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Editorial

Global Tuberculosis Control - Where do we stand?

According to WHO, Tuberculosis is a worldwide pandemic. One third of world population is infected with TB bacilli. In spite of the newer modalities for diagnosis and treatment, TB continues to be a major public health problem world over. Tuberculosis is one among the three top killer diseases - HIV/AIDS kills three million people, TB kills two million and Malaria kills one million every year.[1-10]

Africa and Asia account for the majority of TB cases in the world. It is estimated that among the 15 countries with highest TB incidence, 13 are in Africa. Again half of all new cases in the world are shared by the Asian countries like, Bangladesh, China, India, Indonesia, Pakistan and Philippines.

Attempts for TB control were started by countries world over for many years and were able to achieve some success. Tuberculosis burden was decreasing in industrialised countries even before effective chemotherapy was introduced, with reductions in the rate of infection from 10% to 1%. Introducing effective chemotherapy in the 1950s consolidated the trends in improved TB control. The greatest setback for these attempts accorded with emergence of HIV infection in many countries by 1990.

WHO declared TB as a global emergency in 1993. As per the WHO global Tuberculosis report 2012, the Millennium development goal (MDG) target to halt and reverse the TB epidemic by 2015 has already been achieved. Incidence of new cases of TB have been falling since 2006 and the rate of fall in new TB cases in 2011 was 2.2% . The mortality rate has decreased 41% since 1990 and is aiming towards a reduction of 50% by 2015. Mortality and incidence rates are falling in all the WHO's six regions and in most of the 22 high burden countries. But still the global burden of Tuberculosis is high. Globally 5.8 million new cases were diagnosed in 2011. India and China account for approximately 40% and Africa accounts for 24% of total notified cases of TB in the world. Treatment success rate is 85% for new cases, but it is only 74% in European region. The number of notified MDR- TB cases is increasing. India and China are having the largest number of cases.[13]

Various activities are going on world over towards TB control. In India after the failure of the National Tuberculosis control programme (NTCP), the revised national tuberculosis control programme (RNTCP) was established. RNTCP with the DOTS strategy has great achievements in Tuberculosis control. Today India's DOTS programme is the fastest expanding and the largest programme in the world in terms of patients on treatment, and the second largest in terms of population coverage.[14] RNTCP is targeting 90% case detection and 90% cure rate. India has achieved about 70% case detection and more than 85% cure rate. In May 2012 Tuberculosis was made a notifiable disease in India, which is a landmark step towards Tuberculosis control.

WHO joint monitoring mission (JMM) has lauded the Govt. of India for its efforts in TB control. The govt. of India has endorsed the National strategic plan (NSP) for TB control (2012 - 2017). NSP has set the goal of universal access to early diagnosis and effective treatment.

If implemented properly NSP can save up to 750,000 lives over the next five years. JMM also recommends

Case finding access to community level

Focusing on risk groups

Notifying all- diagnosed cases.

Drug Sensitivity Test for all patients.

Making DOT more patient friendly

Alternate methods for monitoring treatment adherence.

The China Tuberculosis Control Project was the largest Tuberculosis Control Project funded by the World Bank. In this project 94.2% of patients with TB had completed treatment and 93.8% were cured.

By 2002, China had one of the highest "TB burden in the World" after India and was facing particular challenges in MDR TB and HIV-TB co-infection. Some parts of China were among the areas with the highest rates of MDR-TB in the world.

In 1980's health financing in China became decentralized. The Govt. spending on health decreased substantially, and out of pocket spending increased. One survey showed that 37% of TB patients were unable to seek medical help because of financial difficulties and many TB patients became poorer because of the treatment cost.[16]

The TB control project of China covered 16 provinces and it focused on the poor, and adopted the DOTS strategy. The project reduced TB associated deaths by 770,000 and prevented 20 million from being infected. The project exceeded the case detection target of 70% and the cure rate exceeded 85%. Eventhough the project achieved its objectives, TB control remains a major long term public health challenge for China.

In Pakistan the National TB Control Programme and youth has been a strong partner in the fight against TB for last many years. The orientation sessions among youth on TB related issues like TB-HIV and MDR-TB help them to build capacity in TB control activities.

South Africa's rate of Tuberculosis has increased over the last 20 years. Now it is the third highest TB burden country in the world. TB control programme has focused on passively presenting cases. While outcomes for notified TB cases have improved, this strategy failed to contain the TB epidemic. South Africa has the highest per capita risk of TB disease and has the highest TB transmission rates. South Africa's TB notification shows a fivefold increase in TB cases over the last 20 years. About 40% of the notified cases were HIV tested, of which 73% were positive. While effective case management is necessary for TB control, it alone was however insufficient for TB control in scenarios such as South Africa, with a high source of infection, high proportion of latent TB infection and a generalized HIV epidemic. In European region the TB notification rates have been decreasing since 2005, indicating a lower incidence. Despite this, the TB notification rates for the new and relapsed cases in the 18 high priority countries, all from the central and eastern part

of the region, remained almost eight times higher than in the rest of the region. Over the last 5 years the treatment success rate continued to decrease, falling from 72.5% and 50% in 2005 to 68.5% and 47.6% in 2010 in new and previously treated cases respectively.[15]

Even though the TB incidence is decreasing, the drug resistant TB is becoming a major concern in this region. The prevalence of drug resistant TB among new cases was 13.7% in 2010, a slight increase on 2009 (12%). MDR-TB among treated patients also increased to 48.7% in 2010 from 47% in 2008. The majority of TB- HIV co infected patients (85.6%) notified were in the eastern region and it increased from 3.4% in 2008 to 5.5% in 2010.[15]

The incidence of Tuberculosis is declining in USA for the last 20 years and the present incidence is 3.2 cases per 100,000 populations. The TB rate in foreign born persons is 11.5 times as high as US born persons. Asians had the highest TB case rate among all the ethnic groups.

Reaching the Target for TB Control:

In 1991 the 44th World Health Assembly set two targets to be reached by 2000- 70% case detection and 85% treatment success rate.[1,2]Achieving these targets the TB incidence would reduce 10% per year.[3-6] By 2000, 148 countries had adopted WHO DOTS strategy and 27% of global TB cases were being treated in DOTS programme. But it became clear that the target would not be met by 2000 and the date was deferred to 2005.

To reach the target the "Stop TB" Partnership was launched in 2001-2005.[3] Between 1990 and 2004 the global prevalence decreased from 297 to 229 per 1,00,000.[7] By July 2005 more than 36 projects managing MDR- TB was initiated with more than 1,00,00 patients treated in more than 27 countries.[4]

Strengthening TB laboratory capacity will improve the ability to diagnose MDR and XDR TB. This will help to achieve global targets in those countries like Africa and Eastern Europe, where MDR TB is the major deterrent preventing the TB Control Programme to achieve the target.

By the end of 2003, 29 out of 41 countries with high HIV-TB had a national policy for collaborating TB and HIV programme.[4,10] By 2006 the case detection reached 59% in more than 57 countries and treatment success reached 84% in more than 60 countries. However only 25 countries achieved the 1991 World Health Assembly targets for TB control. By late 2006 the global TB epidemic was at the threshold decline. But Africa and Europe were lagging behind with treatment success rate of 72% and 75% respectively.[7]

Problems in TB control:

Many factors affect the effective control of Tuberculosis globally. Neglect of TB control by governments, lack of resources for supervision, weakened health systems and poorly managed TB control programmes are few factors contributing to ineffective control. Poverty, population growth, increase in MDR & XDR-TB, increasing HIV associated TB and lack of newer diagnostic tools are other factors which hampers the progress of TB control.

TB - HIV collaborative activities are improving, to save more and more patient lives. Newer diagnostics like Xpert MTB/ RIF are being widely used for rapid diagnosis. Newer drugs for drug sensitive and MDR -TB are under research. Many new or re-purposed anti TB drugs are on clinical trials. About 11 vaccines for Tuberculosis are on developmental stage. Results of two phase 3 trials of 4 month regimens are expected shortly[13].

Regimens of shorter duration for MDR TB are also under trial. Measures like strict notification of the disease; proper monitoring of treatment, developing newer drugs, regimens and vaccines may make Tuberculosis control a reality in near future.

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Review Article

Upper Airway Cough Syndrome

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Abstract:

Introduction: Chronic cough is a challenge to both the patient and the treating physician. Most common cause of chronic cough in adult nonsmokers is UACS, followed by GERD and asthma. The spectrum of diseases causing UACS includes various rhino sinus conditions.

Pathophysiology: The mechanisms causing cough are post nasal drip, cough hypersensitivity, micro aspiration and rhino bronchial reflex. The altered sensitivity to the cough receptors seems to be the predominant mechanism of cough.

Clinical features and diagnosis: Chronic cough with or without sputum, nasal congestion and discharge, frequent throat clearing and sensation of fluid dripping through posterior pharyngeal wall are the symptoms .In addition to the above symptoms, findings of mucus or secretions in the posterior pharyngeal wall and cobble stone appearance of pharyngeal mucosa on examination suggest a diagnosis of UACS.

Treatment: First generation antihistamines with decongestants are the treatment found to be effective in UACS. Other treatments directed towards the specific causes and non-pharmacologic measures are generally advisable.

Key Words: chronic cough, upper airway cough syndrome, cough hypersensitivity, rhinitis, sinusitis, antihistamines

Introduction

Cough is one of the most common symptoms leading to medical consultations worldwide[1]. Acute cough, lasting up to three weeks is generally curable with initial appropriate therapy or even without treatment sometimes, whereas chronic cough frequently cause discomfort and lead to considerable medical expenditure. The importance of cough as a clinical problem is evident from the number of practice guidelines published by various pulmonary societies over recent years. In spite of these guidelines, chronic cough still remains a challenge for the practicing physician. There are several reasons for this: a lot of diseases cause cough, but many of these do not have any characteristic signs or specific treatment. Many underlying mechanisms related to the pathophysiology and hence treatment options of chronic cough are still not clear. Chronic cough is defined as cough lasting for more than eight weeks. Most common causes of chronic cough are Asthma, Gastro Esophageal Reflux Disease and Upper Airway Cough Syndrome (previously known as Post Nasal Drip syndrome), collectively known as 'diagnostic triad of cough'. In children also upper airway cough syndrome constitutes a major cause of chronic cough, but not the commonest[4]. There are several pulmonary as well as extra pulmonary conditions associated with chronic cough. Studies among different populations have shown that UACS is the commonest cause for chronic cough for which people seek specialist help.

The name 'Upper airway cough syndrome' was coined to encompass diseases affecting upper airways, like rhinitis and sinusitis, which results in chronic cough[1]. Rhinitis is usually associated with nasal discharge and cough. Sinusitis causes secretions dripping down on to pharynx and larynx

from the sinuses. This drainage of secretion was thought to be the mechanism responsible for the cough in UACS. However this could not explain the occurrence of cough in many other situations, which do not produce secretions. A minority of patients with sinusitis who did not have any obvious dripping of secretions were found to have cough. New theories have been brought forward to explain the mechanisms of cough in such situations. Post nasal drip as a mechanism could not explain the cough seen in all the conditions associated with UACS and hence 'post nasal drip syndrome' has been replaced with 'upper airway cough syndrome'.

Pathogenesis

Cough is a protective reflex which helps clearance of secretions and inhaled particles from airways and protects lower airways from aspirations. The afferent limb of cough reflex consists predominantly of Vagus nerve fibers- situated in the airways and upper respiratory tract, Trigeminal and Glossopharyngeal nerves. Cough receptors are present throughout pharynx to terminal bronchioles and comprises two types, rapidly adapting receptors that respond to mechanical stimuli, and nociceptors on C fibers, responding to chemical, immunological as well as inflammatory mediators[3]. The sensory inputs are processed at medulla where the central cough center is situated; which then sends off efferent signals through Vagus, to larynx and tracheobronchial tree, and through Phrenic and various spinal motor neurons, to diaphragm, intercostal, abdominal and perineal muscles to bring about cough. Cough reflex is a polysynaptic reflex and it is modulated by many other sensory inputs in the vagal neurons and out of it. This modulation of reflex is called cough plasticity[6]. In addition to this, a cortical component is also involved in the regulation of cough, as evidenced by the presence of voluntary cough.

In disease states different mechanisms cause cough. Stimulation of sensory receptors by secretions, foreign bodies and mass lesions etc. represents one. Another mechanism is the change occurring in cough receptors, leading to increased sensitivity to cough receptors resulting in either persistent cough or decreased threshold for cough. This abnormal regulation of the cough receptors can either be an up regulation, manifested as enhanced cough reflex and too long cough, as seen in many upper airway diseases like sinusitis and rhinitis. It is believed that this 'cough hyper sensitivity' is the underlying mechanism in many of the cases of chronic cough, in spite of their different aetiology and clinical presentations.

Post nasal drip syndrome has been used to denote conditions associated with upper airway pathology and chronic cough. It was believed that, the draining of secretions from the upper airway caused generation of cough, through direct stimulation of cough receptors situated in the oropharynx and larynx or by inflammatory cells and mediators stimulating cough receptors. However this could not be the reason in all cases of chronic cough associated with upper airway diseases, as there were conditions without secretions being produced. Rhinitis is not always associated with cough, even though it is considered to be the commonest cause of acute cough. Also, in a minority of patients with sinusitis, there were no evidence of secretions draining from sinuses, called silent sinusitis, but were associated with cough. In view of this findings and with the emergence of new hypotheses, the name, post nasal drip syndrome has been replaced with' upper airway cough syndrome'. The recent concepts regarding the pathogenesis of UACS comprise different mechanisms, instead of one as in PNDS. Along with post nasal drip, unified airway concept and cough hypersensitivity may be helpful in explaining the underlying mechanisms in UACS.

Cough hypersensitivity: Increased sensitivity to cough reflex is seen during upper respiratory infections and allergies. This hyper sensitivity has been experimentally proven using challenge tests using capsaicin. The enhanced reactivity is found to be resolving, once the infection is controlled. Morice et al[5] were of the opinion that cough hypersensitivity could be a universal phenomenon in chronic cough, so that, it may be prudent to consider all the causes of chronic cough as part of a separate syndrome with cough as common presentation and cough hypersensitivity as unifying mechanism among them - 'Chronic cough hypersensitivity syndrome'. Studies have shown that there is a gender difference in the occurrence of cough hypersensitivity. Adult females were manifesting more of this phenomenon, compared to males[5].

Recently, Jana Plevkova, and Woo-Jung Song also studied the pathophysiology of UACS more thoroughly[6].

The possible mechanisms suggested were post nasal drip, micro aspiration, nasobronchial reflex, propagation of inflammation via systemic circulation and loss of nasal function while inhaling cold air through mouth breathing during rhinitis. Their speculation was that, this cough hypersensitivity during infections was a protective strategy to prevent spread of diseases from upper respiratory tract to other parts. There was also a cortical component to this, in the form of an' urge to cough' which is considered to be a specific sensation of airway irritation leading on to cough; it represents cortical conscious contribution to the airway defense. Their hypothesis was that, nasal inflammation was a strong trigger for cough in persons with either inherited or acquired cough hypersensitivity or upper airway diseases itself could be the cause of cough hypersensitivity.

Unified airway hypothesis states that there are structural and functional similarities between upper and lower airways, so that insults in the form of infections or allergy occurring in one part may cause changes in the other part. This is brought about by systemic effect of inflammation, through trafficking of inflammatory mediators. According to this model, pathology in one part of respiratory mucosa can evoke a system wide response which can cause pathophysiological changes in other parts of respiratory mucosa, distal to the initial site of insult. This could explain enhanced cough reflex in rhino sinusitis[7].

Thus, the current evidence suggests that, apart from post nasal drip, hypersensitivity to cough receptors in upper airways may be the predominant mechanism leading on to chronic cough in UACS. Other mechanisms like micro aspiration, nasobronchial reflex or systemic propagation of inflammation are likely, but there is lack of evidence to support these mechanisms at present.

Clinical Features and Diagnostic Evaluation

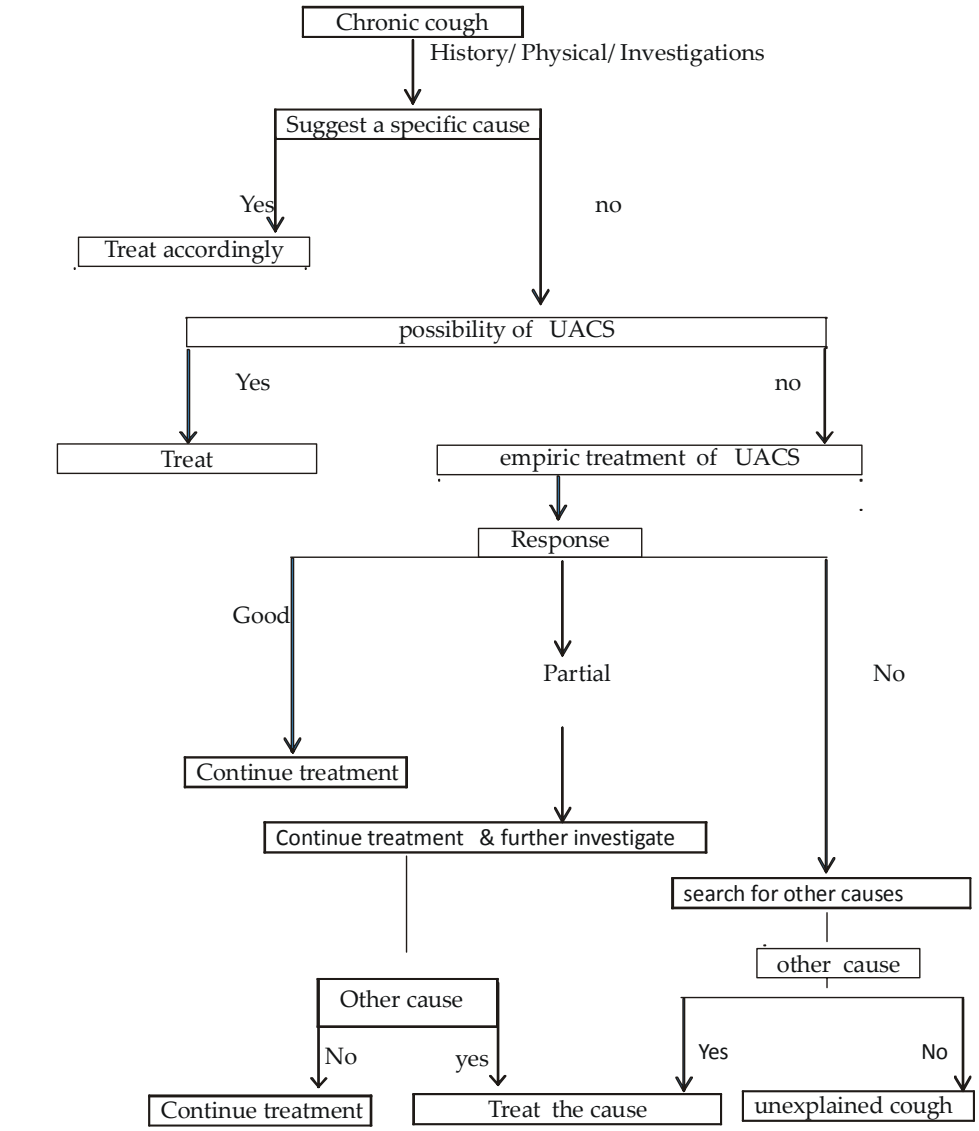
Finding out etiology in chronic cough is often not easy. History as well as patient described symptoms may be useful in some situations, where suggestive symptoms are available, as in the case of Asthma and GERD. In the evaluation of UACS as a cause of chronic cough, symptoms and signs lack specificity. Presence of chronic cough, with or without expectoration, frequent throat clearing, nasal discharge, a sensation of secretions dripping down the throat, and on examination, presence of secretions in posterior pharyngeal wall or cobble stone appearance of the pharyngeal wall mucosa may suggest a diagnosis of Upper Airway Cough Syndrome. However, these symptoms are largely based on patient's subjective sensations. It was reported that nearly 20% patients were unaware of the sensation in the throat, when actually they had sinusitis. Thus, the hallmark of UACS is that, it does not have any pathognomonic finding. Hence response to treatment directed to UACS may also be taken as evidence of diagnosis in UACS. The ACCP guideline suggest a diagnostic approach based on a combination of criteria, including symptoms, physical examination findings, imaging and response to therapy[1]. If symptoms specific to any particular disease is forthcoming, treatment should be directed to that. If the patient does not respond to treatment, further diagnostic evaluations like sinus imaging and nasal endoscopy should be done. It should be remembered that, other conditions like silent GERD or Cough variant Asthma, may occur simultaneously with UACS and when there is only partial or no response at all to treatment, patient should be further evaluated.

Conditions associated with UACS

Rhinitis	Allergic rhinitis
	Perennial non-allergic rhinitis
	Vasomotor rhinitis
	Nonallergic rhinitis with eosinophilia (NARES)
	Post-infectious rhinitis
	Rhinitis due to anatomic abnormalities
	Rhinitis due to physical or chemical irritants
	Occupational rhinitis
	Rhinitis medicamentosa
	Rhinitis of pregnancy
Sinusitis	Bacterial sinusitis
	Allergic fungal sinusitis

Adapted from PratterMR ,Chest 2006, 129:63S-71S1

DIAGNOSTIC ALGORITHM



Treatment

Management of chronic cough is often difficult; though some studies have shown that a guideline based approach may be helpful[10].Treatment of UACS include treatment of specific causes, with pharmacologic and non-pharmacological approach. Avoidance of allergens, antibiotics, methods to reduce inflammation and obstruction are generally advised. When a specific cause is obvious, treatment should be directed to that, and the response to treatment will be good. But many a times a specific cause will not be apparent. In such situations, an empiric therapy initiated before starting further investigations has found to be effective. A first generation anti histamine or decongestant is usually recommended as empiric therapy[8]. Studies have shown that compared to non-sedating second generation antihistamines, first generation antihistamines are effective in relieving cough associated with UACS. The mechanisms of older generation antihistamines in controlling cough in UACS seems to be due to its anticholinergic action, however, other possible explanations being, actions of these drugs on histaminergic and nonhistaminergic receptors in central nervous system[9].

Mechanisms by which antihistamines cause suppression of cough in UAC

Mechanism	Mode of Action
Peripheral action	Antihistamines suppress cough by directly acting on histaminic receptors and modulating peripheral sensory afferents that promote cough. Indirectly antihistamines suppress cough by decreasing mucous secretion induced by histamine receptors and through cholinergic mechanisms.
Central action	H1 receptor blocking drugs act directly on histamine receptors that promote cough and on nonhistaminergic receptors in central nervous system that control cough excitability. Indirectly these drugs act on histaminergic and nonhistaminergic receptors that regulate secretion of mucous, thereby decreasing cough. Another mechanism is the sedative effect that reduces cough excitability

First generation antihistamines and decongestants are the preferred pharmacologic treatment in UACS, because of their cough suppressant effect. Second and third generation antihistamines do not have any effect on cough, hence, are generally not advised. However, second generation, non-sedating antihistamines have a role through reduction in nasal congestion when allergic rhinitis is the causative factor in UACS. In patients with rhinitis prolonged treatment with intranasal corticosteroids may be useful. When empiric therapy is given, patient has to be evaluated for possible causes while continuing treatment. If cough improves in 2-3 weeks, it is suggestive of possible UACS. If response is only partial, possibility of multiple causes for cough has to be considered and should be further investigated. When the patient is not responding to initial therapy, look for other etiologies like sinusitis, for which sinus imaging and prolonged antibiotics may be required. Still the patient continues to be symptomatic further evaluations to rule out other unrelated causes has to be done; since simultaneous occurrence of multiple causes is not uncommon in patients with chronic cough. In children first generation oral antihistaminic drugs are generally not advisable. Antihistamines as nasal preparations and chromolins may be useful.

Treatment of allergic rhinitis include avoidance of allergens wherever possible, antihistaminic drugs, decongestants, topical steroids and allergen immunotherapy. Antihistaminic drugs available are chorpheniramine, cetirizine, fexofenadine, loratidine etc. Topical antihistamines are azelastine and olopatadine. Second generation antihistamines are preferred as first line therapy for their non-sedating advantage. Pseudoephedrine had been the most commonly used oral decongestant, but now it has been replaced by phenylephrine. Leukotriene antagonist, montelukast, inhaled anticholinergic ipratropium, and chromolin sodium are useful in selected cases.

Intranasal steroid sprays are considered to be the first line therapy in Perennial non-allergic rhinitis. Azelastine and olopatadine are topical antihistamines useful in perennial non allergic rhinitis. Ipratropium spray help to control rhinorrhea. Oral antihistamines and decongestants are also useful. But in children, because of safety concerns, many oral antihistaminic drugs are not advised. Surgical removal of allergic mucin, corticosteroids, antifungal treatment and immunotherapy are the usual treatment adopted in allergic fungal sinusitis. Avoidance of offending substances is the mainstay in rhinitis caused by environmental agents and occupational rhinitis. Steroid nasal sprays, cromolyn sodium and antihistamins like chlorpheniramine, loratidine and cetirizine are found to

be safe and effective for treating rhinitis of pregnancy.

There are still unresolved issues in the management of UACS. There is dearth of studies on UACS, so that, the optimum combination of drugs and duration of treatment are not well established.

Conclusion

Chronic cough is caused by a variety of conditions and when initial evaluations do not point to a specific etiology, possibility of UACS has to be considered. Many rhino sinus conditions cause cough through excessive secretions and altered cough reflex mechanisms. Post nasal drip as a possible single mechanism is no longer tenable because, it cannot explain the occurrence of cough due to various causes in UACS. Rhinitis and sinusitis produced by allergens and infective agents play a major role in UACS. Often identification of the underlying cause is unsuccessful and occurrences of multiple underlying conditions are not uncommon. Initial empirical therapy with first generation antihistamines and decongestants are generally effective. However exact duration and treatment responses are still not clear. Emerging scientific evidences point to the role of cough hypersensitivity and other possible underlying mechanisms in the causation of cough in UACS. There is need for the development of newer drugs effective in controlling cough, like transient receptor potential vanilloid receptor (TRPV1) inhibitors.

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Special Article

Management of Chronic Idiopathic Urticaria

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Key words: Urticaria, Chronic urticaria, Idiopathic urticaria, Antihistamines

Urticaria is characterized by wheals, which are superficial itchy swelling of the skin due to transient plasma leakage from small blood vessels. Angio-oedema occurs when the deeper dermis is affected. Urticaria and Angio-oedema can occur alone or in combination.

Appearance of wheals on a recurrent basis more than twice a week and lasting over 6 weeks is Chronic Urticaria. Wheals lasting less than 6 weeks is Acute Urticaria. Urticaria can also be episodic[1]. Chronc Urticaria can last from a few months to several years.

Acute Urticaria: Usually no tests are required for its evaluation. The treatment consists of H1 Anti histamine (oral/parenteral), steroids (oral/parenteral) and Adrenaline.

Episodic or Intermittent Urticaria: Here investigations for Type 1 Allergy (especially food allergens) may be useful. Skin prick test or RAST is done for the detection of allergens. Treatment is the same as in Acute Urticaria. Use of medication is as required.

Classification of Chronic Urticaria

1. Idiopathic - the great majori ty of CU is idiopathic. The probable aetiological agents may be Immune or Non-Immune[2]. The causative agent cannot be identified in most cases.

2. Physical - eg: Delayed pressure urticaria

3. Special types eg: Cholinergic urticaria

4. Diseases related to urticaria eg: Vasculitis

Probable causative agents in chronic Idiopathic urticaria[3] are-

1) Immune

(a) IgE dependent - This is seen rarely in Chronic Urticaria (though common in Acute and Episodic urticaria)

(b) Auto Immune - Constitutes one third of Idiopathic urticaria. Association with Hashimoto's thyroiditis is well documented.

2) Non-Immune

(a) Food pseudo allergens - Non IgE mediated hypersensitivity to food additives and some natural substances found in fruits , vegetables and spices.

(b) NSAIDs

(c) ACE Inhibitors

(d) Opioids

Role of Infections: Role of Helicobacter pylori and parasitic diseases has been proposed, but not proven[5,6.]

Psychological stress has also been postulated[3,7].

Investigations

A detailed clinical evaluation is found to be more useful than laboratory tests in the evaluation of chronic urticaria. In general laboratory tests are not useful[8]. However in some cases it may be possible to identify the aetiology as in Urticarial vasculitis. It may also help to identify any associated auto immune disorder. The tests indicated are:

1. Blood counts
2. ESR
3. Thyroid function tests
4. Serological tests
5. Skin biopsy

6. ASST (Autologous serum skin test)

7. Allergy tests

Estimation of C1 esterase inhibitor is useful only in angioedema without wheals.

Treatment

The ideal management of Chronic Urticaria would be identifying and eliminating the underlying causes and/or eliciting triggers. However this is not possible in the great majority of cases.

Role of Dietary management in Idiopathic urticaria[4]: In the case of Type 1 hypersensitivity, avoidance of triggering agent benefits within 48 hours. But this type is rare in Chronic Urticaria. In pseudo allergy, benefit will appear usually after 3 weeks of stopping the food. Diet with low pseudo allergens is advised in Chronic Urticaria.

The drugs used in the treatment of Chronic Urticaria are Antihistamines, Anti leukotrienes, Immuno suppressants and Omalizumab. Plasmapheresis is useful in Auto immune urticaria.

Antihistamines - The most effective treatment is symptom relief and antihistamines are the most important drugs in Chronic Urticaria.

Histamine is one of the key mediators released from mast cells and basophils[9]. It has an important role in allergic diseases including urticaria. Histamine1 (H1) receptor stimulation is responsible for most of the manifestations of urticaria namely, pruritus, vasodilation, vascular permeability, hypotension and flushing. Histamine2 (H2)receptor stimulation is involved in the manifestation of pruritus and flushing[10].

Antihistamines alleviate itching and reduce the number, size and duration of urticarial lesions. H1 activity in the afferent C nerve fibres cause itching which is mostly relieved by all antihistamines. Axonic reflexes of skin cause erythema. Receptors in the endothelium of post capillary venules cause extravasation (and wheal) formation. Anti inflammatory actions of Antihistamines are by two mechanisms:-1) Stabilization of mast cell and basophil cell membranes[11,12] and 2) Inhibition of cytoplasmic transcription factors[13].

Which Antihistamine to choose?

There are two groups of Antihistamines - the older sedating 1st generation antihistamines and the newer less (non) sedating 2ndgeneration antihistamines

1st generation antihistamines[14]: All drugs of this group are sedating. They are generally regarded safe by health care professionals because of their long standing use. But they decrease REM sleep, impair learning and work efficiency. They have been implicated in accidents (motor, aviation, boating). Deaths have been reported due to accidental overdosing in infants and adults. Intentional overdosing has also been reported in adult deaths. Some exhibit cardio toxicity in over dosage. Their duration of action is short. They have anti cholinergic side effects too.

The advantage of 1st generation antihistamines is that parenteral preparation is available which is useful in some cases of Acute Urticaria. If sedation is needed for insomnia in a patient with Chronic Urticaria, 1st generation antihistamines may be administered at bed time either alone or if necessary, along with a morning dose of 2nd generation antihistamines.

Hydroxyzine, Diphenhydramine, Chlorpheniramine and Promethazine are the drugs belonging to 1st generation antihistamines.

2ndgeneration antihistamines[15,16]: They are a heterogenous group of compounds. In contrast to the highly lipophilic nature of 1st generation antihistamines, the drugs belonging to 2nd generation antihistamines do not cross easily (if at all) through the bloodbrain barrier. Their propensity to occupy the H1 receptors in the CNS varies from 0% for fexofenadine to 30% for cetirizine (for 1st generation antihistamines it is 50-60%). Therefore these drugs are relatively free of sedating effects[17,18]. The duration of action is 24 hours or more.

Astemizole and Terfenadine were withdrawn because of cardiac toxicity. The currently available 2nd generation antihistamines are free from cardiac toxicity even at higher than recommended doses. None of these drugs are available in parenteral form because of their low aqueous solubility.

The drugs belonging to 2nd generation antihistamines are Cetirizine, Levocetirizine, Loratadine, Desloratadine,

Fexofenadine, Rupatidine, Ebastine, Acrivastine and Mizolastine.

Sedation of Fexofenadine and Desloratadine have been compared to placebo. Loratadine has mild sedation compared to placebo[19]. Cetirizine[20] and Levocetirizine were found to have more sedation than the above three drugs.

Combination of Antihistamines: Treatment with two or more drugs of 2ndgeneration antihistamines is not recommended. Instead, up dosing of 2ndgeneration antihistamines is preferred[21]. Also, combined use of 1st generation and 2nd generation antihistamines is not recommended. However, if insomnia is a problem, 1st generation antihistamines may be administered at bed time along with a morning dose of 2ndgeneration antihistamines.

H2 receptor blockers *:* If the patient is not responding to high doses of H1 antihistamines, then H2 antihistamines like famotidine or ranitidine may be given simultaneously. The combination of H1 and H2 antihistamines have been found to be effective in a subgroup of patients with chronic urticaria[27].

Steroids and Cyclosporine: Oral/topical steroids are not recommended in the long term management of chronic urticaria. Cyclosporine 3 mg/kg/day has better safety profile than systemic steroids[22,23]. But short course of oral steroids are indicated in acute or in episodic urticaria[24].

Drug treatment of Chronic Urticaria[21]

The step wise approach is -

1. 2ndgeneration antihistamines for 2 weeks
2. If not responding, 2nd generation antihistamines up dosing (2-4 times) for 1-4 weeks
3. If not responding, add Leukotriene antagonists and/ or change 2nd generation antihistaminesfor 1-4 weeks
4. Other drugs: H2receptor blockers, Cyclosporine, and Omalizumab may be tried in patients with chronic refractory urticaria.
5. Plasmapheresis in auto immune urticaria
6. Systemic steroids (3-7 days) in exacerbations.

Follow up - Re evaluate every 3-6 months as severity may fluctuate and the need for 2ndgeneration antihistamines may stop. Spontaneous remission is seen usually within one year though in some cases it may prolong.

Treatment of Chronic Urticaria in special situations[26]

Pregnancy: Cetirizine, Loratadine and Chlorpheniramine are in 'B' category whereas all other antihistamines are in 'C' category[25]. Avoid 1st generation antihistamines during the third trimester because of risk of neonatal seizures[14]. Safety of up dosing of 2ndgeneration antihistamines is not known.

Children*:* Same line of management as in adults is to be followed. 1st generation antihistamines should be discouraged in children. Liquid formulations of Cetirizine and Loratadine are available.

Liver diseases*:* 1st generation antihistamines and some 2ndgeneration antihistamines undergo metabolism in liver. Safest Antihistamines are Cetirizine, Levocetirizine, Fexofenadine and Desloratadine.

Renal failure: Cetirizine and Levocetirizine are to be avoided in severe renal failure.

Summary

Chronic Urticaria is a "difficult to manage disease." The main reason is that most of the times, a definite cause can not be identified. The most important point is that investigations are of limited use in this disease, nor does it help in the treatment. Moreover it unnecessarily increases the anxiety of patients. The cornerstone of medical therapy is antihistamines. The newer second generation antihistamines are preferred over the older first generation antihistamines. Up dosing of the former is recommended over use of a combination of two 2nd generation antihistamines.

In a minority of patients, where aetiology is identified, its elimination is the most successful treatment measure.

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Original Article

Etiology and clinical profile of pleural effusion in a teaching hospital of south India : A descriptive study.

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Abstract:

Background & objectives: Etiological diagnosis of Pleural effusion (PE) is really challenging to physician. Knowledge of common etiologies of pleural effusion helps us in planning the approach when such a case is encountered. The study was an attempt to identify the common etiologies causing PE in a teaching institute and their clinical profile.

Materials and Methods: A prospective evaluation of 100 consecutive cases of PE. Detailed history and physical examination, thoracocentesis and pleural fluid analysis were done in all cases and closed pleural biopsy using cope needle, ultrasound examination and computerized tomography in indicated cases.

Results: PE occurred more among males (68%) and in the age group between 46 to 60 years (33%). Majority of the cases (95%) were having exudative effusion. Tuberculosis was the commonest cause of exudative effusion (41%) followed by malignancy (38%). Majority of tuberculous PE (63%) was right sided whereas malignant effusion was left sided (57%). The Mantoux test, pleural fluid protein, pleural fluid ADA and age of patients had statistically significant correlation when PE due to tuberculosis and malignancy were compared.

Conclusions: Tuberculosis and malignancy are the two major causes for PE in the hospital. Tuberculous PE predominates slightly than malignant effusion. Tuberculous PE occurred in younger age group. Pleural biopsy should be done in patients with negative pleural fluid cytology. Thoracoscopy should be done if all the other investigative modalities fail to yield a confirmatory result. Knowledge of etiological pattern helps to plan relevant investigations in patients with PE and reduces the delay in diagnosis.

Key words: Pleural effusion, tuberculosis, malignancy, adenosine deaminase, needle biopsy, etiology

Introduction:

Pleural effusion can occur as complication of many diseases. They are classified broadly in to exudative and transudative effusion based on Light's criteria. Common causes of transudative effusions are congestive cardiac failure, cirrhosis, nephrotic syndrome, superior venacava obstruction, peritoneal dialysis, glomerulonephritis, myxoedema, pulmonary emboli and sarcoidosis whereas exudative PE is caused by neoplastic diseases, infections, pulmonary embolism, gastrointestinal diseases, collagen vascular diseases, drug induced, iatrogenic, hemothorax and chylothorax. In an epidemiological study from Czech Republic it was found that four leading causes of PEs were congestive heart failure, malignancy, pneumonia and pulmonary embolism in the order of frequency.[1] When pleural fluid is detected, an effort should be made to determine which among the conditions listed above is responsible and is a challenge to the physician.

Needle biopsy of the pleura is also useful in the diagnosis of malignant PE. The incidence of positive pleural biopsy result ranges from 39-75%.[2] When no pleural fluid is present, but the pleura is thickened, needle biopsy of pleura can still be used to establish the diagnosis of tuberculosis or malignant disease. 20% of PEs remain

undiagnosed even after all investigations. The study was to identify the relative proportion of different etiological conditions and clinical profile of PE encountered in our institute which is a teaching hospital.

Materials and methods:

Objectives: To study the clinical profile and identify the common etiologies of PE in a tertiary care center.

The design of the study: A prospective descriptive study.

Hundred consecutive adult cases of PE attending the outpatient clinic of Institute of Chest Diseases, Medical College Calicut for one year were studied. All cases were subjected to detailed clinical examination which included history and physical examination. Symptomatology included chest pain, cough and dyspnoea on exertion (DOE). Physical examination was done with particular attention to hemi thoracic size, tactile vocal fremitus, percussion, auscultation for decreased intensity of breath sounds and pleural rub. Other systemic examinations included assessing cardiomegaly, neck veins distension or peripheral edema, signs of joint diseases or subcutaneous nodules.

A diagnostic thoracocentesis was done. Gross appearance like colour, turbidity, viscosity and odors were noted. The fluid was sent for various investigations. They include total and differential cell counts, pleural fluid protein and sugar with corresponding serum values and cytological examinations. Pleural fluid was submitted for Gram as well as acid fast bacilli (AFB) staining, aerobic bacterial and AFB culture. Serum adenosine deaminase (ADA) estimation was done in all cases. Pleural biopsy specimens were sent for histopathological examination and mycobacterial culture in indicated cases where other diagnostic clues were lacking. Ultrasound thorax and abdomen, computed tomography (CT) scan thorax and fiber-optic-bronchoscopy (FOB) were done in indicated cases.

Results:

Of the 100 patients studied, 68 patients were males, 32 were females. 18 patients were below 30 yrs, 28 of them between 30 and 45 yrs, 33 patients were between 46 and 60 and 21 patients above 60 yrs.

Basis of diagnosing tuberculous effusion were

1. High ADA level in pleural fluid >70 IU/L
2. Pleural biopsy showing caseating granuloma
3. Positive Mantoux test

Malignant PE was diagnosed on following criteria:

1. Malignant cells in pleural fluid
2. Pleural biopsy suggestive of malignancy
3. Evidence of malignancy in FOB / CT thorax

Of the 100 patients, 41 patients had diagnosis of tuberculosis and 38 patients had malignant PE. The rest belonged to para-pneumonic effusion (n=12), transudative effusion (n=5) and inconclusive (n=4). All transudative PEs were due to cardiac failure (n=5). PEs in which no definite diagnosis was evident with all the investigations, a diagnosis of inconclusive PE was made.

Of the malignant PE (n=38), 23 had diagnosis of adenocarcinoma, 4 squamous cell carcinoma, 4 lymphoma, 5 mesothelioma and 2 small cell carcinoma. 21 patients were male and 17 patients were female. 16 patients belonged to age group 46-60, 10 patients between 31 and 45, 2 patient below 30, and 10 patients above 60 years. (Table 1)

Among the patients with tuberculous PE (n=41), 30 patients were male and 11 patients were females. 27 patients were below 45 years of age and rest above 45 years.

Analysis of symptoms showed that DOE was present in 28 patients with tuberculous PE and 30 patients with malignant effusion, absent in 13 patients and 8 patients respectively. Cough was present in 34 patients with tuberculous effusion and 26 patients with malignant effusion. Chest pain was present in 36 patients with tuberculous effusion and 25 patients with malignant PE. Fever was present in 28 patients with tuberculous effusion where as absent in 13 patients. Fever was present in 20 patients with malignant effusion and 18 patients of this group had no fever. 19 patients with tuberculous effusion and 16 patients with malignant effusion were smokers whereas 22 patients with tuberculous effusion and 22 patients with malignant effusion were nonsmokers. (Table 2)

Colour of effusion was straw in 38 patients with tuberculous effusion and 9 patients with malignant effusion.

PE was hemorrhagic in 3 patients with tuberculous effusion and 29 patients with malignant effusion. (Table 3)

Duration of illness when studied showed 29 patients of tuberculous effusion had more than 1 month history of chief complaints, 12 had duration of less than 1 month. 27 patients with diagnosis of malignant effusion had duration of illness more than 1 month but 11 patients had duration less than 1 month. Out of remaining 21 patients with diagnoses other than tuberculous and malignant effusion, 15 patients had duration of symptoms less than 1 month. When side of effusion were compared between two diagnostic groups 26 patients of tuberculous effusion had right sided effusion and 15 patients had left sided effusion. Malignant effusion group (n=38), 16 patients had right sided effusion and 22 patients left sided effusion.

All patients had undergone pleural fluid gram staining and AFB staining, routine culture and AFB culture (n=100). Gram positive organisms were demonstrated in 2 cases and gram negative organisms in 2 cases. Others were not showing any positive or negative result in gram staining. Routine culture revealed growth of Streptococcus Pneumonia in 2 cases and Acinetobacter in 1 case. One case which showed gram negative organisms in gram staining was found to be sterile on routine culture. AFB smear and culture were negative in all cases. Fibre optic bronchoscopy and CT thorax were done only in cases of PE where diagnosis was not evident by other investigations. CT thorax was done in 1 case and fibre optic bronchoscopy was done in 5 cases and all were suggestive of malignancy. Lymph node fine needle aspiration was positive for malignancy in 3 cases.

Using unpaired 't' test equality of means was measured between the two diagnostic groups. The Mantoux test, protein of pleural fluid, ADA of pleural fluid and age of patients had statistically significant correlation. Other tests did not have any statistical significance in differentiating these two groups. (Table 6)

Pleural fluid cytological examination for malignant cells was done in all cases. 10 cases of adenocarcinoma, 5 cases of mesothelioma, and 2 cases of lymphoma were diagnosed. 3 patients had atypical cells in pleural fluid. Those having malignant cells in pleural fluid were considered as positive, no malignant cells in pleural fluid as negative and those with atypical cells in pleural fluid as inconclusive.

Pleural biopsy was done in 32 cases which revealed 12 cases of adenocarcinoma, 4 cases of squamous cell carcinoma, 5 cases of mesothelioma, 3 cases of lymphoma, and one case of small cell carcinoma. Tuberculous granuloma was demonstrated in 4 pleural biopsy specimens of suspected tuberculous PE. Neutrophilic infiltration was seen in 2 cases.

Comparing pleural biopsy with corresponding pleural fluid cytology in cases of suspected malignancy, positive results were obtained in 25 (96%) cases by pleural biopsy, 17 (65%) cases by pleural fluid cytology, out of total 26 cases. 1 (4%) case was negative by pleural biopsy whereas 6 (23%) were negative by pleural fluid cytology. 3 (12%) cases were inconclusive in pleural fluid cytology; none were inconclusive by pleural biopsy.

Discussion:

Of the 100 patients studied, 68% were male and 32% were female. The age group between 30 and 60 were predominantly affected. Tuberculous effusion occurred in younger age group (n=27 below 45 yrs). This is concordant with various other studies.[2,3] In a study by Berger and Mejia in 1973, they reported that of their 49 patients with tuberculous pleuritis, 15% of the patients were above the age of 70, and 40% were above the age of 35.[3]

While analyzing the frequency of occurrence of each type of PE, tuberculous effusion predominated. In many areas of the world, tuberculosis remains the most common cause of PEs in the absence of demonstrable pulmonary disease. A study from Rwanda by Batungwanayo J et al, tuberculosis was diagnosed in 110 of 127 patients (86%) who presented with PE.[4] Similar result was reported by Khan FY from Qatar.[5]

Male sex predominated in both tuberculous and malignant effusion (n=30) and (n=21) respectively. Duration of illness in cases of tuberculous and malignant effusions was more than 1 month, but in other cases like para-pneumonic effusion it is less than 1 month. In one series, out of 71 patients with tuberculous PE, 50 (62%) had been symptomatic for less than a month.[6]

Tables

Table 1: Etiologies of pleural effusion

Diagnosis	Frequency	Percentage
Tuberculosis	41	41
Adenocarcinoma	23	23
Squamous cell ca	04	04
Lymphoma	04	04
Mesothelioma	05	05
Para-pneumonic effusion	12	12
Transudative effusion	05	05
Small cell carcinoma	02	02
Inconclusive	04	04
Total	100	100

Table 2: Frequencies of major symptoms in 2 major diagnostic groups

Symptoms	Tuberculous effusion		Malignant effusion	
	Present (%)	Absent (%)	Present (%)	Absent (%)
DOE	28 (68.3)	13 (31.7)	30 (78.9)	8 (21.1)
Cough	34 (82.9)	7 (17.1)	26 (68.4)	12 (31.6)
Chest pain	36 (87.8)	5 (12.2)	25 (65.8)	13 (34.2)
Fever	28 (68.3)	13 (31.7)	20 (52.6)	18 (47.4)
H/o smoking	19 (46.2)	22 (53.7)	16 (42.1)	22 (57.9)

Table 3: Comparison of color of effusion in both diagnostic groups

Diagnostic group	Colour of effusion		Total
	Straw coloured	Hemorrhagic	
Tuberculosis	38	3	41
Malignant	9	29	38
Total	47	32	79

Table 4: Duration of illness versus various diagnoses				
Duration of illness	TB	Malignant	Others	Total
<1 month	12	11	15	38
1 - 12 months	29	27	4	60
>12 months	-	-	2	2
Total	41	38	21	100

Table 5: Side of effusion		
Diagnosis	Right	Left
Tuberculosis effusion (n=41)	26 (63.4)	15 (36.6)
Malignant effusion (n=38)	16 (42.1)	22 (57.9)

Table 6: Comparison between tuberculous and malignant pleural effusion					
Diagnostic group		N	Mean	Std. Error mean	P value
Mantoux test	Tuberculous	41	21.17	1.32	0.000
	Malignant	38	5.74	1.29	
Pleural fluid protein	Tuberculous	41	5.005	0.168	0.006
	Malignant	38	4.332	0.172	
ADA-PF	Tuberculous	41	75.06	5.72	0.006
	Malignant	38	35.23	4.27	
Age	Tuberculous	41	40.44	2.78	0.001
	Malignant	38	53.16	2.34	

Table 7: Pleural fluid cytology report	
Adenocarcinoma	10
Mesothelioma	5
Lymphoma	2
Atypical cells	3
No malignant cells	80
Total	100

Table 8: Histopathology results of pleural biopsy specimens	
Adenocarcinoma	12
Mesothelioma	5
Lymphoma	3
Squamous cell carcinoma	4
Small cell carcinoma	1
No abnormality	1
Tuberculosis	4
Neutrophilic infiltration	2
Total	32

Table 9: Comparison of results of pleural biopsy and corresponding pleural fluid cytology in malignant PE		
Result	Pleural biopsy	Pleural fluid cytology
Positive	25 (96%)	17 (65%)
Negative	1 (4%)	6 (23%)
Inconclusive	0	3 (12%)
Total	26	26

Predominant symptoms were fever, cough, chest pain and dyspnoea, of which dyspnoea predominated in malignant effusion; cough, chest pain and fever in tuberculous effusion. In one study by Berger and Mejia in 1973, most patients with tuberculous PE (~70%) had cough, usually nonproductive, and most (~50-75%) had chest pain, usually pleuritic in nature. 7 of 49 patients (14%) were afebrile.[3] In another series, Chernow & Sahn reported that the most common symptom in malignant PEs is dyspnoea, which occurs in more than 50%. Weight loss occurred in 32%, malaise in 21% and anorexia in 14% of patients.[7] Temperature elevation is significantly more common in patients with benign disease (73%) than in patients with malignant disease (37%).[8]

Colour of effusion is diagnostic. Tuberculous effusion was predominantly straw coloured where as malignant effusion was hemorrhagic. But straw coloured malignant and hemorrhagic tuberculous effusions were also seen.

Diagnostic tests like Mantoux test, pleural fluid protein, ADA estimation showed statistical significance in differentiating tuberculous and malignant PE ($P<0.05$).[9] Tuberculin test was negative in majority of diagnosed cases of tuberculous PE. In one Indian study by Hira HS et al. 30% of tuberculous PE were having negative tuberculin test.[10] Ocana and associates measured the pleural fluid ADA level in 221 pleural or peritoneal effusions. All patients with a pleural fluid ADA level above 70 IU/L had tuberculosis, whereas no patient with pleural fluid ADA level below 40 IU/L had tuberculous pleuritis.[11] Fontan Bueso and colleagues reported similar results in a group of 138 patients with PE, which included 61 with tuberculosis and 42 due to malignant disease.[12]

In this study AFB staining and culture of pleural fluid did not yield any positive result. Routine smear for mycobacteria are not indicated because they are almost always negative, unless the patient has a tuberculous empyema.[2] In most series of patients with tuberculous pleuritis, the pleural fluid cultures are positive for mycobacteria in less than 25%.[13]

In the present study, while comparing pleural biopsy and pleural fluid cytology, pleural fluid cytology has low sensitivity than pleural biopsy in case of malignant effusion. Similar studies have shown contradictory results.[14,15] In one series by Levine H et al, the initial pleural biopsy revealed granulomas in approximately 60% of patients with tuberculous pleuritis. If three separate pleural biopsies are obtained the yield increases to approximately 80%. When culture of a biopsy specimen is combined with microscopic examination, the diagnosis can be established in approximately 90% of cases.[16]

In this study pleural biopsy and corresponding pleural fluid cytology were compared and it was found that pleural biopsy is superior in diagnosing malignancy. It has a positive result in 88% when compared to fluid cytology which has a positive result of 32% only. In other studies the pleural fluid cytology was more yielding. In study by Beuno CE et al. the result is consistent with the present study.[2] The proportion of positive pleural biopsy in patients with malignant PEs ranges from 39-75%, according to Bueno et al. In series by Canto A et al, in 1983, pleural biopsy has a lower diagnostic yield than pleural fluid cytologic examination because, in 50% of patients with malignant pleural disease, the costal pleura is not involved.[17] James P et al. reported a diagnostic yield of closed pleural biopsy of 62.2% in all cases of exudative PE.[18] Image guided tru-cut pleural biopsy also increased the yield of this diagnostic test.[19]

Conclusions:

Tuberculosis and malignancy are the two major causes for PE in the hospital. Tuberculous PE predominates slightly than malignant effusion. Tuberculous PE occurs in younger age group and has fever, cough and chest pain as predominant symptoms. DOE is more commonly seen in malignant effusion. Pleural biopsy should be done in patients with negative pleural fluid cytology. Mantoux test, ADA, pleural fluid protein and age has statistical significance in diagnosing PE. Closed pleural biopsy is useful and should be attempted in indicated cases of PE. Thoracoscopy should be done if all the other investigative modalities fail to yield a confirmatory result. Knowledge of etiological pattern helps to plan relevant investigations in patients with PE and reduces the delay in diagnosis.

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Original Article

Food allergy pattern in Alappuzha

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Abstract:

Allergy to food items is often responsible for skin allergy like urticaria. Identifying the offending allergens and avoidance is important in the management of skin allergy. This study was conducted to identify the skin sensitivity to various food allergens in patients with skin allergy and to study the regional pattern of food allergy in Alappuzha District of Kerala. 146 atopic patients with complaints of skin allergy were selected for the study. Allergy testing with 30 food allergens were performed in the above patients by intradermal method. Most common offending allergens identified were wheat (24%), garlic (22.6%), potato (20.54), nuts (18.4%), ginger (16.4%), prawns (13%) and peas (12.3%).

Introduction:

Skin Allergy in the form of urticaria and atopic dermatitis are commonly encountered. Food allergy is often responsible for this clinical situation. Identifying the offending allergens and avoidance is one of the most important measures which may help in the management of skin allergy. Skin test is the most reliable method of identifying food allergens.

MATERIALS AND METHODS

Objectives:

This descriptive study was conducted at Alappuzha, a district of Kerala, India with the following objectives.

1) To study skin sensitivity to various food allergens in patients with skin allergy.
2) To identify the regional pattern of food allergy in Alappuzha District of Kerala

Inclusion criteria

146 atopic patients with complaints of skin allergy (urticaria or atopic dermatitis) were selected for the study. The atopic status were confirmed by doing serum IgE. Serum IgE was estimated in all patients by fully automated Bi-directional Interfaced Chemo luminescent immunoassay method. Patients with serum total IgE levels more than 250 IU/ml were only selected for the study. (The normal value of IgE in adult is less than 158 IU/ml.)[1]

Exclusion criteria

1. Patients with normal or mildly elevated serum Ig E levels (less than 250 IU/L).
2. Patients with age less than 15 and more than 60.
3. Patients with other causes of urticaria (eg. Malignancy, hereditary angioneurotic edema, etc).
4. Contact allergic dermatitis.
5. Patients with extensive eczema were not included, because of difficulty in doing skin testing in such patients.
6. Since the study was aimed to identify the regional pattern of food allergy, patients outside Alappuzha District of Kerala were excluded from the study.

Methodology

Allergy testing with 30 food allergens were performed in the above patients by intradermal method. List of the

allergens tested are given in table 1. Buffered saline was used as negative control and histamine as positive control. Skin testing and reading were conducted as per criteria laid by American Academy of Allergy Asthma and Immunology (AAAAI)[2]. Patients were asked not to take antihistamines or steroids for prior 7 days of testing.

Results:

Total number of patients : 146

Sex distribution : Male -69 (47%), Female -77 (53%)

Age : ranged from 15 to 60 with an average of 36 years

Skin disease: Atopic dermatitis (eczema) - 32, Urticaria - 101, Mixed - 13

Serum IgE levels: The serum IgE values ranged from 254 IU/L to 8747 IU/L, with an average value of 1769 IU/l.

Pattern of allergy:

All the patients, except one were found to be allergic to at least one of the food allergens tested (145 out of 146, ie. 99.3%) 131 patients (89.7%) had allergy to more than one antigen. Only 14 patients were found to be allergic to a single food allergen. While 19 were allergic to two antigens, 16 were allergic to three allergens and the rest 96 patients (66%) were allergic to more than three antigens. One patient was found to be allergic to none of the allergens tested. None of the 146 patients developed any immediate or late complications following intradermal allergy testing.

Most common offending allergens were wheat (24%), garlic (22.6%), potato (20.54), nuts (18.4%), ginger (16.4%), prawns (13%) and peas (12.3%).

No relation could be established between age and sex of the patient and the number or variety of food allergens could be established.

Table 1: List of food allergens tested

Sl No	Allergen	Number of patients found to be allergic	Sl No	Allergen	Number of patients found to be allergic
1	Apple	2	16	Haldi	10
2	Banana	3	17	Lemon	12
3	Black pepper	15	18	Mutton	13
4	Cashew nut	11	19	Mustard	11
5	Chicken	8	20	Milk	8
6	Coffee	3	21	Orange	8
7	Dal urud	2	22	Onion	9
8	Dal arhar	1	23	Prawn	19
9	Dal moong	1	24	Rice	8
10	Egg white	11	25	Tea	7
11	Fish	9	26	Tomato	4
12	Garlic	33	27	Potato	29
13	Ground nut	27	28	Wheat	35
14	Ginger	24	29	Beef	8
15	Gram	2	30	Pea	18

Discussion

Skin allergy is most often due to ingested food allergens. Detection of food allergens responsible for the disease helps in prescribing avoidance diet, which is an important step in the management of food allergy. Intradermal allergy testing is an efficient method of doing allergy testing.

Food allergy pattern varies regionally. In order of prevalence, the most common food allergens at all age in Western countries are citrus fruits, tomato, egg, strawberry, soy, wheat and fish[3]. It has been reported that common food allergens among Indians are cashew nut, coconut, wheat, fish (especially shellfish), peanut, milk, egg, meat, rice, etc[4].

In this study, most common offending allergens were wheat, garlic, potato, nuts, ginger, prawns and peas. This pattern is somewhat different from the previous studies. Earlier studies have documented that allergy to spices are rare except for mustard and garlic. But in this study, allergy to spices like pepper and ginger are also frequent. Unlike in the western population, allergy to citrus fruits like orange, lemon and tomato are not common in Kerala.

Conclusions:

1. Food allergy is common among patients with skin allergy (99.3%).
2. Intradermal skin testing is an efficient and safe method to identify food allergens.
3. Most patients with food allergy are allergic to multiple allergens (90%).
4. Most commonly encountered allergens, in the order of prevalence are wheat, garlic, potato, nuts, ginger, prawns and peas.
5. Allergy to spices is not rare as previously reported.
6. Allergy to citrus fruits is not as common as in Western population.
7. There is no apparent relation between age & sex of the patient with food allergy.

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Radiology Quiz

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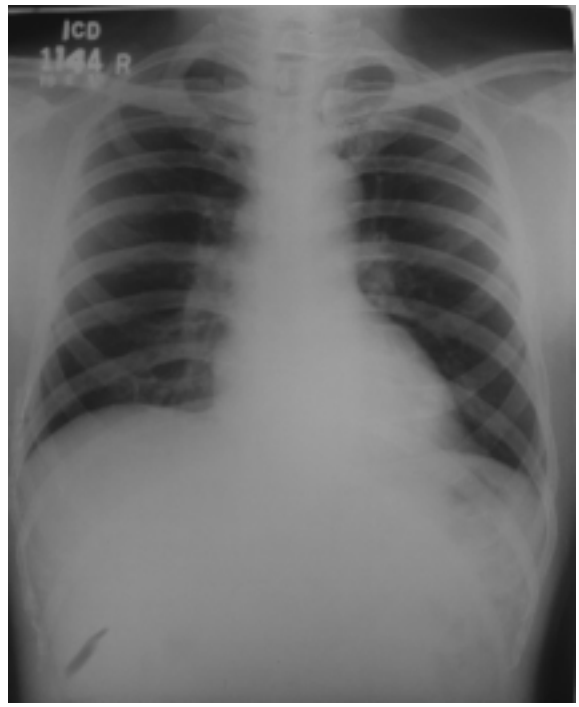

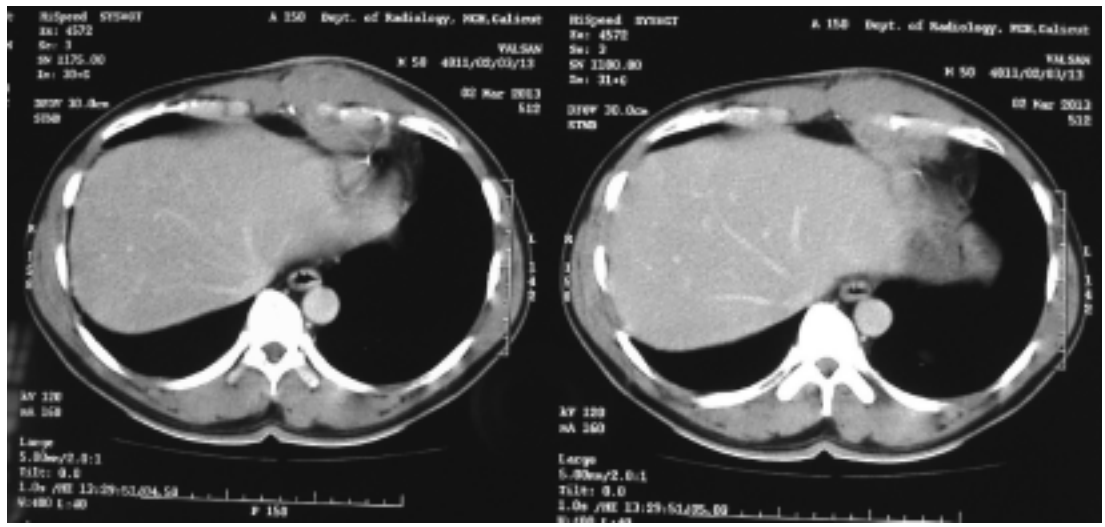

50 yr old male with Diabetes, presenting with this chest X-ray &
CT chest was started on CAT-I DOTS. Diagnosis?

Answer in Page : 109

Case Report

Malignant behavior of a benign lesion

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Abstract:

Metastasis to lung is a term almost synonymous to malignant lesions with only very few exceptions being benign. Giant cell tumor of the bone is one such disease capable of causing benign pulmonary metastasis. We here report the case of a young female who presented to us with multiple lung lesions which turned out to be benign metastatic implants from an earlier resected giant cell tumor of the tibia. Planning resection of metastatic lesions may prove beneficial with good survival benefits in this rare situation. These lesions may even show the classical pattern of doubling time observed with malignant lesions.

Key words: Giant Cell tumor (GCT), benign implants, pulmonary metastasis

Case report

A twenty year old female presented to us with left sided chest pain of four months duration. She gave history of loss of appetite of three months duration. She did not have fever, cough, expectoration or haemoptysis. There was history of a major surgery done for pain and swelling of her left Knee joint two years back. At that time an X-Ray AP view of Left Knee Joint, (fig 1) and an MRI of the knee, (fig 2), revealed a well defined lesion in the upper end of the tibia in the medial epimetaphyseal region extending to subarticular region measuring nearly 5x3 cm size. Open biopsy was done and it turned out to be giant cell tumor.

Curettage of the lesion with cementing was done, (fig 3), as part of conservative local management of the tumor as the patient was an otherwise healthy unmarried young female.

She was asymptomatic for about one year following which she developed again pain and swelling at the same site. A repeat MRI of the Knee revealed hypo intense signals in the tibia close to the tibial tuberosity on T1 weighted images which was minimally hyper intense on T2 weighted images and the lesion showed minimal contrast enhancement, (fig 4). Hence the radiologist suggested repeat biopsy to rule out a recurrence. Biopsy proved the lesion to be that of local recurrence and hence an Enneking resection with arthrodesis, K wire fixation and fibular grafting was performed as a definitive procedure, (fig 5)and the patient was moving around in crutches and was leading a near normal life till she presented to us with trivial chest symptoms.

On examination her vitals were stable; she was not dyspnoeic and was maintaining 100 % saturation on room air. Her chest movements were reduced on the left side as compared to the right, trachea was deviated to right, vocal fremitus was decreased over the left interscapular, infrascapular areas .Dull note on percussion was observed in these areas. The intensity of breath sounds and vocal resonance were reduced in the above areas. There was no evidence of any bronchial breathing or added sounds. Her routine blood investigations showed Hb- 13.8 g/dl ;

TC - 7800 DC: P64 L 22 M 12 ; Plt - 2.8 L/ml ; ESR - 32 mm / 1st hr; RBS - 112 mg/dL ; renal function tests were normal,Liver function tests were normal; Sputum AFB - Negative; Sputum cytology showed no malignant cells. Her Chest X-ray revealed a large homogenous opacity involving the left upper and mid zone extending to the lower zone with well defined medial and lateral margins silhouetting the aortic knuckle and the lateral part of the opacity merging with the lateral chest wall. Nodular opacities were seen over the lower zones on both sides. There was no evidence of pleural effusion or mediastinal widening, (Fig 6).However a Chest X-ray taken seventeen months back showed an ill defined lesion over the same area with less than half the size of the present upper lobe mass,(fig 7).

Her CT chest, (fig 8), revealed a soft tissue density lesion of size 6.6x4.3x5 cm in the left upper lobe abutting the descending thoracic aorta and extending to the lateral chest wall. Multiple enhancing nodules of varying sizes were noted scattered in both lung fields of which some showed feeding vessels and the CT picture was consistent with Pulmonary metastasis.

CT guided FNAC was done and it came as Benign implants from Giant cell tumor. Our patient was hence planned for a resection of the left upper lobe mass and radiotherapy for tumorlets.

Discussion

Secondary tumours are a common form of lung neoplasm. Lungs receive the most secondary tumours of any organ as it is the only organ to receive the entire blood and lymph flow and have the densest capillary network in the body. Metastasis to lung usually occur from primary in breast, colorectal, thyroid, head and neck, renal cell carcinoma, testicular tumors, prostate, Ewing's sarcoma, osteosarcoma and Wilm's tumor. Rarely, lung metastasis can occur from a benign primary such as Leiomyoma of uterus. Approximately 3% of Giant cell tumor (GCT) metastasizes to the lung[1]. The metastases appear as clusters of GCT located within the lung. GCT metastases generally appear at an average of 3-5 years after the initial diagnosis of the primary lesion as seen in our case[3]. The natural history of GCT varies widely and can range from local bony destruction to local metastasis, metastasis to the lung, metastasis to lymph nodes (rare), or malignant transformation (rare). GCT of the bone is a benign tumor which is locally invasive and can cause local recurrence despite wide excision and may even produce distal benign metastasis very rarely[4]. Benign histological features include absence of atypia, mitosis & necrosis. It may occasionally undergo malignant transformation as well. Lung metastasis is the cause of death in 20 - 25 % of cases.

GCT has been described as the most challenging benign bone tumor. Although benign, GCT shows a tendency for significant bone destruction, local recurrence, and occasionally metastasis[1]. The natural history of these lung metastases is unpredictable. Pulmonary metastases may spontaneously regress[2], remain stable, continues to grow slowly, or rapidly progress. In our case the size of the lesion has doubled in a manner as expected for malignant lesions with other newer lesions appearing in both lung fields. Early treatment is advocated because of the possibilities of hemorrhage, tissue necrosis and rarely, malignant transformation . These complications have been implicated as the cause of death in 16-25% of reported cases. Hence prompt detection and treatment of these metastases has been emphasized. Wide resection, chemotherapy, radiation therapy, and interferon alpha are the proposed modalities for management. Wherever possible, wide surgical resection or metastatectomy is the treatment of choice. Adjuvant treatment, such as chemotherapy or radiation therapy, has been advocated.

When the metastases are unresectable, both chemotherapy and radiation have been used as solitary agents. Interferon has been used with promising results. Malignant transformations may result in osteosarcoma, fibrosarcoma, or malignant histiocytoma.

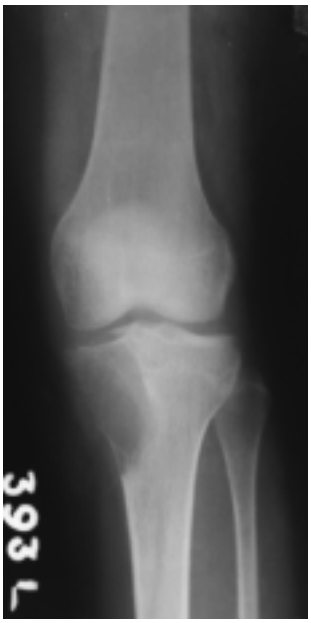
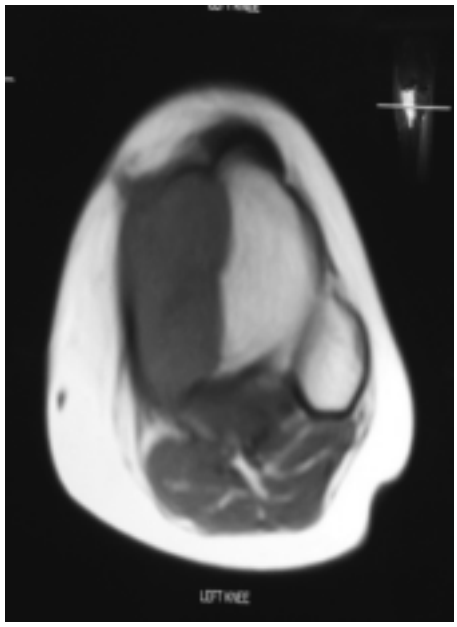


Fig 1 : X-ray Left Knee



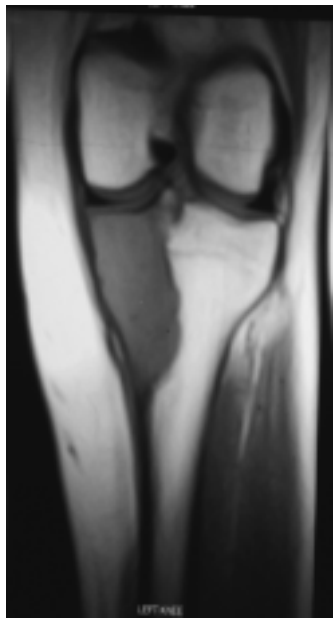


Fig 2 : MRI Left Knee

Lesion in the upper end of the left tibia in the medial epimetaphyseal region

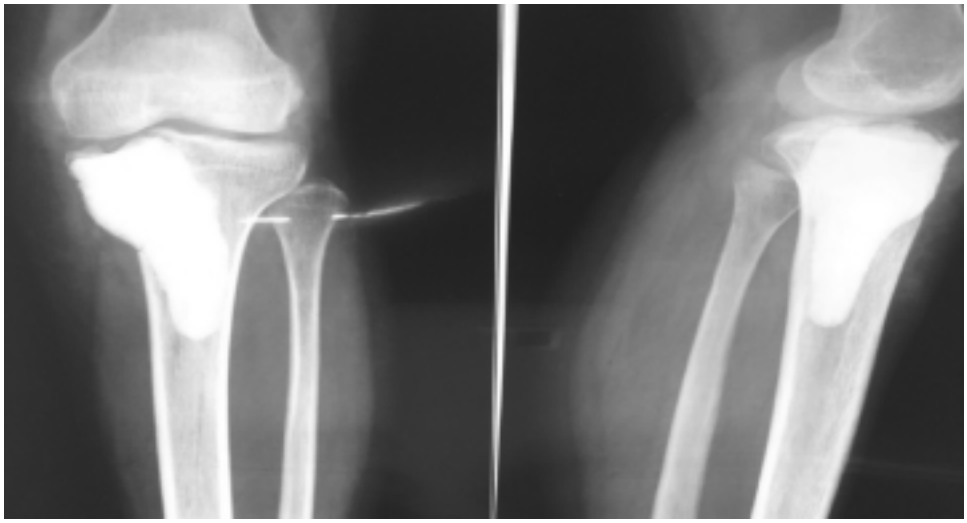


Fig 3 : Post Curettage and cementing

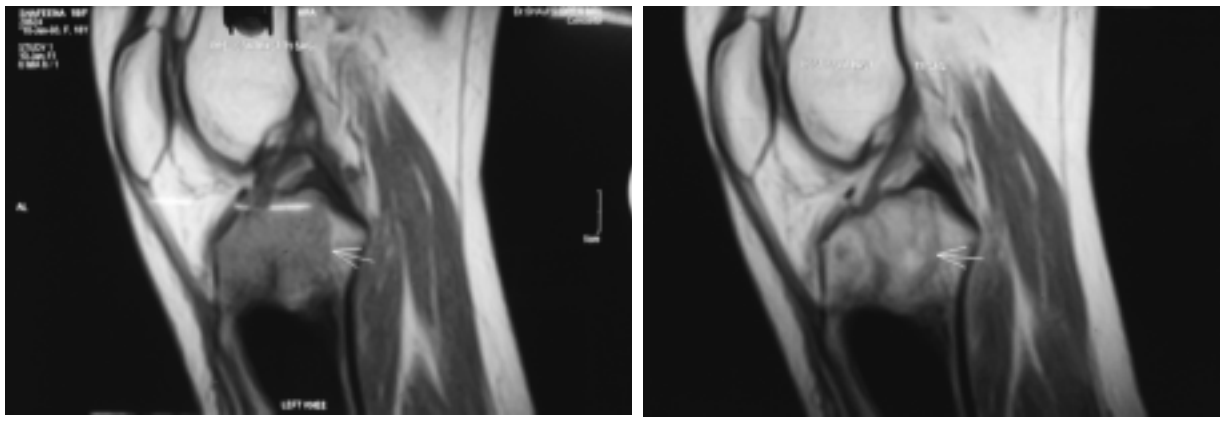


Fig 4 : Pre and Post Contrast sagittal T1 weighted Images of left Knee joint shows enhancing lesion (white arrow)

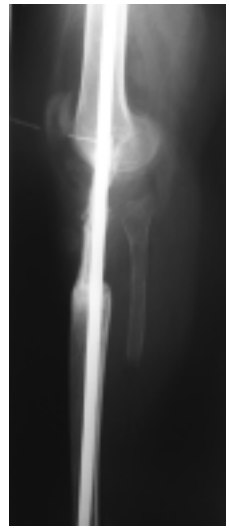


Fig 5 : X-Ray Left Knee

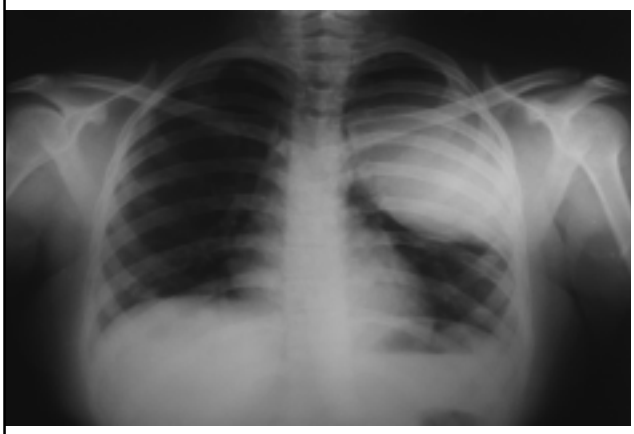


Fig 6 : Present Chest X-ray Pa view showing homogenous mass left upper lobe

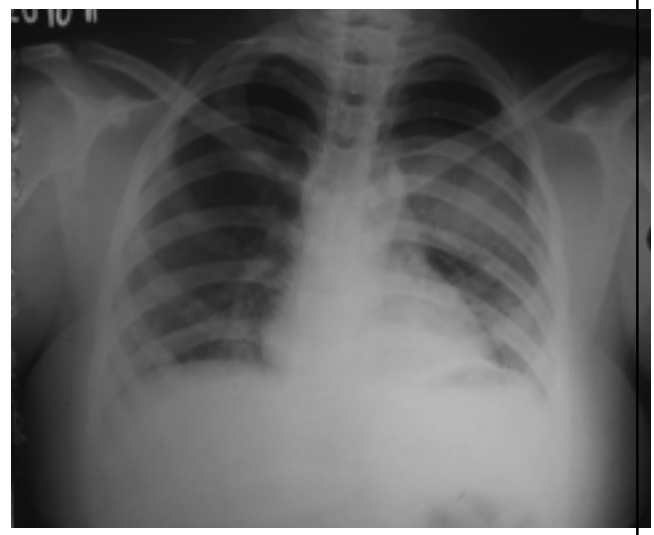


Fig 7 : Chest X-ray taken seventeen months back showed ill defined lesion left upper zone

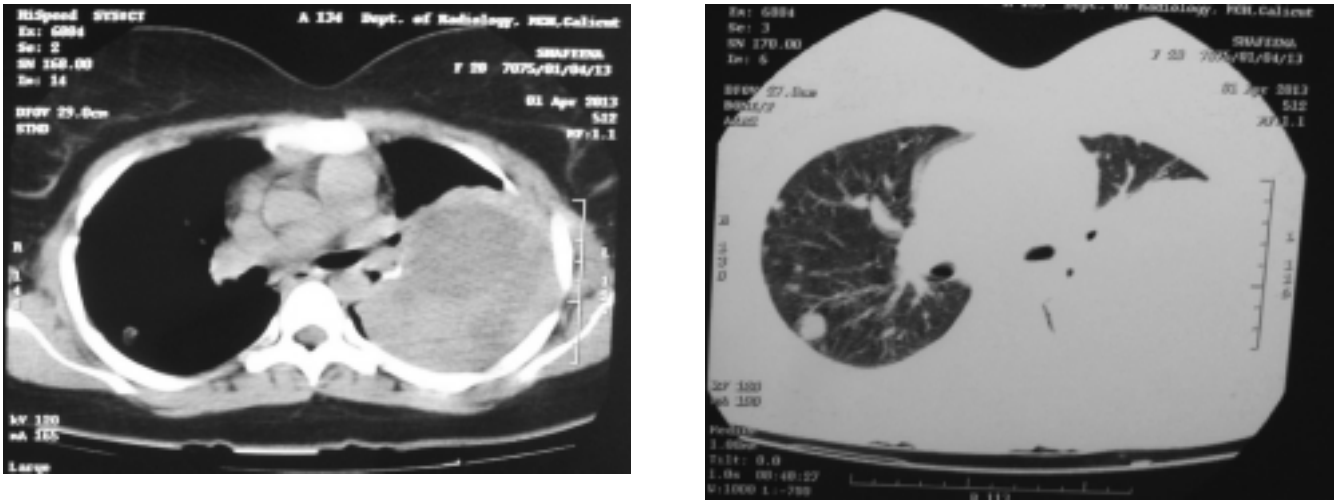


Fig 8 : CT-Chest showing metastatic lesions of varying sizes

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Case Report

Scimitar Sign and Scimitar Syndrome

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Introduction

Scimitar syndrome is a rare congenital cardiovascular anomaly with an incidence of 1-3 per 1,00,000 live births. The radiological description "Scimitar sign" may occur in isolation which is more frequently encountered in clinical practice. It can also be part of the full blown Scimitar syndrome wherein other congenital anomalies are also present. This case report is intended to high light Scimitar syndrome with particular emphasis on the radiological characterization of the individual components of the syndrome.

Key words: Scimitar syndrome, Scimitar sign

Case report

A 35 year old lady presented to our outpatient clinic with symptoms suggestive of asthma. Clinical examination of the respiratory system revealed the presence of polyphonic wheezes over both lung fields. On routine evaluation she was found to have an abnormal chest radiograph (Fig 1). There was evidence of volume loss in the right hemithorax with ipsilateral shift of mediastinum and a linear opacity parallel to the right heart border. With a suspicion of Scimitar sign, she was further evaluated with a contrast enhanced computed tomogram of the chest which revealed the presence of the following abnormalities - hypoplasia of the right lung, dextroposition of the heart, hypoplastic right descending pulmonary artery and an enlarged and elongated anomalous pulmonary vein having tributaries from the hypoplastic right upper lobe, middle lobe, lower lobe and the right inferior pulmonary vein and finally joining the inferior vena cava at the diaphragmatic hiatus level. (Fig 2). This was better delineated by the technique of Maximum Intenstiy Projection, which is a method of three dimensional reconstruction using the computed tomogram images. (Fig 3). The left pulmonary artery is of normal caliber (Fig 4) where as the right pulmonary artery is hypoplastic (Fig 5). These constellation of radiological signs are consistent with a diagnosis of Scimitar syndrome, a rare but well known congenital cardiovascular anomaly.

Discussion

The radiological sign, coined by Naill in 1960, is called Scimitar sign because the characteristically curved anomalous right pulmonary vein that drains into the inferior vena cava resembles the curved Middle Eastern (Turkish) sword called "Scimitar". A variety of congenital thoracic abnormalities are associated with this specific type of partial anomalous pulmonary venous return first described by Cooper in 1836 [1,2]. Associated anomalies are variable and include hypoplasia of the right lung, dextroposition of the heart, hypoplasia of the right pulmonary artery (RPA), and anomalous systemic arterial supply from the aorta to the right lung [3]. This rare anomaly has an incidence of approximately 1 to 3 per 100,000 live births[4]; the true incidence may be higher because many patients are asymptomatic.

Scimitar syndrome overlaps with pulmonary sequestration and the term "venolobar syndrome" has been

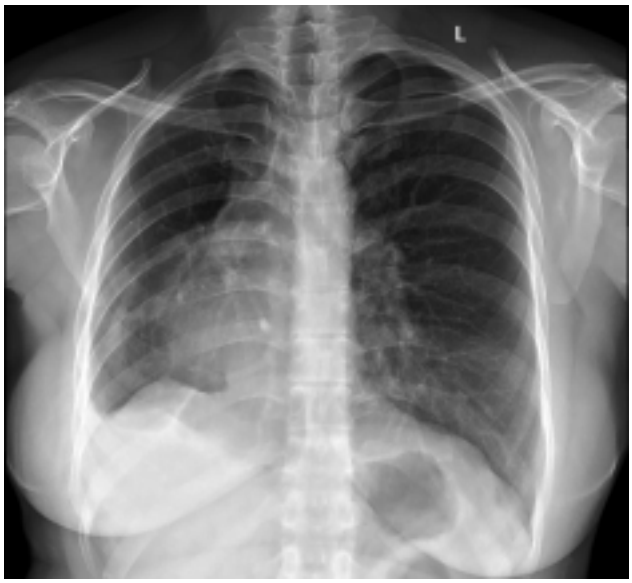

Fig 1: Chest X ray PA view depicting the anomalous vein (Scimitar sign) and hypoplastic right lung

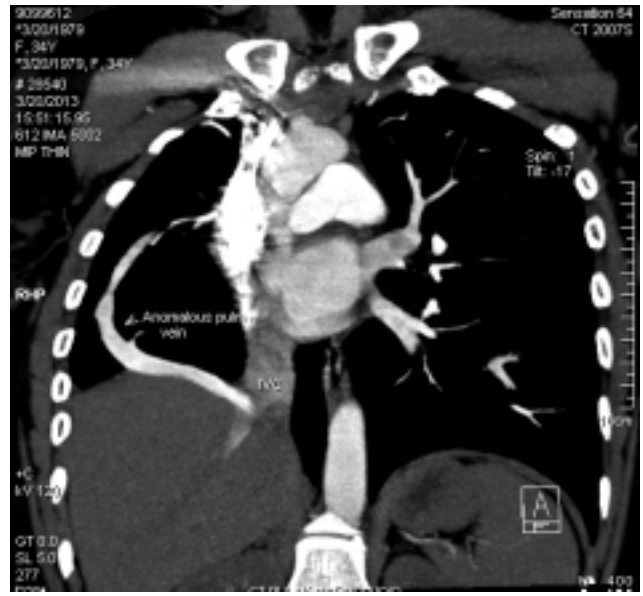

Fig 2: Contrast enhanced CT scan clearly delineating the anomalous course of the inferior pulmonary vein

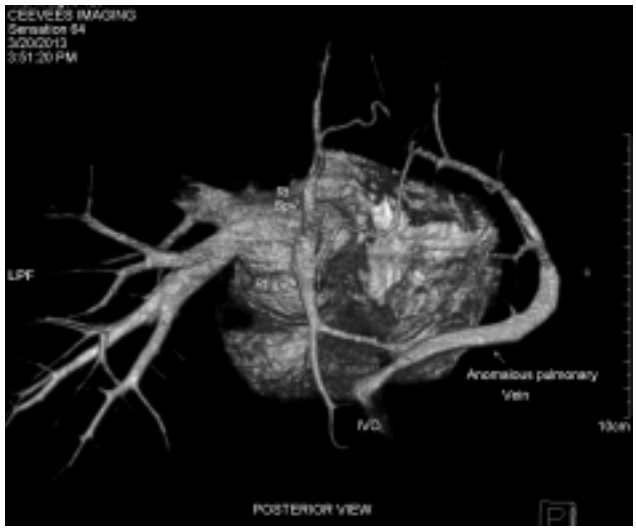

Fig 3: Maximum intensity projection image which gives a three dimensional view of the anomalous course of the inferior pulmonary vein

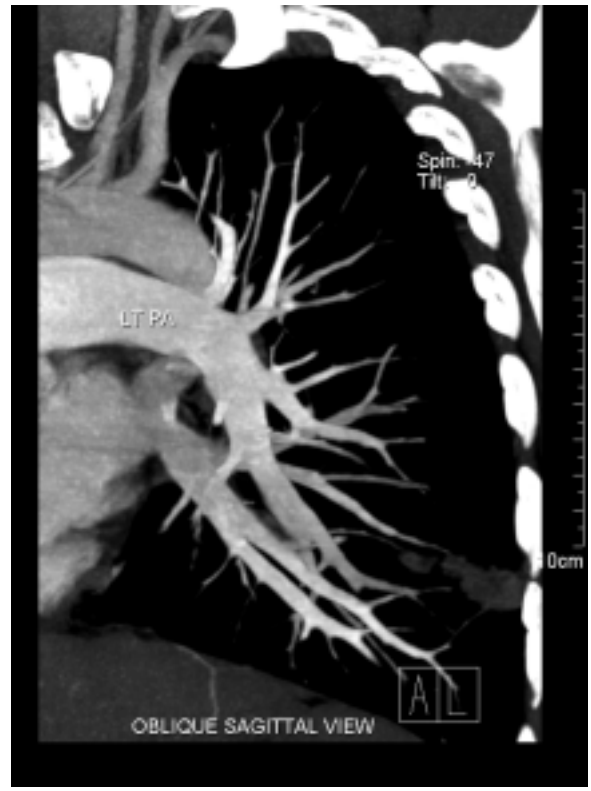

Fig 4: Left pulmonary artery which is normal in caliber

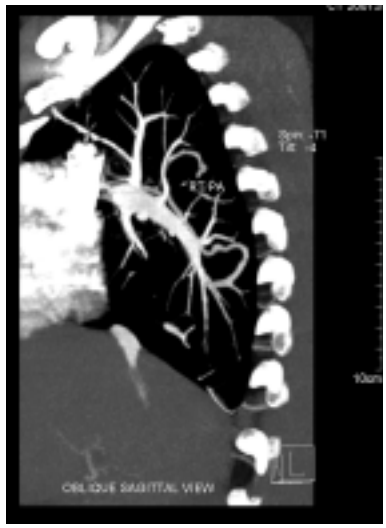

Fig 5: Hypoplastic right pulmonary artery

coined to include these associated pulmonary and vascular malformations[5]. This condition is associated with:

1. Partial agenesis or hypoplasia of the right lung with bronchial isomerism.
2. Diverticulum or hypoplasia of the right bronchial system.
3. Hypoplasia or agenesis of the right pulmonary artery. This may cause mediastinal shift to the right side and Scimitar vein may be difficult to appreciate or even completely obscured.
4. Abnormal systemic blood supply to at least part of the right lung, most frequently the posterior basal segment of the lower lobe, usually arising from the infra diaphragmatic descending aorta.
5. Dextroposition of the heart due to right lung hypoplasia with mediastinal shift.
6. Accessory diaphragm, eventration or partial absence of the diaphragm.
7. Phrenic cyst.
8. Horseshoe lung.
9. Esophageal and gastric lung.
10. Absence of the pericardium.
11. Other congenital cardiac malformations (25% of cases) including ASD, ventricular septal defect, coarctation of the aorta, tetralogy of Fallot, pulmonary stenosis, absent inferior vena cava with azygous continuation to superior venacava

Three-dimensional computed tomography (CT) and cardiac-gated magnetic resonance imaging (MRI) are useful in visualizing the anomalous pulmonary vein. . Scimitar syndrome has been reported most widely in adults and older children and is usually found during a workup for dyspnea, fatigue, recurrent respiratory infections, or as an incidental finding on a routine chest radiograph [4]. This adult form of Scimitar syndrome usually is not associated with pulmonary hypertension and typically has mild symptoms and a benign prognosis.

Most patients require only medical follow up. The indications for surgical repair include the presence of Scimitar syndrome, especially in association with ASD, pulmonary hypertension, or stenosis of the anomalous vein. Several methods with cardiopulmonary bypass have been recommended to repair this anomaly, including direct anastomosis of the Scimitar vein to the left atrium, or division with reimplantation of the anomalous pulmonary vein into the right atrium with baffle insertion to redirect the flow into the left atrium[6].

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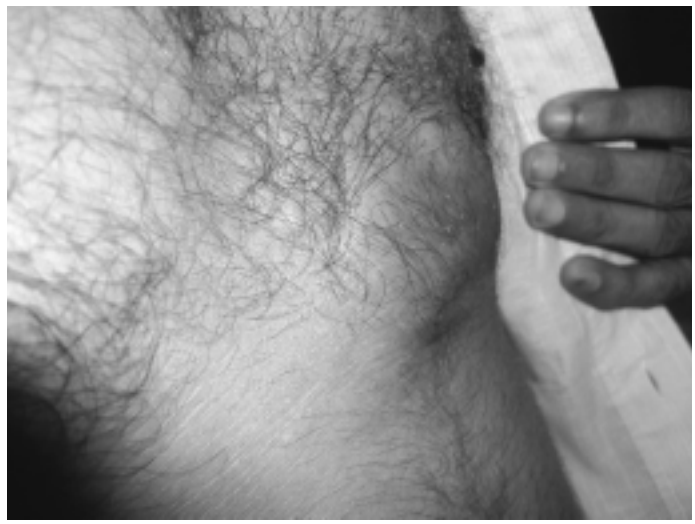
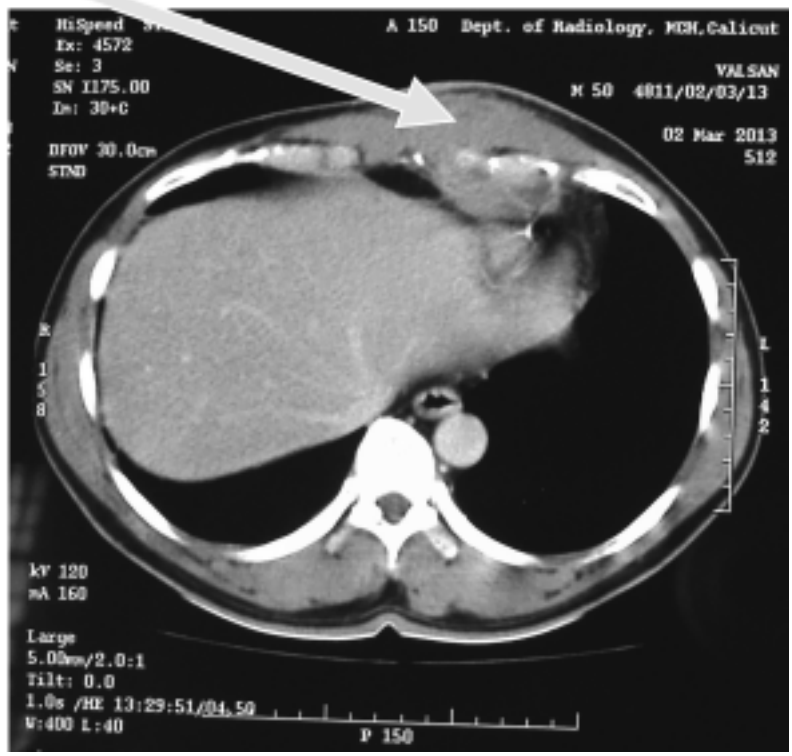
Answer

Collar stud abscess (bold arrow).

FNAC of the lesion revealed granulomatous disease suggestive of Tuberculosis. The most likely gland involved is the internal mammary gland which results in periadenitis causing these nodes getting adherent to each other. The caseous node perforates through the anterior chest wall and the caseous matter escapes into the subcutaneous plane resulting in the characteristic collar stud abscess.





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