyroid and overt hypothyroid groups. Age and BMI were statistically non-significant ($p>0.05$). Therefore groups were comparable with respect to age and BMI. Total T3 and total T4 levels in subclinical hypothyroid group were statistically significantly low ($p<0.001$), while TSH level was statistically significantly high ($p<0.001$) in overt hypothyroid group as we compare all the three groups together. QTc interval in overt hypothyroid group was statistically significantly higher ($p<0.001$) as compared to euthyroid group.

Table III shows comparison between euthyroid and subclinical hypothyroid, euthyroid and overt hypothyroid, subclinical hypothyroid and overt hypothyroid for total T3, total T4, TSH levels and QTc interval. T3, T4 levels in between euthyroid and subclinical hypothyroid were not significantly different ($p>0.05$). But, the difference between euthyroid and subclinical hypothyroid for TSH was statistically significant ($p<0.05$). Whereas comparison between euthyroid and overt hypothyroid, subclinical hypothyroid and overt hypothyroid for total T3, total T4 and TSH were significantly different ($p<0.001$). For QTc interval comparison between euthyroid and subclinical hypothyroid was statistically significant ($p<0.05$), while the difference between euthyroid and overt hypothyroid was statistically highly significant ($p<0.001$). The difference between subclinical hypothyroid and overt hypothyroid for QTc interval was statistically non-significant ($p>0.05$).

Graph 1: Showing comparison of the mean values of corrected QT interval (QTc) in euthyroid, subclinical hypothyroid and overt hypothyroid groups.



Graph 2: Showing correlation between TSH levels and QTc interval for all patients and control subjects.



Graph 2 shows positive correlation between TSH levels and QTc intervals of 114 subjects ($r = 0.4268$, $p<0.001$).

Discussion

QT interval reflects the total duration of ventricular myocardial depolarization and repolarization. It can be corrected for heart rate by commonly used Bazett's formula where QTc = QT /$\sqrt{}$ RR interval. The QTc (corrected QT interval) effectively is the QT interval estimated at a rate of 60/minute.[11] QT interval prolongation is an irregularity of the electrical activity of the heart that places patients at risk for ventricular arrhythmias.[3] Prolongation of the QTc is believed to be due to an imbalance in the sympathetic drives from the right and left stellate ganglia. It is generally agreed that parasympathetic has little influence on QTc modulation.[12]

In our study we found that QTc interval (seconds) in subclinical hypothyroid was 0.41 ± 0.04, in overt hypothyroid it was 0.42 ± 0.04 while in euthyroid it was 0.39 ± 0.02 seconds (Table II and Graph 1). The corrected QT interval was significantly high in overt hypothyroid and subclinical hypothyroid group as compared to euthyroid group. In overt hypothyroid it was higher as compared to subclinical hypothyroid group. The difference was found to be statistically significant among all these groups (Table II). Also we compared QTc interval in between euthyroid and subclinical hypothyroid groups, it was found statistically significant ($p<0.05$) (Table III). Whereas QTc interval difference was statistically highly significant ($p<0.001$) among euthyroid and overt hypothyroid groups (Table

III). But the difference was statistically non-significant among subclinical hypothyroid and overt hypothyroid groups (Table III). Our results were compatible with previous studies.[7,8,9,13,14]

Increased QTc interval i.e. prolonged repolarization time may be due to an increase in the depolarizing currents or to a decrease in repolarizing currents. Bakiner O et al and Wickenden AD et al proved that overt hypothyroidism reduces some cardiac repolarizing K^+ currents such as the transient outward potassium current (I_{to}) and increases the L-type calcium current (Ica-L).[14,15] In overt hypothyroidism most of the repolarization abnormalities found are due to a reduction of the I_{to}, and an increase in the I_{Ca}-L.[16,17,18] T3 regulates the I_{Ca}-L calcium current at transcriptional and posttranscriptional level.[19] The Cav 1.2 channel expression is reduced by T3 and the calcium current is also modulated by T3 through cAMP.[17,20] Thus, decreased T3 in overt hypothyroid could explain the increase in I_{Ca}-L current, but does not show the decrease in I_{to} current.

However, previous studies observed cardiac repolarization abnormalities in patients with subclinical hypothyroidism, which were having many similar characteristics of cardiac repolarization found in overt hypothyroidism.[9,13] Also some studies correlated elevated serum TSH levels with repolarization abnormalities in patients with subclinical and overt hypothyroidism,[13,14] which coincides with our study (Graph 2). H. Alonso et al in their work found that TSH decreases the repolarizing K^+ current (I_{to}) and no effect on the I_{Ca}-L current in adult ventricular myocytes, thus prolonging action potential.[21] Thus, elevated serum TSH level prolongs ventricular repolarization in subclinical hypothyroidism, while in overt hypothyroidism decreased serum T3 and elevated serum TSH levels prolong ventricular repolarization.

Summary and conclusion

The aim of the present study was to test the hypothesis that subclinical hypothyroidism modulate ventricular repolarisation similar to that found in overt hypothyroidism. We detected increase in ventricular repolarization time in patients of subclinical hypothyroidism and overt hypothyroidism, which may predispose to the risk of ventricular arrhythmia. Thus measurement of QTc interval and its correlation with serum TSH level can predict about further complications.

Limitations

The limitations of the study were small number of subjects included in each group. Also only female subjects were included and to overcome this further population based studies including male and female subjects are needed.

Conflict of Interest: None

Funding source: None

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ORIGINAL ARTICLE

Placental Morphology In Pregnancies Complicated By Toxemia

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ABSTRACT

INTRODUCTION : Hypertensive disorder of pregnancy is most common medical problem complicating 3-8% of pregnancies. As pathophysiology lies in placenta most attention is drawn on placenta. In recent years it acts as valuable indicator for maternal and fetal diseases. Objectives: The objective of study was to assess the morphological changes of placenta and to correlate the findings with severity of disease. Materials and Methods: Total 102 placentae of which 52 placentae from cases of toxemia and 50 placentae from normal full-term pregnancy cases were studied. The morphometric parameters of placenta like weight, thickness, diameter, shape, umbilical cord insertion, retroplacental hematoma and microscopic lesions were recorded. Fetal birth weight was also recorded. Results: Placental morphometric features like mean placental weight, thickness were significantly low in toxemia group compared to control group. There was a positive correlation between placental weight and fetal birth weight ($P<0.001$). Mean fetoplacental (F/P) ratio was significantly low in toxemia group compared to control group ($P<0.05$). Microscopic lesions showing increased incidence of syncytial knots, fibrinoid necrosis, infarction and calcification were found in toxemia group. Conclusion: In this study it was found that placenta in toxemia group definitely had morphometric changes attributed to uteroplacental insufficiency, duration of disease, onset early or late affecting perfusion and oxidative stress. Further intensive workup with histo-pathological correlation is needed to come up with more promising recommendations that may help to resolve issues in future studies.

KEY WORDS : Toxemia, Syncytial knots, Infarction, Fibrinoid necrosis.

Introduction

Placenta is transient organ that forms during pregnancy to support growth and development of fetus. Human placenta is hemochorial which means maternal blood is in direct contact with fetal trophoblast. Growth and functions of placenta are precisely regulated and coordinated to ensure exchange of nutrients and waste products between maternal and fetal circulatory systems, operates at maximal efficiency.[1]

Placenta not only record and reflects the intrauterine environment, it also provides valuable information or the cause and timing of many adverse events and conditions. The placental examination reveals etiology and timing. Acute lesions may be associated with catastrophic events whereas other more chronic lesions lead to decreased placental reserve.[2]

Hypertensive disorders complicating pregnancy are common. In India incidence is 5%.[3] Conditions with the risk of recurrence can be recognized such as toxemia resulting in counseling and management of subsequent pregnancies. Despite the understanding and appreciation of placental disease, great resistance still exists in performing placental examination routinely.[4] So the detail study of placentae morphologically done in cases of toxemia to know significant changes compared to normal and was carried out in present study.

Material and Methods

This study is a cross sectional comparative study. The study comprised 102 cases obtained from department of obstetrics and gynecology at our institution. 50 placentae formed control group from normal full term

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pregnancies with 28 to 42 weeks gestation attending our institution and 52 placentae of toxemia cases complicating pregnancy were studied. Detail medical and obstetric history and consent were taken in all cases and clinical examination carried out with emphasis on following parameters.

Clinical data : History with findings by obstetrician including gestational age, pregnancy related preexisting medical diseases.

Examination of placenta :

- Gross: Size, shape, weight.
- External examination: Adherent clots, infarcts, calcification, hematoma.
- Cut surface: Infarct fresh /old, hematoma, calcification.
- Umbilical cord: Length, thickness, insertion, number of vessels, knots true/false.
- Membranes: Colour, opacity, meconium staining, amionnodosum.
- Microscopy: Syncytial knots, Fibrinoid necrosis, Infarct, Calcification.

At the time of delivery fetal birth weight was noted. Placental changes were correlated with duration and severity of underlying maternal disorder.

Statistical analysis

The results were given as Mean ± Standard Deviation and range values. Comparisons were performed using the unpaired type Student 't' test and Chi-square test. A "p" value of less than 0.05 was considered as statistically significant and “p” value of less than 0.001 as statistically highly significant. Statistical software namely Graphpad Prism for windows, version 5.01 dated Aug.7th 2007 was used for the analysis of the data and Microsoft word and Excel 2013 have been used to create text documents, graphs, tables etc.

Observation and Results

In present study 102 placentae were studied out of which 52 placentae were from toxemia group and 50 placentae from normal full term pregnancy formed control group. All mothers from cases and control group satisfied selection criteria. Gestational age of mothers were recorded from clinical record.

Table: I showing incidence of various placental parameters in control and cases (toxemia).

Table I shows shape of placenta and umbilical cord insertion among control and cases. Thirty three placentae were circular in control group whereas 20 placentae in toxemia group. 17 placentae were oval in shape of control group and 32 in Toxemia group. 35 placentae showed central cord insertion in both control and toxemia group, while 15 showed eccentric cord insertion in control group and 17 in toxemia group. No abnormality was found on fetal surface in control and toxemia group. No other pathological findings, like velamentous cord insertion, battledore cord insertion, single umbilical artery and knots in umbilical cord were seen in toxemia group. But retroplacental hematoma was seen in 10 placentae of toxemia group.

Parameters	Control group (n=50)	Toxemia (n=52)
Shape of placenta		
Circular	33 (66%)	20 (38.4%)
Oval	17 (34%)	32 (61.5%)
Fetal surface	Normal	Normal
Membranes	Normal	Normal
Umbilical cord insertion		
Central	35 (70%)	35 (67.3%)
Eccentric	15 (30%)	17 (32.6%)
Velamentous	Nil	Nil
Battledore	Nil	Nil
Single umbilical artery	Nil	Nil
Knots in umbilical cord	Nil	Nil
Maternal surface		
Retroplacental Hematoma	Nil	10

Table: II showing comparison of different parameters like fetal birth weight, placental weight, placental thickness, placental diameter and fetoplacental ratio between control and cases (toxemia).

Parameters (Mean±SD)	Control (n=50)	Toxemia (n=52)	Student ‘t’ test (p value)
Mean birth weight (gms)	2645±79.60	2099±71.51	<0.001
Placental weight (gms)	450.1±15.68	372.5±15.18	<0.05
Thickness (cms)	1.77±0.08	1.40±0.05	<0.05
Diameter (cms)	16.18±0.39	15.98±0.38	>0.05
Fetoplacental weight ratio	6.081 ± 0.2066	5.498 ± 0.1981	<0.05

$p<0.05$ = significant, $p<0.001$ = highly significant, SD= standard deviation.

Table II shows comparison of mean values of birth weight, placental weight, thickness, diameter, fetoplacental weight ratio between control and toxemia group. Fetal birth weight was highly significantly low ($p<0.001$) in toxemia as compared to control group. Also placental weight and placental thickness were significantly low ($p<0.05$) in toxemia as compared to control group. Whereas placental diameter was nonsignificant ($p>0.05$) in toxemia as compared to control group. Fetoplacental weight ratio was significantly low ($p<0.05$) in toxemia as compared to control group.

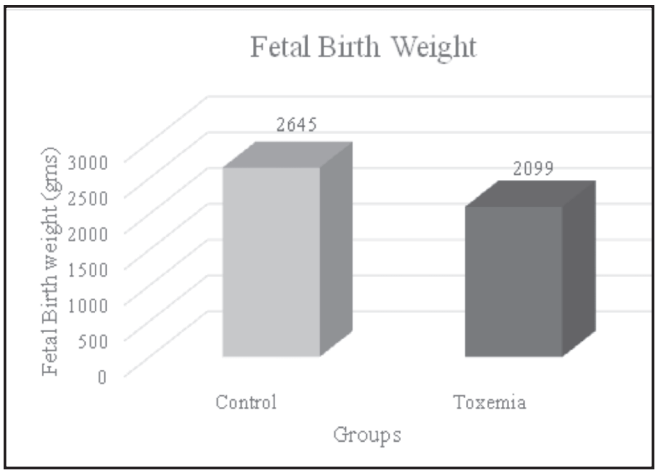
Table: III comparison of microscopic lesions like syncytial knots, fibrinoid necrosis, infarct and calcification between control and cases (toxemia).

Parameters	Control (n=50)	Toxemia (n=52)	Chi-square test (p value)
Syncytial knots			
⩽	44	33	<0.05
>30%	6	19	
Fibrinoid necrosis			
⩽3%	44	35	<0.05
> 3%	6	17	
Infarct			
Present	5	32	<0.001
Absent	45	20	
Calcification			
Present	16	30	<0.05
Absent	34	22	

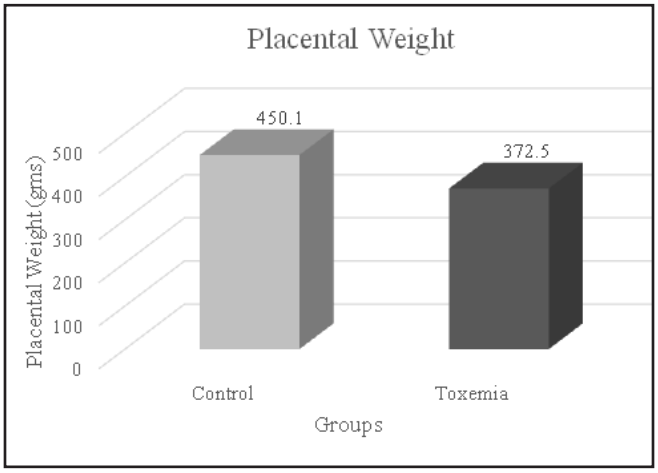
$p<0.05$ = significant, $p<0.001$ = highly significant.

Table III shows comparison of microscopic lesions between control and cases. In toxemia group syncytial knots, fibrinoid necrosis and calcification were significantly increased ($p<0.05$) as compared to control group. While presence of infarct was highly significant in toxemia when compared to control group.

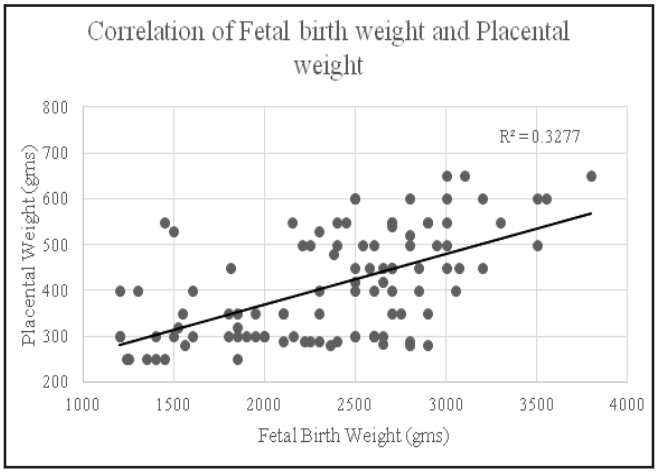
Graph: 1 showing comparison of mean birth weight between control and cases (toxemia).



Graph: 2 showing comparison of mean placental weight between control and cases (toxemia).



Graph: 3 showing correlation between fetal weight and placental weight of control and cases (toxemia).



Graph 3 shows positive correlation between fetal birth weight and placental weight of 102 subjects (Pearson r = 0.5725, p<0.001).

Discussion

Although the study of the placenta is retrospective in nature, yet it provides a reflection of hazards, the foetus has been subjected to during its growth and development.[4] With this background the present study was undertaken to analyse the spectrum of morphological changes in toxemia during pregnancy and to compare them with normal full term pregnancy.

Shape of placenta : In the present study, shape of the most placentae were oval 32 (61.5%) in toxemia group and most being circular 33 (66%) in control group (Table I). Our finding correlates with previous study of Sengupta K et al.[5] Navbir et al found discoidal shape of placenta in majority of toxemia group[6], whereas Shah found no clinical significance in oval or round shaped placentae. Oval shaped placentae were seen in toxaemia probably due to prematurity.[7]

In this study we found retroplacental hematoma in 10 placentae of toxemia group. Furthermore, no other pathological findings, like single umbilical artery, knots in umbilical cord found in toxemia group.

Mean birth weight: Mean Fetal birth weight (grams) in toxemia was significantly low (p <0.001) as compared to control group (Table II). The above findings are in coherent with Shirpurkar M et al (2015).[8] The low birth weight in toxemia group can be attributed to uteroplacental insufficiency and its duration.[9]

Weight of placenta: The placental weight is significantly low (p<0.05) in toxemia group as compared to control group (Table II). Similar results were found in the study done by Shirpurkar M et al (2015)[8]. Also similar results were depicted in the studies done by Dutta DC et al (1989)[10] and Nobis P et al (1991).[11]

The main reason for reduced placental weight in toxemia could be uteroplacental insufficiency. Toxemia adversely affects placental morphology. It has been recorded that maternal vasospasm in preeclampsia leads to decreased maternal uteroplacental blood flow. Hypoxia and reduction in blood flow could be responsible for morphological alterations of placenta in toxemia. Long standing hypoxia, which depending on duration time, primarily results with hypertrophy but as pregnancy advances, changes implicate the placental growth restriction and development of small, hypotrophic placenta.[12,13]

Thickness and Diameter: We found reduced thickness and diameter in toxemia group as compared to control group. There was no significant correlation when diameter was compared (p>0.05), while the difference was statistically significant (p<0.001) with thickness (Table II). Similar results were observed in the study of Das B et al (1996) they found reduction in both diameter and thickness hypertensive group but there was more reduction in thickness than in diameter.[14]

The mean external diameter of uterine spiral arterioles in toxemia is less than half of the diameter of these arterioles in normotensive women. This results in reduced uteroplacental blood flow due to which placenta becomes extremely ischemic as gestation continues. Placenta tries to compensate for reduced supply however these compensatory changes are insufficient and thus fails to develop adequate placental mass.[15]

Fetoplacental weight ratio: At term the fetoplacental weight ratio varies between 6:1 and 8:1 in normotensive pregnancies. In this study difference of fetoplacental ratio was statistically significant between control and toxemia groups (P<0.05) (Table II). Similar results were obtained by Das B et al (1996)[15] and Kher AV et al in 1981.[16]

Syncytial knots: Syncytial knots are normally present at term in 11% to 30% of the villi. Formation of knots on more than a third of the villi is considered excessive. We found syncytial knots (>30%) in 19 cases out of 52 cases of toxemia (Table III). The difference being statistically significant (p<0.05). Syncytial knots are also reported to occur as a result of hypo perfusion of villi secondary to obliterative lesion of fetal stem arteries.[17]

Fibrinoid necrosis: Placentae in which fibrinoid necrosis involving up to 3% of placental villi is considered as normal and placentae in which the percentage of villi showing fibrinoid necrosis of greater than 3% is considered as abnormal.[18] In the present study we found fibrinoid necrosis (>3%) in 17 cases out of 52 cases of toxemia (Table III). The difference was statistically significant (p<0.05) between control and

toxemia group.

Infarction: In the present study we found infarct in 32 cases out of 52 cases of toxemia (Table III). The difference was statistically significant ($p<0.001$) among control and toxemia group. The pathogenesis of placental infarcts is similar to that of infarction in other organs that is rapid loss of arterial blood supply. Most placental infarcts are due to thrombotic occlusion of the maternal arteries.[29]

Calcification: We found calcification in 30 cases out of 52 cases of toxemia (Table III). The difference was statistically significant ($p<0.05$) among control and toxemia group. Grossly identifiable calcification is seen in 14-37% of placentae at term.[20]

Das B et al (1996)[14] found higher incidence of syncytial knots, fibrinoid necrosis, infarct and calcification in hypertensive group which depicts similar finding of our study.

Summary and Conclusion:

The aim of present study was to test the hypothesis that underlying maternal medical disorders like toxemia adversely affect placenta during pregnancy.

We found decreased fetal birth weight, placental weight, thickness, diameter and fetoplacental ratio in toxemia group as compared to control group. Whereas increase in syncytial knots, fibrinoid necrosis, infarct and calcification in toxemia group compare to control group.

Our results confirm strong association of toxemia with low placental weight and low fetal birth weight. This data indicates that low placental weight is associated with placental dysfunction. Thus we can conclude that severity of toxemia has adverse effect of morphology of placenta and consequently affects the fetal weight.

Conflict of Interest: None

Funding source: None

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Case Report

Sequestrectomy Of Long Tubular Diaphyseal Sequestrum In Chronic Hematogenous Osteomyelitis Of Humerus In 4 Year Old Child - A Rare Case

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ABSTRACT

Introduction : Acute hematogenous osteomyelitis is usually seen in children, if not properly managed, results in chronic osteomyelitis and sometimes extensive sequestration. We are reporting a case 4 year child with chronic osteomyelitis of humerus with long tubular diaphyseal sequestrum treated by removal of entire tubular diaphyseal sequestrum.

Case Report

4 year old male child with previous history of trauma and massage to left arm was presented at with two chronic discharging sinuses at medial aspect of left elbow and arm. Further investigations like X-ray, CT scan, culture sensitivity, blood investigations were done. Patient was diagnosed to have with chronic osteomyelitis of left humerus shaft with long sequestrum. (Fig1) But sequestrum was not completely separated from involucrum. So he was treated with splinting and antibiotics for 1 month.

After 1 month, surgical removal of entire sequestrum was done by making a bony window on anteromedial aspect of lower end humerus (Fig 2). Bone and wound was irrigated with antibiotic solution and closed in layers over drain.

Wound healed with primary intension. Sinus tracks dried completely. After 6 months , he had 20 degree fixed flexion deformity of left elbow with further flexion possible upto 100 degree.(Fig 3) He resumed daily activities 2 months after surgery.

Fig 1- X-ray of humerus with long diaphyseal sequestrum a) AP view b) lateral view

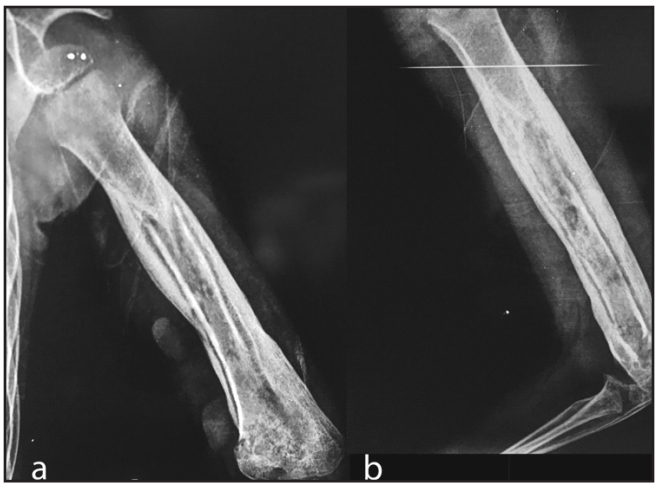

Fig 2- X-ray of humerus after sequestrectomy

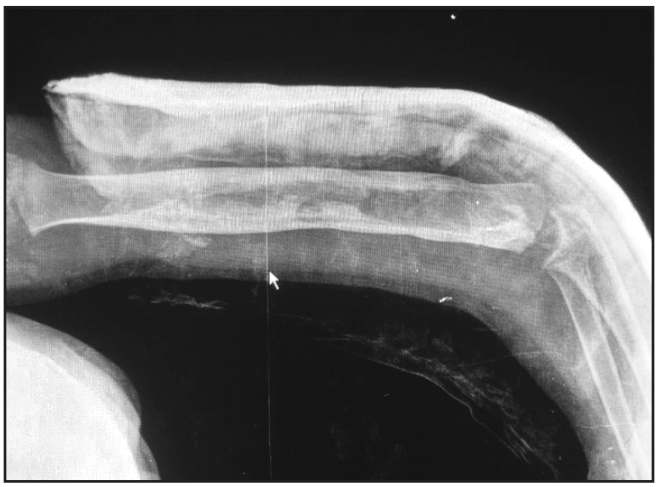

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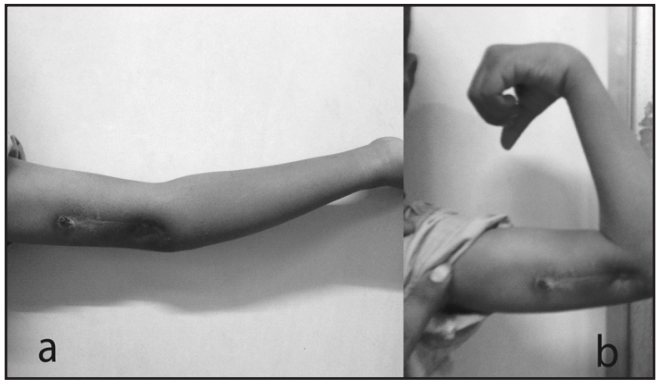
Fig 3- Elbow ROM and dry wounds after 6 months of surgery a) 20 ° FFD b) upto 100 ° elbow flexion possible



Discussion

Hematogenous osteomyelitis is more common in male child [1]. The physis acts as a barrier to the spread of a metaphyseal abscess in children older than 2 years. If the infection spreads into the diaphysis, extensive diaphyseal sequestration occurs due to damage to endosteal and periosteal blood supply. [1]

Management of chronic osteomyelitis with long diaphyseal sequestrum is very challenging. Laboratory tests like white blood cell count, erythrocyte sedimentation rate, C-reactive protein should be performed first.[1,2,3] CT scan is useful for extension of sequestra. MRI is more useful to detect soft tissue involvement.[1] Early sequestrectomy with incomplete involucrum formation obliterates the space between the periosteal tube and may damage the periosteum leading to mechanical instability and risk of pathological fracture.[4,5] Long diaphyseal sequestrum should be treated initially by antibiotics and prolonged protection of the limb.[2,5,6] Few cases of long diaphyseal sequestra treated no surgically were reported in literature.[4,5] If incorporation of sequestrum does not occur after series of follow-up xrays, sequestrectomy should be carried out after complete formation of involucrum.[5]

Conflict of Interest: None

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Case Report

Autologous Fat Injection Laryngoplasty

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ABSTRACT

Injection laryngoplasty is a surgical technique that can be used in vocal cord palsy causing glottic insufficiency. Lots of material are available for injection laryngoplasty technique of which autologous fat is a good material that can be easily harvested from the patient at the time of surgery which can be used without any allergic or tissue reaction and with less expenditure. It is a material which has comparably good longevity and maintains the visco-elasticity of the vocal fold, post procedure.

Our case, a 56 year old lady who had a unilateral vocal cord palsy following total thyroidectomy was evaluated and underwent autologous fat injection laryngoplasty. Post operatively she had adequate glottic closure and a good voice.

Key words - Injection laryngoplasty, unilateral vocal-cord palsy, autologous fat injection, glottic insufficiency

Introduction

Injection laryngoplasty is a surgical procedure used to treat glottic insufficiency. Glottic insufficiency is a condition whereby patients suffer from weak and breathy voice due to air escaping through incompletely opposed vocal cords. Thyroid surgery, malignancies, trauma and neurologic diseases are the main causes for recurrent laryngeal nerve paralysis leading to glottic insufficiency. However, the incomplete glottic closure can also result in aspiration and cough with the risk of developing pneumonia from aspiration.

Injection laryngoplasty is aimed at medializing the vocal cords to aid voice production by opposing the gap. This procedure allows for correction of glottic insufficiency, and is typically used to treat temporary or permanent mild-to-moderate glottic insufficiency (<1 to 3 mm glottal gaps). Since its first description in 1911 by Bruening[1],injection laryngoplasty has evolved in its approaches and materials. In literature, Mikaelianet. al were the first to report the use of autologous fat for intracordal injections in patients with a recurrent laryngeal nerve paralysis. Since then various animal, clinical, radiological and pathological studies have documented fat survival once transplanted within a paralyzed true vocal cord.

Case

A 56-year-old lady, clerk by occupation, presented to ENT out-patient department of our hospital with weak and husky voice after she underwent total thyroidectomy for follicular neoplasm of thyroid. She had neck swelling for 2 years which was evaluated and found to be follicular neoplasm of thyroid and underwent thyroidectomy in February 2015. Immediately following the surgery, she noticed a change in voice. She came to our out-patient department, underwent indirect and direct laryngoscopic evaluation and was found to have palsy of left vocal cord.

She was advised a course of voice therapy and was kept under follow up. As the voice did not improve by the therapy and she wanted to have a better voice which is essential for her profession, she was advised and worked up for injection laryngoplasty with autologous fat injection by microlaryngoscopic approach under general anesthesia. Pre-anesthesiacheck-up was done and fitness was obtained for the procedure and the patient was taken for surgery on July 2017.

Intubation was done with an endotracheal tube number 6. Abdominal incision measuring 2.5cm was made in the right iliac fossa and a small chunk of abdominal fat was obtained. This fat was minced into a slurry like consistency, cleaned and filtered and was kept loaded in the barrel of the Broening syringe.

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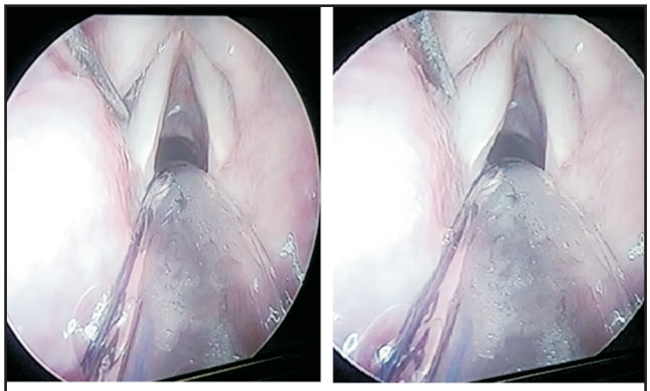
Figure 1:

Microlaryngoscopywas done, by keeping a pillow under the shoulder, withKleinsasser laryngoscope, which was applied and fixed to chest piece after adequate visualization of glottis. The fat loaded syringe was attached to Bruening's syringe holding system and an18 gauge, 25 cm long needle with malleable tip was attached. Under microlarygoscopic visualization fat was injected to the lateral aspect of left vocal cord in the middle and posterior third and middle third of vocal cord achieving sufficient medialisation. Smooth extubation was done without allowing coughing.

Figure 2:



Glottis with paralysed left vocal cord

Glottis with left vocal cord after fat injection showing medialisation

Post op care was given with antibiotic coverage, steroids, supportive care and voice rest. Post-operative video directed laryngoscopy was done and was found to have a favourable result with adequate glottic closure. The voice quality was good for her satisfaction. The patient was discharged with advice of oral antibiotic and relative voice rest of 2 weeks.

The patient was kept on regular follow up. Diagnostic laryngoscopy was done every quarterly and was found to have adequate glottic closure. The patient is having a satisfactorily good voice following the laryngoplasty procedure.

Discussion

Injection laryngoplasty[13] is indicated in glottic insufficiency caused by conditions that lead to vocal cord paresis or paralysis, vocal cord atrophy, vocal cord bowing and vocal cord scarring. These conditions include infection, laryngopharyngeal reflux, tumour, thyroid disease, voice abuse, alcohol abuse, Parkinson's disease, radiotherapy, as well as iatrogenic causes such as recurrent laryngeal nerve injury following surgery.

Injection laryngoplasty is considered advantageous in:

i) Patients with small glottic gap, from 1 – 3mm.[2,3,4]

ii) Patients with previous neck surgery or irradiated neck, as other surgical options likethyroplasty or nerve re-innervation are not feasible.

iii) Patients with a possibility of full functional recovery as an interim intervention.

iv) Patients who had previous laryngeal framework surgery requiring fine tuning of their voice function.

There are scenarios where patients would be better served by a different procedure. Patients with large glottic gap or involvement of arytenoids would achieve better results from thyroplasty or arytenoids adduction[5]. Patients with glottic insufficiency caused by an irreversible etiology would benefit more from a more permanent procedure such as thyroplasty. There are no absolute contraindications for this procedure.

The ideal injection material should be:

1. Biocompatible, inert and does not cause local tissue reaction or fibrosis
2. Easy to prepare and easy to use. The injection material should be readily available, easy to measure in quantity and easy to inject through a small needle
3. Low cost
4. Is durable, and resistant to resorption or migration
5. Maintains the visco-elasticity of the vocal cord post-injection

There is no perfect injection material that meets the all the criteria above. The materials used for injection are

classified based on their longevity to short lasting and long lasting ones.[15]Materials that are long lasting are autologous fat,autologous fascia,[16, 17,18] calcium hydroxylapatite (Radiesse™), polydimethylsiloxane (PDMS or particulate silicone), and polytef paste (Teflon™). Temporary short lasting materials include bovine gelatin (Gelfoam™, Surgifoam™), collagen-based products (Cymetra™, Zyplast™, Cosmoplast/Cosmoderm™), hyaluronic acid (Restylane™, Hyalaform™), and carboxymethylcellulose (Radiesse Voice Gel™).

Autologous fat injection has a longer lasting effect compared to other materials above. It has been shown to provide long term improvement of voice function comparable to thyroplasty[6]. Its effect has been shown to last 26 months and more[7, 8]. However, the actual duration is variable as the rate of resorption is unpredictable. Fat tissues are harvested in theatre, typically from subcutaneous tissues in the abdominal wall. Its autologous nature makes it biocompatible and safe for use.[9, 10]

It is also one of the materials that maintain the visco-elasticity of the vocal fold post injection.[11]The disadvantage of fat injection is the prolonged harvest time and variability in its results due to unpredictable fat survival. Complication rate is low although there have been reports of donor site haematoma, poor voice quality due to over-injection[12]andfat extrusion. In addition, patients will have to undergogeneral anaesthesia. Patients also tend to suffer prolonged post-operative dysphonia up to a few weeks, owing to the necessary over-injection.

There are 3 approaches to injection laryngoplasty - Transcutaneous, transoral and microlaryngoscopic injection.

1) Transcutaneous approach can be further divided into cricothyroid, thyrohyoid and trans-cartilaginous approach, depending on the site of injection.

2) Transoral injection can be performed in theatre or clinic setting. Flexiblenasoendoscope is used to visualize the vocal cord and paraglotticarea. A distinct 25cm long needle with 16-gauge malleable shaft and 25-gauge needle tip is used to inject the injection material. The needle is bent as appropriate to suit the contour of the pharynx and larynx and then introduced orally. Injection material is injected lateral to the vocal cord where it arises from the vocal process. This will oppose the middle and posterior gap between the vocal cords.

3) In microlaryngoscopic injection, patient is taken under general anesthesia. A 25cm long needle with 18-gauge malleable tip is passed through a rigid laryngoscope under microscopic visualization. Injection site is the same as for transoral approach.

Injection laryngoplasty generally carries fewer risks compared to laryngeal framework surgery. General risks such as bleeding, infection and pain are seen. The most significant but rare risk of the procedure is airway obstruction. Airway obstruction can occur secondary to laryngeal spasm, over-medialization of both vocal cords and laryngeal edema secondary to over-manipulation of the larynx. Adequate depth of anesthesia reduces the risks of laryngeal spasm. When bilateral injections are necessary, it should be done with caution, avoiding over-injection.

Patients are also at risk of a less than satisfactory outcome. This can be attributed to migration or increased rate of resorption of the injection material. Rarely, it could be due to accidental injection into the wrong site, thereby giving no effect to the patient's voice. In some instances, the materials can be wrongly injected into the vocal cords, causing edema and therefore hoarse voice, discomfort or even breathing difficulties.

Conclusion

Injection laryngoplasty is a useful procedure as a means of treatment for glottic insufficiency. Fat injection is a good autologous implant and may be considered as an option in management of patients with vocal fold scar, defect, or atrophy. Reabsorption of fat is a problem, but the procedure may be repeated.

Conflict of interest –None

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Case Report

Vancomycin-Induced Leukocytoclastic Vasculitis

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ABSTRACT

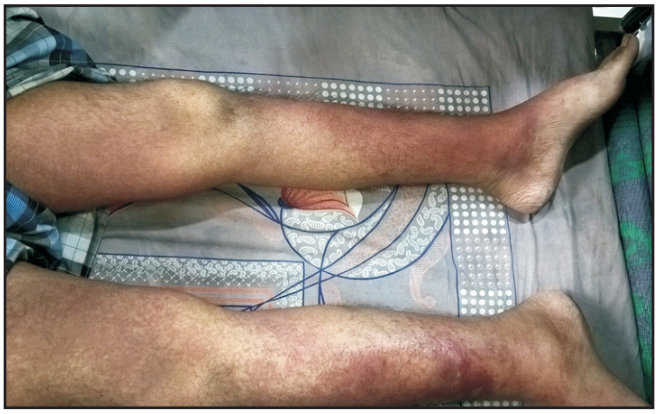
Vancomycin is well recognized for causing nonallergic skin reaction known as red man syndrome; however, it is rarely suspected as causative agent in the setting of an immune-mediated skin reaction. We describe a 30-year-old chronic alcoholic admitted with complaints of high grade fever,oligouria, altered sensorium, yellowish discoloration of eyes. He was treated for hepatic encephalopathy.With the management of hepatic encephalopathy, patient's sensorium improved but fever was persistent. Urine culture showed enterococcus, sensitive to vancomycin. On 2nd day of treatment with vancomycinof renal adjusted dose patient developed blanching purpuric rash with small blisters on lower extremities with pruritus which progressed to trunk, upper limb, and oral mucous membrane. Skin biopsy performed was suggestive of leukocytoclastic, necrotizing small-vessel vasculitis. Six days after discontinuation of vancomycin, skin lesion showed regression.

Key words: vancomycin, vasculitis, purpuric rash

Case

A 30-year-old male chronic alcoholic presented to hospital with chief complaint of yellowish discoloration of eyes since 20 days, decreased urine output since 10 days, high grade fever since 6 days and altered sensorium since 3 days. On examination he was conscious but disoriented, his pulse was 102/minute, regular and BP of 100/60mmHg. His respiratory rate was 16/minute. He had pallor, icterus, and pitting edema over feet. He developed ecchymotic patches & asterixis. On systemic examination he had ascites but no organomegaly. Air entry was decreased bilaterally at bases. Other systemic examination was unremarkable. On investigation Hb was 10.5gm/dl, WBC 20,000/mm3, Platelet count normal, Serum Urea 60mg/dl, Serum Creatinine 5.1mg/dl, ALP was 60 IU/L, SGOT- 74U/L, SGPT- 26U/L, T. Bilirubin7.4mg/dl, Direct 4.6mg/dl, Serum Sodium and Potassium were 136 mEq/L & 3.5 mEq/L respectively. Serum albumin was 1.8g/dl. All hepatotropic viral markers were negative. His urine routine and microscopy revealed albumin-trace, RBCs was 6-8/hpf; and WBC of 40-50/hpf. Ascitic fluid - no growth. USG abdomen - normal sized kidneys with raised renal cortical echogenicity and altered echo texture of liver. Diagnosis of chronic liver disease with ascites with hepatic encephalopathy with urosepsis and acute kidney injury was kept and treatment of hepatic encephalopathy was started along with antibiotics. In view of progressive rise in creatinine with decreased urine output hemodialysis was started on 2nd day of admission. Patient improved clinically from hepatic encephalopathy and serum creatinine was dropped downed to 3.2 mg/dl on 3th day of hemodialysis but fever was continuous. On urine culture enterococcus sp. was grown which was sensitive to vancomycin. Inj. Vancomycin 500 mg every 48 hr according to eGFR was started. After first dose of vancomycin patient developed blanching purpuric rash on bilaterally lower extremities with blister on right leg. Rash progressed over trunk and bilateral upper limbs which was palpable and non-blanching, sparing the palms and sole. (fig 1)

Figure1. Purpuric rash on bilateral lower extremities with blister on Right Leg



Peripheral blood smear was sent for absolute eosinophil count which was 100 cells/ul and urinary eosinophils

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were absent. Connective tissues work up like P-ANCA, C-ANCA etc. was not done as patient had developed lesion after he received vancomycin injection. The dermatologist was consulted and a skin biopsy was done. Biopsy revealed the pattern of a busy dermis with a superficial and mid perivascular inflammatory pattern containing neutrophils and lymphocytes, a population of predominantly neutrophils in a perivascular and interstitial pattern in addition to those undergoing extravasation from the vessels. Leukocytoclasis (neutrophil degeneration) forming nuclear dust, extravasated numerous erythrocytes which is characteristic of leukocytoclastic vasculitis (fig 2). Vancomycin was stopped and the other medications were continued. Patient improved gradually over period of 7 days, with normalization of liver and kidney functions. Repeat urine examination revealed no pus cells and no growth on culture after 7days of treatment. Rash completely disappeared on 14th day

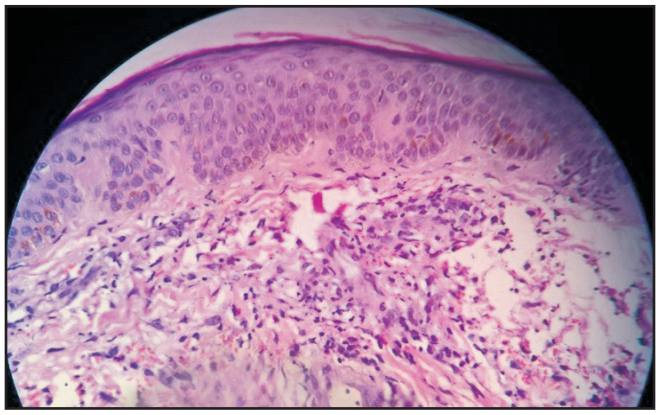

Figure 2. Busy dermis with a superficial, mid perivascular inflammatory pattern with neutrophils and lymphocyte (small arrow). There is a population of predominantly neutrophils in a perivascular and interstitial pattern (arrow head) in addition to those undergoing extravasation from the vessels. Leukocytoclasis (neutrophil degeneration) forming nuclear dust (Broad black arrow). Extravasated numerous erythrocytes (white arrow) characteristic of leukocytoclastic vasculitis.

Discussion

Leukocytoclastic vasculitis (LV) is a small vessel inflammatory disease. Predominantly involves the lower extremities, limited to skin but usually spares palms and soles. Palpable purpura is the most common skin manifestation. It can also manifest as maculopapular rash, bullae, papules, nodules, ulcers, and livedo reticularis. High index of suspicion with clinical picture and skin biopsy for histopathological correlation gives the diagnosis. Basic principle of histopathological diagnosis for cutaneous vasculitis is the morphological evidence of both angiocentric infiltration of inflammatory cells and damage of vessel wall. Other minor features, including erythrocyte extravasation and nuclear dust, are not crucial but supportive findings for the diagnosis of small vessel vasculitis [(1)]. Deposition of immune complexes into vessel walls and activating the complement pathway is thought to be the cause of LV. LV can be caused by drugs, infection, connective tissue disease, and malignancy. Drugs may act as haptens and activate the immune response. Drugs most frequently associated with vasculitis were propylthiouracil, hydralazine, colony-stimulating factors, allopurinol, cefaclor, minocycline, D-penicillamine, phenytoin, isotretinoin, and methotrexate [(1)]. Antibiotics are the most common drugs reported to cause cutaneous vasculitis, mainly β-lactams [(2)]. Vancomycin is known for its different types of hypersensitivity reactions, including red man syndrome, immune-mediated skin reactions like vancomycin-related linear IgA bullous dermatosis, and IgE-mediated anaphylaxis [(3–5)]. Till date very few cases of vancomycin-related leukocytoclastic vasculitis have been reported[(3–6)]. Even after single dose of vancomycin, small vessel vasculitis has been reported [(6)]. The onset of vasculitis can vary from days to months after administration [(4, 5)]. The time to recovery also varies between days to weeks. Preferred treatment is withdrawal of the suspected drug [(5)]. Role of steroids in treatment of LV is not proven. Steroids do not change the course of disease but relapse can occur after discontinuation of steroids in such cases. Colchicine and dapsonemay be used because of their immunomodulatory and anti-inflammatory properties in patient with limited skin involvement [(6)].

In our patient there was no history and clinical features of connective tissue diseases, his viral markers were negative for chronic viral infection of HBV and HCV. With this clinical scenario and temporal correlation with drug administration and development of the vasculitis, we have considered the diagnosis of vancomycin-associated LV. Patient on treatment with vancomycin if developes palpable purpura, vancomycin has to be

considered as a potential cause of leukocytoclastic vasculitis. Discontinuation of the offending medication and supportive treatment with steroid is the most effective approach.

Conflict of Interest: None

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Case Report

Uterus Didelphys With Double Vagina With Successful Pregnancy Outcome

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ABSTRACT

Uterus didelphys results when there is complete failure of midline fusion of two mullerian ducts. The cause of fusion failure is unknown. In these conditions, there is duplication of uterus, cervix and sometimes vaginal canal. It occurs one in 3000 cases. Due to higher risk of obstetric complications and increased perinatal morbidity, these patients need special antenatal care. This case report describes one case of successful pregnancy outcome in uterus didelphys bicollis with double vagina, which was misdiagnosed as bicornuate uterus during antenatal period. A 20 years old primigravida with postdated pregnancy was admitted with labour pain. Pelvic ultrasound showed a bicornuate uterus with pregnancy in right horn with foetal growth restriction and oligohydraminos. Patient had a thick inelastic longitudinal vaginal septum; however patient was unaware until that day. Due to foetal distress emergency caesarean section was performed and female baby of 2170gms was delivered.

Key words - uterus didelphys, vaginal septum, bicornuate, postdated.

Introduction

Congenital anomaly of mullerian duct is relatively common and incidence varies from 3-4%[1.] Mullerian duct anomaly can originate due to either failure of mullerian duct to fuse in midline, failure of development, canalization or resorption. Uterus didelphys is an anomaly which results in two uteri, two cervices and some women may have two vaginal canals. Patients are usually asymptomatic but may present with dysmenorrhoea, dyspareunia in presence of varying degree of longitudinal vaginal septum. Pregnancy with uterus didelphys is associated with increased risk of spontaneous abortion, malpresentation, premature labour and foetal growth restriction. Due to very low incidence of anomaly in the population and an individual clinician's experience with these abnormalities is limited hence it is worthwhile to report individual cases. Thus, it will be useful for planning clinical management and care of these patients and it will be useful in the review of didelphys uterine anomaly.

Here, we discuss an undiagnosed case of uterus didelphys with double vagina in a woman who successfully conceived, carried her pregnancy to term. During labour complete longitudinal vaginal septum was detected and she was delivered by caesarean section, during which didelphys uteri was diagnosed.

Case

This patient is a 20 year old primigravida from Pune, Maharashtra, who was referred to us on 21/12/2016 with ultrasound report of bicornuate uterus with pregnancy in right horn with foetal growth restriction and oligohydraminos. Patient went in labour at the gestation of 40 6/7 weeks .

At gestational age of 22 6/7 weeks ultrasound scan showed uterus bicornis bicollis with pregnancy in right horn and showed no renal anomaly. Patient had uneventful antenatal period. On abdominal examination uterine fundal height was corresponding to 32 week gestation. Baby was in cephalic presentation and patient had uterine contractions.

Longitudinal, thick, inelastic vaginal septum was found on per speculum examination (Figure-1). However patient and her husband were not aware of such vaginal septum until that day. Patient did not report any dyspareunia and dysmenorrhoea.

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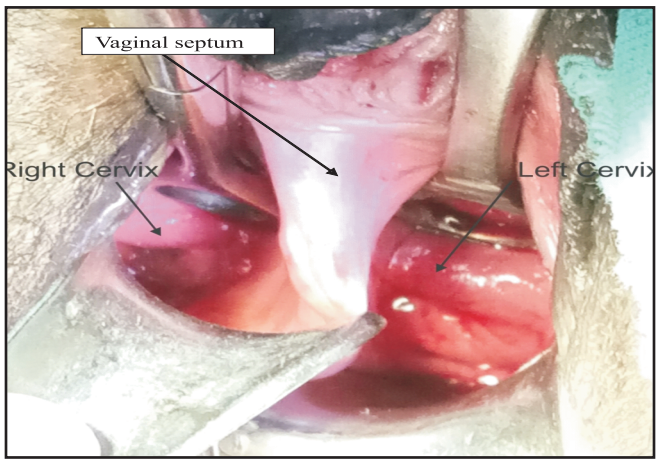
Figure 1: Longitudinal Vaginal septum with two cervices.



There was a separate cervix on each side of vaginal septum. Per vaginal examination confirmed presence of two cervices. Right cervix was 1.5 cm dilated minimally effaced and left cervix was closed. Ultrasound report showed bicornuate uterus, foetus of 35 weeks gestation in cephalic presentation and AFI of 4.2 cm with growth lag between abdominal circumference and biparietal diameter of foetus suggesting foetal growth restriction. Cardiotocography monitoring indicated foetal distress and hence patient was posted for emergency caesarean section immediately.

On opening the abdomen, uterus didelphys with pregnancy in right uterus was noted. Left uterus was nongravid. Female baby of 2170 gms was delivered. Both uteri were explored and they were found to be completely separate. One fallopian tube and ovary was attached to each uterus separately. An intervening thick antero-posterior fibrous band in between both uteri was seen and palpated (Figure-2). Right uterine incision was sutured (Figure-3).

Figure 2: Uterus didelphys with two separate uteri

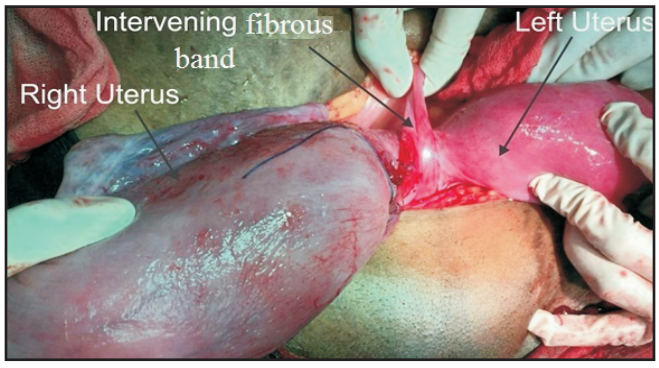
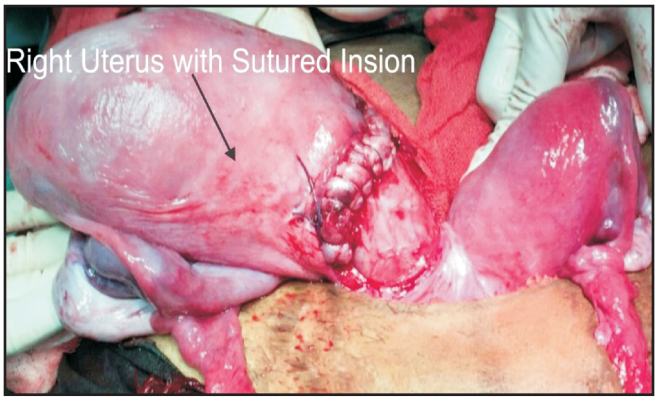


Figure 3: Two separate uteri with sutured incision on right uterus



Patient had uneventful post-operative period, both mother and baby were discharged on 28/12/2016. Vaginal septum was left alone as she had no coital difficulty. The couple was counseled about nature of anomaly and they were reassured about no need of special intervention for future fertility. With respect to future pregnancies, couple was counseled about associated obstetric risks and necessity of antenatal care at appropriate centre.

Discussion

A didelphys uterus belongs to American Fertility Society class III and account for 8% among all mullerian duct anomalies[1]. Most women with didelphys uteri are asymptomatic however depending on presence of varying degree of longitudinal vaginal septum some cases may present with dyspareunia or dysmenorrhoea. These anomalies are often discovered during pregnancies or at the time of delivery and abortion or during infertility evaluation. Many cases of didelphys uteri remain undiagnosed and some cases may be misdiagnosed as uterus bicornis bicollis. Similarly, present case was misdiagnosed as bicornuate uterus on ultrasound but at the time of labour longitudinal vaginal septum was diagnosed. Sometimes such anomalies are discovered during caesarean section. In the present case, uterus didelphys was diagnosed during caesarean section, when 2 separate uteri with thick intervening fibrous band in between them.

Grimbizis[1] et al (2001) in a review of 152 pregnancies by 114 patients with untreated didelphys uteri revealed a mean abortion rate of 32.9% , a mean preterm delivery rate of 28.9%, a mean term delivery rate of 36.2% and

live birth rate of 56.6%. Similarly poor reproductive performance in women with didelphys uteri is demonstrated in a large retrospective longitudinal study of 3181 patients by Raga etal[2] (1997). There are some case reports of undiagnosed uterus didelphys in a term pregnancy with adverse foetal outcome[3,4,].

Heinonen[5] (2000) studied 49 cases of didelphys Uteri and evaluated reproductive outcome. He observed the foetal survival rate of 75%, prematurity in 24%, foetal growth restriction in 11% cases and perinatal mortality of 5.3%. Hence special prenatal care should be given to the women with this type of uterine anomaly for its associated risks. There are successful pregnancy reports available including pregnancies in each uterus of didelphys uteri as well. Most of the single pregnancies in didelphys uteri are observed in right uterus as reported in literature and in the present case also pregnancy was noted in right uterus.

In the present case report, emergency caesarean was done for foetal distress. Vaginal delivery should be considered in these patients as some vaginal septa get easily displaced by head while thick and inelastic septa might require excision to prevent laceration of septa and hence bleeding. But due to high chances of abnormal presentations and cervical dystocia, caesarean section is preferred by many obstetricians. Caesarean section rate of 82-84% is reported in earlier studies.

Conclusion

Uterine anomalies should be detected early during pregnancy for appropriate clinical management of these cases. Patients with didelphys uteri need special antenatal care and birth planning, anticipating obstetric complications and perinatal morbidity associated with it.

Conflict of Interest - None

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Case Report

Jejunal Perforation As The First Presentation Of Non-Hodgkin's Lymphoma In A Seropositive Patient

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ABSTRACT

A 44-year-old man presented with sudden-onset abdominal pain, vomiting and constipation since two days. He had features of shock and peritonism. Radiological investigations showed gas under diaphragm. Hence, he was posted for exploratory laparotomy. Preoperative blood tests revealed patient to be positive for HIV-1 antibodies.

Upon exploration, a 2x2 cm sized perforation was found 10 cm from the DJ flexure, just proximal to intraluminal mass involving the jejunum. Resection of the bowel segment containing the mass and the perforated bowel was done. Bowel continuity was established by jejuno-jejunal anastomosis. Histological examination showed diffuse large B-cell lymphoma. The patient had an uneventful recovery and was subsequently started on a course of R-CHOP regimen. While gastrointestinal perforation secondary to Anti-lymphoma treatment is a well-recognized complication, primary perforation is rare. Hence the case report.

Key words: Non-Hodgkin's lymphoma; Small bowel perforation; Peritonitis; Gastrointestinal tract; Seropositive Patient

Introduction

Diffuse large B-cell lymphoma (DLBCL) can present as either primary lymph nodal disease or with involvement of extra-nodal sites. Gastrointestinal involvement of DLBCL is often insidious presenting as abdominal pain, nausea, vomiting, anemia, weight loss, fever, and occasionally small bowel obstruction or a palpable mass. Although small-bowel rather than large bowel perforation corresponding to diffuse large B-cell non-Hodgkin's lymphoma has been reported in literature, jejunal perforation due to diffuse large B-cell non-Hodgkin's lymphoma in a seropositive patient is extremely rare.

Case

A 44-year-old man, of Indian origin presented with 2 days' history of severe, sudden-onset abdominal pain, vomiting and constipation. Past medical and surgical history was not significant. His height was 170cm and weight was 65kg. On examination, his temperature was 38.8°C, heart rate was 117 bpm, respiratory rate was 22 breaths/minute, blood pressure was 111/73 mm Hg and oxygen saturation was 97% on room air. On per abdominal examination, there was guarding, tenderness to palpation. There was absent stools on per rectal examination.

Laboratory investigations demonstrated WBC count 5.1×10^{9}/L; hemoglobin 13.7 g/dL and platelet count $282x10^{3}$/µl. Chest X-Ray showed gas under diaphragm (Figure 1). Ultrasonography scan showed hollow viscous perforation. HIV testing as part of routine preoperative investigations diagnosed the patient to be positive for HIV-1 Antibodies. He was enrolled for antiretroviral therapy.

Patient was taken to the operating room after adequate fluid resuscitation, grouping and cross matching. An emergency laparotomy was performed under general anesthesia via midline incision following universal precautions of operating a seropositive patient. An intraluminal mass was noted 10 cm distal to the ligament of Treitz involving the proximal jejunum. There was a 2x2 cm jejunal perforation on the mesenteric side, just proximal to the mass (Figure 2). Resection of the bowel segment containing the mass and the perforated bowel was done. Bowel continuity was established by jejuno-jejunal anastomosis done in four layers using 3-0 silk. Abdominal closure was done in layers. Resected specimen was sent for histopathology and was reported as intermediate grade Non Hodgkin Lymphoma (Figure 3a & 3b).

Subsequent IHC typing showed diffuse large B cell lymphoma positive for LCA, CD20, Bcl-2 Protein and negative for CD3 and CD10 with MiB-1 labeling index of 80%.

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During the course of stay in the hospital patient was tested for CD_4 count and was found to be immune-compromised with most recent CD_4 count being 24 cells per cubic millimeter of blood. His sputum was sent for AFB in view of cough and co-existent seropositive disease, which came out negative for AFB. He was started on R-CHOP(Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone) regimen for Non-Hodgkin's lymphoma and was discharged in a vitally stable condition.

Fig.1 Erect Chest XRay Showing small amount of Free Gas Under Right Hemidiaphragm (Indicated by Red arrow)

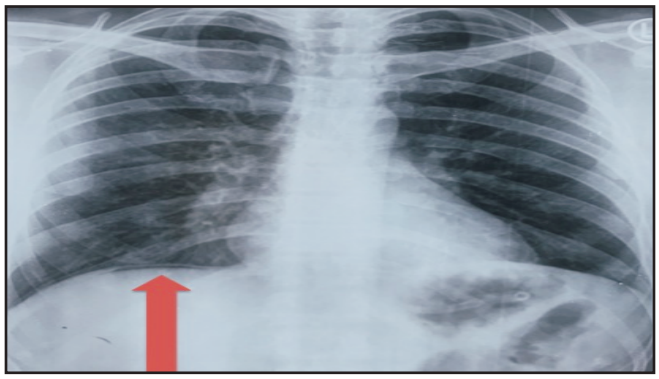


Fig.2 Resected jejunal Specimen Showing perforation with Intraluminal mass on Mesenteric Side

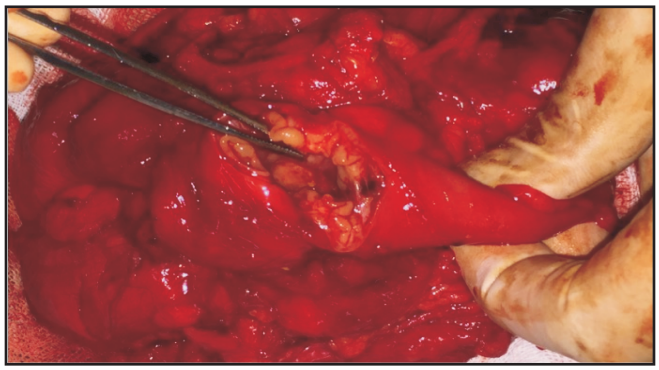


Fig. 3a : Dense Lymphocytic Infiltration seen extending upto muscular layer, of atypical lymphocytes

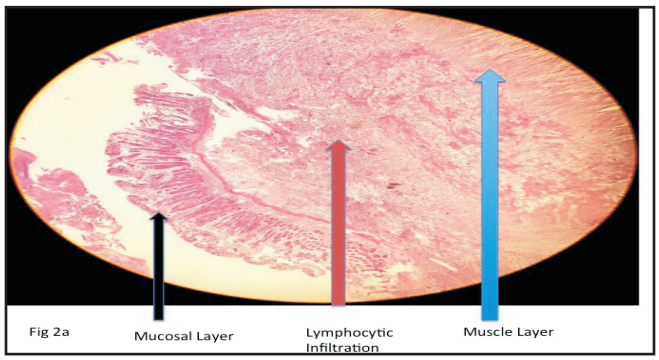
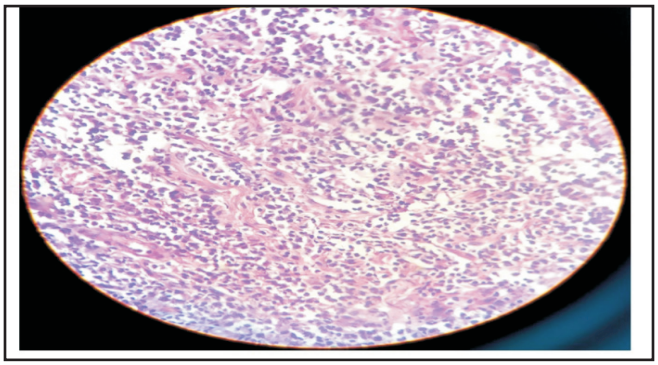


Fig. 3b : High Resolution photomicrograph showing dense lymphocytic inflitration with typical and atypical lymphocytes



Discussion

Lymphoma is a group of blood cell tumors that develop from lymphocytes; the name often refers to cancerous ones.[1] Non-Hodgkin's lymphoma (NHL) is a condition that frequently occurs in lymph nodes of the chest, abdomen, neck, tonsils and skin. Rarely, it can also invade the GI tract and the central nervous system. Approximately 5% of peripheral NHL's are primarily located in the intestine,[2] and comprise 5 to 10% of all GI tumors. The lymphoma most frequently associated with perforation was of the diffuse large B-cell variety.[3]

High grade B cell NHL is the second most common malignancy affecting HIV infected individuals. Diffuse large B cell lymphoma (DLBCL), which includes all immunoblastic lymphomas, is the most frequent histological type occurring in HIV infected individuals and accounts for 80% of the cases.[4] There is a clear correlation between declining CD_4 cell count and risk of developing NHL.[5]

Bowel perforation as a consequence of anti-lymphoma chemotherapy treatment is well documented. Perforation as a primary presenting feature of DLBCL in a seropositive patient, that too pre chemotherapy is a rare entity altogether. Also, it presented as a small bowel lesion, instead of large bowel as the perforated intestine is difficult to come by. This case illustrates a rare complication of large B-cell non-Hodgkin's lymphoma of the jejunum that was responsible for small-bowel perforation and resultant peritonitis. This clinical pattern may appear as a leading presentation of small intestinal neoplastic disease in which surgical resection needs to be considered.

Diffuse Large B Cell Lymphoma (DLBCL) is a set of

heterogeneous aggressive lymphoma, which occur in germinal center or extra-germinal sites in adults. For the diagnosis of DLBCL, intestinal microscopy and immunohistochemistry pattern plays a crucial role. Complete surgical excision in combination with chemotherapy might be the main modality of treatment of diffuse large B cell lymphoma[6]. Long-term follow up with serial imaging techniques may be recommended for possible aggressive behaviour and recurrence. Doctors firstly should pay attention to the clues of the symptoms, signs and related inspection, look for a more reasonable explanation.

Conflicts of Interest - None

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Case Report

A Rare Case Of Breast Metastasis From Carcinoma Rectum

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ABSTRACT

Carcinoma of rectum is disease of older age group and is rarely seen in the young population. Very few cases of carcinoma rectum in pregnant women have been reported in literature. A 28-year- old female patient with 7 months pregnancy presented with per rectal bleeding. Rectal biopsy was suggestive of adenocarcinoma. She underwent abdominoperineal resection 15 days after delivery and was given postoperative chemoradiotherapy. Six months later, she presented with lump in right breast and palpable axillary node. FNAC from axillary node was positive for malignant cells. Hence, modified radical mastectomy was done. Immunohistochemistry was suggestive of metastatic carcinoma of the breast. As carcinoma rectum in pregnancy is very rare and also its metastasis to breast is extremely rare, we are presenting this case.

Key words - Carcinoma Of Rectum, (CG Retum), Abdomino-Perineal Resection, Metastatic Carcinoma Of Breast, Modified Radical Mastectomy

Introduction

Primary tumors which metastatise to breast are melanoma, sarcomas, prostate cancer (most frequent primary cancer in men), lung cancer, gastric cancer, ovarian cancer and renal cell cancer[1,2]. Clinically primary breast cancer and metastatic lesion to breast both present as lump in breast. Differentiation can only be done on histopathological evaluation and by immunohistochemistry.

Case

A 28- year-old female patient with 28 weeks gestational age presented with bleeding per rectum since one week. On per rectal examination, growth was palpable. Colonoscopy demonstrated a proliferative growth at 5-6 cm from anal verge. Scope could not be negotiated beyond the growth. Tumor biopsy was taken and sent for histopathology. Histopathology report was suggestive of well differentiated adenocarcinoma of the rectum. As patient was 28 weeks pregnant, surgery for ca rectum was planned after delivery, in consultation with gynecologist and patient herself. She was admitted for further evaluation of ca rectum 15 days after delivery. Ultrasonography showed hepatomegaly with evidence of irregular wall thickening at rectosigmoid region with few enlarged parailiac nodes. CT - scan of abdomen and pelvis showed short segment asymmetric polypoidal wall thickening 6cm in length involving the distal rectum. Wall thickness was 3cm and was causing narrowing of the rectal lumen. Liver was enlarged. However, there were no liver metastasis. Lung and rest of the solid organs were normal. Patient underwent Abdomino- perineal resection with end colostomy. Histopathology report confirmed well differentiated adenocarcinoma –lower 1/3rd of rectum with infiltration of muscularis propria and perirectal tissue(pT3) with metastasis to two out of three lymph nodes i.e. TNM stage III (T3N1M0), Duke's stage C[11]. Proximal surgical margin was free of tumor. Patient was given 6 cycles of chemotherapy with Leucovorine (30 mg) and 5-FU (650 mg) over 5 days at 4 weekly intervals with 6 cycles with adjuvant radiotherapy. She was advised to stop breastfeeding in view of ongoing chemotherapy. She completed 6 cycles of chemoradiotherapy and was on regular follow up.

After 6 months following completion of chemoradiotherapy, she presented with a lump in right breast. The lump was painful since 1 week. There was no discharge or bleeding through nipple. On clinical examination, there was a hard, mobile, tender lump about 6x5 cm size in right upper and outer quadrant of the right breast. There was no evidence of retraction or ulceration of nipple. A 2x2 cm sized hard, mobile, non-tender node was palpable along the anterior axillary line.

As patient had not breast fed, clinical diagnosis of galactocoele was considered. But Local ultrasonography was suggestive of large ill-defined

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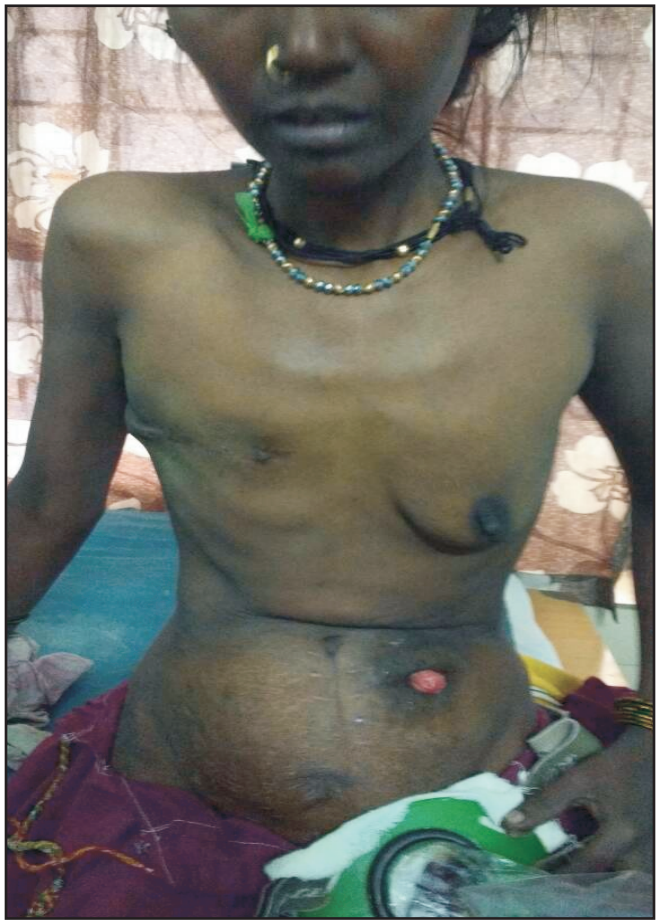
mixed heterogeneous lesion of size 6x5 cm with no vascularity. Though FNAC of right breast lump was inadequate, FNAC of the axillary node was positive for malignancy.

Hence, she underwent modified radical mastectomy (Fig1). Histopathology showed breast with infiltrative tumor composed of round to oval cells having pleomorphic vesicular nuclei with focally prominent nucleoli and eosinophilic cytoplasm arranged in sheets, clusters, glandular and tubular pattern. Well to moderately differentiated adenocarcinoma suggestive of metastasis to breast and axillary lymph node (2 out of 4) in known case of carcinoma of rectum. Resection margin was free of tumor.

This tumor was negative for hormonal receptors estrogen and progesterone. Immunohistochemistry examination showed tumor to be positive for CK20 and CDX2 and negative for CK7, thus confirming it's origin from the rectum rather than a primary breast cancer.

Fig 1: Post-operative photograph of the patient showing well healed scar of MRM. Also note the end colostomy.



Discussion

Incidence of cancer in pregnancy ranges from 0.07%to 0.1%. Most common cancers reported during pregnancy are lymphoma, leukemia, melanoma, carcinoma of breast, cervix, ovarian, thyroid and colorectal cancer.

Carcinoma of rectum is very rare in pregnancy. Its incidence is about 0.002% all over world [3]. Very few cases have been reported in literature[4]. Carcinoma of rectum most commonly metastatise through blood born route to liver 33%, lung 22% and adrenals 11%.

In this case, clinically it was hard to differentiate primary breast cancer, infected galactocoele or metastasis from rectum. Histopathology report showed adenocarcinoma but immunohistochemistry was required to confirm the diagnosis of metastasis to the breast from carcinoma rectum.

For carcinoma of breast, immunohistochemistry includes estrogen receptor, progesterone receptor, HER 2/new. Cytokeratin study is shows CK5/6 positive for basal cells of breast ductal epithelium while CK7 for luminal cells[5]. Most commonly in normal practice estrogen, progesterone receptor study is done to determine plan for chemotherapy regime and also for prognosis of disease. These are prognostic biomarkers for ca breast. Oncogenic markers for ca breast include human epidermal growth factor 2(HER 2/new)[5]. Cytokeratin markers are helpful to confirm the origin of primary colorectal carcinoma in their metastasis. Most colorectal carcinomas show typical CK7 negative and CK 20 positive pattern. CDX2 is nuclear transcription factor for intestinal development and is expressed in intestinal epithelium and adenocarcinomas[6].

In our case, the tumor marker is CK 20 positive, CDX2 positive, CK 7 negative, ERPR(estrogen receptor progesteron receptor) negative, which confirmed that the breast metastasis was from colorectal carcinoma.

Report of colorectal carcinoma metastatising in the breast without involving other organs in young pregnant female is extremely rare. It is difficult to differentiate primary breast cancer from metastatic rectal carcinoma involving the breast without involving other organs. Immunohistochemistry is very essential to confirm the diagnosis. Further research is required to find out why rectal cancer in this case metastatised to breast without

involving other organs.

Conflict of Interest: None

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Case Report

An Extremely Rare Case Of Aneurysmal Bone Cyst Of Skull Base

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ABSTRACT

Aneurysmal bone cysts (ABC) are benign expansile tumour-like bone lesions of uncertain aetiology, composed of numerous blood filled channels. They usually are muticystic or multi septated with fluid-fluid levels within them. ABCs are extremely rare in the head and neck region and even rarer in sinuses as presented in our case. In this article, we present a 20 year old male patient with a large nasopharyngeal mass lesion. The patient after thorough imaging was diagnosed with this condition on histopathology. Owing to the widespread extension and aggressive nature of the lesion, it was deemed as inoperable with the patient being treated on conservative management.

Key words: aneurysmal bone cyst, orbit, CT MRI, fluid-fluid levels, blood.

Case Report

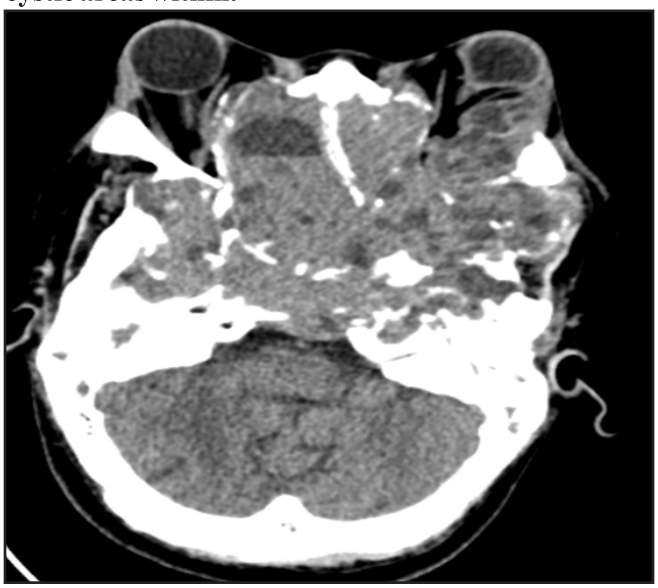
The patient was a 20-year-old male who presented to our clinic with symptoms of chronic headache since 3 years and now had developed symptoms of nasal blockade and proptosis in the last 4 months. No H/o any fever, trauma or bleeding diathesis were elicited from the patient. He had no previous medical or surgical history.

Nasal examination revealed a firm nasal mass with bloody discharge on touch. Ophthalmological examination revealed bilateral proptosis with perception of light on right side and complete vision loss on left.

Plain radiographical films of the skull revealed an ill-defined expansile lytic bony lesion involving bilateral maxillary sinuses and base of skull with narrow zone of transition.

A plain Computed Tomography (CT) scan of facial skeleton was done subsequently for better appreciation of the bone involvement. CT revealed a large lytic expansile bony lesion in the basi-sphenoid region with the mass lesion having a narrow zone of transition. Extensive soft tissue component with multiple hypo dense cystic areas and few hyper dense foci of calcifications were also noted within this lesion.

Non contrast axial CT image of skull showing lytic expansile bony lesion in the basi-sphenoid region with soft tissue component and multiple hypo dense cystic areas within.



Magnetic Resonance Imaging (MRI) revealed a large heterogeneously enhancing extra axial mass lesion in base of skull measuring approximately 9 x 11 x 8 cm. It appeared iso to hypo intense on T1W images and iso to hyper intense on T2W and FLAIR images. Multiple areas of cystic and haemorrhagic changes were noted within the lesion. Superiorly it was seen abutting the right basifrontal region with compression of left temporal lobe and displacement of left hippocampus medially. Inferiorly, it showed extension into the nasal cavities, nasal septum and bilateral maxillary sinuses. Anterior extension was seen into the frontal and ethmoidal air cells, encasing left orbit and partially encasing right orbit and displacing left optic nerve laterally with splaying of optic chiasma. Posteriorly, the sella and sphenoid sinus were involved; however pituitary gland was seen separately from the lesion.

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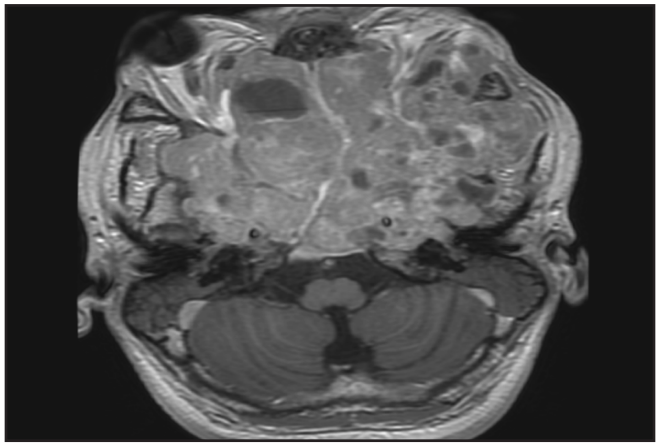
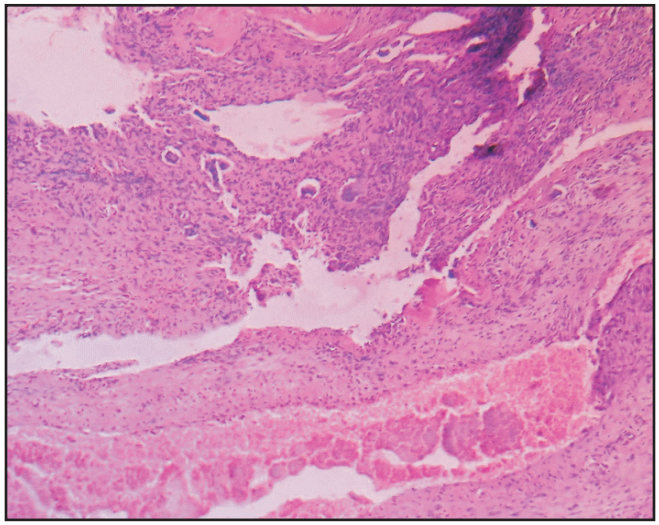
Contrast enhanced T1W axial MRI image of skull showing heterogeneously enhancing extra axial mass lesion in base of skull with multiple areas of cystic and haemorrhagic changes within.



The patient had presented with such extensive involvement that the lesion was termed inoperable by the surgery and maxillofacial consultants. Subsequently, the patient was posted for a trans-sphenoidal endoscopic biopsy. The histopathological examination showed numerous variably sized blood filled cystic spaces separated by fibrous septae containing spindle shaped fibroblasts and scattered multinucleated giant cells. The final diagnosis was given as an aneurysmal bone cyst.

Histopathological micrograph of biopsy specimen showing multiple blood filled cystic spaces separated by fibrous septae containing spindle shaped fibroblasts and scattered multinucleated giant cells.



Patient was discharged and is being followed up for palliative treatment.

Discussion

Aneurysmal bone cysts (ABC) are benign expansile tumour-like bone lesions of uncertain aetiology, mostly composed of numerous blood filled sinusoidal spaces which expand from the affected bone. The most common location of ABCs are the metaphysis of long bones, followed by flat bones. Only 2% of ABCs are found in the head and neck region; among these maxilla and mandible are the most common sites. Involvement of ethmoid sinus is extremely rare [1–4]. It is usually found in individuals less than 20 years old. There is no predilection for gender [5]. Aneurysmal bone cyst has been widely regarded a reactive process of uncertain aetiology since its initial description by Jaffe and Lichtenstein in 1942. Based on recent studies, WHO has redefined Aneurysmal bone cysts as “benign cystic lesions of bone composed of blood filled spaces separated by connective tissue septa containing fibroblasts, osteoclast type giant cells, and reactive woven bone [6,7].These are usually found within bones with high venous pressure and marrow content. 65% are primary or simple, and 35% are secondary in nature as per Bonakdarpour et al [8]. ABCs can be primary or secondary to another skeletal lesion. Secondary ABCs may be related to fibrous dysplasia, giant cell tumours, chondromyxoid fibroma, chondroblastoma, non-ossifying fibroma, fibrous histiocytoma, osteoblastoma, and osteosarcoma [9]. Symptoms are caused due to compression of adjacent structures or as a result of pathological fracture, rather than by the lesion itself. [10]

The radiological imaging show an eccentric lytic lesion with an expanded remodeled "blown-out" or "ballooned" bony contour of the affected bone, with a delicate trabeculated appearance, and fluid-filled spaces on CT scans and MRI [11].

The differential diagnosis for a case of ABC in the head and neck region includes giant cell tumour, giant cell reparative granuloma, hemorrhagic cyst, telangiectatic osteosarcoma, metastasis, fibrous dysplasia plasmocytoma and clivus chordoma [4,12,13].

Histopatholgically, giant cell tumour, fibrous dysplasia, ossifying haematoma and cavernous haemangioma present similarly due to the presence of multi nucleated giant cells in all of them [4].

A recent genetic basis for ABC has been demonstrated

by clonal chromosome band 17p13 translocations that place the USP6 oncogene under the regulatory influence of highly active CDH11 promoter [14].

Although the treatment of choice for cranial ABCs remains surgical excision, conservative management may be done in the form of curettage, enucleation and endoscopic surgery. Larger aggressive lesions may even warrant a bifrontal craniotomy. Selective pre-operative arterial embolization in large lesions may help to improve results of surgery. Other forms are medical management such as interferon alfa-2a and radiation therapies for unresectable lesions [1,4,15]. Due to the high recurrence rates after surgical excision newer modalities such as the use of cement, high-speed burr, argon beam, phenol, and cryotherapy have been used recently.

Conclusion

In conclusion, our case presented with an extremely aggressive nasopharyngeal mass lesion with multiple cystic and hemorrhagic components with associated extensive bone destruction and remodelling. Imaging modalities (CT and MRI) were helpful in characterising the lesion and its extent and also in deciding the management in this patient. Histopathology confirmed our imaging findings to be an aneurysmal bone cyst though the occurrence in such an anatomical location with widespread bony destruction is a very rare entity.

Acknowledgement

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Conflict of Interests : None

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Case Report

Intensive Management Of Complex Symptomatology In Severe Preeclampsia With Super Added PRES

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ABSTRACT

Posterior Reversible Encephalopathy Syndrome (PRES) is a cliniconeuroradiological syndrome characterized by headache, seizures, vision impairment or blindness, altered mental status and focal neurological signs. The lesions in the PRES are thought to be due to vasogenic oedema predominantly in posterior cerebral hemispheres.

We report a case of severe Pregnancy induced hypertension (PIH) with PRES presented with severe headache, visual impairment scheduled for emergency caesarean section. She was stable clinically during intra-operative period under general anaesthesia but after extubation there were blood pressure changes and altered mental status due to which she was reintubated and shifted to ICU. Postoperative CT brain was suggestive of PRES. Patient's clinical condition was further deteriorated due to development of cardiomyopathy in postpartum period. Early diagnosis of PRES, vigorous ICU monitoring and prompt treatment lead to the dramatic improvement in patient's clinical condition preventing any long term neurological deficits in reversible condition like PRES.

Keywords- PRES, PIH, cardiomyopathy, vasogenic oedema.

Introduction

Posterior Reversible Encephalopathy Syndrome (PRES) is a cliniconeuroradiological condition with multifactorial etiology. Causes include pregnancy induced hypertension (PIH) and eclampsia,[1] hypertensive encephalopathy, renal failure with hypertension, immunosuppressants and autoimmune disorder,[2] postdural puncture and spinal anaesthesia.[3] Clinically it is characterized by headache, generalized seizures, vision impairment, lethargy, confusion, changes in mental status and focal neurological signs. The global incidence of PRES is unknown. It has been reported in patients aged 4 to 90 years, most cases occur in young to middle aged adults and death has been reported up to 15%.[4] This study describes a case of PRES in association with PIH.

Case Presentation

20 year old 60 kg primi with 34weeks of amenorrhea in labour came with complaints of severe headache, blurring of vision since 2 hours. Her past history was not significant. Her blood pressure (BP) on admission was 180/110 mmHg and pulse rate was 110/min. She was given stat dose of 8gm magnesium sulfate intramuscular and labetolol 20mg intravenous. When received for emergency Caesarean section she was obeying commands but unable to perceive hand movements. Her respiratory rate was 20/min with clear chest on auscultation and 99% O2 saturation on room air with BP - 170/110mmHg and pulse rate- 100/min, regular; Fundus examination, Laboratory investigations, ECG were normal.

Patient was subjected to anaesthesia with risk of high BP explained to relatives and post-operative ventilator consent was obtained. Rapid sequence induction was done with thiopentone 4mg/kg and succinylcholine 1.5mg/kg intravenous. Anaesthesia was maintained on 50% N2O in O2 and sevoflurane as inhalational agent and intravenous atracurium as muscle relaxant. As the intra-operative period was uneventful and BP was maintained around 140/90mmHg without requirement of labetolol, it was decided to extubate the patient. After confirming the good respiratory efforts, tone, power, reflexes and consciousness, patient was extubated and observed on operation table. 15 minutes after extubation there was sudden rise in BP up to 190/110mmHg and patient's consciousness started deteriorating. Patient was therefore given loading dose of labetolol 20mg intravenous. With no satisfactory result from first dose after 5 min, second dose of 20mg repeated. But 5min after second dose, BP was still 180/110mmHg, consciousness was deteriorating further and she was desaturating, immediate decision was taken to start

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nitroglycerine infusion with initial drip rate of 5g/min and reintubate the patient. With nitroglycerine BP was lowered up to 150/90mmHg gradually over 30min and she was shifted for CT brain before ICU suspecting PRES. In ICU patient was put on elective mechanical ventilation till clinical improvement. CT brain was suggestive of PRES and tiny subarachnoid hemorrhages. As 5 hours after shifting, BP was controlled around 140/90mmHg, nitroglycerine was tapered off and patient was conscious, oriented with improvement in vision, she was extubated and vigorous monitoring was done. Patient was managed on magnesium sulfate 1gm/hour, labetolol 100mg through RT bd and 100ml mannitol tds. 7 hours after extubation she had first episode of generalized tonic clonic convulsions which required reintubation and loading dose of inj phenytoin 600mg. After 6 hours she regained consciousness and maintained vitals, she was given extubation trial. Next 18 hours ICU stay was uneventful; there was single episode of sudden rise in BP resulting in appearance of ST depression on ECG. Desaturation up to 85% on ventimask at 4L/min got stabilized after adding lasix 40mg. 2D-ECHO done after stabilization showed cardiomyopathy, left ventricular global hypokinesia and ejection fraction 30-35%. Tablet metoprolol and lasix were added to current medications.

After 24 hours of uneventful ICU stay patient was shifted to ward and was discharged after 5 days. She was advised follow up after 6 weeks for MRI brain and 2D-ECHO.

Discussion

Posterior reversible encephalopathy syndrome was introduced into clinical practice in 1996. The exact mechanism of PRES is currently not well understood. One of the dominating hypothesis is that severe hypertension exceeds the autoregulatory ability of cerebral blood vessels, leading to compromise of the blood brain barrier and vasogenic oedema.[5] Other postulated theories include physical disruption of the endothelial layer, blood brain barrier compromise in inflammatory conditions such as sepsis or autoimmunity or vessel abnormalities leading to cerebral vasoconstriction and hypoperfusion states such as in eclampsia and cyclosporin toxicity.[6] Posterior circulation is more susceptible to this type of damage because there is less sympathetic innervation of the vertibrobasilar vasculature to protect parenchyma from rapid increases in arterial BP.[2]

At presentation we suspected impending eclampsia but as there was sudden increase in BP with deteriorating consciousness after extubation, postoperative CT brain was done suspecting PRES. CT showed ill defined hypodensity involving bilateral posterior parieto-occipital region at grey white matter interface and helped in early diagnosis of PRES. With early diagnosis and prompt treatment this syndrome reverses completely without sequels. Treatment of PRES revolves around strict blood pressure control using JNC guidelines for hypertensive emergencies, anticonvulsants as well as correction of any potential causative factor. The essence of controlling hypertension is not to normalize the blood pressure but rather to decrease the mean arterial pressure by 20%- 25% within the first 2 hours. BP of our patient at presentation was 180/110mmHg and aim was to control around 140/90 mmHg. Though magnesium sulphate was used prophylacticaly to prevent postpartum seizures and mannitol as antioedema therapy, there was an episode of seizure on second postoperative day and phenytoin was added as second anticonvulsant. In addition to cerebral ischaemia the cause of seizures in this case was cerebral oedematous areas due to PRES. In addition to PRES patient's clinical condition was worsened by presence of cardiomyopathy. Clinical symptoms of cardiomyopathy were improved by addition of beta blocker and diuretic. So in ICU patient's treatment strategy included antihypertensive, anticonvulsant, magnesium sulfate, diuretic and supportive care to which she responded dramatically.

Conclusion

PIH is one of the most common medical disorders affecting pregnancy, may present with complications like eclampsia, intracerebral haemorrhage, renal failure, hemolysis, elevated liver enzymes and low platelets viz. HELLP syndrome and recent entity of PRES. The above case highlights importance of anticipation, early diagnosis and prompt treatment to avoid permanent complications in reversible condition like PRES.

Conflict of Interest: None

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Verrucous Nodules On Foot : A Diagnostic And Therapeutic Challenge

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ABSTRACT

Verrucous nodules over foot can occur due to chronic lymphatic obstruction arising from inflammatory, infective, neoplastic or endocrine causes.We report a middle-aged housewife with multiple long-standing verrucous nodules and edema over left foot.History of frequent attacks of pain, swelling and fever with chills pointed to recurrent cellulitis contributing to the dermal fibrotic changes.Lymphoscintigraphy confirmed lymphedema.Microbiological investigation ruled out filariasis.Nodule histopathology revealed papillomatous hyperplasia, moderately dense dermal inflammatory infiltrate composed of mature lymphocytes and plasma cells suggestive of elephantiasis nostras verrucosa with chronic inflammation.No evidence of carcinoma was detected.Elephantiasis nostras verrucosa (ENV) is a rare condition associated with chronic non-filarial lymphedema caused by bacterial or non-infectious lymphatic obstruction.Clinically it is characterized by verrucous nodules or plaques with non-pitting edema.The potential for debilitating deformities and malignant transformation necessitates timely management and extreme vigilance.The mainstay remains identification and amelioration of the cause of the lymphatic obstruction.This case highlights the challenges involved in the diagnosis and treatment of such verrucous nodules .

Key Words : Lymphedema, Elephantiasis nostras verrucosa

Introduction

Lower extremity is involved in various common and unusual dermatological conditions. Verucous nodular lesions over foot may have a wide array of differential diagnoses like verrucous carcinoma, pretibial myxedema, filariasis, lipedema, chromoblastomycosis, lipodermatosclerosis and venous stasis, tuberculosis verrucosa cutis, erythema nodosum, lipoma, warts, verrucous skin lesions associated with diabetic neuropathy (VSLDN), verrucous hemangioma and xanthoma.Herein we report a case which illustrates the approach and challenges involved in the management of such baffling lesions.[1]

Case Report

A 47 year old housewife presented with swelling over left foot since 10 years with skin lesion over that foot since 4-5 years.Five years ago she noticed a single lesion over second toe that gradually increased in size and number involving adjacent toe with swelling of foot and fever with chills.She denied history of weight loss, trauma, any crops of painful lesions, habitual or occupational prolonged erect position, similar lesions over other body parts, non healing ulcer over foot, and walking barefoot.

General examination was unremarkable except for pallor, there was no lymphadenopathy.BMI was 24.88 kg/m^2.

Dermatological examination showed non-pitting edema of left foot involving dorsum, ankle, malleoli above ankle joint, four non-tender firm verrucous nodules involving first,second, third toes and dorsum of foot (sized 2x3 cm to 4x5 cm) with crusting and oozing (Figure 1).Pitted keratolysis over sole and interdigital maceration were noted.Systemic examination was unremarkable.Investigations were performed considering the differential diagnosis of deep fungal infection,tuberculosis verrucosa cutis,elephantiasis and verrucous carcinoma.Hemogram, liver and renal function tests were within normal limits.ESR was elevated (60 mm/hr). ELISA/HIV and VDRL were non-reactive,CRP was positive.RA Factor, Mantoux test were negative and absolute eosinophil count was within normal limits.Serum lipid profile was normal.KOH mount, pus culture and sensitivity and ultrasound abdomen-pelvis were non-contributory.Local ultrasound (left foot) revealed extensive subcutaneous edema and thickening (1.6cm) involving dorsum of foot. X ray left foot and chest, electrocardiogram and Doppler left lower limb were normal. Sputum for acid fast bacilli

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was negative.

Histopathology of verrucous lesion demonstrated stratified squamous epithelium with marked hyperkeratosis and papillomatous hyperplasia.Dermis was filled with large dilated spaces lined by single layer of endothelial cells containing clear fluid, channels appeared partially enclosed by acanthotic epidermis.There was moderately dense dermal inflammatory infiltrate composed of mature lymphocytes and plasma cells suggestive of lymphedema with chronic inflammation (Figure 2).PAS stain and Z N stain for acid fast bacilli were negative.

Lymphoscintigraphy confirmed lymphedema and a final diagnosis of elephantiasis nostras verrucosa secondary to chronic lymphedema was reached.She was empirically started on tab diethycarbamazine and tab daflon (flavanoid fractions) with physiotherapy and elastic stockings. Patient followed up monthly with gradual regression in swelling and nodule sand no further febrile episodes or new lesions.

Discussion

Elephantiasis nostras verrucosa (ENV) is an exaggerated form of secondary non-filarial lymphedema.It was originally defined as a condition resulting from lymphatic blockage caused by recurrent bacterial infection and also called lymphangitis recurrens elephantogenica as in our case.A recent study has included neoplastic, traumatic, and other non-infectious causes of lymphatic obstruction in the definition.[2] Although the lower extremities are the most commonly affected site, any area with chronic lymphedema can be affected.The term *elephantiasis* is used to describe a body part that becomes enlarged and disfigured due to edema and fibrosis of the skin.Several conditions that block lymphatic drainage can induce lymphedema including bacterial and filarial infections, neoplasms, surgery or trauma, radiation therapy, congestive heart failure, obesity, hypothyroidism, chronic venous stasis, obesity and scleroderma.

Castellani classified elephantiasis into four subtypes: 1) elephantiasis tropica - due to filariasis; 2) elephantiasis nostras - due to bacterial infection; 3) elephantiasis symptomatica - due to mycotic, syphilitic, tuberculoid, neoplastic, or traumatic causes of lymphatic obstruction; and 4) elephantiasis congenita - associated with inherited disorders such as Milroy's disease.[3]

In our case, detailed history, meticulous clinical examination and investigation ruled out most of the documented causes.However insidious course and frequent bouts of fever with rigors were clues pointing towards the chronic infectious etiology.Although recurrent streptococcal lymphangitis may contribute to the origin of ENV,the exact pathogenesis of the disorder is not yet clear.It is conceivable that first the lymphatic channels are damaged and blocked, excessive protein-rich fluid accumulates in the dermis and subcutaneous tissues.Second, the protein-rich fluid decreases oxygen tension and the immunity of the skin.Third, poor immunity increases the skin's susceptibility to infection by micro-organisms.In chronic venous disease, activated leukocytes may migrate out of the vasculature and release TGF-β1,stimulating collagen production by dermal fibroblasts, which culminates in dermal and lymphatic fibrosis and dis- figuration of the affected areas. Thus, a vicious cycle begins.

Clinically, ENV is characterized by hyperkeratotic verrucous papules, plaques and nodules with woody fibrosis of dermis and subcutaneous tissue. If left untreated, skin changes are almost always progressive with potentially permanent disfigurement and gross dysfunction.Chronic dermal inflammation and collection of toxic metabolites may induce a small percentage to undergo malignant transformation into squamous cell carcinoma, verrucous carcinoma and angiosarcoma.Management of advanced stages usually results in unsatisfactory outcomes. Therefore it is imperative to recognize this rare condition in its initial stages and control infection and edema as soon as possible to prevent debilitating deformities.ENV can be very difficult to treat and comprehensive long-term studies on the management of elephantiasis are unfortunately lacking.There is no standard of care in patients with ENV and the clinician is left with a handful of case reports and literature reviews to guide management.The most important challenge is to investigate the underlying cause of lymphedema which should be treated as best as possible.The initial therapy should be directed at alleviating lymphedema with massage, multilayer inelastic bandaging and compression stockings after confirming adequate vascular perfusion and control of any infection.Pharmacological intervention with oral or

topical retinoids has been successfully employed to treat ENV and can be considered as an adjunct to physiotherapy.For cases that have not responded well to conservative or medical treatment, surgical intervention should be attempted.Surgical debridement has been reported to successfully reduce verrucous lesions in several case reports.[4,5,6]

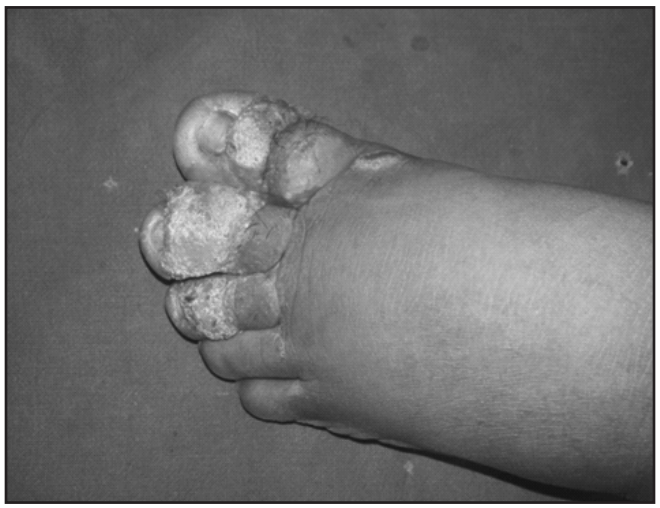

Figure 1. Verrucous nodules involving first, second and third toes & dorsum of left foot

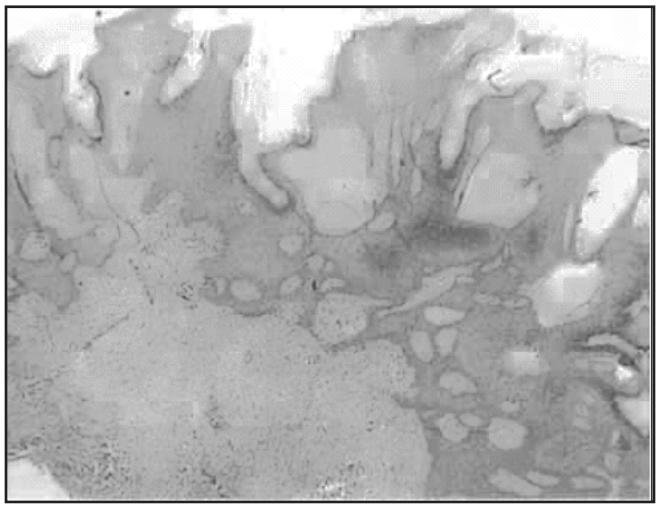

Figure 2. Hyperkeratosis and papillomatous hyperplasia.Dermis filled with large dilated spaces lined by single layer of endothelial cells containing clear fluid, dense dermal inflammatory infiltrate composed of mature lymphocytes and plasma cells

Conflict of Interest: None

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