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Editorial

This issue brings 'surgical safety' into focus. It was the 'saving a million lives' campaign which focuses the human errors made in patient care led to irreversible damage sometimes. Learning from the aviation industry - any aeroplane that is about to fly has to undergo rigorous tests by a successive line of personnel each armed with a check-list. Nothing is left to the 'sab theek hai' (all is well) attitude which prevails elsewhere. This is the perfectionist attitude that we need to adopt to save precious human lives and decrease errors in the surgical setting.

Medical Education is another topic on which this journal is going to focus in the coming issues. Philosophically, we physicians have conceived of ourselves as, and taught students that we are advocates for each patient, obligated to eschew all consideration other than benefit to that patient and his / her preferences.

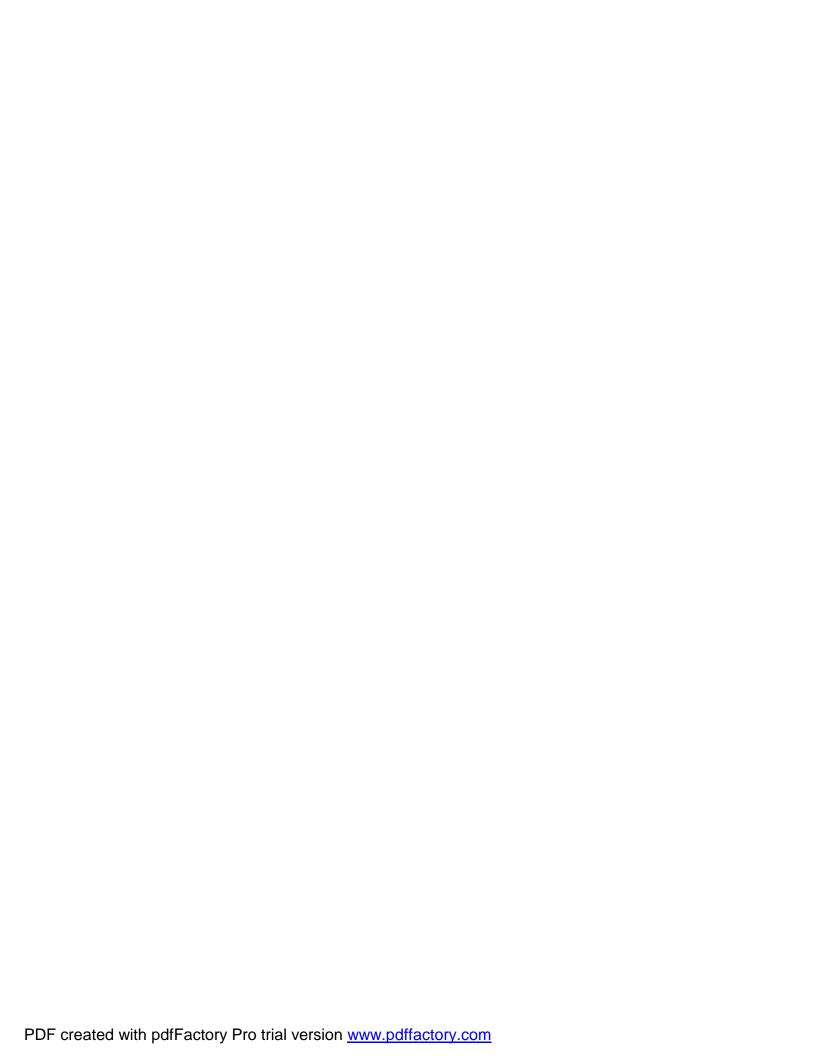
Academia celebrates the high knowledge of medicine: pathophysiology, molecular biology, genomics.² Evidence based medicine is the new mantra. But we are too high and mighty to teach the 'low brow' things like cost of treatment. It is common knowledge that in theory questions regarding management, each student will write all the diagnostic tests available. What we do not realize is that after getting a degree, he has no real-life insight into how to go about treating actual patients. Most of his working knowledge is going to be from sales-persons of various pharmaceutical companies. He is going to ask for an MRI even when the diagnosis is obvious from the history and sonography. The rich patient may actually be happy with this kind of medicine but what of the poor patient who has barely enough to eat? What about the ethics - who tells them that good medicine should be irrespective of patients status.³ Each patient has to be managed so as to receive the best therapy but if the cost of 'best' is twenty times more than the 'nearly-best' then the 'nearly-best' is appropriate for a person who is marginalized and poor. We invite views on these topics from our readers. Happy reading.

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Guillain Barre syndrome: Evidence based management

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ABSTRACT

Guillain barre syndrome is a neurological disorder with a wide clinical spectrum and significant morbidity and mortality. Several proven treatment strategies are in use, yet scope is there for more effective and individualized treatments. Supportive management is equally important area requiring further research.

Key words: Guillain barre syndrome, IV immunoglobulins, Plasmapheresis, Steroids

INTRODUCTION

Guillain barre syndrome (GBS) is a common neurological emergency. The incidence of GBS throughout the world is 1-4/100,000. It is a major cause of flaccid paralysis in developed countries where poliomyelitis has been eradicated. It is typically a monophasic illness. Its clinical variants are acute inflammatory demyelinating polyradiculoneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), and the Fisher syndrome (FS). Bickerstaff brainstem encephalitis (BBE) is also considered to be related to GBS. Males are more commonly affected. Exact incidence of various types of GBS is not known in India, but in western countries AIDP is commoner whereas AMAN is more common in countries like China and Japan. 5

GBS is an autoimmune polyneuropathy; evidence suggests that microbial agents by molecular mimickery trigger the autoimmune process and thus cause injury to nerves.⁶

Because of its autoimmune etiology various immunotherapies have been tried with or without success. IV immunoglobulin and plasmapheresis are the standard treatment nowadays. Despite advances in treatment and critical care mortality rate is between 3.5% - 12% in the acute phase. Apart from that, persistent disability is found in around 20% of cases and fatigue in 67% of cases. 8

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Clinical presentation: The clinical spectrum of GBS is heterogeneous regarding clinical severity, course of disease and outcome. It can present with vague symptoms of weakness, neck or back pain and paraesthesia. Some patients develop mild limb paresis and recover spontaneously, whereas others develop oculomotor, bulbar, respiratory muscle and limb paralysis and remain bedbound for several weeks or months. Neuromuscular respiratory function becomes compromised in 17% to 30% of patients with GBS. Autonomic instability in the form of sinus tachycardia or bradycardia, fluctuating hypertension or hypotension, flushing of the face, loss of or excessive sweating occurs in majority (70%) and can cause sudden death. 10

The Fisher syndrome presents as an acute onset of ataxia, areflexia and ophthalmoplegia; when there is associated disturbance of consciousness the condition is known as Bickerstaff brainstem encephalitis.^{11,12}

The severity of disease and improvement can be graded by the following scale given by Huges et al.¹³

- 0- Healthy
- 1- Minor symptoms or signs of neuropathy but capable of manual work/capable of running
- 2- Able to walk without support of a stick (5m across an open space) but incapable of manual work/running
- 3- Able to walk with a stick, appliance or support (5m across an open space)
- 4- Confined to bed or chair bound
- 5- Requiring assisted ventilation (for any part of the day or night)
- 6- Death

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INVESTIGATIONS

Although the diagnosis can be made clinically, investigations are helpful especially in atypical presentations. Electrodiagnostic studies like nerve conduction velocity and electromyography help in making diagnosis. Cerebrospinal fluid examination done after first week shows raised proteins and normal or mildly raised cell count (albuminocytological dissociation). Antiganglioside antibodies can also be given if available.

Treatment: It includes immunotherapy and supportive management.

Immunotherapy: Since it is an immune mediated disorder, several type of immunotherapies are in use.

IV Immunoglobulin: For the first time it was used for GBS in 1988. ¹⁴ Its efficacy is well established. IVIG acts by several mechanisms. It suppresses antibody production complement activation and membrane attack complex formation and provides anti-idiotypic antibodies for neutralizing autoantibodies. It also modulates expression and function of Fc receptors on macrophages and other effector cells. ¹⁵ Thus it prevents further injury to nerves and ensures faster recovery.

In a recent Cochrane systematic review by Hughes et al in 2010, it was seen that in severe disease, IVIG started within two weeks from onset hastens recovery as much as plasma exchange. Adverse events were not significantly more frequent with either treatment but intravenous immunoglobulin is significantly much more likely to be completed than plasma exchange. Also according to moderate quality evidence, giving intravenous immunoglobulin after plasma exchange did not confer significant extra benefit. In children, according to low quality evidence, intravenous immunoglobulin probably hastens recovery compared with supportive care alone. More research is needed in mild disease and in patients whose treatment starts more than two weeks after onset.

The current dosage of IVIG used in the treatment of GBS is 0.4 g/kg/d given over 5 days, or a total of 2 g/kg. This dose is based on its use in other autoimmune conditions.¹⁷ The optimum dosage of IVIG in GBS is not known but administering IVIG over 3 days compared to 6 days showed no significant difference in the outcome.¹⁸ Difference in pharmacokinetics can cause variability in IgG rise in different patients, in patients with lower rise prognosis is usually poor. In such patients, further doses

of IVIG might be beneficial.¹⁹ Recent systemic review recommends more dose ranging studies.¹⁶

Usually IVIG has only mild infusion-related adverse effects such as chills, headache and myalgias, which resolve after stopping the infusion and resuming it 30 min later at a slower rate. Rarely some serious adverse effects like anaphylaxis, thromboembolic events or renal failure can occur. Severe adverse events vary from 1.7 - 4.5%. Usually these complications occur in older patients with coexisting cardiovascular and renal morbidities.²⁰

Its major disadvantage in developing countries is high cost.

Plasmapheresis: Plasmapheresis or plasma exchange (PE) was first used in GBS in 1978. A large trial in 1985 established its role.²¹ It is hypothesized that PE probably works by eliminating the pathological autoantibodies.¹⁷

The usual regimen is PE 5 times during 2 weeks, exchanging a total of about 5 plasma volumes. Cochrane systemic review published in 2008, concluded that in mild GBS, two sessions of PE are significantly superior to none, in moderate variety four sessions are significantly superior to two and in severe variety six sessions of PE exchange are not significantly better than four. PE was more beneficial within seven days of onset rather than later, but was still beneficial in patients treated up to 30 days after disease onset. The value of PE in children less than 12 years old is not known. ²²

The facilities for PE are not available in all hospitals. It is an invasive procedure. It is usually well tolerated but hemodynamic instability, dilutional coagulopathy, hypocalcemia and allergic reactions can occur.²³ Severe cardiac disease or coagulopathy are relative contraindications for PE.

Fisher syndrome and Bickerstaff brain stem encephalitis: Although both IVIG and PE have been used in the treatment of FS and BBE, no randomized clinical trials have been done for treatment of FS or BBE.²⁴ In FS, IVIG slightly hastens recovery but the final outcome does not change much. In the FS or BBE cases presenting with a GBS overlap, treatment with either PE or IVIG is recommended as randomized controlled trials have established the efficacy of both treatments in GBS.²⁵

Combination therapy: Various trials have been done to look for the effect of combination of IVIG and PE but metaanalysis of these trials indicates that, combination

of IVIG and PE is no better than either alone. 16

Steroids: Steroids are useful in several immune mediated disorders but in several trials it was seen that steroids alone do not confer any added benefit in the treatment of GBS as compared to placebo or supportive treatment. In animal models it was seen that macrophages act as scavengers during remyelination process in AIDP and steroids inhibit them thus delaying the healing process.²⁶

In a systematic review done in 2011 it was concluded that corticosteroids given alone do not significantly hasten recovery from GBS or affect the long term outcome (moderate quality evidence). According to low quality evidence oral corticosteroids delay recovery.²⁷

Thus steroids are not recommended in management of LGBS at present.

Newer Research areas: In the pathogenesis of GBS, complement activation is a very important step. Extensive research is being done regarding role of complement inhibitors like Nafamostat mesilate and Eculizumab in management of GBS. They are supposedly more specific and fast acting form of treatment.^{28, 29}

Since anti-ganglioside antibodies are associated with myelin damage their selective removal seems an attractive option, specific immunoadsorption has been tried but it is practically a very tedious procedure.³⁰

Mycophenolate mofetil, Brain-derived neurotrophic factor (BDNF) and IFN-b were tried in GBS patients but no significant effect was noted. 31,32,33

CSF filtration has also been tried and some studies found it to be comparable to PE.³⁴ In a Cochrane review done in 2011, it was observed that interferon beta-1a, brain-derived neurotrophic factor and cerebrospinal fluid filtration, showed no significant benefit or harm.³⁵

Supportive management: Since GBS can present with serious problems like respiratory insufficiency, autonomic instability and sometimes altered sensorium (BBE), supportive management is of utmost importance.

Respiratory monitoring and airway management: Respiratory problems can occur due to respiratory muscle weakness or bulbar dysfunction. Important predictors for mechanical ventilation as seen in various studies were time from onset to admission being less than 7 days, "inability to cough", inability to stand, inability to flex the arms or head and vital capacity less than 60%. 36, 37 So, Respiratory functions should be monitored in all severely

affected individuals.

Often these patients require prolonged ventilation (after six weeks)³⁸ Early tracheostomy increases patient comfort and airway safety and may help weaning but the decision to place a tracheostomy may be postponed for 2 weeks. If after 2 weeks the pulmonary function tests do not show any significant improvement from baseline, tracheostomy should be performed.³⁹

Autonomic instability: As fatal autonomic dysfunction like arrhythmias and blood pressure disturbances can occur, monitoring of pulse and blood pressure is recommended in all severely affected patients.

Constipation can occur due to autonomic dysfunction, immobility and opiate analgesics. Bowel sounds and abdominal girth should be monitored.

Voiding dysfunction can occur but bladder is usually catheterised in all severely affected patients.

Deep venous thrombosis: In GBS, immobilization is a risk factor for the development of deep vein thrombosis (DVT). It can develop any time from 4-67 days after onset.⁴⁰

Since enoxaparin is indicated in all acutely ill medical patients, it should be used prophylactically in GBS patients also till they become able to walk independently.⁴⁰

Neuropathic Pain: Pain has been reported in 33-70% of cases. Gabapentin, carbamezapine and tricyclic antidepressants may be used for pain relief. Opioid analgesics should be used with caution in setting of autonomic instability.⁴⁰

Rehabilitation: Gentle strengthening exercises should be done because excessive exercise can cause paradoxical weakening of muscles.⁴⁰

Proper nutrition is especially important during recovery.

Fatigue: In 80% of GBS patients, severe fatigue persists which is unrelated to age, duration, or severity of the initial illness.⁴¹ It might be a sequel of forced inactivity and general muscle deconditioning. With supervised exercise programmes marked improvement is noted.⁴⁰

CONCLUSION

Management of GBS includes supportive and definitive treatment. In definitive management IVIG and PE are equally effective and steroids are either not effective or harmful. IVIG and PE are strongly recommended in severely affected patients but evidence is still poor for mildly affected patients and patients with FS and BBE. For children less than 12 years IVIG is better than PE. Management of respiratory failure and autonomic instability is of utmost importance for patient survival.

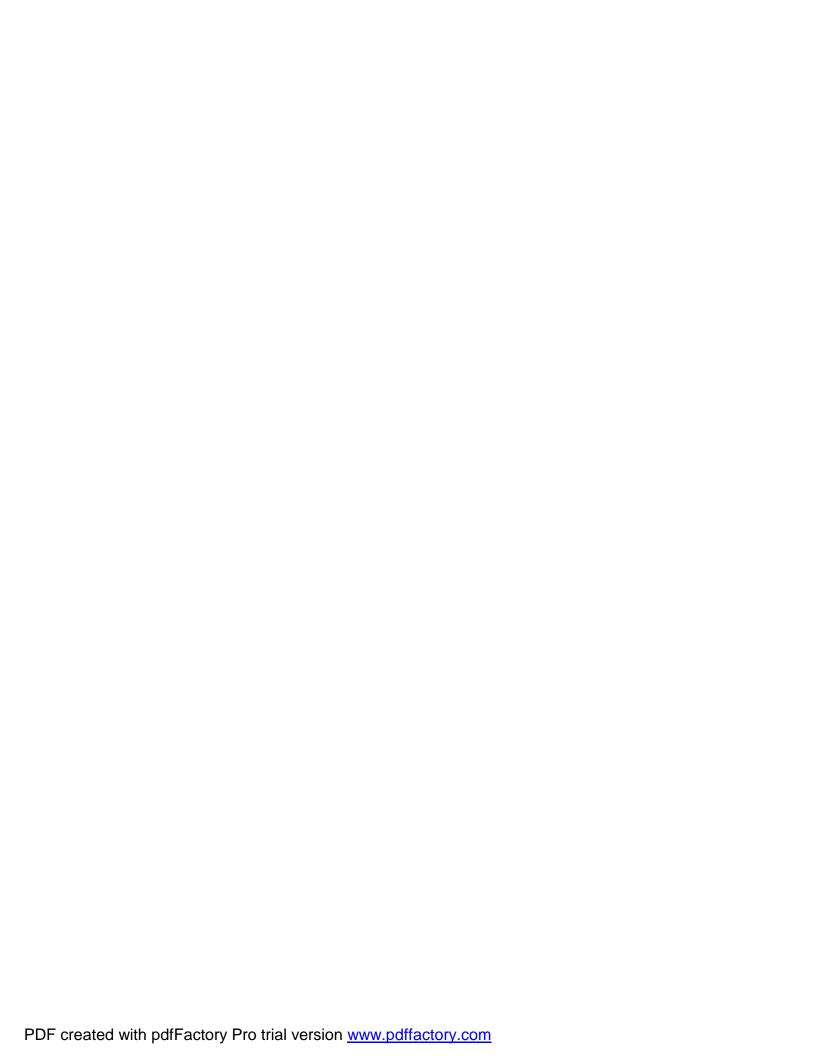
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Treatment Compliance in Glaucoma

Innludhhəl lund

INTRODUCTION

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VBSTRACT

The compliance to treatment of glaucoma patient has a big importance on the long term vision preservation, as well as on the quality of life of our patients. The body of literature on adherence interventions in chronic diseases such as systemic hypertension and glaucoma shows there are myriad causes of non-adherence or non compliance. The interventions to improve compliance need to be multifaceted and tailored to the individual patient.

Keywords: Adherence, compliance, motivation, persistence

Some researchers prefer the term" adhevence," since it suggests a treatment alliance between the patient and provider.

Medication persistency is defined as the total time on therapy.¹¹ Measures of persistency allow for some degree of patient noncompliance; for instance, a patient who takes a daily prescribed medication every other day is persistent with therapy, although his level of compliance is 50%. Persistency reflects not only the patient's satisfaction with an agent's tolerability but also the physician's satisfaction with the degree of intraocular prescribe control.¹²

Prevalence of Noncompliance

The reported proportion of noncompliers ranged from 4.6% 12 to 80%. 13 Medication compliance has been measured using a variety of methods.

a. Medication possession ratio: This is calculated as the number of days' supply the patient received divided by the number that should have been received if the medication had been taken as prescribed.

b. Medication monitor: This is regarded as the gold standard in compliance measurement, as it provides the most objective data on patients' dosing histories.

Effect of Noncompliance on Intraocular Pressure or

Six main studies, 3 with a cross-sectional design, 2 with a longitudinal design, and 1 intervention study, assessed the relation between noncompliance and IOP or the progression of VF loss. 7.23-27

To sum it up, there is no consistent evidence of the existence of a relation between noncompliance and IOP or the progression of VF loss.

Glaucoma is the second leading cause of blindness worldwide. Ocular hypotensive treatment prevents the occurrence of glaucoma in persons with raised intraocular pressure (IOP) and delays the progression of visual field (VF) loss in patients with glaucoma. L-5 From mice to molecules to clinical therapies to the larger socioeconomic impact of glaucoma, the ongoing research aims at better understanding of glaucoma. But amidst all these revolutionary concepts, the quintessential concept of compliance with ocular hypotensive treatment in glaucoma patients can not be forgotten.

Medication compliance is an important factor in the prevention of visual impairment. 6-9 The absence of symptomatology in almost all untreated glaucoma patients increases the risk of nonadherence and other visually related problems among these patients. Moncompliance with topical therapy may result in unnecessary switching to other drugs or in a surgical procedure, with additional risks and costs.

Let's get to know the key players: Compliance,

Adherence and Persistence.

Compliance can be defined as the degree of correspondence between the prescribed treatment regimen and the patient's actual dosing history. 10

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Determinants of Noncompliance:

Determinants of noncompliance can be subdivided into 4 groups:

- i. Communication Skills and Information Exchange. This encompasses a broad spectrum that includes patient expectations and discussion between the doctor and patient. Factors like diagnosis and prognosis; the use of clear language; honesty; and the doctor's experience, empathy, and listening skills all contribute to the use of medication. Patients have a need for more understanding, evidenced by the fact that glaucoma suspects are less likely than glaucoma patients to use medications or to maintain follow-up, and those with lower literacy levels are less likely to refill prescriptions. ^{28,29,30}
- *ii.* The Choice of Medications or the Treatment Regimen. Approximately one third or more of follow-up treatment problems relate to the choice of regimen.³¹ The prostaglandin class of agents has a better adherence and persistence than other classes, with once-daily dosing preferred (the more frequent the instillation regimen, the lower the adherence³²). The costs of medications (identified by up to 42% of patients³¹), side effects, and problems getting prescriptions refilled are also all associated with poor compliance.
- *iii.* Situational and Environmental Factors. These include life events as well as other challenges or diseases, lack of social support (for example, living alone, transportation issues, emotional support, lack of reminders to use drops), and challenges posed by travel (timing of instillations, loss of routine, distance from home and work).
- *iv. Miscellaneous Factors.* These include costs, varying motivation to use therapy and to maintain follow-up care, the impact of other physical and emotional conditions (depression and personal reaction to illness), and physical barriers to drop instillation (such as arthritis and tremor).

Another compliance issue is the supply of eye drops that insurance companies or government dispensaries allow patients to obtain. Many insurance companies have a policy that an empiric number of drop bottles must last 90 days. However, daily eye drop usage is not an exact measurement, such as daily prescribed pills can be.

We know how many drops may be in a bottle or what the volume of an eye drop bottle is, but the angle at which the patient administers a drop, and the force that he/she uses to squeeze the bottle and the temperature of the air when the bottle is squeezed, all influence the number of drops there are per bottle.

Interventions to Enhance Patient Compliance:

- **1.** *Education-and-tailoring program*: Norell tested an education-and-tailoring program in which the patients received information on glaucoma and its treatment. Patients were helped by an assistant to identify suitable times when application of eyedrops could be fitted in with their daily routines.²²
- **2.** *Use of a memory aid*: Chang et al evaluated the use of a memory aid (C Cap Compliance Cap, Allergan Pharmaceuticals, Irvine, CA) that displays the number of the dose the patient should take next.²⁷ In Sclar et al's study, the effect of the same cap was tested over a 13-month period. In addition, patients were counseled twice during this period on how to instill eyedrops correctly and on the importance of compliance with treatment.³³
- 3. *Medication alarm device*: Laster et al, in a crossover trial with 13 subjects, evaluated a medication alarm device (Prescript Time Cap, Wheaton Medical Technologies, Millville, NJ) that provides an audible as well as a visual reminder.³⁴

How to identify potential non compliers in clinical practice?

Patients are universally reluctant to acknowledge nonadherence because they do not want to be perceived as bad patients by their doctors.

Intraocular pressure: Intraocular pressure is a poor surrogate for compliance/adherence since patients commonly increase their adherence in the days prior to their scheduled visit to their ophthalmologist.¹⁷

Pharmacy records: Pharmacy records may be valid for measuring compliance of large groups, but can be inaccurate for individual patients ³⁵ and difficult to attain. In countries like ours, where the concept of directing the patients' prescription directly to the pharmacy close to his/her residence is not there, pharmacy tracking is not possible.

Friedman found lower adherence with low patient education, low-risk of vision loss, higher costs of medications, longer travel distance, increased side effects, and in those aged <50 years and those >80 years.³⁶



Figure 1: Xalease (with XalatanTM, Pfizer); Travatan Eyopt (with TravatanTM, Alcon)



 $Figure~2: Medication~Reminder~device~(with~Lumigan^{TM}, Allergan)$

Medication Tick Chart

Brand / Generic Names:	Time	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
		1	Š.		2			
Colour / Shape:	Instructions:							
Brand / Generic Names:	Time	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
Colour / Shape:	Instructions:		\$ 54.					
Brand / Generic Names:	Time	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
Colour / Shape:	Instructions:			2 1 2 1				
Brand / Generic Names:	Time	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
Colour / Shape:	Instructions:	12 12 12 13 14						
Brand / Generic Names:	Time	Mon	Tues	Wed	Thurs	Fri	Sat	Sun
Colour / Shape:	Instructions:]						

Figure 3: Medication Reminder chart

Lacunae in knowledge:

It is impossible to perform a meta-analysis, due to the great heterogeneity between studies concerning the definition of compliance, the assessment method, and the studied medication regimens.

RECOMMENDATIONS

Communication, Communication, Communication: Optimal treatment of patients with a chronic condition such as glaucoma requires a detailed conversation between the patient and the

ophthalmologist that continues over the years. These conversations must regularly reinforce the benefits of ocular hypotensive therapy and regular follow-up visits.

- 2. Regular assessment of the medication regimen: Consider the simplest feasible medication regimen that will meet the patient's needs. Be alert to side effects that might reduce compliance and persistency and consider changing the regimen if problems arise.
- 3. Ensure patient understanding of correct drop instillation technique: When starting a patient on

drops for the first time, consider a "practice bottle" of artificial tears.

At each visit, have a staff observe the patient instilling drops in the office. Instruct patients regarding the timing/spacing of drops and, depending on the regimen, consider a device to administer the drop (Figure 1: Xalease for Xalatan; Travatan Eyopt for Travatan).

- 4. **Be attuned to cost issues:** Patients may be embarrassed to admit they cannot afford the medication or follow-up visit fee, and ophthalmologists need to be sensitive to the possibility that cost is an issue. Some patients adopt the "pill-splitting" technique of using one drop every other day of a once-daily medication to lengthen medication use. Patient assistance programs from pharmaceutical companies can be offered to patients having difficulty paying for medications.
- 5. Help patients remember eyedrops into their routines: Cues such as teeth brushing, morning coffee, or administration of other medications may help patients remember to instill the eyedrops. Some drug companies provide a medication reminder alarm with the drug (Figure 2: Alarm with Lumigan) Ask patients to keep a calendar and check off when drops are instilled (Figure 3: Medication Reminder chart).

Advise patients who work, especially those who work shifts, to consider keeping an extra bottle at the work site.

CONCLUSION

Just like flossing prior to a dentist's visit, medication adherence goes up just before and after a visit to the ophthalmologist. Accurately assessing both compliance and persistency is important to optimizing patient care. Physicians may mistake either medication noncompliance or lack of persistency with poor efficacy. Such errors would likely increase health care costs if they result in unnecessary changes to a patient's therapeutic regimen or in surgery.

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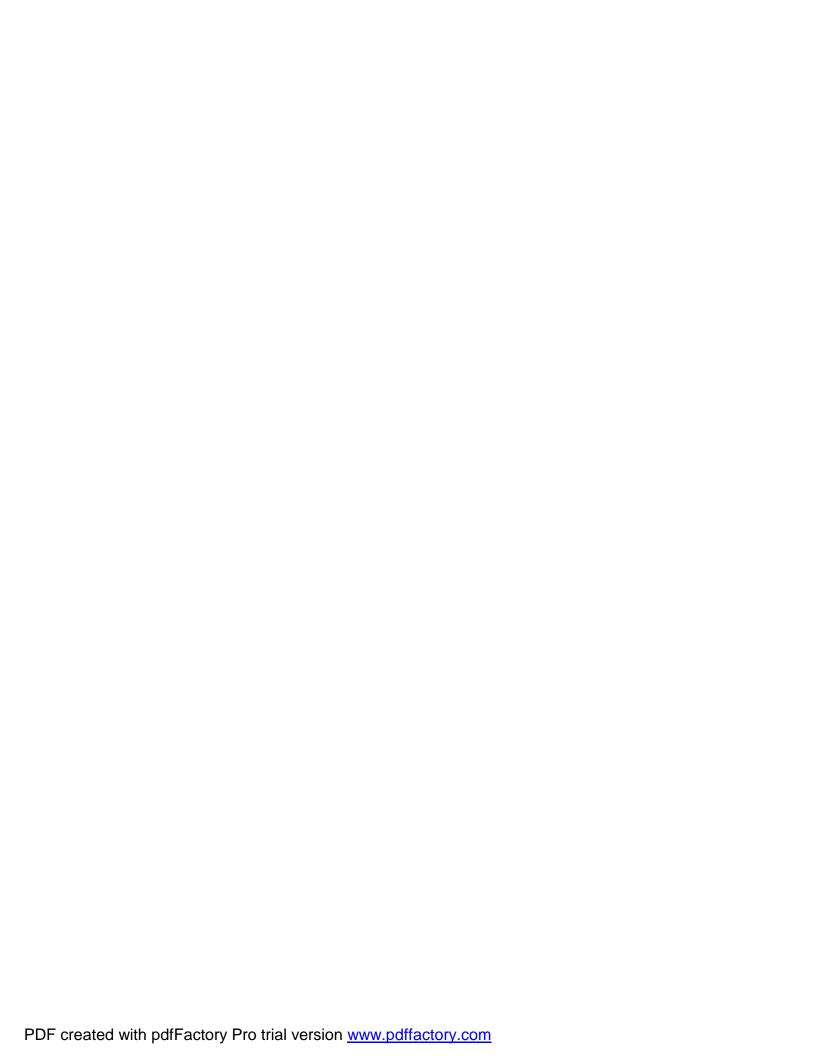
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Surgical Safety Checklist

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INTRODUCTION

Adverse event (harm caused to the patient as a result of medical care not the disease) is a major cause of morbidity and mortality. Worldwide, the incidence of adverse events in hospitalized patients ranges from 3-17%, with an associated mortality of 0.4-0.8%.^{1,2} With estimated 187-281 million procedures per year, surgical care is associated with significant risk of such adverse events.3As per WHO communication, almost seven million surgical patients suffer from complications each year, one million of whom die during or immediately after surgery. The consequences of surgical adverse events are found to be more severe as compared to other type of adverse events, resulting in permanent disability, prolonged hospital stay, extra costs and unplanned readmissions. Furthermore, with the reports that 50% of these adverse events are preventable, surgical safety is posing a big challenge to health care delivery systems.4Despite of the best efforts, preventable complications resulting from human factors are frequent. Simple measures like appropriate and timely administration of antibiotics, venous thromboembolism prophylaxis, preparation for blood loss, confirmation of equipment sterility, surgical counts and appropriate labeling of surgical specimens are often missed. Impaired cognition due to stress or fatigue and lack of team coordination is generally considered to be responsible for such errors.⁵ To overcome these limitations experts felt the need of surgical checklist for patient's safety after learning its success in aviation industry.

SURGICAL CHECKLIST

As a part of "Safe Surgery Saves Life" project, the WHO working group designed a surgical safety check list based on ten essential elements of safe surgery ⁶(Table:1). The

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Dr Sanjay Gupta, Department of Surgery, Govt. Medical College and Hospital, Chandigarh 160030 Email: sandiv99@me.com aim was to reinforce accepted safe practices, build team work and improve communication. Although, the checklist was designed to be suitable for any surgery in any surgical specialty, still WHO encourages additions and modification as per local requirement. However, the removal of any safety step from checklist is strongly discouraged, as it will have negative impact on achievement of safe surgery goal.

The safety steps are divided into three phases, each corresponding to critical period during normal operative procedure- (i) "sign in": before administration of anesthesia; (ii) "time out": immediately before surgical incision; (iii) "sign out": at the end of operation before the patient is shifted from the operating theatre. ⁶(Fig:1). It is recommended that single person usually the nurse should be made responsible for performing safety checks on the list and all steps must be checked verbally with the appropriate team member. In each phase, the checklist helps to confirm that the surgical team has completed its critical safety tasks before proceeding on to the next phase. This checklist is clear, concise and user friendly and also brings together members of surgical team at different critical time points. The "sign in" addresses patient's identity, surgical site and procedure, airway patency, allergies, pulse oximetry and need for blood and fluids. In "time out" team members introduce themselves, confirm loudly that they are performing the correct operation on the correct patient and site and also verbally communicate any anticipated critical element of the operation. Finally, in "sign out" phase, the completion of sponge and instrument count, labeling of surgical specimens and any equipment related problem is confirmed. The surgeon, anesthetist and nurse also review the key concerns for recovery and post-operative management.

To check the efficacy of this checklist, a trial was conducted (2007-2008) in eight hospitals in eight different countries having different economic status and diverse patient populations⁷. In this pilot study, after the introduction of checklist, death rate reduced from 1.5% to 0.8% and rate of inpatient complications reduced from 11.0% to 7.0%. Combined effect of team work and local culture modification was adjudged to be responsible for

Table 1

Ten Essential Objectives for Safe Surgery

- 1. The team will operate on the correct patient at the correct site.
- 2. The team will use methods known to prevent harm from administration of anesthetics, while protecting the patient from pain.
- 3. The team will recognize and effectively prepare for life-threatening loss of airway or respiratory function.
- 4. The team will recognize and effectively prepare for risk of high blood loss.
- 5. The team will avoid inducing allergic or adverse drug reaction for which patient is known to be at significant risk.
- 6. The team will consistently use methods known to minimize the risk for surgical site infection.
- 7. The team will prevent inadvertent retention of instruments or sponges in surgical wounds.
- 8. The team will secure and accurately identify all surgical specimens.
- 9. The team will effectively communicate and exchange critical information for the safe conduct of the operation.
- 10. Hospitals and public health systems will establish routine surveillance of surgical capacity, volume and results

these results. Although the authors pointed out some limitations of this study,the results attracted global attention and further studies were carried out to check the effectiveness of surgical checklist. Weiser TG et al, observed its utility even in emergency conditions and reported 6.7% reduction in rate of major complications and a 2.3% reduction in mortality rate.8The Surgical Patient Safety System (SURPASS) checklist, which follows the patient from admission to discharge, also showed decline in total number of complications per 100 patients from 27.3 to 16.7 and mortality from 27.3 to 16.7%. There are studies which fail to reproduce similar results. 10,11 However, the authors of these observed that introduction of check-lists does improve communication among surgical team members and compliance for safe surgery practices like appropriate antibiotic prophylaxis and deep vein prophylaxis.

After the encouraging results of these initial reports, various state governments started incorporating surgical checklist in to their health care delivery systems. In January 2009, United Kingdom National Patient Agency mandated the implementation of WHO version of checklist with in the entire National Health Service. A 'Safe Surgery 2015" program was launched by Harvard School of Public Health, with aim to implement the checklist in every hospital in the United States and in 7,500 hospitals worldwide by 2015. According to the WHO, over 4000 hospitals worldwide have implemented surgical safety checklist in their day to day practice. ¹² Not only this, various specialties like neurosurgery, cardiothoracic, interventional radiology and orthopedic

surgery*etc*. have also developed their own checklists with modification as per requirement of particular specialty.^{5,} 13, 14

Implementation of Checklist

Despite the evidence that the checklist reduces surgical morbidity and mortality, lack of awareness is one of the major barriers to its implementation in day to day practice.15Mere pasting of laminated WHO surgical checklist on the wall of surgical wards and operation theatres does not serve any purpose. Even when it becomes part of patient record file, resident doctor or nurse is given responsibility to confirm safety steps and surgical team members never shares their concerns among themselves regarding safe surgery. Another factor which resists its implementation is prevalent operation theatre culture. 10 The loud and clear verbal interaction among team members as a means of confirming that appropriate standards of care are ensured for every patient may be found embarrassing. Highly educated professional may not accept that they are susceptible to simple mistakes like forgetting or miscommunication. Similarly, a nurse leading the checklist may not be acceptable to surgeons or anesthetists. Bringing together team members at different points of surgical pathway is found to be another challenging task. It is also possible that in many hospitals these checks may have already been done at different points by different individuals before patient "signs in". Therefore, confirming of these checks again may be considered as repetition and wastage of time.

Surgical Safety Checklist



Before induction of anaesthesia	Before skin incision	Before patient leaves operating room
(with at least nurse and anaesthetist)	(with nurse, anaesthetist and surgeon)	(with nurse, anaesthetist and surgeon)
Has the patient confirmed his/her identity, site, procedure, and consent?	Confirm all team members have introduced themselves by name and role.	Nurse Verbally Confirms: The name of the procedure
Is the site marked?	 Confirm the patient's name, procedure, and where the incision will be made. 	 Completion of instrument, sponge and needle counts
☐ Yes ☐ Not applicable	Has antibiotic prophylaxis been given within the last 60 minutes?	 Specimen labelling (read specimen labels aloud, including patient name) Whether there are any equipment problems to be
Is the anaesthesia machine and medication check complete?	☐ Yes ☐ Not applicable	addressed To Surgeon, Anaesthetist and Nurse:
Yes	Anticipated Critical Events	☐ What are the key concerns for recovery and
Is the pulse oximeter on the patient and functioning? Yes Does the patient have a:	To Surgeon: ☐ What are the critical or non-routine steps? ☐ How long will the case take? ☐ What is the anticipated blood loss?	management of this patient?
Known allergy? No Yes Difficult airway or aspiration risk? No Yes, and equipment/assistance available Risk of >500ml blood loss (7ml/kg in children)? No	To Anaesthetist: Are there any patient-specific concerns? To Nursing Team: Has sterility (including indicator results) been confirmed? Are there equipment issues or any concerns? Is essential imaging displayed? Yes	
Yes, and two IVs/central access and fluids planned	☐ Not applicable	

This checklist is not intended to be comprehensive. Additions and modifications to fit local practice are encouraged.

Attri & Gupta: Surgical SafetyChecklist

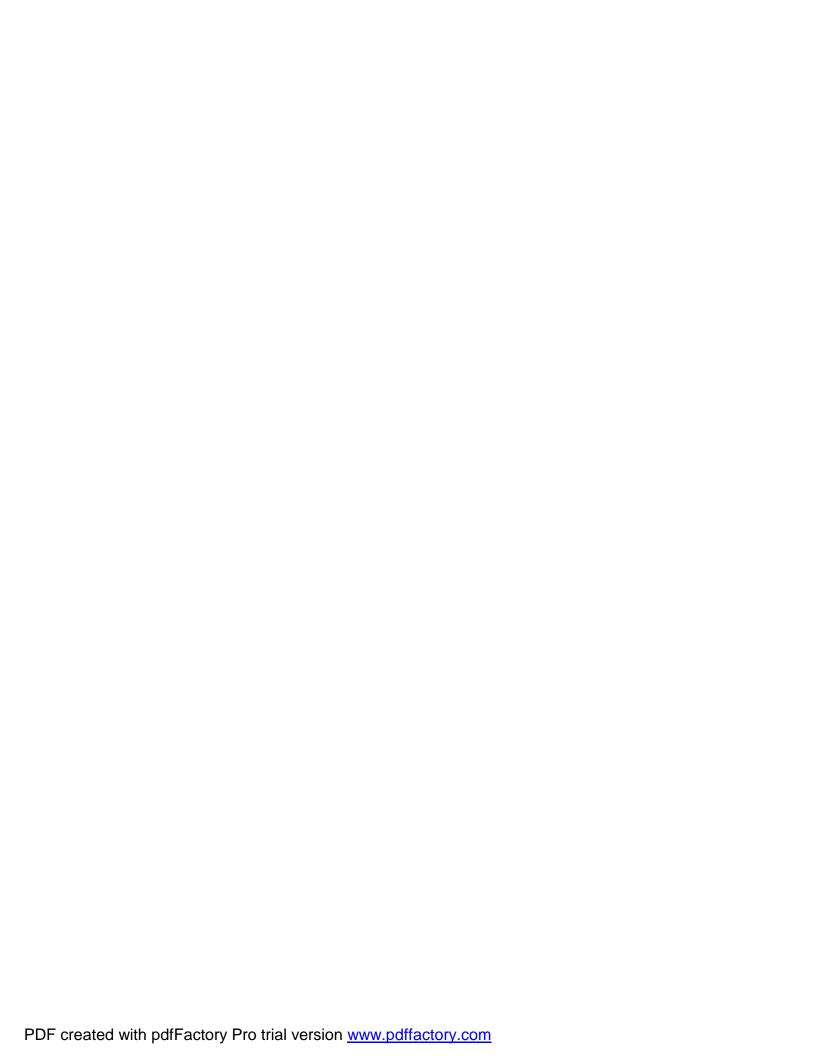
To overcome these barriers, stepwise approach and commitment is necessary. Clinicians and other supporting staff should be made aware of what the checklist is, how it works and why it is important. To promote sense of "ownership", its contents must be discussed and modified as per local culture and practices. In the initial phase rather than insisting everyone, the people who are interested, should be given the responsibility to run the project. Over time, with positive results, people who are initially reluctant will start adopting it in their practice. Active support of hospital leaders is also very important. Patient safety should be one of the priorities. Clinical staff will accept it more easily when their senior colleagues are serious about improving the quality of patient care. Further, periodic check on progress, regular feedback, audit of outcome and sharing of the results is also essential for the checklist to sustain in a system.¹⁶ An integrated and coordinated effort for all sectors and intersectoral coordination is required for best patient outcome.

To conclude, in the era of quality assurance, simple intervention like checklist can serve as an important tool to reduce morbidity and mortality due to human errors, but to achieve desired results its effective implementation is essential.

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Prevention of backflow of blood in the intravenous tubing during ipsilateral arm measurement of non-invasive blood pressure and its effect on blood pressure measurement readings - a randomized prospective study

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ABSTRACT

Certain surgeries necessitate and it becomes very essential to put intravenous line and non invasive blood pressure (NIBP) monitor cuff on the same arm. But this may cause retrograde blood flow in the infusion set and its occlusion may occur whenever the blood pressure cuff inflates. The technique as described by Mackawa et al¹ for preventing backflow, appears to be effective. But the presence of a tube with a solid stylet as described by Mackawa et al¹ may alter the blood pressure measurement by the non invasive blood pressure measurement. Keeping this view in mind we evaluated the impact of this assembly on the blood pressure measurement.

This prospective study was done in one hundred patients requiring insertion of intravenous cannula and NIBP measurement in the same arm. Patients with any deformity of the upper limb, limb edema and any cardiovascular disease were excluded from the study. The patients were randomized to receive the 18 G intravenous cannula either on left or right dorsum of hand. One arm had the assembly incorporated in the sphygmomanometer cuff as described by Maekawa et al and other arm has cuff tied in the conventional method (control arm). For comparison of the blood pressure, the other arm was taken as control (NIBP cuff directly applied without an intravenous tubing or stylet). The readings were obtained immediately at application of both cuffs, 5 minutes, 10 minutes and 15 minutes later using automated NIBP monitor. Three readings at all times were noted and mean reading was noted.

The blood pressure measurements (systolic and diastolic blood pressure) in the two groups were comparable (p value -0.893, 0.937). The backflow in the intravenous infusion tubing was not observed in any of the patient.

To conclude, the technique of using infusion tubing between coiled stylet and sandwiched between the velcro layers of sphygmomanometer cuff is an effective method of preventing the backflow of the blood during ipsilateral arm blood pressure measurement. The blood pressure measurements are reliable and are comparable with the true value.

Key Words: Intravenous tubing, backflow of blood, prevention, blood pressure

INTRODUCTION

Intravenous access for administration of drugs is essential for patient care during intraoperative period. In certain surgical procedures like upper extremity procedures (orthopedic, neurovascular), having AV fistula or mastectomy, it becomes necessary to put intravenous line and NIBP monitor cuff on the same arm. But this may cause retrograde blood flow in the infusion set and may

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occlude it most often. This usually occurs when the blood pressure cuff gets inflated.

The methods employed to counteract increase in peripheral venous pressure (PVP) include elevation of intravenous solution bag, routing the infusion tubing through the BP cuff so that it is compressed between the Velcro layers of NIBP cuff or placing a check valve within the intravenous tubing etc. However, these methods are used empirically without any randomized trials based evidences.

The accuracy of oscillometry method of blood pressure measurement is maintained by adoption of number of standards, including appropriate cuff size, its application, and its operation. These standards are well followed but any alteration like putting an extra object in the cuff may alter the blood pressure measurements.

The technique as described by Mackawa et al¹ for preventing backflow (intravenous tubing between a coiled infant ET tube ultrathin stylet sandwiched between two velcro layers of sphygmomanometer cuff) appears to be effective. This stylet is often available in the operation room and does not require any other special material.

Presence of a tube with a solid stylet as described by Mackawa et al¹ may alter the blood pressure measurement by the non invasive blood pressure measurement.

Keeping this view in mind, the present study was designed prospectively to evaluate the impact of this assembly on blood pressure measurement.

MATERIAL AND METHODS

This randomized, prospective study was conducted in one hundred patients of average built ,requiring insertion of intravenous cannula for intravenous fluid administration. Written informed consent was taken from all patients. Patients with any deformity of the upper limb, limb edema and any cardiovascular disease were excluded from the study. All the patients who were selected, were operated in supine position where blood pressure variability is minimum. The patients were randomized to receive an 18 G intravenous cannula (BD Venflon ProTM) on left dorsum of hand and similar brand of intravenous cannula and intravenous infusion set (Angiplast private limitedTM) was used in all patients. Immediately in one arm the assembly was incorporated in the adult sized sphygmomanometer cuff as described by Maekawa et al³ (study arm) (Figure 1 & 2) and in other arm the cuff was tied in the conventional method (control arm). For comparison of the blood pressure, the other arm was taken as control (NIBP cuff directly applied without an intravenous tubing or stylet). Both the arms were kept aside on the operation table. The blood pressure readings were obtained in each of the 100 patients from both the arms simultaneously using automated NIBP monitor (Datex S5®) and recorded. The readings were obtained immediately at application of both cuffs, 5 minutes, 10 minutes and 15 minutes later. Three readings at all intervals were noted and the mean of all three was noted at all intervals.

After pilot cases and previous limited literature it was estimated that at least 86 patients were required for this

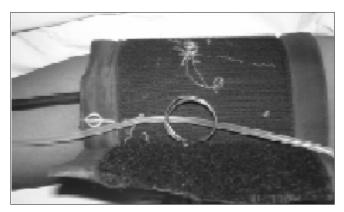


Figure 1: Coiled stylet with IV tubing kept in BP cuff (cuff partially opened to show the assembly)

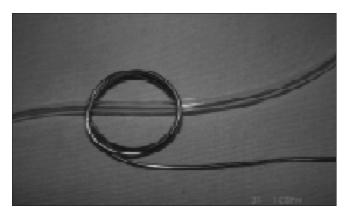


Figure 2: Coiled stylet with IV tubing assembly

study and the blood pressure readings were compared using student 't' test. The p value < 0.05 was considered as significant.

RESULTS

The mean age of the patients was 36.4 ± 12.4 yrs. The mean weight was 61.7 ± 11.2 kg with 56 males and 44 females(Table 1). The blood pressure measurements (systolic and diastolic blood pressure) in the two groups were comparable (p value -0.893, 0.937) (Table 2) and backflow in the intravenous infusion tubing was not observed in any of the patient.

Table 1
Demographic Profile

	No. of patients: 100
Mean Age ± SD	$36.4 \pm 12.4 \text{ years}$
Mean weight± SD	$61.7 \pm 11.2 \text{ kg}$
Male: Female	56:44

Table 2

The Systolic and Diastolic blood pressure in two arms

	No. of patients	Study arm	Control arm	P value
Mean systolic blood pressure (mm Hg)	100	127.5 <u>+</u> 16.6 (89-160)	127.1 <u>+</u> 17.9 (90-162)	0.893
Mean diastolic blood pressure (mm Hg)	100	82.2 <u>+</u> 8.8 (58-100)	82.1 <u>+</u> 9.1 (60-98)	0.937

Values are mentioned as Mean \pm *SD (range)*

DISCUSSION

The heart rate and blood pressure are most fundamental cardiovascular vital signs, that reflect the force that derives perfusion of the body. Consequently, frequent measurement of arterial blood pressure is a critical part of monitoring anaesthetized or seriously ill patients. The importance of monitoring this vital sign is underscored by the fact that standards for basic anesthetic monitoring mandate measurement of arterial blood pressure at least every 5 minutes in all anaesthetized patient.

Techniques for measuring blood pressure are categorised into two major types: indirect Riva Roci cuff devices and direct arterial cannulation with pressure transduction. A variation of the Riva Roci method commonly employed today is generally the return-to-flow technique where the pressures are recorded during cuff deflation. Many limitations of manual intermittent blood pressure measurement have been overcome by automated NIBP devices.

These techniques of blood pressure measurement can be altered by decreased peripheral blood flow (cardiogenic shock, high dose vasopressor infusion), shivering patient, severe calcific arteriosclerosis, inappropriate cuff size, The Oscillometric technique, first demonstrated by Marey (1876). He measured non invasive blood pressure and it this technique single cuff is applied to the patients arm. he machine inflates it to a level assumed to be greater than systolic pressure and then the cuff is deflated gradually. A sensor then measures the tiny oscillations in the pressure of cuff generated by pulse. The signals are detected by a pressure transducer and converted to blood pressure values. An algorithm is used to convert these values to systolic and diastolic pressure readings.

Various techniques and options have been mentioned in the literature regarding prevention of backflow of blood in intravenous cannula and infusion tubing during measurement of blood pressure in ipsilateral arm. Though the option of securing intravenous access in foot is present but it becomes uncomfortable most of times for the anesthesiologist to administer drugs. The option of measuring NIBP by cuff on thigh is always present, but the large size cuff is often not available. The invasive blood pressure may not be warranted in every patient. The simple technique of closing the stopcock / drip regulator every time the cuff inflates for blood pressure measurement, is not feasible and becomes quiet cumbersome when surgical site is cleaned and draped.

Brin et al ² developed simple technique to prevent backflow by placing a length of intravenous line in a blood pressure cuff between the velcro layers. Similar technique was described by Wait et al³ which was supported by Nishina et al⁴ also. When the cuff inflates, the tubing is squashed flat and is occluded, and retrograde flow is automatically prevented. However, this simple method often does not work effectively because the low compliance of the tubing in most of the infusion sets does not allow easy compressibility. Another technique was given by Malhotra et al⁵ where tubing of an intravenous set is placed along the arm of the patient and the sphygmomanometer cuff is applied over the arm .The intravenous tubing is again sandwiched between the velcro layers which is again not fully effective.

Sim et al⁶ studied the changes on peripheral venous pressure during cuff inflation and deflation during NIBP measurement. Peripheral venous pressure (PVP) waveforms were recorded from 6 subjects during NIBP measurement. They found that PVP change was biphasic in shape during NIBP monitoring and PVP peak was

higher during deflation as compared to PVP peak during inflation of cuff. These patterns and the range of PVP change should be kept in mind when we apply methods to counteract venous regurgitation during NIBP monitoring. This increase is more during deflation period of cuff and thus necessitating the efficient compression of tubing even during phase of deflation. Most of the time the methods used for preventing backflow may help during inflation but may be ineffective during deflation of cuff due to ineffective compression of the infusion tubing. Probably, this was the reason for less effectiveness of earlier techniques of preventing backflow.

Jeaney et al⁷ used modified squeeze-clamp into portion of intravenous tubing that is to be placed between the velcro layers to prevent the backflow of blood. When the intravenous tubing with clamp inserted is placed between the velcro layers, the occlusion-reflow of the tubing occurs synchronously with the blood pressure cuff inflation-deflation cycle. They concluded that this clamp was easy to use and effective in stopping the retrograde flow each time the blood pressure cuff is inflated. The clamp is reusable and does not need sterilization. It is probably less expensive than a commercial infusion set with check valve.

Maekawa et al¹ modified the technique of wait for effective prevention of backflow and to increase the success rate. A stylet (FUJI System, Tokyo, Japan) is coiled twice around a laryngoscope handle to form a spiral before use. The stopper of the stylet is removed. The infusion line is placed between the two turns of the coil. The device is then sandwiched between Velcro layers. This technique gives effective compression over the infusion tubing during cuff inflation and thus preventing backflow of blood.

Misuzu et al⁸ described an yet another technique using a spectacle case to prevent backflow. A three-way stopcock or T-connector is placed in the air line connecting the sphygmomanometer and blood pressure cuff. The open limb of the stopcock or connector is connected to another small blood pressure cuff. The intravenous tubing is inserted between the halves of the spectacle case, and the case is then rolled up in the smaller cuff. When the

blood pressure cuff on the patient's arm is inflated for a measurement, the smaller cuff is also inflated, pinching the intravenous line placed between case covers. The device completely stops flow through the line only during blood pressure measurements. Possible problems of this device are influence on blood pressure measurement and damage to intravenous tubing.

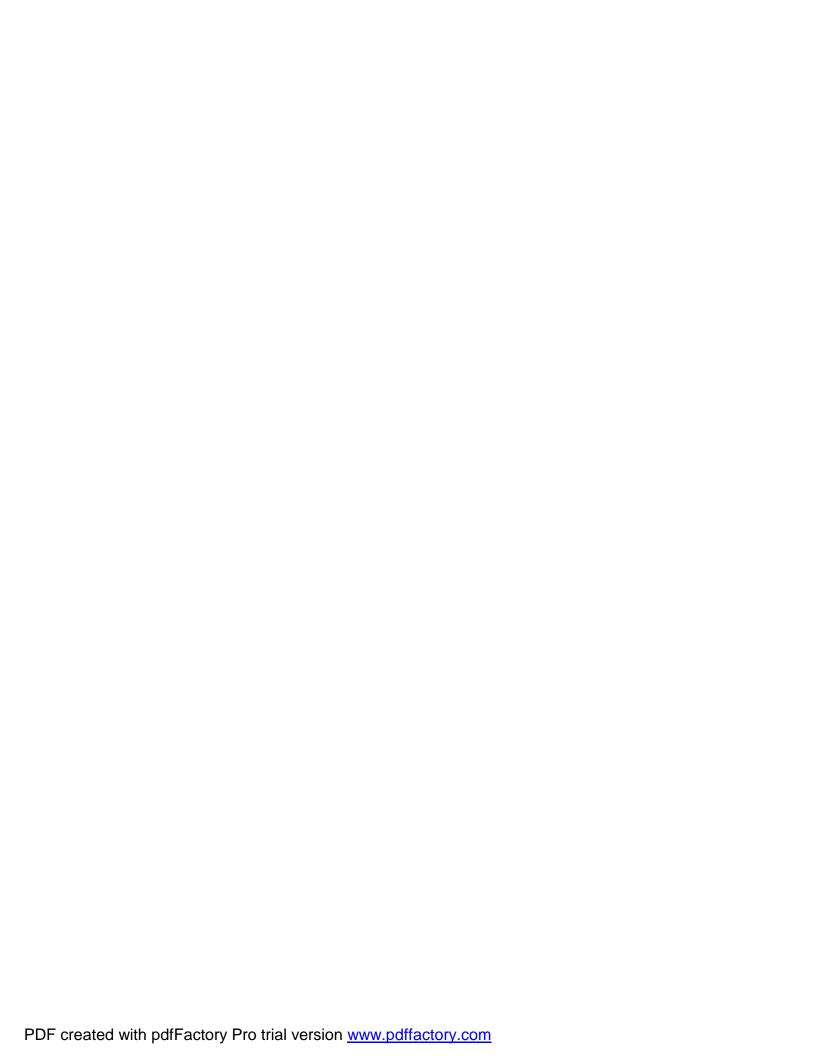
Some commercially available intravenous tubings incorporate a one-way valve but are not available everywhere.

The presence of coiled stylet and intravenous infusion tubing did not affect blood pressure measurements in our study. The blood pressure readings did not alter much and were comparable to each other in both arms at all times.

To conclude, the technique of using infusion tubing between coiled stylet and sandwitched between the velcro layers of sphygmomanometer cuff is an effective method of preventing the backflow of the blood during ipsilateral arm blood pressure measurement. The blood pressure measurements are reliable and are thus comparable with the true value.

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Rate of Speech of Punjabi Speaking Children

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ABSTRACT

The rate of speech is one of the important aspects of speech that affects both fluency and intelligibility. Studying rate of speech is important because it may be deviated in many speech-language disorders such as stuttering. The aim of present study was to find the normal rate of speech of Punjabi speaking children. Forty subjects (20 males and 20 females) in the age range of 10-14 years participated in the study. All the subjects were native Punjabi speakers and had normal speech fluency. It was investigated whether their speech rate differed in various speech tasks, that is, reading, picture description and spontaneous speech. The results obtained showed that the rate of speech was in the range of 148-216 words-per-minute (wpm) during reading; 139-171 wpm during picture description and 127-156 wpm during spontaneous speech. The rate of speech of male children does not differ significantly from female children. The rate of speech in reading was highest. It was significantly higher in reading than picture description and spontaneous speech for both male and female children. The difference was not significant for the tasks of picture description and spontaneous speech. The rate of speech of Punjabi speaking children was highest for the speech task of reading followed by picture description and then by spontaneous speech. Either of the speech tasks could be used to assess rate of speech.

Keywords: Rate of speech, stuttering, Punjabi

INTRODUCTION

Speech is a unique character of human beings. It is the audible manifestation of language and serves the purpose of communication. Normally acceptable speech should, apart from other aspects, be fluent and intelligible. The speed with which a speaker speaks, that is, the rate of speech is one of the important aspects of speech that affects both fluency and intelligibility.

The rate of speech may be defined as the number of linguistic output units, words or syllables, per unit time, including pause interval which may separate uninterrupted articulatory sequence¹. In speech-language pathology, studying rate of speech is important because in many speech-language disorders rate of speech deviates from the normal. These disorders include fluency disorders such as stuttering², neurogenic language disorders and some motor speech disorders.

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Ravi Kapoor Audiologist cum Speech Therapist Department of ENT, 3rd Floor B Block, Govt. Medical College Hospital, Chandigarh,India E-mail: ravikapoor2002@yahoo.co.in Rate of speech is generally expressed in range. Reported normal speaking rate in English language is in the range of 115 to 165 words per minute and 162 to 230 syllables per minute³, whereas normal reading rate has a range of 150 to 190 words per minute and 210 to 265 syllables per minute.⁴

In Western literature, several studies related to rate of speech in different languages have been done for establishing normative values for various groups of speakers and for different speaking tasks.^{5,6} In Indian languages, studies with respect to rate of speech have been carried out in Kannada, Marathi, Oriya languages^{7,8}. The norms of one language cannot be used for another language because of differences in the sociolinguistic environment and probable differences in the neuromuscular skills. Kaushal et al ⁹ studied rate of speech for adults in Punjabi. To the best of our knowledge, there has been no exclusive study done for establishing rate of speech for Punjabi speaking children population.

AIM

The aim of present study was to obtain the rate of speech of Punjabi speaking children having normal speech fluency.

METHODOLOGY

Subjects

Forty subjects in the age range of 10-14 years participated in the study. Twenty children were males and twenty were females having normal speech fluency. All the subjects were native Punjabi speakers. They were explained, in their own language, about the purpose of speech recording, that is, to find the norms for rate of speech for Punjabi speakers. Any subject with past history of any speech-language-hearing disorder was excluded from the study. All the subjects studied Punjabi as a subject in their curriculum.

Speech Tasks

Reading: The subjects were given the same passage to be read aloud without any prior familiarization. The passage was selected from fifth standard text book of Punjabi.

Picture description: Two stories with picture sequence cards were shown to the subjects and were asked to describe one of them of their choice and convenience in their own words. The picture sequence was as follows:

- 1 a) A crow flying, b) Crow sitting on a pot having little water, c) Crow putting pebbles in the pot, water level rises, d) Crow drinking water, e) Crow flying away.
- 2 a) A dog with a bone going over a bridge, b) Sees his own reflection in the river, c) Barks, and bone fells in the river, d) Walks away sadly.

Spontaneous Speech: The subjects were asked to speak spontaneously for 2-3 minutes on one of the topics-1) Daily routine; 2) Recent movie that the subject has seen; or 3) Ones own family.

Instruments and Recording method: Sony stereo audio cassette recording system with external microphone placed at 5 centimeters distance from mouth was used with Sony-90 cassettes for speech recording in sound treated rooms of the Audiology and Speech Rehabilitation Unit of Department of ENT, Government Medical College and Hospital, Chandigarh. It was ensured that the speech sample was no less than 5-minute duration of the child's talking. A speech sample of 500-word from each child was taken for analysis during the study. Conture (1990) noted that the sample size should be sufficient to permit averaging across several 100-word samples¹⁰. During the analysis the cassette was replayed and the time taken

by each subject to complete the material was recorded using a digital stopwatch (least count 0.01 seconds). The words spoken during the three speech tasks were analyzed in terms of words per minute (WPM). Any pauses that were greater than 3 seconds were omitted and not included in the analysis.

Speech analysis: Two experienced Speech Therapists calculated the words spoken during the three speech tasks and the total time taken for a given sample with the help of a stopwatch. They analyzed all the speech samples as judges at two different times in a gap period of two weeks to determine the inter-judge and intra-judge variability.

RESULTS

The rate of speech in terms of words per minute (WPM) for the speech tasks of reading, picture description and spontaneous speech was calculated by analyzing the recorded speech samples. The data were then subjected to statistical analysis by student t-test and co-efficient of correlation. The range, mean and standard deviation of words per minute (WPM) for the tasks of reading, picture

TABLE 1
The Rate of Speech of Punjabi Speaking Children in words per minute (WPM)-----Reading

	Males	Females	Statistical Significance
Range	148-204	149-216	No significant
		difference	
Mean	186.3	187.1	
SD	16.3	17.1	

t-value=0.328; p>.05

TABLE 2

The Rate of Speech of Punjabi Speaking Children in words per minute (WPM)----Picture description

	Males	Females	Statistical Significance
Range	139-162	143-171	No significant
		difference	
Mean	152.1	155.5	
SD	14.6	16.2	

t-value=0.286; p>.05

TABLE 3
The Rate of Speech of Punjabi SpeakingChildren in words per minute (WPM)---Spontaneous Speech

	Males	Females	Statistical Significance
Range	127-156	130-152	No significant
		difference	
Mean	149.5	145.3	
SD	13.2	15.1	
t rroling	$-0.207 \cdot n > 0$	5	

t- value=0.297; p>.05

description and spontaneous speech are shown in tables 1 to 3.

Since there was no significant difference between males' and females' rate of speech in three different speech tasks, the data were combined for further analysis (Table 4).

Table 4 shows the normative values of the rate of speech of Punjabi speaking for male and female children in words per minute (WPM) in terms of range, mean and standard deviation.

TABLE 4
The Rate of Speech of Punjabi speaking Children in words per minute (WPM) for Males and Females

Speech Task	Range	Mean	S.D
Reading	148-216	185.7	18.3
Picture description	139-171	153.6	15.4
Spontaneous Speech	127-156	148.3	14.7

TABLE 5
Comparison between reading and picture description speech tasks (WPM)

	Reading	Picture description	Statistical significance
Range	148-216	139-171	Significant difference
Mean	185.7	153.6	
SD	18.3	15.4	

t-value=5.384; p<0.05

TABLE 6
Comparison between reading and Spontaneous Speech tasks (WPM)

	Reading	Spontaneous Speech	Statistical Significance
Range	148-216	127-156	No significant difference
Mean	185.7	148.3	
SD	18.3	14.7	

t-value=4.749; p<0.05

TABLE 7

Comparison between picture description and Spontaneous Speech tasks (WPM)

	Picture description	Spontaneous on Speech	Statistical significance
Range	139-171	127-156	No significant difference
Mean SD	153.6 15.4	148.3 14.7	
SD.	13.7	17.7	

t-value=0.243; p>0.05

TABLE 8

Co-efficient of correlation for words per minute WPM				
Co-efficient of correlation by two judges	0.981 (98%)			
Co-efficient of correlation by the same				
judge at different times	0.997 (99%)			

The student t-test showed that there was no significant difference between the rates of speech of male and female subjects. The difference was significant between the tasks of reading and picture description as well as reading and spontaneous speech, while the difference was not significant between the tasks of picture description and spontaneous speech, as shown in the tables 4 to 6.

The co-efficient of correlation for measurements at different times and different judges is shown in the table 8.

DISCUSSION

This study was carried out with an aim to determine the rate of speech of children in Punjabi language. In order to minimize the effect of age, the children in the age range of 10-14 years were selected. It was observed that there were no significant differences between the rate of speech of male and female children. This corroborates with most of the adult studies carried out in western languages as well as Indian languages such as Punjabi, ⁷ Kannada¹¹ and Oriya.⁸

According to Yuan, Liberman, Cieri (2006)⁶ males tend to speak faster than females, the difference between them is, however, very small, only about 4 to 5 words or characters per minute. Whereas, Robb, Maclagan, Chen, (2004)⁵ state that there were no gender differences in speaking rate or articulation rate found for either variety of English. Kaushal et. al. also reported no statistically significant difference between rate of speech for males and females in the Punjabi speaking adults for the speech tasks of reading and picture description. Venkatesh, Purushottam and Poornima (1982)¹¹ reported no significant difference between males and females in reading or spontaneous speech in Kannada. Similarly, Banik and Sashidhar (1989)⁸ compared the spontaneous speech rate of Oriya speakers between males and females and observed no significant difference.

The rate of speech of Punjabi speaking children was highest for the speech task of reading followed by picture description and then by spontaneous speech. The rate of speech in the task of reading was significantly higher from that in the other speech tasks of picture description and spontaneous speech, the difference was not significant between the tasks of description and spontaneous speech. Similar findings have been reported by Rathna and Bhardwaj (1977)⁷ for adults.

While further comparing the present study on Punjabi speaking children with the cross- linguistic study,⁷ it was found that in reading and picture description speech tasks, in terms of words-per-minute, Marathi, Kannada, and Tamil languages are slower than Punjabi language.On comparing the present study with a study⁹ of Punjabi speaking adults, it was observed that on an average in the speech task of reading the children spoke faster than the adults.

Further the investigators⁷ studying the languages Hindi, Punjabi, Kannada, Tamil and Marathi, reported that the rate of speech in spontaneous speech tasks in terms of WPM was slower than rate of speech in reading tasks in all above mentioned languages except Kannada language. These findings for Punjabi language are in accordance with the present study. This could be because in the task of reading uncertainty is reduced due to presence of written text which tends to eliminate the need for word retrieval.

The inter-judge and intra-judge variability was assessed for measurement of words-per-minute. High co-efficient of correlation between the calculations made by two judges {0.981 (98%)} and the two calculations made by the same judge at different times {0.997 (99%)} was observed. In concordance with the present study, Alpermann A et al, ¹² in a recent study, reported satisfactory inter-judge and intra-judge agreement above 80%. This indicates that the calculations of words per minute were considered to be highly reliable measure.

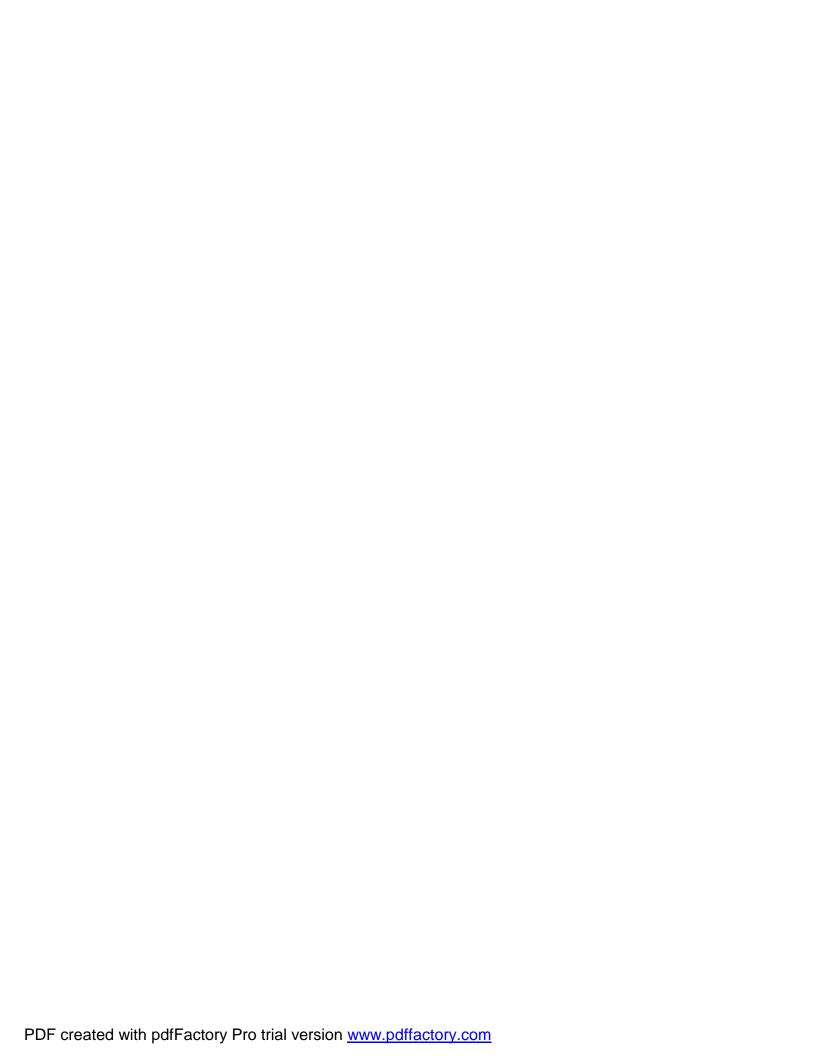
CONCLUSIONS

The rates of speech for male and female children speakers in the age range of 10-14 years were not significantly different for Punjabi language. It was in the range of 148-216 words-per-minute (wpm) during reading; 139-171 wpm during picture description and 127-156 wpm during spontaneous speech. It was significantly higher in

the task of reading than the tasks of picture description or spontaneous speech. There was no significant difference between the tasks of picture description and spontaneous speech. Therefore either of the speech tasks could be used to assess rate of speech. Therefore, it may be concluded that, in order to reliably assess rate of speech, either of the speech tasks could be used by measuring words per minute.

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Spontaneous rupture of spleen: A case report and review of literature

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ABSTRACT

Splenic rupture is a well-known complication of abdominal trauma. Splenic rupture without history of trauma also has been reported. Atraumatic splenic rupture is an uncommon and potentially fatal clinical entity. Immediate diagnosis and early surgical treatment can be lifesaving. We present a case report of splenic rupture with no history of trauma and not abnormal findings on pathologic examination of spleen that was successfully treated with splenectomy.

Keywords: Splenic rupture; abdominal trauma

INTRODUCTION

Rupture of spleen is a common occurrence associated with trauma, infectious diseases, neoplastic and many systemic disorders affecting the reticuloendothelial systems (eg.CML, Hepatitis, malaria).

There have been reports of spontaneous rupture of spleen in the absence of disease, but a trivial insult such as coughing and vomiting but non traumatic spontaneous rupture is extremely rare entity. Orloff and Peskin¹ had suggested few criteria for labelling any case as spontaneous rupture of spleen: (i) no history of trauma; (ii) absence of any disease affecting spleen directly or indirectly; (iii) absence of perisplenic adhesions or scarring; and (iv) presence of normal spleen, macroscopically and microscopically. Ultrasound by experienced investigators is reliable method of diagnosis.

CASE REPORT

We report a case of 36 yrs old male who developed fever, moderated to high grade, not associated with chills and rigors but headache and bodyache. He had 1-2 episodes of vomiting. After 3 days he had severe pain in left upper quadrant pain which was sudden in onset, radiating to back and left shoulder. He was taken to hospital after initial treatment from village. He was referred to our hospital in view of shock. At the time of admission patient

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was having dyspnea with altered mental status. Pulse was 110 min. BP 60 mm Hg. Pallor present. Per abdomen examination revealed tenderness. Chest was bilaterally clear. Patient was intubated due to respiratory distress. CECT (Fig. 1) abdomen was done which showed gross hemoperitoneum with perisplenic hematoma. Investigations were: Hb: 8 gm%. Platelets: 45000. TLC: 5000. Tbil 1.85, BU/S Cr: 27/1.3, SGOT/PT: 35/ 31. Blood group: B positive. PTI: 80%. BT/CT: 2.44/ 7.58 min, Dengue serology negative, malarial parasite antigen negative. Patient was taken up for exploratory

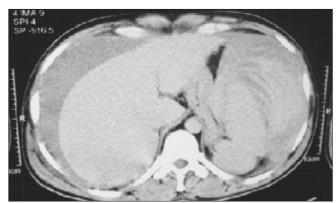


Figure 1: CECT scan revealing large hematoma of spleen



Figure 2: Intraoperative picture showing hematoma around spleen

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laparotomy which showed gross hemoperinoneum with hematoma around spleen which was intact except for capsular tear on surface (Fig 2). Splenectomy was done. Patient was discharged on 6th post-operative day and he is still alive and healthy.

DISCUSSION

Spontaneous splenic rupture is a rare entity and is initially very difficult to diagnose. Rupture of the spleen has been described in varieties of medical and surgical conditions such as infections, haematologic diseases, neoplastic, SLE² or even pancreatitis³. Traumatic rupture of a normal spleen is a common result of high velocity trauma. However, spontaneous rupture (in the absence of either trauma or disease) can also occur following trivial insults such as vomiting^{4,5} and coughing^{6,7}. Some 632 publications reporting 845 patients were identified by Renzulli P et al⁴. Six major aetiological groups were defined: neoplastic (30.3 per cent), infectious (27.3 per cent), inflammatory, non-infectious (20.0 per cent), drugand treatment-related (9.2 per cent) and mechanical (6.8 per cent) disorders, and normal spleen (6.4 per cent). Treatment comprised total splenectomy (84.1 per cent), organ-preserving surgery (1.2 per cent) or conservative measures (14.7 per cent). The ASR-related mortality rate was 12.2 per cent. The spleen was normal in 7.0 per cent (atraumatic-idiopathic rupture). Spontaneous splenic rupture requires a high index of suspicion for diagnosis with abdominal pain and should be considered in the differential diagnosis when a patient without any trauma history has abdominal pain with unexplained hypotension.

There are many different speculations regarding the cause of this rare clinical entity, but most of these theories lack strong evidence to support them. These theories include^{1,8}

- Localized involvement of the spleen with a pathologic process, which upon rupture all evidence of pathologic changes are destroyed.
- 2. Reflex spasm of splenic vein causing acute splenic congestion.
- 3. Portal venous congestion with chronic splenic congestion.

- 4. Abnormally mobile spleen that undergoes recurrent torsions and the resultant
- 5. congestion leads to rupture. Rupture of a degenerative or aneurysmal splenic artery.
- 6. Forgotten or unnoticed trauma.
- 7. Sudden increase in abdominal pressure leads to rupture (i.e. defecation, weight lifting, sexual intercourse).

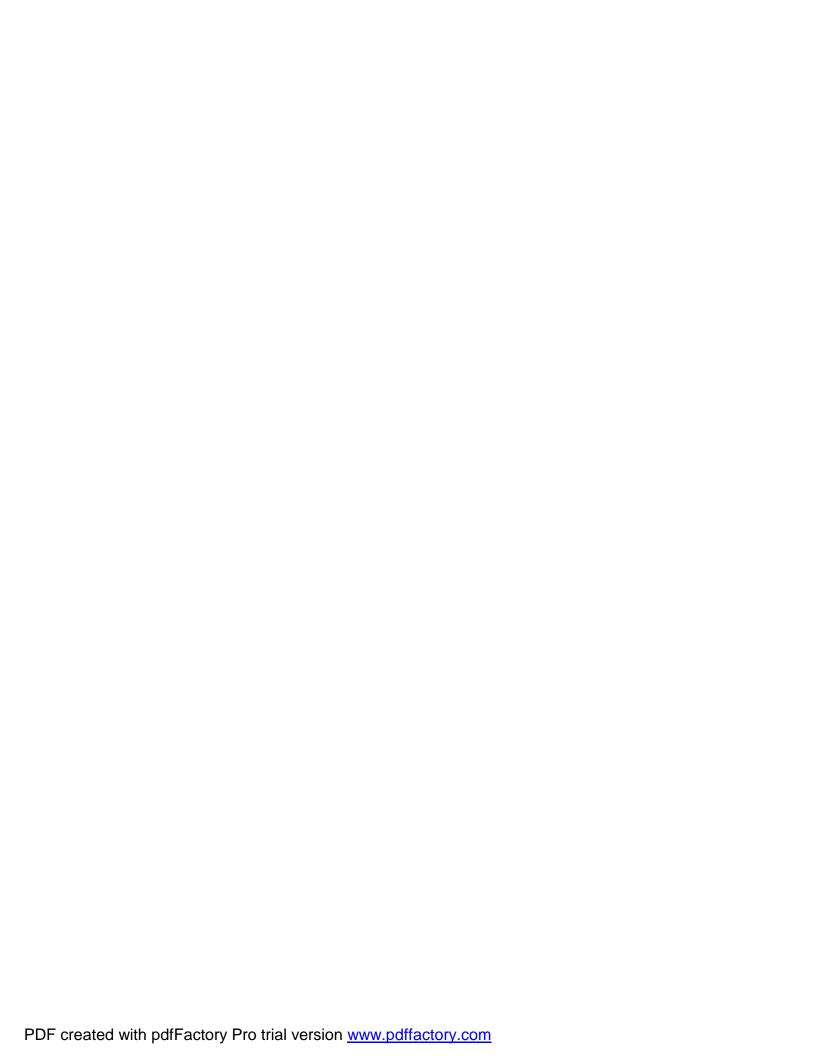
Splenic rupture with hemoperitoneum should be managed with laparotomy and splenectomy. High index of suspicion is needed to detect this patholgy early.

CONCLUSION

In summary, primary spontaneous splenic rupture is a rare entity and needs a high index of suspicion for diagnosis. Abdominal CT scan is very helpful to detect this potentially fatal condition. Other causes like inflammatory, neoplastic, and infectious should be considered in differential diagnosis.

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Rare foreign body in airway- an anesthetic challenge

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ABSTRACT

Foreign body (FB) in airway is a potential life threatening clinical situation. Rigid ventilating bronchoscope is usually required for its removal under general anesthesia (GA). Removal of FB from airway is an anesthetic challenge due to sharing of common airway by otolaryngologist and anesthesiologist. It requires utmost skills and thorough knowledge of the physiological changes associated with lodgment of the FB and closed loop communication of anesthesiologist with ENT surgeon during perioperative period. Here, we are presenting a case with successful anesthetic management for removal of rare FB which was accidentally lodged in left main bronchus.

Keywords: Foreign body; General anesthesia; Bronchoscopy, Airway

INTRODUCTION

Foreign body (FB) aspiration is one of the common emergencies seen in pediatric age group particularly in infants. ^{1,2} Moreover, otolaryngologist and anesthesiologist share common ends for working in operation theatre and thus anesthetic management for removal of FB has always been a challenge. These patients are prone to bronchospasm due to associated inflammatory changes and edema in airways. ² Here, we are presenting a case of rare foreign body aspiration posted for rigid bronchoscopy with successful anesthetic management.

CASE REPORT

A 4 year old female child weighing 12 kg was admitted to otolaryngology department for evaluation of intractable dry cough since last one month. The cough was associated with fever and shortness of breath. Father of child revealed history of unknown foreign body aspiration about 2 months back. The fever was low grade and continuous for last 7 days with loss of appetite. The patient developed difficulty in breathing which aggravated since 2 days. No other significant history was noted. General physical examination of the child was normal. Systemic examination of child was done. There was mild intercostal

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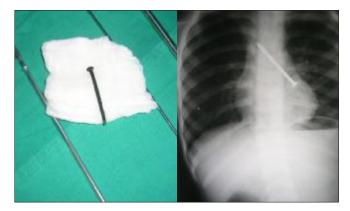


Figure 1 Showing radiological appearance of foreign body (nail)

recession with tracheal tug seen on examination of the chest. On auscultation, coarse conducted breath sounds with occasional ronchi were heard, more on left upper and middle zone of the chest. Routine investigations were done which includes hemoglobin -11.2 gm/dl, total lymphocyte count (TLC)–13600/mm³, and erythrocyte sedimentation rate (ESR)-13 mm in first hour.

Chest X-ray (AP view) showed left sided FB in main bronchus about 2.5 cm long and it was shaped like a nail (Figure 1).

Rigid bronchoscopy to extract the FB was planned under general anesthesia. Written informed consent with risk involved about the procedure and the anticipated complications were explained to the parents. Preoperatively before administration of general anesthesia, child chest condition was optimized. Child was administered antibiotics (Ceftriaxone 500 mg IV) and was nebulized with bronchodilators (.3 mg of levosalbutamol)

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prior to the institution of general anesthetics. Child was transferred immediately to operating room (OR) for planned rigid bronchoscopic procedure. Standard monitoring was instituted, comprising electrocardiograph (ECG), noninvasive blood pressure (NIBP) and pulse oximeter (SPO2) in Datex S5® monitor. Premedication included glycopyrrolate (60micro gm IV), hydrocortisone (25mgIV) and fentanyl (30 micro gm IV). Preoxygenation was done with 100% oxygen for 5 minutes using Mapelson E circuit. Induction of anesthesia was done gradually with sevoflurane (4%) in 100% oxygen preserving the spontaneous ventilation. After ensuring adequate mask ventilation, suxamethonium (10mg IV) was given for muscle relaxation. A nasal airway of size 5.0 cm was introduced in right nostril. A universal connector of standard endotracheal tube was mounted on top of the nasal airway to which oxygen tubing was attached. An oxygen flow of 4l/min was allowed for oxygen enrichment during the period of apnea when the airway manipulation was to be done by the surgeon. Once the ventilating bronchoscope was introduced beyond glottic opening, the anesthesia circuit was attached to the side arm of the bronchoscope. Sevoflurane in 100% oxygen and intermittent dose of suxamethonium was used for maintenance of anesthesia. Suction of secretion was permitted to a short period to prevent hypoxia during surgical intervention. FB was extracted after a period of 18 minutes with the help of long forceps under bronchoscopic vision without any complication. Child was ventilated with 100% oxygen till the spontaneous respiratory efforts were resumed. Post intervention, child was given injection dexamethasone (2mg IV) in view of anticipated airway edema due to surgical intervention. Ondansetron (2 mg IV) was immediately given to counteract incidence of postoperative nausea and vomiting (PONV). Once the child was fully awake and has adequate respiratory efforts the child was shifted to postanesthesia care unit (PACU) for further monitoring of the vitals. Afterwards the child was shifted to pediatric intensive care unit (PICU) for next 24 hours for further optimization of the chest condition. Child was then shifted to pediatric ward thereafter and was discharged on seventh day post operatively. No complication was observed in postoperative period and child went home.

DISCUSSION

Infants and children are most commonly affected from aspiration of foreign body. ^{1,2} History of aspiration may not always be elicited in all patients. ³For removal of foreign

body open rigid ventilating bronchoscope is most widely used in children. Aspiration of non vegetative FB (like metallic nail, ball) and its presence in left main bronchus is not very common. Metallic FB causes mucosal irritation but fortunately they take time to completely occlude the bronchial lumen. Vegetative FB ingestion, its incidence, pathophysiology and management is somewhat different when compared to the metallic FB. They tend to cause chemical bronchitis and mucosal edema which lead to atelectasis or obstructive emphysema. Rechest X-Ray is diagnostic in majority of cases. Here, chest X-ray (AP view) showed a 2-3 cm long FB, probably of metallic nature, in left main bronchus. There was no other abnormality detected in lung fields may be due to partial patency of left main bronchus.

A good team effort amongst the anesthesiologist, otolaryngologist is required for successful intervention and appropriate management. Rigid bronchoscopy may lead to reflex vagal stimulation, severe cardiovascular compromise, hypoxia and bronchospasm. The incidence of cardiac arrhythmia is always increased in presence of hypoxia. An appropriate and safe planning of anesthetic technique is required in managing these patients in perioperative period. This includes adequate analgesia, adequate anesthetic depth, good muscle relaxation. Rapid recovery of cough reflex is desirable.

Difficult airway cart should always be prepared prior to these surgical manipulations to manage any unintentional catastrophic events due to intense airway manipulations. An anticholinergic agent (preferably glycopyrrolate) should be given prior to the intervention, acting as an antisalogougue and to counteract reflex vagal stimulation by the instrumentation. Hydrocortisone is generally used to prevent post operative subglottic and airway edema. Preoxygenation provides additional safety by preventing hypoxia during apneic period of surgery. Inhalational induction in these patients is preferred as it preserves the patient spontaneous respiratory efforts, much needed in managing difficult airway. Sevoflurane is the inhalational agent of choice particularly in pediatric patients due to its property of providing smooth and quick induction without irritating the lower airway structures. Short acting muscle relaxant like suxamethonium is preferred as it increases the margin of safety in these patients with anticipated difficult intubation. Prolong controlled ventilation is avoided as they may increase the possibility of lodgement of FB further distal in smaller airways, leading to severe airway obstruction and lung atelectasis. Oxygen enrichment can be done to avoid hypoxia, as done in this child via nasal airway to provide oxygenation during the period of apnea created by the surgeon for instrumentation. The maintenance of anesthesia was done by ventilating the patient through side arm of bronchoscope with oxygen, sevoflurane and intermittent dose of suxamethonium. Non depolarizing muscle relaxants were generally avoided in anticipation of short period of surgery. If in case there is suspicion of impaction of the FB which might prolong the surgical period of intervention, an intermediate acting muscle relaxant can be given. Suctioning of secretions and blood should be restricted to a limited duration to prevent hypoxia and atelectasis. 10,11

Other techniques of ventilation during bronchoscopy can be used beside conventional ventilation through side arm of bronchoscope. There is venturi injector (manual jet ventilation) which basically provides oxygenation with high pressure source (50psi) via pressure regulator. The in line manual switches with one to one and half inch 16-18 gauge needle is connected to side arm of bronchoscope. Intermittent jet of oxygen can be delivered without interruption of ventilation. Another simpler yet effective technique is by providing oxygen through small size suction catheter introduced along the side of bronchoscope into larynx and connected to the oxygen source. An oxygen of flow rate of approximately 10l/min is administered via this catheter into the subglottic airway path. The major disadvantage of this technique is continuous rise in carbon dioxide levels and hence not recommended for prolong procedures.

The peculiar history of foreign body ingestion at any time should never be ignored. This can provide us the information of the nature of the FB and its appropriate management thereafter. This should always be followed by detail general and systemic examination to find out the severity of infliction caused by it.

CONCLUSION

Removal of tracheobronchial FB requires utmost skills

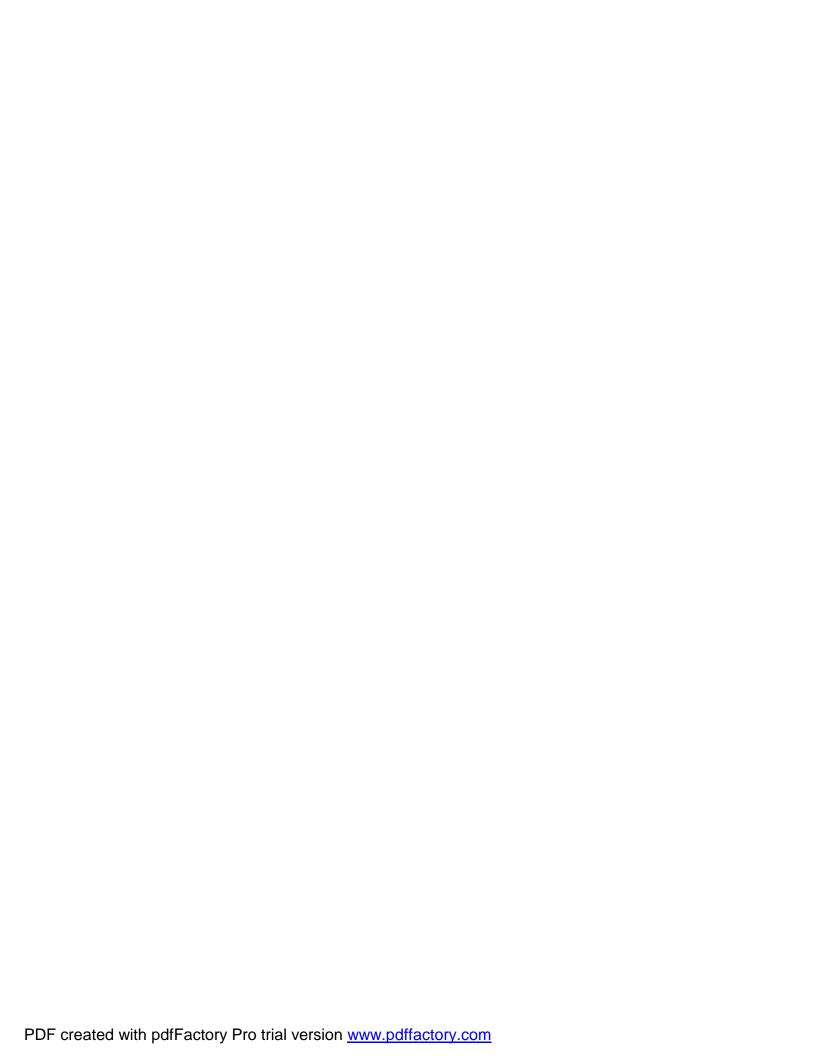
and experience of the anesthesiologist and concerned surgeon. Comprehensive preoperative preparation and effective team work is required for managing these cases. Ensuring proper functioning of the ventilating bronchoscopes and preventing period of hypoxia during the intervention is the crux of the management during intraoperative period. The post-operative care with intensive monitoring is mandatory to avoid any further complications. This also provides us a window for rapid optimization of patient general condition ensuring fast tracking for discharge from the hospital.

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Erratum

This is with reference to manuscript entitled "Cardiopulmonary Resucitation Teaching and Traning Programmes: Our Experience" published in JMCC 2011, Vol 1, No. 2 with authors Manpreet Singh, Lakesh Anand, Dheeraj Kapoor, Satinder Gombar. On the page No. 59 in title 'Abstract' para 2 line 1, Introduction para 2 line 3, and on page 60 title Methods para 1, line 2 the October 2011 and November 2011 may be read as August 2011.



Ancient cystic schawannomas: case series and review of literature

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ABSTRACT

Schwannomas can occur virtually anywhere in body where peripheral or cranial nerves are present, and they correspond to 8% of primary intracranial and 29% of primary spinal tumours. Interestingly, large schwannomas within the lumbar spine may go unnoticed for a large time span mainly due to indolent growth of the tumor and the paucity of symptoms generated. With a more malleable structure, a cystic schwannoma may pose a challenge to diagnosis.

We aim to emphasize the differential diagnosis of cystic masses of the intraspinal region by illustrating the clinical picture, imaging findings, treatment and prognosis of this unique disease by presenting two case reports.

Keywords: Ancient Schwannomas; Cystic Schwannomas; Intraspinal Tumours

INTRODUCTION

Schwannomas can occur virtually anywhere in body where peripheral or cranial nerves are present and they correspond to 8% of primary intracranial and 29% of primary spinal tumours.^{1,2} Schwannomas occurring within the lumbar spine are not rare, but large and predominantly cystic schwannomas occurring in the Dorso-lumbar spine have rarely been demonstrated. Interestingly, large schwannomas within the lumbar spine may go unnoticed for a large time span mainly due to the indolent growth of the tumor and the paucity of symptoms generated. With a more malleable structure, a cystic schwannoma may pose a challenge to the diagnosis.3 Few cases of cystic nerve sheath tumours have been described in the literature. There is no report of multiple cystic nerve sheath tumours in literature as is the second case we are presenting.

We aim to emphasize the differential diagnosis of cystic masses of the intraspinal region by illustrating the clinical picture, imaging findings and treatment of this unique disease by presenting two case reports.

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CASE 1

A 60-year-old female without remarkable previous medical history was admitted in our Hospital with 18-month history of lumbar pain and radiation to both lower



Figure 1: T1 sagittal view showing hypointense SOL in thoracolumbar spine.

limbs. There was a progressively increasing difficulty in walking. Her general physical examination was normal. Her neurological examination disclosed signs of paraparesis with motor power grade 3/5 and spasticity in both lower limbs. She had decreased sensations below L1 dermatome.

Magnetic resonance imaging (MRI) depicted an extensive lesion 10cm x 2cm x 2cm extending from D11 to upper border of L2 level completely constituted by a large cyst and a small nodule. The lesion was hypointense (Figure 1) on T1 weighted image and hyperintense on T2 weighted images (Figure 2). The differential diagnosis of haemangioblastoma and ependymoma was kept.

Laminectomy (D11 to L2) was performed using a posterior midline approach to expose the dura, which was found to be thinned out, and tense. The Cystic mass had a greyish nodule measuring 10x10x8 mm.Complete excision by microsurgical technique was done. Water tight Duroplasty was done.



Figure 2: T2 sagittal view showing bright hyperintense SOL with a hypointense nodule in thoracolumbar spine

CASE 2



Figure 3: T2 sagittal view showing bright hyperintense SOL at cervico medullary junction and dorsal spine

A 45 year old male presented with inability to walk since 2 months and pain radiating to all four limbs (lower limb>upper limb)since last five years. On examination patient had spasticity in both lower limbs with ankle clonus bilaterally. Sensations were preserved. Bowel and bladder sensation was preserved.

MRI of whole spine was suggestive of two lesions one at cervicomedullary junction (Figure 3) and other at D2-3 level of dorsal spine. The lesions were of 1.5X1cm and 1.5x1.5 cm respectively. They were hyperintense on T2 signal. Differential diagnosis of arachnoid cyst and infectious cyst was kept.

Laminectomy at both levels i.e. C1 and partial C2 and D2-D3 was done and the lesion excised completely by microscopic technique. Both were cystic lesions with membrane and a small solid part.

Histological examination of the excised specimen revealed tumor composed of hypocellular and hypercellular areas showing interlacing bundles and



Figure 4: Showing cyst with membrane, solid and cystic parts

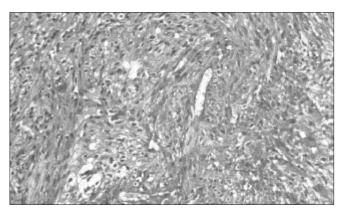


Figure 5: Photomicrograph of the specimen showing alternating Antoni A (hypercellular) and Antoni B (hypocellular) areas in a fibrillar background without any axons suggestive of cystic schwannoma (H&E, x100).

fascicles of spindle shaped cells with nuclear pallisading forming verocay bodies at places suggestive of schwannoma cell nuclei (Figure 5). The hypocellular areas showed areas of cystic change. There was no evidence of nerve infiltration or mitoses to suggest malignancy.

After an unremarkable postoperative period, both patients experienced a complete remission of preoperative symptoms. At a follow-up visit performed 6 months after surgery, the patients had reduced spasticity, were pain free and could walk without support.

DISCUSSION

Schwannomas are slow growing benign tumours. They are usually encapsulated, and rarely undergo malignant transformation. Schwannomas arise from the Schwann cells of the nerve sheath, and they comprise the most common tumor type affecting the peripheral nerves. Conspicuously, schwannomas are more frequently observed in patients with neurofibromatosis type 2. Women and men are equally affected by schwannomas, and the literature is prolific in showing cases of schwannomas affecting a large age range, albeit there is a predefined predilection for occurrence in between the fourth to sixth decades of life. 1,2

Benign schwannomas can occasionally display degenerative changes that are encompassed by cyst formation, calcifications, haemorrhage and hyalinization. When multiple degenerative changes are encountered, schwannomas fit into the category of "ancient schwannomas", which are extremely benign in course, rarely demanding any form of treatment. Specifically, the cystic degeneration of schwannomas occurring in isolation, i.e., without additional features of ancient

schwannomas, is rarely encountered. Cystic degenerations have been observed in the orbital region,⁵ in the olfactory groove,⁶ in the tentorial hiatus and posterior cavernous sinus,⁷ in the presacral region,^{8,9} within the pancreas,¹⁰ in the maxillary sinus,¹¹ within the spinal cord,¹² and intraventricular.¹³ Cystic schwannomas have also been observed surrounding cranial nerves such as the vestibular nerve,¹⁴ and within the jugular foramen.¹⁵

No radiographic findings are pathognomic for intraspinal schwannomas. However, imaging studies may reveal widening of the neural foramen, erosion of the pedicle, increased interpedicular distance, and scalloping of the adjacent vertebral body. MRI is the preferred imaging modality. Schwannomas generally have low-tointermediate signal intensity on T1-weighted images. On T2-weighted images, they may be heterogeneous with focal areas of hyperintensity and hypointensity, corresponding to cyst formation, haemorrhage, dense cellularity, and collagen deposition.[16] Very high intensity regions seen on T2- weighted images correspond to cystic degeneration with surrounding collagenous ûbrous tissue. Schwannomas do not always have the typical T2 appearance of benign neurofibromas, specifically a hyperintense rim of myxomatous tissue surrounding a hypointense centre of fibrocollageneous tissue. 17

Surgical treatment of cystic schwannomas can be very demanding because of the adhesion of the tumour capsule to the surrounding structures, fragile tumour capsules, and difficulty in identifying the arachnoidal planes. Early identification of the arachnoidal planes without opening of the cyst and sharp dissection may be useful. Complete excision without resultant neurological deficits may be feasible provided that there is no entrapment of nerve roots. ¹⁵ Prognosis is usually excellent with the exception of the melanotic variant, malignant forms, and cases of neurofibromatosis.

The differential diagnosis of such a large cyst includes a cystic neurofibroma, ¹⁸ ependymoma, epidermoid cyst, arachnoid cyst, cystic lymphangiomas, ¹⁹ cystic teratoma, ²⁰ and cystic meningioma. ²¹ Histopathological examination remains the mainstay of differentiation as clinicoradiographic features can be indistinguishable.

Less than fifty cases of cystic schwannoma or ancient schwannoma are reported in literature and only two of giant proportion are reported.²² Multiple Cystic schwannomas are not reported in literature.

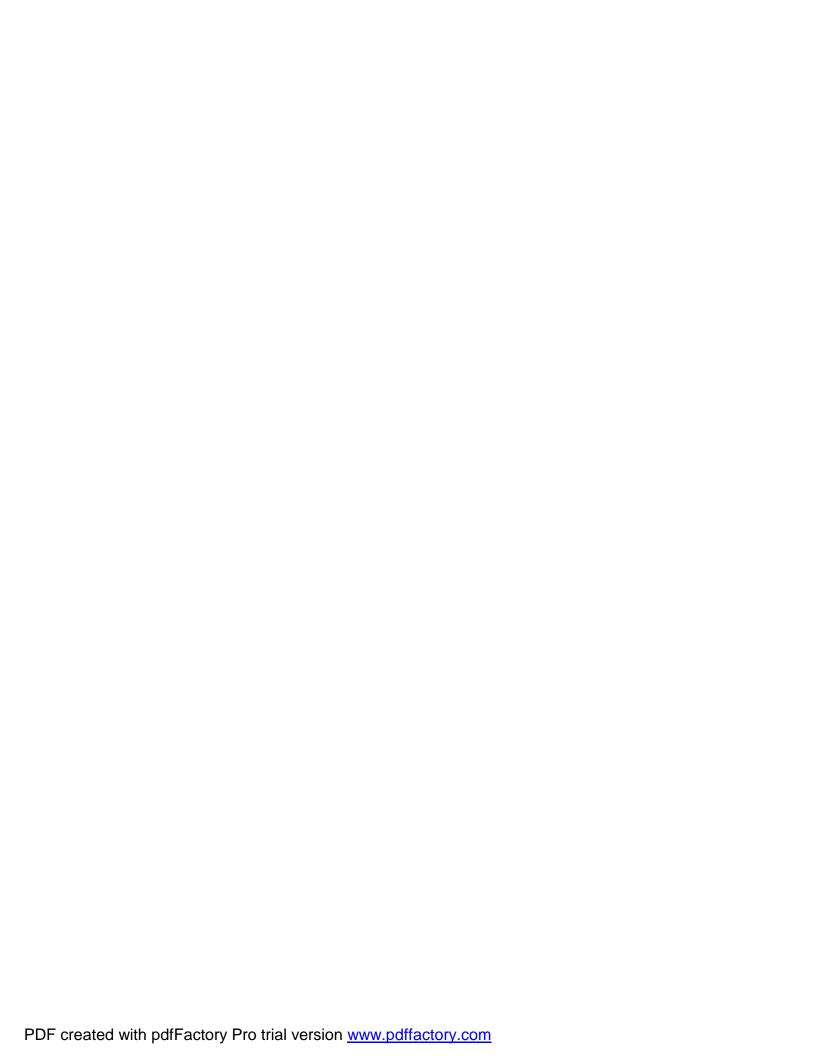
CONCLUSION

Cystic schwannoma is a rare entity and must be kept as a differential diagnosis of all cystic masses in spine. It is curable with good prognosis.

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Pyomyoma: a rare cause of acute abdomen in pregnancy

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ABSTRACT

Pyomyoma (suppurative leiomyoma) is an acute complication which occurs as a result of infarction and infection in a fibroid. Only a few cases are reported in literature some of which were seen in post menopausal women where they were presumed to be caused due to ischemia resulting from atherosclerosis associated with diabetes or hypertension. Amongst the rest, pyomyomaoccurred either post abortion or post partum and the cause was generally presumed to be ascending infection. This report documents a pyomyoma that presented spontaneously, as acute abdomen in an ongoing pregnancy.

Prompt identification and surgical treatment of a pyomyoma is important because its perforation and subsequent spillage of pus can lead to pyoperitoneum, acute respiratory distress syndrome and septic shock in the patient.

We know that diagnosis of acute abdomen during pregnancy can be difficult as a result of the anatomical and physiological changes associated with pregnancy. Hence, if a patient of acute abdominal pain with a previous history of uterine fibroid does not improve upon conservative management, we must think beyond the known red degeneration and keep a possibility of pyomyoma in mind.

Keywords: Pyomyoma, acute abdomen, red degeneration of fibroid

INTRODUCTION

Pyomyoma, or suppurative leiomyoma, is a rare and potentially fatal complication of uterine leiomyomas. Some cases occur as complications of pregnancy, while others are idiopathic occurring in postmenopausal women. As per literature there are 20 case reports of pyomyoma since 1945. The occurrence of pyomyoma after pregnancy termination, either spontaneous or induced, demonstrates the role of ascending infection. However the findings in our case suggest that it can insidiously develop following red degeneration of a fibroid during pregnancy. Since the perforation of pyomyoma with subsequent spillage of pus into the peritoneal cavity can lead to pyoperitonitis, septicemia and acute respiratory distress syndrome(ARDS); it needs timely intervention. The aim of this report is to highlight a potentially fatal condition for which we need to keep a high index of

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Dr. Bharti Goel, Assistant Professor Department of Gynecology & Obstetrics Government Medical College & Hospital Sector 32 B, Chandigarh, INDIA Email: bhartigoel14@gmail.com suspicion in a pregnant lady presenting with acute abdomen along with coexisting leiomyoma of the uterus.

CASE REPORT

A primigravida, aged 22 yrs presented in outpatient department at 38 wks of gestation with complaint of generalized pain in abdomen for three days. The pain was dull aching, non-radiating, with no aggravating or relieving factors. It was not associated with painful uterine contractions, leaking or bleeding per vaginum. There were no gastrointestinal or urinary complaints. She was a booked and supervised patient with no antenatal complications other than a small uterine fibroid 5 cm X 5 cm in anterior wall of body of uterus detected on a routine obstetric ultrasound at 20 weeks gestation. On examination her vitals were stable. Uterus corresponded to term size gestation with a single live fetus in cephalic presentation. There was a small swelling in the umbilical region approximately 5cm x 5cm in size. There was mild tenderness all over the uterus. Tone was not raised. There was no guarding over abdomen. Liver and spleen were not enlarged. Bowel sounds were normal. Ultrasound confirmed the findings. In addition, there was no retroplacental clot. The fibroid showed a variegated appearance and probe tenderness. Her routine



investigations were normal. A provisional diagnosis of red degeneration of the fibroid was made and the patient was managed conservatively with non-steroidal antiinflammatory drugs. She was kept in the labour ward for observation with a plan of normal vaginal delivery. Severity of pain in abdomen increased over the next two days. Repeat haemogram showed leucocytosis with neutrophilia. There was guarding and generalized tenderness associated with nausea and vomiting. Umbilical swelling became tender, soft, warm and fluctuant. There was no fever. On ultrasound examination a breach was noted in the anterior abdominal wall with bowel loops herniating in the periumbilical area. A diagnosis of strangulated paraumbilical hernia was made and the patient was taken up for laparotomy. Peroperatively we found a pedunculated fibroid of size 8cm X 6cm with pus pointing. The same was removed and sent for histopathology, the findings of which were consistent with pyomyoma. Aspirated pus was sent for culture which was reported as sterile. A live healthy baby boy was delivered by caesarean section. Rectus sheath did not reveal any defect or hernial sac. Patient received broad spectrum antibiotics. Her post-operative period was uneventful. She was discharged after stitch removal on day eight of surgery in satisfactory condition.

DISCUSSION

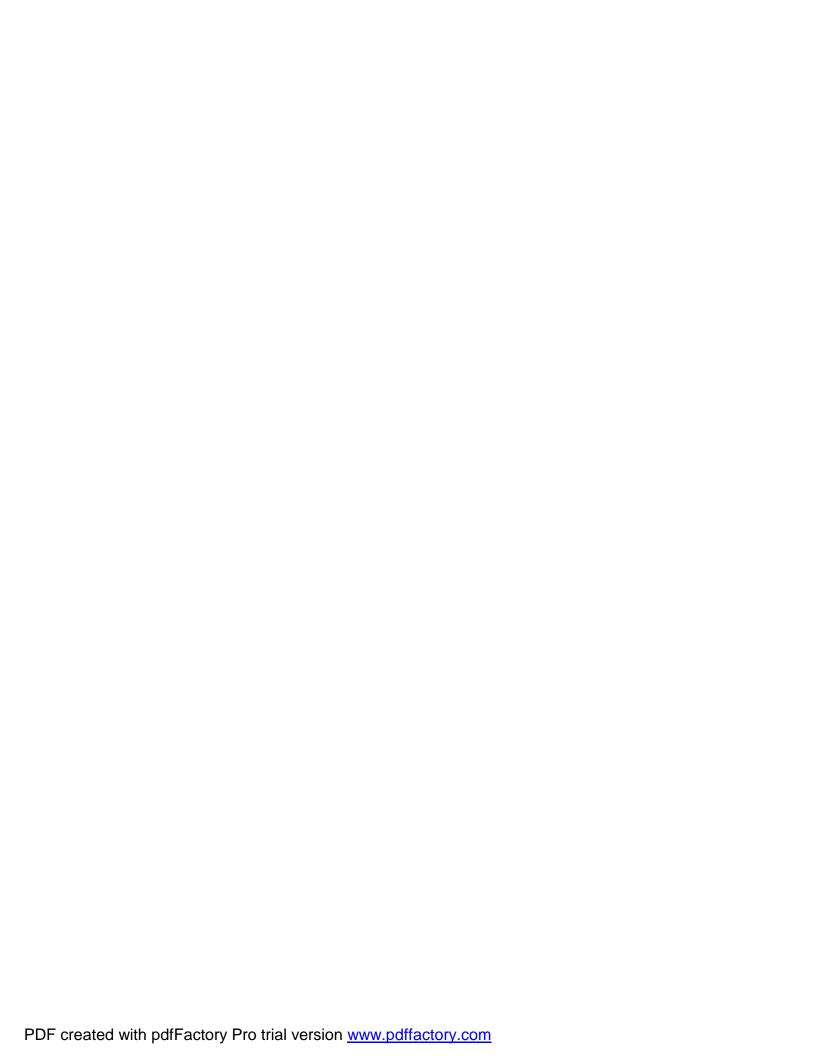
Pyomyoma, or suppurative leiomyoma, is a rare but potentially fatal complication of uterine leiomyomas. Etiology of pyomyoma is mainly infarction or infection of fibroid. Out of nearly hundred cases reported in the literature, only about 20 have occurred in the postantibiotic era. This implies a preventive role of antibiotics. More commonly reported in postmenopausal women;

atherosclerosis causing ischemia in association with diabetes or hypertension is presumed to be the cause. Amongst the rest, ascending infection post abortion or postpartum appears to be the preceding event¹. Our patient presented spontaneously and uniquely, as acute abdomen in an ongoing uncomplicated pregnancy with no high risk factor. Only one more case of sepsis in second trimester of an ongoing pregnancy due to pyomyoma has been described in literature².

The commonest complication of fibroid in pregnancy is the 'syndrome of painful myomas' variously described as red degeneration, hemorrhagic infarction or aseptic necrobiosis. In our patient the insidious development may have followed red degeneration of the fibroid. The site and presentation of the fibroid in the region of umbilicus and the ultrasound picture lead to misdiagnosis. Perforation of pyomyoma with subsequent spillage of pus can cause pyoperitoneum, ARDS and septic shock. Early diagnosis of pyomyoma is critical because of associated morbidity and mortality³. Ultrasound findings suggestive of pyomyoma have been described as presence of echogenic debris and reverberation artifact in a preexisting fibroid. Contrast enhanced CT scan in a non-pregnant patient can also demonstrate the presence of gas and debris in a pyomyoma⁴. The definitive treatment of a pyomyoma is hysterectomy or myomectomy with aggressive antibiotic therapy³. Nonsurgical treatment using ultrasound/CT guided drainage of pyomyoma has been tried successfully in two cases⁵. However, in absence of adequate response to this treatment, hysterectomy should be done. Although the condition is rare yet diagnosis should be considered in a patient presenting with acute abdomen when there is sepsis, coexisting uterine leiomyoma and no other source of infection especially if patient is not responding to conservative management.

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Ileosigmoid knot- an unusual volvulus : A case report

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ABSTRACT

The "ileo sigmoid knotting" (ISK) is a rare cause of acute intestinal obstruction. In ISK, the terminal ileum wraps around the base of redundant sigmoid colon and forms a knot. Term "compound volvulus" is also used for this condition. Hypermobile loop of ileum forms the active knot component, which wraps around the narrow base of the dolichosigmoid colon. Depending on the tightness of the knot - gangrene of both or single component of knot occurs. Incidence of gangrenous bowel in ISK has been found to be around 88%. Severe shock ensues due to sequestration of large volume of blood, peritonitis and endotoxemia. There is high mortality unless prompt and correct treatment is undertaken.

INTRODUCTION

Parker credited with having described the first patient with Ileosigmoid knot in 1845.¹ Ileosigmoid knot is an unusual clinical entity of small bowel obstruction in which the ileum wraps around the base of the sigmoid colon and forms a pseudoknot.² As the knot tightens, a double loop obstruction with rapid progression to gangrene of ileum as well as sigmoid colon. Preoperative diagnosis is difficult because of its infrequency and atypical radiographic findings.³ Here we report a case of 22 year male in whom diagnosis of ileosigmoid knot was made at emergency surgery.

CASE REPORT

A 22 year male presented with complaint of pain abdomen for 2 days, vomiting and constipation for one day. On examination, patient was having tachycardia, abdominal distension, generalized tenderness, guarding and positive rebound tenderness with absent bowel sounds. Investigations revealed Hb 14.5 gm/dl, total leucocyte count 28,900/cu mm with predominance of neutrophils count (90%), blood urea 49mg%, Serum creatinine 1.8mg%, S. amylase 51 IU/l, S. Na⁺/ k⁺ 132/4 meq/ L. X-ray abdomen erect film revealed multiple air-fluid levels with dilated gut loops. There was no free air under domes of the diaphragm. Provisional diagnosis of acute intestinal

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Dr. Rajesh Bansiwal Department of General Surgery, Block D (Level III) GMCH, Sector- 32, Chandigarh (India-160030) Mobile No. 9646121566 E-mail - rajbansiwal 72@yahoo.co.in obstruction was made. Patient was shifted to emergency operation theatre after resuscitation. Exploratory laparotomy was performed through midline vertical incision. There was one liter of foul smelling, blood stained fluid in the peritoneal cavity, Complex knotting was present between terminal ileum and sigmoid colon with gangrene of the sigmoid colon and distal one and half feet of terminal ileum, except for the last 6cm of the terminal ileum (Figure 1-4). Resection of gangrenous distal ileum and sigmoid colon was done with colorectal anastomosis with proximal ileostomy. Intraoperatively, diagnosis of "ileosigmoid knotting" was made also known as "compound volvulus". Post operative period was uneventful and patient was discharged on 7th post operative day. He was advised regular follow up and ileostomy closure after 6 weeks.

DISCUSSION

Ileosigmoid knot is an uncommon lesion; however it is a well recognized condition in certain African, Asian and middle east region. Although what causes an ileosigmoid knot is still unclear, three factor have been found responsible: a long small bowel mesentery and freely mobile small bowel; a long sigmoid colon on a narrow pedicle; and finally the ingestion of high bulk diet in the presence of an empty small bowel.²

Ileosigmoid knot has been categorized into three types. In type I, the ileum (active component) wraps itself around sigmoid colon (passive component) in a clockwise or anticlockwise direction (type A when clockwise and type B when anticlockwise). In type II, the sigmoid colon (active component) wraps itself around a loop of ileum (passive component) in a clockwise or anticlockwise

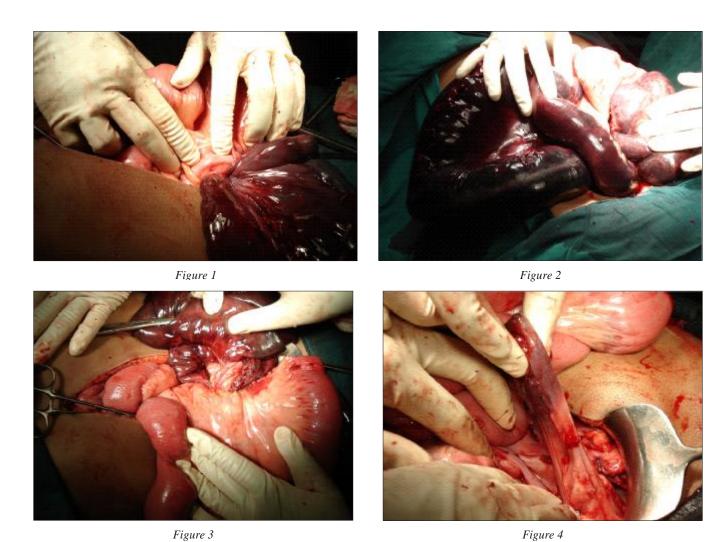


Figure 1-4 shows operative steps

direction. In type III, the Ileocaecal segment (active component) wraps itself around the sigmoid colon (passive component).

Predominant clinical features of ileosigmoid knot are that of acute intestinal obstruction. General condition of the patient deteriorates rapidly as ileosigmoid knot can rapidly progress to gangrene of ileum as well as sigmoid colon.

The radiographic findings of ileosigmoid knot include a double close loop obstruction, with the small intestinal loops in the upper left quadrant and dilated sigmoid loop in right.³ The finding in a CT scan suggestive of ileosigmoid knot include the 'Whirl sign' created by the twisted intestine and sigmoid mesocolon in ileosigmoid knot, medial deviation of the caecum and descending

colon.⁴ Preoperative diagnosis of ileosigmoid is difficult because of its infrequency and atypical radiographic findings. Consequently, this entity is usually diagnosed during exploratory laparotomy.³

Prompt laparotomy and resection of non viable or doubtful intestine in a patient with antibiotic therapy and adequate fluid and electrolyte resuscitation are key factors to diminish the mortality rate.³

The anatomical and pathological changes dictate the operative procedure. Various surgical procedures have been conducted in these patients.

When loops of the knot assessed as viable with certainty, untying of the knot after deflation is the sole operative maneuver required. This is also worth trying when the bowel is of questionable viability.⁵ When one

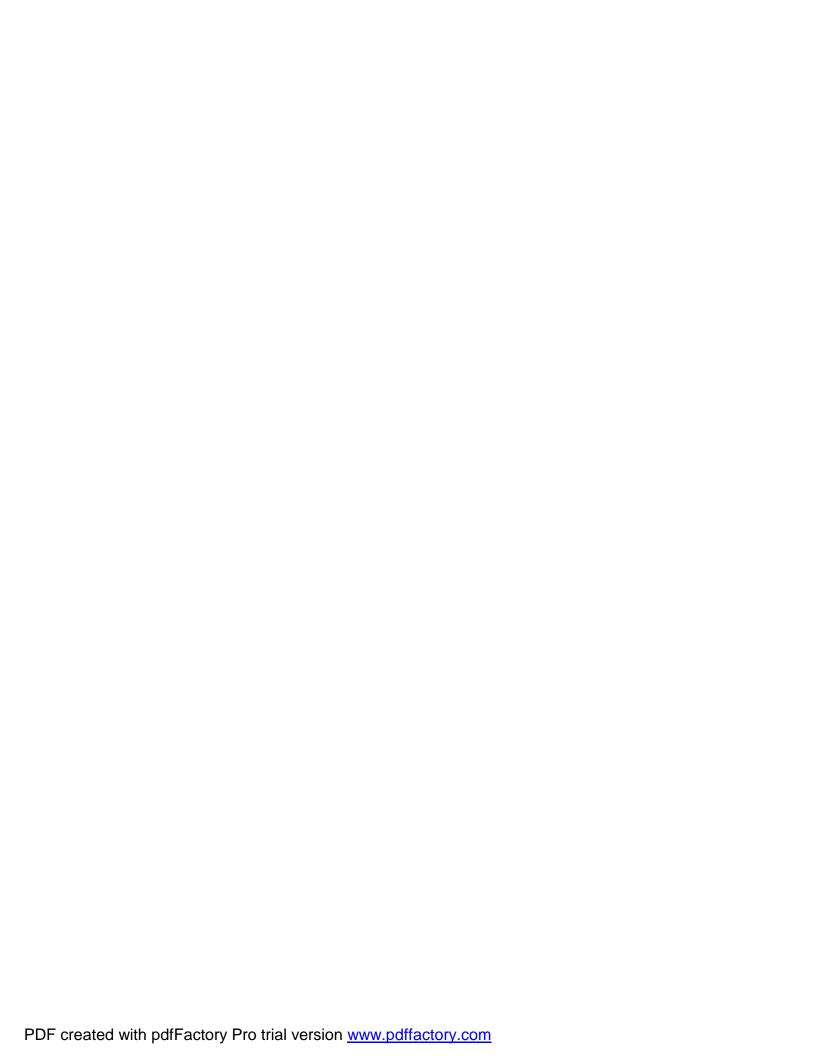
of the components of the knot develop gangrene, resection of the involved loop at its point of ingress and egress, simplify the untying of the knot. This result in preservation of the viable component.⁶ In the presence of gangrene of both loops of ileosigmoid knot, any attempt to untie the necrotic knot should be condemned. En bloc resection of both gangrenous components of knot is recommended.⁵ After resection of gangrenous small bowel, intestinal continuity is restored by end-to-end enteroenterostomy. If less than 10 cms of the terminal ileum proximal to the Ileocaecal valve appears frankly gangrenous or of doubtful viability, entero-enteric anastomosis should not be attempted. Terminal ileum is closed and enterocecal anastomosis performed bypassing the ileocaecal valve.⁵ After resection of the gangrenous sigmoid colon, Hartmann procedure is usually considered suitable; when the viability of the distal rectum is doubtful or the viable limb is too short to be exteriorized.⁵ The reconstruction of the colonic continuity may be established by immediate colorectal anastomosis, if the distal limb has good blood supply.6

CONCLUSION

We conclude that the Ileosigmoid knot is a rare cause of intestinal obstruction. It may rapidly progress to gangrene and shock so, early diagnosis, aggressive fluid resuscitation, preoperative antibiotic and prompt effective surgery are essential for better outcome despite difficulty in making a preoperative diagnosis.

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Subcutaneous emphysema in bronchial asthma: misdiagnosed as a drug reaction

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ABSTRACT

Pneumomediastinum and subcutaneous emphysema are unusual complications of acute asthma in children. Here, we present such a case which was misdiagnosed as drug reaction. The need for increased awareness among physicians dealing with children is being emphasized to diagnosis early and to treat effectively the mediastinal and subcutaneous emphysema during acute asthma in children.

Keywords: Asthma, pneumomediastinum, subcutaneous emphysema.

INTRODUCTION

Asthma is the most common chronic disease in children, with prevalence between 10% and 23%.¹ Children frequently visit pediatric emergency department for acute exacerbation of asthma. Mediastinal and subcutaneous emphysema are unusual complications of acute asthma in children but are important because of their sudden and usually unexpected onset. Mediastinal and subcutaneous emphysema may cause significant morbidity and rarely mortality if undiagnosed and untreated.².³ We present here a case of bronchial asthma with subcutaneous emphysema and pneumomediastinum with an emphasis to identify the condition timely and correctly to avoid delay in treatment and to prevent morbidity from asthma.

CASE REPORT

An 11 year old boy, presented to pediatric emergency with history of cough for five days and swelling of face for two days. He was known case of asthma but was not on regular inhaler therapy. On second day of cough, patient had consulted a local physician and was started on theophylline tablets. Cough did not respond to medication and next day patient had developed swelling of face. It was diagnosed as drug reaction to theophylline by local physician. Patient was administered pheniramine maleate and hydrocortisone and was referred to our

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Figure 1: A child with bronchial asthma complicated by subcutaneous emphysema; A. at presentation, B. after seven days of treatment.

centre. There was no history of fever, rash, itching, loose stools, oedema of feet, abdomen distension or seizures. At presentation, patient was afebrile, had heart rate of 106/min, respiratory rate of 34/min with minimal retractions and blood pressure of 106/68 mmHg. The child had subcutaneous swelling over chest, neck and face extending up to upper eyelids (Figure 1 A). Crepitus was present all over the swelling. Hamman's sign (the crunching sound synchronous with the heart beat) was also positive. Chest examination revealed bilateral wheezing. Rest of the systemic examination was unremarkable. Chest x-ray showed bilateral subcutaneous emphysema and pneumomediastinum without obvious pneumothorax (Figure 2). Hemogram, renal function and liver function tests were within normal limits. Based on history and examination findings diagnosis of acute asthma complicated by extensive subcutaneous emphysema and pneumomediastinum was considered which was confirmed by chest x-ray findings.

Child was managed conservatively as an acute exacerbation of asthma with oxygen supplementation, salbutamol and ipratropium nebulisation and steroids (initially intravenous hydrocortisone followed by oral prednisolone). He responded to treatment; respiratory



Figure 2: Chest x-ray of a child with asthma showing bilateral subcutaneous emphysema and pneumomediastinum.

distress settled completely within 12 hours and subcutaneous emphysema resolved gradually over seven days (Figure 1 B). He was discharged on inhaled fluticasone and salmeterol combination therapy and was asymptomatic on follow-up.

DISCUSSION

Kahn reported first case of subcutaneous emphysema as a complication of childhood asthma in 1927.⁴ Since then, there are case reports and case series on mediastinal and subcutaneous emphysema as a complication of childhood asthma.^{2,3,5-10} Air leak complications of asthma had been reported in about 1.1% of the severely asthmatic children.⁶ These complications may also recur in same individual.

Over-distension of alveoli from partial or complete airway obstruction during asthma exacerbations causes escape of air along perivascular sheath into mediastinum resulting in pneumomediastinum. Accumulation of large quantity of air in mediastinum under tension may compress large vessels and cause decrease in cardiac output. Further extension of air may then produce pneumothorax, pneumopericardium, retroperitoneal, epidural and retropharyngeal emphysema. 6.8,10,11 Air may also dissect through carotid perivascular sheaths producing subcutaneous emphysema in neck and face.

Causes of mediastinal and/or subcutaneous emphysema, other than acute asthma may include: forceful resuscitation of newborn, congenital stenosis of larynx, infections (pneumonia, laryngeal diphtheria, pertussis, acute obstructive laryngitis, measles, and

pulmonary tuberculosis), foreign body aspiration, anesthesia under pressure, surgical complications (surgery of chest, tracheotomy and tonsillectomy), trauma to chest and spontaneous mediastinal emphysema.^{2,5,12}

Clinical features of mediastinal emphysema, also called as pneumomediastinum, include: sudden onset dyspnea, anterior chest pain, associated subcutaneous emphysema of neck area, decreased cardiac dullness, Hamman's sign (cracking or crunching sound heard by auscultation over precordium) and venous distension of neck and head.^{2,3,5} Chest x-ray (antero-posterior and/or lateral view) usually confirms the diagnosis of mediastinal and subcutaneous emphysema. Although difficult to diagnose, pneumothorax should be suspected in presence of decreased/absent breath sounds with hyper-resonance on one side of chest in such cases with confirmation by chest x-ray. 6 The present case had typical clinical features of mediastinal and subcutaneous emphysema, but it was misdiagnosed by a local physician as drug reaction to theophylline. The reason for misdiagnosis may be unawareness of the physician of such sudden onset and extensive subcutaneous emphysema (including even upper eyelids) in acute asthma. The diagnosis was confirmed on chest x-ray. There was no evidence of pneumothorax in index case. The subcutaneous emphysema complicating acute asthma most frequently occur in the neck, face, anterior chest, axilla and sometimes extending to arms, dorsum of hands and upper thighs.^{2,3} The involvement of upper eyelids in particular, as in index case, is rarely described in literature.

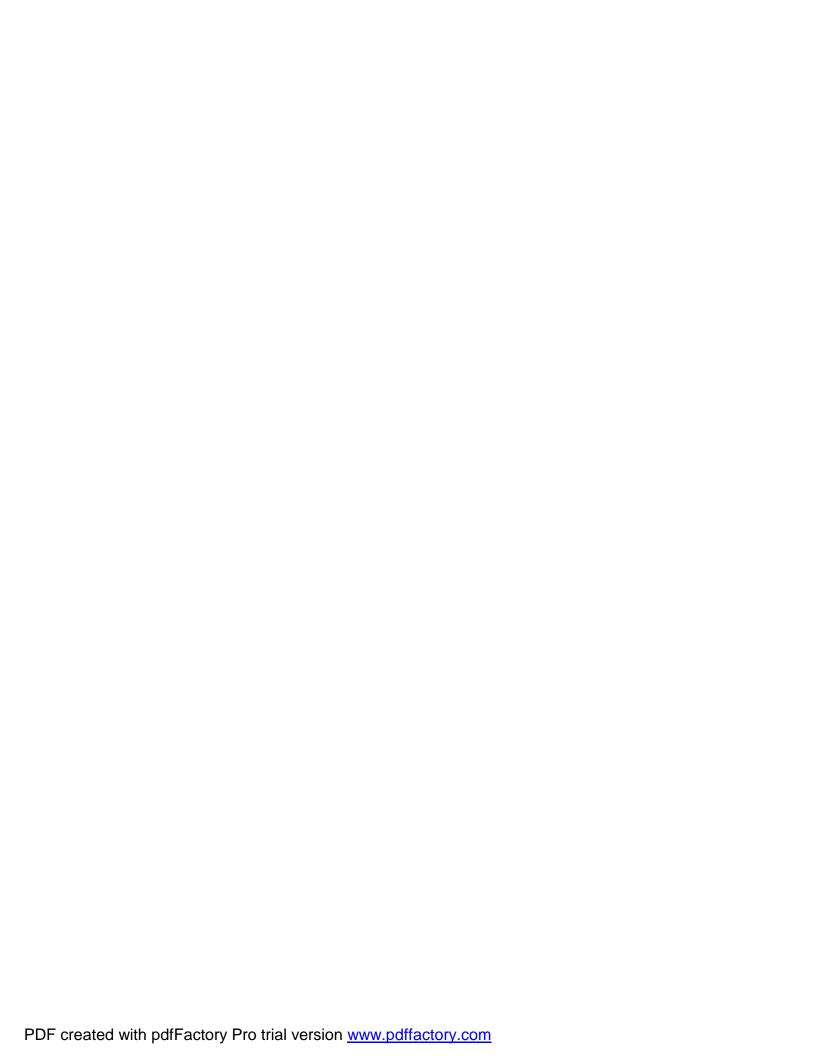
The management of mediastinal and subcutaneous emphysema is usually conservative and include treatment of underlying acute exacerbation of asthma by oxygen supplementation, bronchodilators and steroids with careful monitoring.^{2,3,13} Effective asthma treatment stops further flow of air in mediastinum by decreasing alveolar over distension and air already present there is absorbed gradually. Positive pressure ventilation should be avoided in these patients as much as possible because it may worsen the condition. Surgical intervention is usually not required except in cases of progressive worsening dyspnea, cyanosis, poor perfusion and tension pneumomediastinum despite adequate medical therapy and may include cervical mediastinotomy, needle aspiration of air or incision of the skin in the suprasternal notch by experts.^{5,13,14} The associated pneumothorax, if more than 20 percent, progressively increasing or under tension, may require chest tube drainage. We also managed the case conservatively and it responded. In 52 cases, reported by Odajima, average duration of subcutaneous emphysema was 6.2 days (range 3-11 days) and average duration of mediastinal emphysema was 6.5 days (range 3-11 days).³ In index case, the subcutaneous emphysema resolved in 7 days.

To conclude, increased awareness by physicians is needed to diagnosis early and to treat effectively the mediastinal and subcutaneous emphysema, an unusual complication of acute asthma in children.

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Unusual foreign body in male urethra - a sewing needle

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INTRODUCTION

Foreign body, especially sharp object is rare in male lower urinary tract. Most of them are self-inflicted as a result of exotic impulses, psychosexual problems, sexual curiosity or sexual practice while intoxicated.

CASE

A 14- year old boy presented with complaint of single episode of bleeding per urethra and dysuria since one day. There was no history of any abdominal pain or trauma. Patient was having no psychological problem. On physical examination, hard pointed mass was protruding from the ventral surface of the penis near penoscrotal junction (Fig 1). The distal end of swelling was not palpable. Digital rectal examination was normal. On urinalysis, RBCs were present . X-ray examination revealed a long needle in the penile area (Fig 2). On repeatedly asking, the patient admitted to have inserted the needle during masturbation. The needle was removed by ureatherotomy near penoscrotal junction under spinal anaesthesia. Wound was closed in layers and patient was catheterised. On seventh post operative day catheter and skin stitches were removed. After two weeks patient had epididmo-orchitis, which was managed conservatively.

DISCUSSION

The most common reason for self infliction of foreign object in male urethra is of erotic or sexual nature, especially mastrubation or sexual gratification. ¹⁻⁴ When the foreign body is inserted into the urethra it gets slipped into urinary bladder itself due to involuntary perineal muscle contraction. The length of passage that a foreign body can migrate from urethral meatus to bladder is approximately 20-25 cm in an adult erected penis.

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Figure 1: Needle protruding near penoscrotal junction.

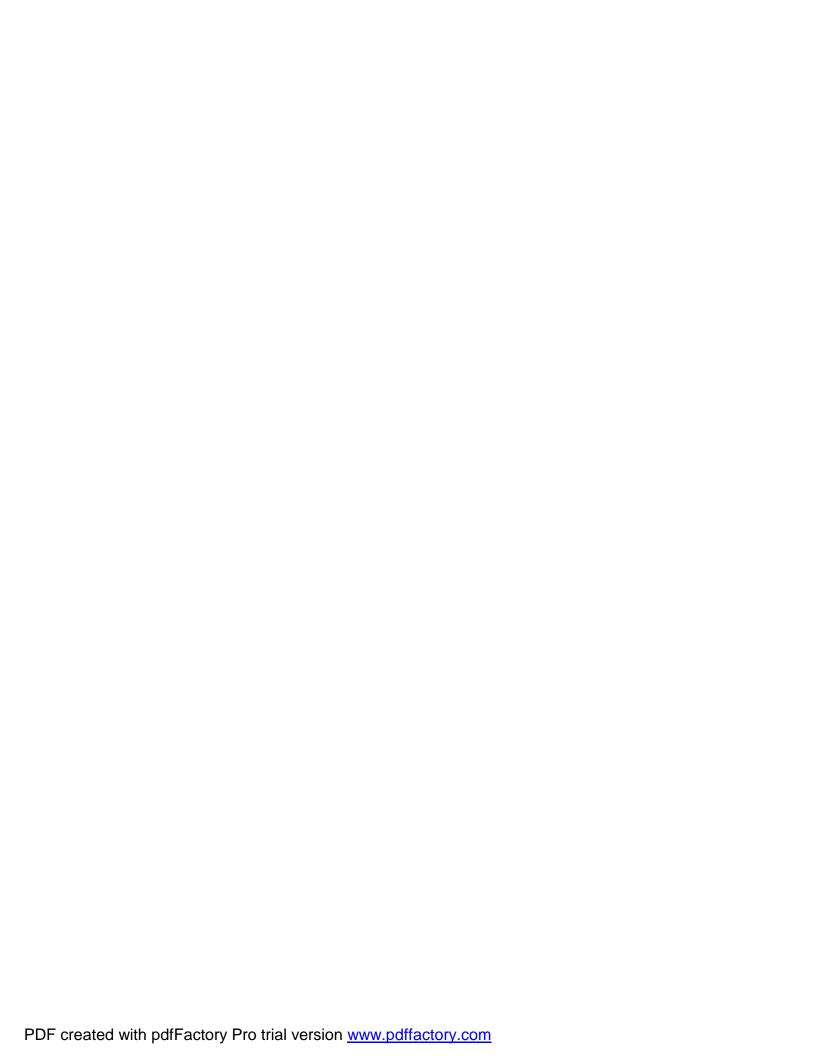


Figure 2: X-ray showing sewing needle in the penile area

Migration through the bulbous urethral curvature without significant injuries is surprising and still not fully explained.⁵ The suitable method of removing a urethral foreign body depends on the size and mobility of the object. Whenever possible endoscopic or minimally invasive techinques of removal should be used. In case of severe inflammation, surgical retrieval should be done. Common complications of urethral foreign body are urethritis, urethral tear with periurethral abscess and or fistula, haemorrhage and urethral diverticulum.⁶

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News We Can Use

1. Take aspirin a day, keep cancer away

We all know the role of Aspirin in reducing risk of vascular events. Recently aspirin is established as having antineoplastic effect particularly in colorectal tumours. A number of epidemiological studies, ^{1,2} randomised controlled trials on colon polyp recurrence, ³ and hereditary colorectal cancer syndromes ⁴⁻⁵ have shown that aspirin reduces incidence of colorectal cancer.

First convincing proof reveals - aspirin can prevent death from several cancers. Aspirin use daily at any dose is associated with a 21% risk reduction of cancer death and this benefit is evident after 5 years,⁶

In six primary prevention trials, low-dose aspirin has reduced risk of cancer incidence by 12%. Despite its effects in causing bleeding in the short-term, (it proved to be diminished over time). Finally, for most of us, after weighing risk-benefit of aspirin it seems to favour aspirin's long-term anticancer benefit.

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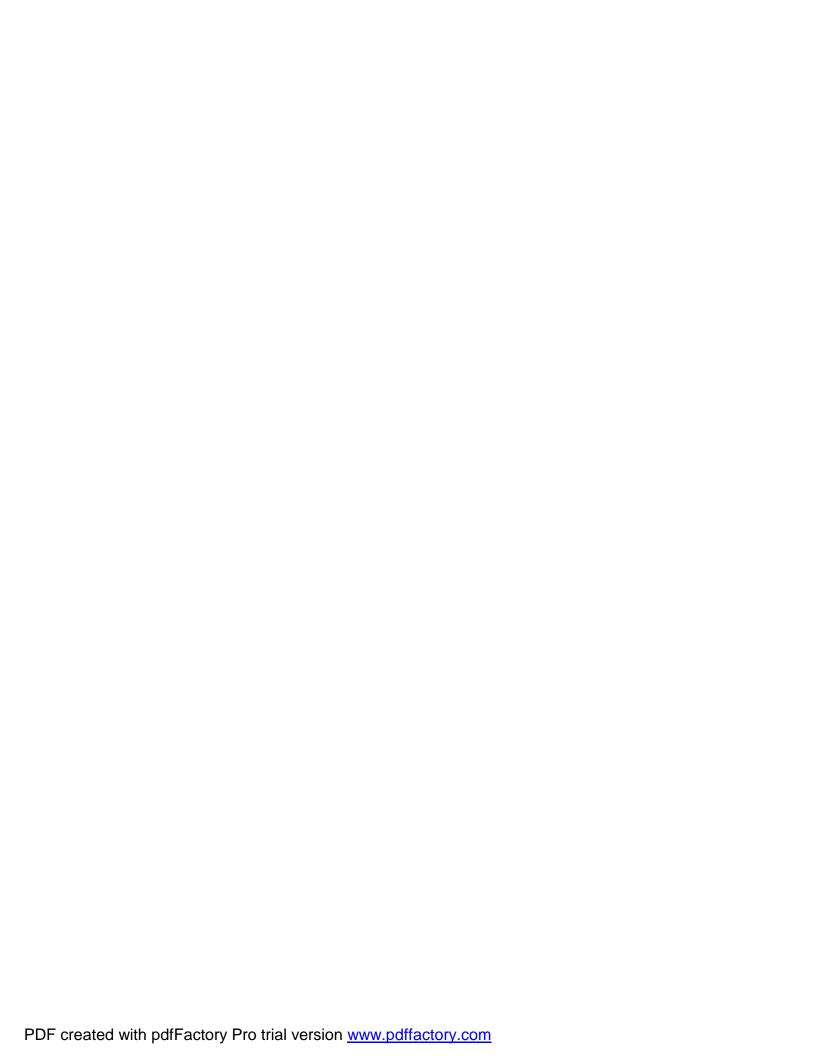
2. Boosting coffee - a paradigm shift

Contrary to our belief that coffee might increase the risk of cardiac disease as coffee drinking is associated with increased low density lipoprotein(LDL) cholesterol levels and short term increases in blood pressure, recently published prospective U.S. cohort study involving 400,000 participants and 52,000 deaths have revealed a dose-dependent inverse association between total mortality and mortality due to heart disease, respiratory disease, stroke, injuries and accidents, diabetes, and infections, but not cancer. 'As compared with men who did not drink coffee, men who drank 6 or more cups of coffee per day had a 10% lower risk of death, whereas women in this category of consumption had a 15% lower risk.' The contents of coffee like antioxidants, including polyphenols might be attributed for the benefit.

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Other:

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I. Standard journal article

If less than six authors, list all the authors.

Halpern SD, Ubel PA, Caplan AL. Solid-organ transplantation in HIV- infected patients. N Engl J Med. 2002;347:284-7.

If more than six authors, list the first six authors followed by et al.

Rose ME, Huerbin MB, Melick 1. Marion DW, Palmer AM, Schiding JK, et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res. 2002;935: 40-6.

2. Books and other monographs

Personal author(s)

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical Microbiology. 4th ed. SI. Louis: Mosby; 2002.

Chapter in a book

Meltzer PS, Kallioniemi A, Trent JM. Chromosome alterations in human solid tumors. In: Vogelstein B, Kinzler KW, editors. The genetic basis of human cancer. New York: McGraw-Hill; 2002. p. 93-113.

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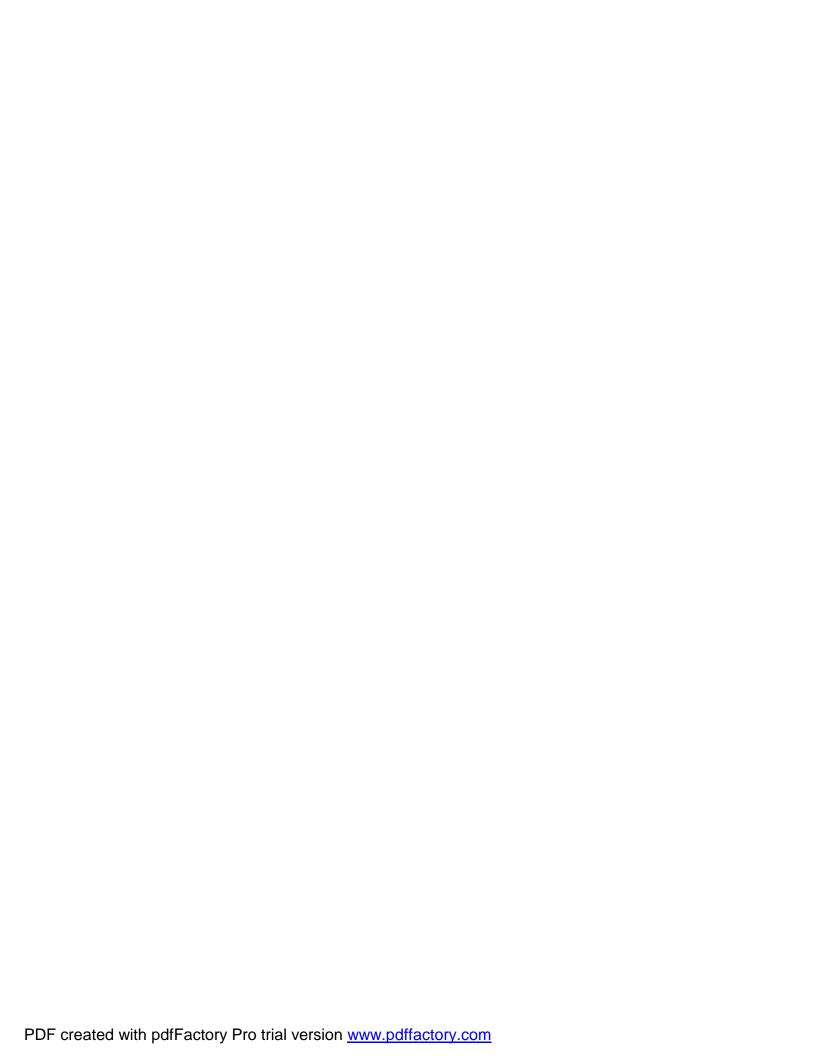
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