Pulmon

The Journal of Respiratory Sciences

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Academy of Pulmonary & Critical Care Medicine

Pulmon

The Journal of Respiratory Sciences

Editorial

Allergic Bronchopulmonary Apergillosis Do We Need More Studies ?

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Allergic Bronchopulmonary Apergillosis (ABPA) is a hypersensitivity response to the Aspergillus fungi mostly seen in patients with Asthma and Cystic Fibrosis (CF). CF being rare in India, ABPA is almost a disease of patients with Naso Bronchial Allergy (NBA). The first description of the disease was given by Hinson KF et al in 1952[1]. From India the first case report of ABPA was by Shah JR in 1971[2], after few sporadic reports Agarwal R et al published the experience of 126 patients from North India in 2006. The prevalence of ABPA is approximately about 2% in Asthma. In India prevalence is relatively high that varies from 7.5% to 27.2%[3,4].

ABPA is mostly seen in the age group 30- 40 years but it can occur in children and elderly. The common presentation of the disease is asthma which may be uncontrolled or controlled. Rarely it may present in those without asthma. The other features are fleeting lung infiltrates with or without, bronchiectasis, eosinophilia, elevated serum total IgE, Aspergillus specific IgE, IgG, precipitin antibody and skin test positivity to Aspergillus antigen. The criteria followed by most centers to diagnose the disease are the one put forward by Rosenberg in 1977[5] which was later modified by Greensberger in 1997[6].

There is no single diagnostic test for the disease and all patients might not present with the classical features of the disease. As ABPA mimics tuberculosis it is often misdiagnosed and treated as tuberculosis[4] . Better awareness of the disease can improve the detection rate. It is extremely important to make an early diagnosis. A delay in the diagnosis probably may lead to bronchiectasis and lung fibrosis.

ABPA is generally treated with corticosteroids (CS) to suppress the immune response[10]. Treatment has to be continued for 6 to 12 months[11]. Different centers follow different treatment schedules. Antifungal can be added to CS[12]. This will reduce the burden of fungi and thereby prevents further antigenic stimulation. The most effective antifungal in the treatment of ABPA at present is Itraconazole[13]. Combination therapy is more effective than steroids alone[14]. The monoclonal anti IgE Omalizumab was also found to be benificial[15].

Availability of an effective treatment may demand for an early diagnosis. The main obstacles for early diagnosis are

1) Absence of a single specific test

2) Masking of the criteria's used for diagnosis by concomitant steroid administration

3) Resemblance with common diseases like tuberculosis and malignancy

Considering the need of an early diagnosis focus now is to find out new tests with more sensitivity and specificity. Recombintant Aspergillus antigen synthesized from c DNA of Aspergillus fumigates may improve the specificity of skin testing and measurement of specific IgE[10]. Thymus and Activation Regulated Chemokines (TARC) which is a chemo attractant to Th2 cell has more specificity and sensitivity compared to specific igE in CF associated ABPA. FACS basophil CD 203c is being evaluated for the diagnosis and follow up patients with ABPA. These may emerge as the future tests for ABPA[11]

Two investigations, Computed Tomography (CT) of thorax and bronchoscopy which have only a supplementary role today, has to be utilized in a better way for an early diagnosis. Apart from its advantage in differentiating TB and bronchogenic carcinoma CT features like high attenuation mucus (HAM) in airways have relatively high specificity in ABPA[12,13,14]. There is lack of specificity of central bronchiectasis and that term has been removed from the radiologic classifications of ABPA. The revised radiologic classification for ABPA is ABPA-S (Serological), ABPA- B (Bronchiectasis), ABPA -HAM and ABPA –CPF (chronic pleuropulmonary fibrosis) based on findings of High Resolution CT. Bronchoscopy may also play an important role in the diagnosis. Many ABPA patients presents as collapse of a lung, lobe or a segment mimicking malignancy. Brochoscopy is helpful not only to rule out malignancy but also to support the diagnosis of ABPA. The thick mucus plugs along with the presence of Aspergillus fungus in bronchial wash and biopsy will help in confirming the diagnosis. Presently it is reserved for patients presenting with collapse. Can it help in the diagnosis of ABPA in those without obvious collapse? If so bronchscopy can be upgraded to a routine test in the evaluation of

ABPA. Combining CT thorax and bronchscopy will also help in eliminating tuberculosis and malignancy much more easily.

There are lots of other issues related to ABPA. In the recent years there is an increase in case reports of ABPA.Is this because of the increased awareness and improved facilities to diagnose the disease or an actual increase in the incidence? If there is actual increase what are the factors leading to this? Is there a better alternative to eosiophil count and IgE in the screening of ABPA? Will ABPA respond to antifungal alone? What is the optimum dose and duration of Itraconazole? Considering the complexity of the disease there is no end to the queries and only specific dedicated research can answer these questions.

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Review Article

Role of Probiotics in Preventing Acute Respiratory Tract Infections

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Introduction

The beneficial effects of food with added live microbes (probiotics) on human health, and in particular on children and other high-risk populations, are being increasingly promoted by health professionals. It has been reported that these probiotics can play an important role in immunological, digestive and respiratory functions and could have a significant effect in alleviating infectious disease in children. "Probiotics" are defined as "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.(Food and Agriculture Organization 2001.U.S)[1]. At the same time, Food and Drug Administration (FDA) has not approved any specific health claims for probiotics. The amounts of probiotics that studies have found to be beneficial vary from strain to strain and condition to condition.

Probiotic strain characteristics

- Human Origin
- Adherence to oral surface
- Acid Stability
- Production of antimicrobial substances
- Antagonism against cariogenic and pathogenic bacteria
- Safety in food and clinical use
- Clinically documented and validated health effects

Common Strains

- Lactobacillus acidophilus.
- Lactobacillus reuteri.
- Lactobacillus rhamnosus.
- Lactobacillus casei.
- Bifidobacteriumlactis.
- Saccharomyces cerevisiae (S. boulardii).
- Streptococcus thermophilus
- Enterococcus faecium

Frequently used strains

1) Lactobacillus

This is the most common probiotic. It's found in yogurt and other fermented foods. Used for treating and preventing diarrhea, including rotavirus diarrhea in children and traveler's diarrhea[2]. Used to prevent and treat diarrhea associated with antibiotics use. Prevent common cold in adults, and respiratory infections in children. Also used for high cholesterol, lactose intolerance, Lyme disease, hives, and to boost the immune system.

2) Bifidobacteria

This is also found in some dairy products. Bifidobacteria are used for many conditions affecting the intestines, such as preventing diarrhea in infants and children; as well as traveler's diarrhea in adults. Other uses for Bifidobacteria include treating atopic eczema in infants, candidiasis, cold, flu, reducing flu-like symptoms in children attending day-care centers.

Common conditions where probiotics are useful

- Irritable bowel syndrome
- Inflammatory bowel disease (IBD)
- Infectious diarrhea (caused by viruses, bacteria, or parasites)
- Antibiotic-related diarrhea
- Skin conditions, like eczema
- Urinary and vaginal health
- Preventing allergies and colds
- Oral health

Mechanisms of action

The beneficial role of intestinal microflora, is by "colonization resistance" or "barrier effect".[3] Mechanism used by bacteria already present in the gut to maintain their presence in this environment avoid colonization of the same sites by new microorganisms, including pathogens. Therefore, it is assumed that dietary manipulation of gut microflora, increases the relative numbers of beneficial bacteria which contribute to the wellbeing of the host.

- Competitive exclusion of enteric pathogen by adhesion
- Triggers cytokine production by enterocytes
- Maintenance of normal intestinal flora
- Cholesterol lowering effects
- Increase of turnover of enterocyte
- Neutralization of dietary carcinogen such as nitrosamines
- Growth inhibition of pathogen by Lactic acid and Bacteriocin
- Food allergy reduction
- Paediatric gastroprotection
- Immunomodulatory effects

Role of probiotics

The scope of these micro-organisms is broad, concerning many areas including that of infectious diseases, especially respiratory infections. Rational use of probiotics may be beneficial in respiratory infections such as nosocomial or community acquired pneumonia, or on specific grounds such as cystic fibrosis. The results are sometimes contradictory, but the therapeutic potential of probiotics seems promising. Implementing research to understand their mechanisms of action is critical to conduct therapeutic tests.

A 2011 Cochrane review suggested that probiotic prophylaxis significantly reduced URTIs and antibiotic prescriptions for URTIs in randomized controlled trials of specific populations. One small pilot study in patients with asthma found that probiotics in combination with acupuncture reduced respiratory infection rates, but the study was underpowered (n = 17), and the results were not statistically significant (P =0.18). Controlled trials in younger children demonstrated that probiotics reduce respiratory tract infections and hence reduce antibiotic prescription rates. They established the reproducibility of these findings in older children and adults with asthma using information leaflets[5].

Lactobacillus acidophilus and Lactobacillus casei commercial strains exhibit antibacterial activity against clinical MRSA isolates. Their effects were mediated both by direct cell competitive exclusion as well as production of acids or bacteriocin-like inhibitors. In vitro antimicrobial activity did not necessarily assure efficacy in vivo in animal infectious models. Very few clinical data were found on the interactions between probiotics and MRSA, but the few identified clinical cases pointed to the feasibility of elimination or reduction of MRSA colonization with probiotic use.

Randomised controlled trials (RCTs) studying the effects of probiotics for the prevention of upper or lower RTIs were systematically identified. Fourteen RCTs (twelve involving healthy subjects and two involving patients with RTIs) were included[6]. Various Lactobacillus strains were used in seven RCTs, combinations of Lactobacillus and Bifidobacterium strains were used in five RCTs, and a Bifidobacterium strain and a non-pathogenic Enterococcus faecalis strain were used in one RCT, respectively.

In ten RCTs no difference was found regarding the incidence of RTIs in the probiotic arm compared with the control arm, whereas the remaining four RCTs favoured the use of probiotics. Reduction in the severity of symptoms related to RTIs was noted in five of six RCTs that provided relevant data. In three of nine RCTs that provided relevant data, the clinical course of RTIs was shorter in the probiotic arm, whereas no difference was found in the remaining six RCTs. In conclusion, probiotics may have a beneficial effect on the severity and duration of symptoms of RTIs but do not appear to reduce the incidence of RTIs

Probiotics were better than placebo in reducing the number of participants experiencing episodes of acute URTI, the mean duration of an episode of acute URTI, antibiotic use and cold-related school absence[4]. This indicates that probiotics may be more beneficial than placebo for preventing acute URTIs. However, the quality of the evidence was low or very low.

The proportion of study subjects who experienced 1 or more week with URTI symptoms was not different from that of placebo (PRO .58, PLA .59; p = .947). The number of URTI episodes was similar in the 2 groups (PRO 1.6 ± 0.3, PLA 1.4 ± 0.3; p = .710). Severity and duration of symptoms were not significantly different between treatments. Regular ingestion of L. salivarius does not appear to be beneficial in reducing the frequency of URTI and does not affect blood leukocyte.

Studies showed a positive effect of probiotics on reducing the number of pulmonary exacerbations and decreasing gastrointestinal inflammation. The findings suggest that probiotics may improve respiratory and gastrointestinal outcomes in a stable CF clinic population with no reported evidence of harm. There is inadequate evidence at this time to recommend a specific species, strain or dose of probiotic as likely to be of significant benefit[7].

Evidence suggests that use of probiotics is associated with a reduction in the incidence of VAP. However, the quality of the evidence is low. The available evidence is not clear regarding a decrease in ICU or hospital mortality. Three trials reported on the incidence of diarrhoea. The results of this meta-analysis do not provide sufficient evidence to draw conclusions on the efficacy and safety of probiotics for the prevention of VAP in ICU patients[8].

1,302 participants were randomly assigned to a control group (n = 650) or intervention group (n = 652). There was no significant difference in the primary outcome measure, with 27.7% receiving antibiotics in the intervention group and 26.9% receiving antibiotics in the control group. There is no evidence of an effect on respiratory tract infections or asthma exacerbations. In this pragmatic community-based trial there is no evidence to suggest that use of winter probiotics reduces antibiotic prescriptions in asthmatics[9].

A fatal case of community acquired pneumonia and lung abscess due to Lactobacillus caseissrhamnosus was reported. Clinicians should be aware of this type of pneumonia[10].

According to data, probiotics reduced URTI episodes (average 7 days) by -0.77 days [-1.5;-0.04]. Extrapolating these results to the French population, probiotics would save 2.85 million URTI-days, the number of antibiotic courses would drop from 1,004,000 to 674,000 (difference about -330,000) and the number of sick leave days avoided in adults would be 653,000. According to Cochrane data, probiotics would reduce the probability to have an URTI episode by 0.58 [0.36;0.92] and antibiotic prescription by 0.67 [0.45;0.98]. The probiotic impact would become larger in terms of URTI-days avoided (-7.1 million), antibiotic courses (-509,000) and workdays lost (-1.2 million) [11].

Conclusion

There is good evidence that specific strains of probiotics are safe for human use and able to confer some health benefits on the host, but such benefits

cannot be extrapolated to other strains without experimentation. The health benefits for which probiotics can be applied include conditions such as gastrointestinal infections, certain bowel disorders, allergy, and urogenital infections, which afflict a large portion of the world's population.In addition, there is emerging evidence to indicate that probiotics can be taken by otherwise healthy people as a means to prevent certain diseases and modulate host immunity. Number of studies performed so far in the field of respiratory tract infections is small, though some data show that probiotic administration might display clinical advantages. Current laboratory and clinical data regarding the possibility of the role of probiotics on preventing the development of respiratory tract infections are contradictory, and are somewhat insufficient to recommend their routine use.

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Original Article

Prevalence of Allergic Bronchopulmonary Aspergillosis Among Patients with Asthma Attending a Tertiary Care Centre

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Abstract

Background : Allergic bronchopulmonary aspergillosis (ABPA) is a complex hypersensitivity reaction to Aspergillus species, often seen colonizing the airways in patients with asthma and cystic fibrosis. Repeated episodes of airway obstruction, inflammation and mucoid impaction can lead to bronchiectasis, parenchymal fibrosis and respiratory compromise.

Objectives : To study the prevalence of allergic bronchopulmonary asergillosis (ABPA) in patients with asthma in a tertiary care centre in South India. To assess the complications like central bronchiectasis and parenchymal fibrosis in such patients.

Materials and Methods : 120 consecutive patients with asthma diagnosed on basis of clinical and spirometric findings who presented to respiratory medicine department of KIMS, Trivandrum over a period of one year were included. All were initially screened for skin test for immediate skin test reactivity to 5 common Aspergillus species antigens namely A. fumigatus, A. flavus, A. niger, A.tamari and A. versicolor. Those who had positive skin test were further evaluated for the diagnosis of ABPA with serology and HRCT.

Results : A total of 120 patients (43 males, 77 females) were included in this study with mean age of 48.16 years (18 to 70 years). 38 patients (31.7%) were found to be skin test positive. 16 patients (13.3%) were diagnosed to have ABPA using standard criteria. HRCT showed central bronchiectasis in 7 (43.8%) patients and parenchymal fibrosis in 1 (6.3%) patient.

Conclusion : In our study, the prevalence of allergic bronchopulmonary aspergillosis (ABPA) among studied population was 13.3%. Any patients of long standing asthma and need for regular oral corticosteroids for control of symptoms, should always be investigated for ABPA. Efforts should be emphasized to improve the awareness level about this disease in high tuberculous prevalence area, as patients with ABPA are often misdiagnosed as having tuberculosis due to the radiological similarities. Early diagnosis and initiation of appropriate therapy with oral corticosteroids could alter the natural course of the disease and prevent end stage parenchymal fibrosis.

Key Words : ABPA, asthma, central bronchiectasis, parenchymal fibrosis

Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a immune mediated response to chronic airway colonization by Aspergillus species, often seen in patients with asthma and cystic fibrosis [1,2]. Aspergillus is a ubiquitous fungus that is found throughout the world. Spores are tiny and easily aerosolized and deposit in distal and terminal airways, where they germinate if the airway environment is favourable. Over 150 species of this fungus have been identified, of which A.fumigatus (AF) is responsible for about 95% of Aspergillus related illness in humans. Host characteristics are a major determinant of the type of pulmonary disease that may develop in response to Aspergillus exposure. Various Aspergillus-associated pulmonary disorders can be broadly classified into three clinical categories, viz allergic aspergillosis, saprophytic colonisation and invasive diseases[3]. ABPA is the most frequently recognised presentation of allergic aspergillosis and is worldwide in distribution. ABPA is being recognised as an upcoming disease in India also. There is no single test that can establish diagnosis of ABPA. A set of minimal essential criteria (Table-1) has been advocated by Greenberger[4] . Using this criteria, ABPA may be considered to exist in two forms: ABPA-seropositive (S) and ABPA-central bronchiectasis (CB). When central bronchiectasis is not present, the disease entity is termed serological ABPA, which could possibly be an earlier or a milder form of presentation[5]. The ISHAM working group has proposed revised criteria for the diagnosis of ABPA[6]. Five clinical stages of ABPA were identified[7,8] based on clinical, serologic and radiographic characteristics: 1) acute, 2) remission, 3) exacerbation, 4) corticosteroid-dependent asthma and 5) fibrotic lung disease. Staging of the disease should be done at the time of diagnosis and re-evaluated periodically. A new clinical staging of ABPA in asthma proposed by the ISHAM working group has not been widely adopted[6]. The goal of treatment for ABPA include[9] prevention and treatment of exacerbation, management of underlying asthma and prevention of end stage parenchymal fibrosis. Oral corticosteroids are the mainstay for the treatment of ABPA[10], as they aid in suppressing the immune hyper-reactivity in patients with asthma and ABPA by their anti-inflammatory properties.

Table 1 : Diagnostic Criteria for ABPA (patients without cystic fibrosis)[4]

Major Criteria

- Asthma
- Immediate type-1 skin test reactivity to A.fumigatus
- Elevated total serum IgE >417 kU/L(>1000 ng/ml)
- Elevated A.fumigatus specific serum IgE and/or IgG
- Peripheral blood eosinophilia (not essential for diagnosis)
- Precipitin antibodies to A.fumigatus (not essential for diagnosis)
- Presence of chest roentgenographic infiltrates (not essential for diagnosis)
- Central bronchiectasis in the absence of distal bronchiectasis

Minor Criteria

- Expectoration of brown mucus plugs
- Positive sputum culture for A.fumigatus
- Late (Arthus–type 3) skin reactivity to A.fumigatus

The true prevalence of ABPA among asthmatics is not known. This may be attributed to the lack of a uniform diagnostic criteria and standardized tests[11] and delays in the diagnosis of patients with long-standing disease. The prevalence of allergic bronchopulmonary aspergillosis (ABPA) among patients with persistent asthma is estimated at 1 to 2 percent, although rates up to 28 percent have been reported[12]. Reported rates are higher in patients seen in asthma clinics and those admitted to the hospital with an asthma exacerbation. Despite of high prevalence of ABPA reported in different studies, ABPA is still under diagnosed in our country. A number of factors may be responsible for this situation. There is high prevalence of tuberculosis in our country and a large number of ABPA cases may be misdiagnosed as having tuberculosis due to the radiological similarities[13]. The present study is carried out to determine the prevalence of ABPA among patients with asthma catered by Kerala Institute of Medical Sciences (KIMS), a tertiary care hospital in Trivandrum, Kerala.

Materials and Methods

All patients (120) with symptoms suggestive of asthma presenting at outpatient clinic and those admitted as inpatient in the department of respiratory medicine, Kerala Institute of Medical Sciences (KIMS), Trivandrum over a period of one year were included in this study. Patients with history of smoking, previous history of tuberculosis, pregnant and lactating women were excluded from the study. After getting informed consent clinical history of all patients were taken. It included present symptoms, history of allergic rhinitis, atopic history. Co-morbidities were enquired along with relevant personal history. Thorough general and respiratory system examination were done and positive findings were noted. All patients underwent spirometry and bronchodilator reversibility testing. Reversibility was defined as 12% and 200 ml increase in the FEV1 following 400μg of inhaled Salbutamol[14].

All asthma patients underwent aspergillus skin test for 5 common Aspergillus antigens namely A.fumigatus, A.flavus, A.niger, A.tamari, A.versicolor. There is no additional harm or risk to the life due to this test. The intradermal skin test was performed as follows: (i) The skin test was performed by injecting 0.01 ml of the aspergillus antigens intradermally in the forearm. For negative control, 0.01 ml of normal saline was injected intradermally in the same forearm. (ii) The injection site was examined after 20 min. Aspergillus sensitisation was defined if a wheal and erythema developed within 1 min, reached a maximum after 10–20 min and resolved within 1 hour. The result of the test was considered as positive if the reaction to the antigen was at least twice that of the control. Only those asthma patients showing positive response to any of the aspergillus antigens were investigated further for the diagnosis of ABPA. The diagnosis was made by using either four or five of minimal essential criteria advocated by Greenberger, as described above (table-1). The peripheral blood eosinophil count was carried out by standard Hematoxylin and Eosin (HE) staining - an eosinophil count greater than 350 per cubic mm was taken as eosinophilia. The total serum IgE was assessed by the ELFA (enzyme-linked fluorescent immunoassay) method. Serum aspergillus specific IgE was determined by FIA (Fluorescent immunoassay) method. Serum aspergillus specific IgG was determined by ELISA (enzyme linked immunosorbent assay) method. Serum precipitin test could not be done due to logistic reasons as these precipitating antibodies may also be present in 10% of asthmatics who do not have ABPA[15]. High levels of serum precipitating antibody against A.fumigatus have also been shown in various other forms of chronic pulmonary aspergillosis[16]. Chest radiographs were reviewed for the presence of fleeting opacities in serial chest radiographs, toothpaste or gloved finger shadows indicative of mucus impaction, ring shadows or tramline shadows indicative of bronchiectasis and for evidence of fibrosis. High resolution CT (HRCT) scan of the chest was done to look for any central bronchiectasis, parenchymal fibrosis, consolidation, atelectasis and mucous plugging. Sputum culture for A.fumigatus was done on sabouroud's dextrose agar.

Statistical Analysis

The collected data were analyzed using the statistical software SPSS Version 16. All the categorical data were expressed in frequencies (n) and percentages (%). A chi square test has applied to know the statistically significant association between the variables. A p value <0.05 is considered as significant.

Table 2 :
List of clinical features assessed

Findings	Yes	No
1. Breathlessness		
2. Cough		
3. Chest tightness		
4. Fever		
5. Expectoration		
6. Wheeze		
7. Allergic rhinitis		
8. Atopic dermatitis		
9. Chest finding • Rhonchi • Crackles		

Table 3 :

List of characteristics assessed

1. PFT findings	
• FVC((litre/min)	
• FEV1(litre/min)	
• FEV1 %	
• Reversibility	
2. Absolute eosinophil count (AEC)	
3. CXR Findings	
• Normal	
• Fleeting infiltrates	
• Toothpaste/Gloved finger shadow	
• Ring/Tramline shadow	
4. Intradermal skin test for Aspergillus antigen	
• Positive	
• Negative	
5. Total serum IgE level	
6. Serum specific IgE to A.fumigatus	
• Positive	
• Negative	
7. Serum specific IgG to A.fumigatus	
• Positive	
• Negative	
8. HRCT findings	
• Normal	
• Consolidation	
• Atelectasis	
• Central bronchiectasis	
• Parenchymal fibrosis	
9. Sputum culture for Aspergillus species	
• Positive	
• Negative	

Results

All 120 consecutive patients with asthma who had fulfilled the inclusion and exclusion criteria were included in the study. Among them males were 43 (35.8%) and females were 77 (64.2%). The age of patients ranged from 18 years to 70 years with mean age of 48.16 years. Among those asthmatic patients, presenting symptom of episodic breathlessness 113 (94.2%) was predominant symptom followed by cough in 93 (77.5%), fever in 52 (43.3%), expectoration in 47 (39.2%), chest tightness 30 (25%), wheeze in 25 (20.8%). Allergic rhinitis was present in 92 (76.7%) and Atopic dermatitis was present in 30 (25%). Most common chest findings were rhonchi in 72 (60%) followed by rhonchi & crackles in 18 (15%), crackles in 14 (11.7%), normal in 16 (13.3%). Chest radiographs were normal in 83 (69.2%), fleeting pulmonary infiltrates in 32 (26.7%), Tooth paste/ gloved finger shadow in 1 (0.8%) and ring/tram line shadow in 4 (3.3%). Absolute eosinophil count were <350 cells/cumm in 69 (57.5%), 351-500cells/cumm in 26 (21.7%), 501-1000 cells/ cumm in 18 (15.0%), >1000cells /cumm in 7 (5.8%). Serum total IgE was positive in 35 (29.2%) patients. Out of 120 asthma patients 38 (31.7%) patients were found to be positive for aspergillus skin test for at least one or more aspergillus antigen. Those asthma patients who found to be positive for aspergillus skin test were further evaluated for ABPA. ABPA was diagnosed on basis of presence of at least four or five minimal criteria described above (table-1). Among these 38 patients with intradermal skin test positive asthma, 16 (42.1%) patients were subsequently diagnosed to be suffering from ABPA. This was 13.3% of our 120 patients with asthma, 4 (25%) males and 12 (75%) females. Their mean age was 54.0 years with standard deviation ± 16.8. Mean duration of illness was more than 10 years. Breathlessness was main complaint in all of them (100%), followed by cough in 13 (81.3%), fever in 10 (62.5%), chest tightness in 6 (37.5%), expectoration in 10 (62.5%) with brownish expectoration among 2 of them, wheeze in 3 (18.8 %) patients. Allergic rhinitis was present in 13 (81.3%) and Atopic dermatitis was present in 8 (50%) patients. Skin hypersensitivity to aspergillus antigen with type-1 reaction was present in 16 (100%) patients with ABPA. Total serum IgE was positive in 16 (100%) patients of ABPA. A.fumigatus specific IgE was positive in 15 (93.8%) and A.fumigatus specific IgG was positive in 6 (37.5%) patients with ABPA. HRCT showed normal lung parenchyma in 1 (6.3%), consolidation in 6 (37.5%), atelectasis in 1 (6.3%), central bronchiectasis in 7 (43.8%), parenchymal fibrosis in 1 (6.3%) patients with asthma diagnosed to have ABPA.

Table - 4 : Characteristics of Skin Test Positive Patients with Asthma

		ABPA (N=16) N	%	Non ABPA (N=22) N	%	N	X^2	df	P	
							%			
Age in years		54.0±16.8		49.5±16.6						0.423
Sex	Female	12	75	14	63.6	26	68.4	.554	1	0.457
	Male	4	25	8	36.4	12	31.6			
Cough	Present	13	81.3	19	86.4	32	84.2	.182	1	0.67
	Absent	3	18.8	3	13.6	6	15.8			
Chest tightness	Present	6	37.5	3	13.6	9	23.7	2.918	1	0.088
	Absent	10	62.5	19	86.4	29	76.3			
Fever	Present	10	62.5	9	40.9	19	50	1.727	1	0.189
	Absent	6	37.5	13	59.1	19	50			
Expectoration	Present	10	62.5	10	45.5	20	52.6	1.080	1	0.299
	Absent	6	37.5	12	54.5	18	47.4			
Wheeze	Present	3	18.8	3	13.6	6	15.8	.182	1	0.67
	Absent	13	81.3	19	86.4	32	84.2			
Allergic rhinitis	Present	13	81.3	17	77.3	30	78.9	.088	1	0.767
	Absent	3	18.8	5	22.7	8	21.1			
Atopic dermatitis	Present	8	50	5	22.7	13	34.2	3.061	1	0.08
	Absent	8	50	17	77.3	25	65.8			
Chest findings	Normal	0	0	3	13.6	3	7.9			
	Rhonchi	8	50	11	50	19	50			
	Rhonchi and crackles	4	25	6	27.3	10	26.3			
Intradermal skin test type 1	Present	16	100	22	100	38	100			
S.Total IgE	Present	16	100	15	68.2	31	81.6	6.240	1	0.012
	Absent	0	0	7	31.8	7	18.4			
Specific IgE to A.fumigatus	Present	15	93.8	0	0	15	39.5	34.076	1	0
	Absent	1	6.3	22	100	23	60.5			
Specific IgG to A.fumigatus	Present	6	37.5	0	0	6	15.8	9.797	1	0.002
	Absent	10	62.5	22	100	32	84.2			
HRCT finding	Normal	1	6.3	9	40.9	10	26.3			
	Consolidation	6	37.5	6	27.3	12	31.6			
	Collapse	1	6.3	2	9.1	3	7.9			
	Central bronchi-ectasis	7	43.8	5	22.7	12	31.6			
	Parenc-hymal fibrosis	1	6.3	0	0	1	2.6			
Absolute eosinophil count	<350	8	50	11	50	19	50			
	350-500	1	6.3	5	22.7	6	15.8			
	501-1000	5	31.3	4	18.2	9	23.7			
	>1000	2	12.5	2	9.1	4	10.5			
Sputum culture for Aspergillus species	Present	2	12.5	0	0	2	5.3	2.903	1	0.088
	Absent	14	87.5	22	100	36	94.7			
Chest X-RAY	Normal	4	25	12	54.5	16	42.1			
	Fleeting infiltrates	9	56.3	8	36.4	17	44.7			
	Tooth paste/ gloved finger shadow	0	0	1	4.5	1	2.6			
	Ring/Tram line shadow	3	18.8	1	4.5	4	10.5			

Discussion

ABPA is the best recognized manifestation of hypersensitivity to aspergillus species in patients with long standing asthma. In an asthma patient, an occurrence of a significant eosinophilia or unexpected infiltrates in the chest X-ray raises the suspicion of ABPA making it important to determine if the patient is skin test positive to aspergillus antigens. The true prevalence of ABPA in patients of asthma is still not known. This may be due to lack of a uniform diagnostic criteria and standard tests[11]. Greenberger *et al*[17,18] suggested that ABPA could complicate 1-2% of all cases of asthma. Eaton *et al*,[19] suggested that the prevalence of ABPA in a typical asthma clinic was likely to exceed 5%. Kumar and Gaur,[20] reported 16% ABPA prevalence in their asthma subjects. Maurya *et al*,[21] reported an ABPA prevalence of 7.5% in their asthma subjects from Delhi. Agarwal *et al*,[13] reported an ABPA prevalence as high as 27.5% in their study of 564 asthma patients from north India. In our study, the prevalence of ABPA among patients with asthma in a tertiary care referral hospital in Kerala was 13.3% in one year, which represent about 42.1% of skin test positive asthmatics. In our study ABPA was predominantly found in patients belonging to 4th to 6th decade of life with female predilection. Most of our ABPA cases had history of asthma for more than 10 years and had moderately severe airway obstruction. A positive skin test should prompt evaluation for the diagnosis of ABPA. Among asthmatics various studies show skin test positivity to Aspergillus ranging from 14 to 46%[19,22-25]. In India Maurya *et al*[21] reported aspergillus skin test positivity in 28.5 and Agarwal *et al*[13] reported aspergillus skin test positivity in 39.5% of studied patients, respectively. In our study skin test positivity to aspergillus antigen was found in 31.7% of the asthma patients. Total serum IgE concentration was more than 1000ng/ml in all 16 (100%) patients with ABPA. Eosinophil count has neither proved to be sensitive nor specific for the diagnosis of ABPA in our study. The radiographic shadows were present in 12 patients with ABPA as four out of sixteen patients with ABPA had normal radiograph. High-resolution CT emerged as the investigation of choice for the demonstration of bronchiectasis[26,27]. Study has been shown that HRCT, in comparison to bronchography has 83% sensitivity and 92% specificity in detecting central bronchiectasis in patients with ABPA[29]. CT scanning also provides the explanation for radiological findings in non-ABPA skin test positive asthma patients. In our study central bronchiectasis was found in 7 (43.8%) and lung parenchymal fibrosis was found in 1 (6.3%) patients with ABPA. In our study 15 (93.8%) were positive for specific IgE to A.fumigatus and 6 (37.5%) were positive for specific IgG to A.fumigatus among those diagnosed to have ABPA. The positive sputum culture among ABPA patients were 1.8% and fungus isolated from sputum was A. fumigatus.

Conclusion

The prevalence of ABPA among studied population with asthma was 13.3%. Any particular test lacks reliability for establishing or excluding the diagnosis of ABPA if performed alone. Any patient of long standing asthma with peripheral blood eosinophilia, fleeting pulmonary infiltrates on serial chest radiographs, and persistently require systemic corticosteroid for control of asthma, should always be investigated for ABPA. Intradermal skin test should be the first step in an asthmatic being evaluated for ABPA. A negative intradermal reactivity to aspergillus antigen virtually excludes ABPA. Patients with ABPA are often misdiagnosed as having tuberculosis due to the radiological similarities. Such patients are often mistreated with antitubercular drugs for a long duration while lung damage continues to progress silently. Efforts should be emphasized to improve the awareness level about this disease in high tuberculosis prevalent area. Systemic corticosteroids are the mainstay of therapy for ABPA. Early diagnosis and initiation of appropriate therapy with oral corticosteroids may prevent significant irreversible lung damage due to bronchiectasis and parenchymal fibrosis.

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Radiology Quiz

The Bubbly Lung

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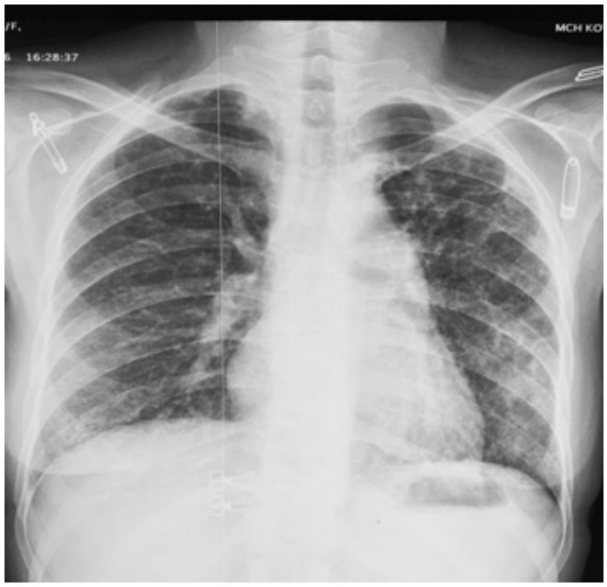

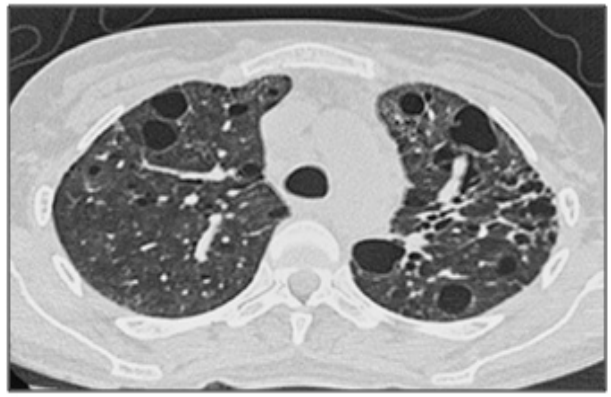

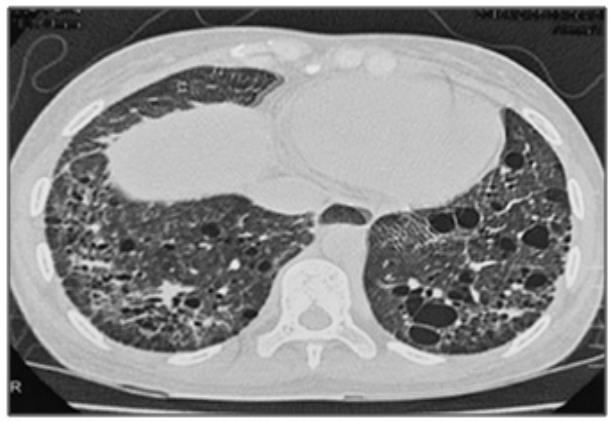

A 34 year old female with complaints of dry cough and progressive shortness of breath over the past 3 months. On examination she had hypo pigmented skin patches, Raynauds phenomenon and bilateral basal crepitations. Examine the available cuts to deduce the radiological pattern.

ANSWER

Lymphocytic Interstitial Pneumonitis (LIP)

She was diagnosed to have a phenotypic pattern of Mixed Connective Tissue disease with Scleroderma- Sjogrens overlap and Autoimmune thyroiditis. Her ANA profile showed U1-RNP and SS-A positivity. The Chest skiagram showed normal Lung volumes with reticulonodular opacities and widening of Main Pulmonary Artery. HRCT Thorax axial cuts revealed bilateral randomly distributed cysts with centrilobular nodules and ground glassing. The bases show evidence of fibrosis with traction bronchiectasis and subpleural sparing.

Differential Diagnosis and approach

1. **Centrilobular Emphysema -** Most common cause of cystic lucencies in HRCT. Usually seen in the upper part, associated with panacinar emphysema in smokers. Characterised by lucencies without walls, and maybe accompanied by the centrilobular arteriole displaced to the periphery.

2. **Idiopathic Interstitial Pneumonias -** Cysts maybe seen in Hypersensitivity pneumonitis(HP) but other features like centrilobular nodules,mosaic attenuation may be evident. Cysts in HP are also usually in the upper and mid lung zones. In smokers,cysts maybe seen in Respiratory bronchiolitis (RBILD) and Desquamative Interstitial Pneumonitis(DIP).

3. **Multifocal Cystic bronchiectasis** - maybe difficult to differentiate from clustered cysts.The accompanying pulmonary arteriolar branch along with the lucencies(Signet ring sign) will help in differentating cysts. In addition evidence of peribronchial thickening and mosaic attenuation due to bronchiolectasis maybe seen.

4. **Lymphangioleiomyomatosis -** Female in the reproductive age having diffusely distributed thin wall cysts with the intervening lung parenchyma being normal.Complications of Recurrent Pneumothorax, Chylothorax, Pulmonary Hypertension and Renal Angiomyolipomas seen.

5. **Langerhans cell Histiocytosis -** Exclusively in males and smokers with significant pack years.Bizzare shaped irregular variable sized cysts and centrilobular nodules distributed in the upper and mid lung with relative sparing of lingula and middle lobes.

6. **Birt hogg dube syndrome -** Young males with positive family history.Characterised by facial fibrofolliculomas, Cysts in lung and bilateral renal tumours. Presents with reccurent pneumothorax. Cysts are usually in the lower zones.

7. **Metastatic cystic disease -** seen in Colorectal carcinomas,Endometrial stromal sarcoma and Soft tissue sarcomas.

8. Cysts can also be seen in Follicular bronchiolitis, Primary Amyloidosis and Light chain depositional disease.

9. In the clinical context, infectious causes of cystic disease like Pneumocystic jirovecii Pneumonia must be kept in mind. Multiseptated thin walled subpleural cysts occuring in areas of consolidation are a clue to this.

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Case Report

Aspiration Pneumonia due to Esophageal Cause in the Elderly

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Abstract

Aspiration pneumonia in the elderly is usually caused by dysphagia with or without dementia. In such situations it is mandatory to rule out structural diseases of esophagus. Here we report a case of a seventy two year old female patient who presented with pneumonia and pleural effusion. Tracheo-esophageal fistula was diagnosed as the cause of aspiration and subsequent pneumonia and pleural complications in this case. We also highlight a diagnostic CT scan finding to pin point structural abnormality of esophagus in elderly debilitated patients in whom all the investigations may not be easily possible.

Introduction

Aspiration pneumonia has to be considered in most of the cases of pneumonia in the elderly[1]. As age advances, the ratio of aspiration pneumonia among cases of hospitalized pneumonia increases considerably[2]. Therefore when treating pneumonia in the elderly, we should think of aspiration pneumonia rather than pneumonia due to infective cause. Structural diseases of esophagus such as trachea-esophageal fistula, esophageal diverticulum, achalasia cardia and esophageal obstruction are frequent causes of aspiration apart from age related dysphagia and impaired cough reflux. Eventhough plain x-ray of the chest is useful for diagnosing pneumonia, it may not help in identifying esophageal abnormality. Barium contrast x-ray, upper GI endoscopy and CT scan are needed to diagnose esophageal abnormality. When the patient is elderly with debility, dementia or delirium, it might be difficult to subject the patient for all these investigations. It will be better to look for signs in the CT scan which is always employed to evaluate unresolved pneumonia. Here we present the case of a 72 year old cachectic female presenting with pneumonia and pleural effusion which turned out to be aspiration pneumonia due to trachea-esophageal fistula.

Case Report

A seventy two year old female patient was admitted in medical ward with cough and breathlessness of one month duration. She had two previous admissions during the past one month and was treated as COPD exacerbation. During the last hospitalization she was intubated and mechanically ventilated for 4 days. There was mild disturbance in renal and liver functions. She was an emaciated patient with difficulty in swallowing and loss of appetite. This was attributed to her drugs

including inhalers. There was tachypnea and hypotension. Total WBC count was 13200cells/mm^3 with neutrophilic predominance. Hb was 10.1 gm%. Blood sugar was normal. Blood Urea was elevated with normal creatinine. Liver enzymes were elevated. Albumin was 3 gm/100ml. She was on inotropic support. X- Ray showed multiple fluid levels on the right side (Fig-1A). A thoracic CT scan was performed which showed pleural effusion with multiple air fluid levels (Fig-1B). Dilated air filled esophagus was seen suggesting communication with airways (Fig-2A & B). Based on her X-ray and CT findings, a diagnosis of aspiration pneumonia (dysphagic pneumonia) with pleural complication was made. Upper GI endoscopy showed a fistulous communication. Edge of the fistula appeared smooth and there was no evidence of acute inflammation or ulceration. Fibreoptic bronchoscopy was done in the ICU. A fistulous communication was detected on the posterior wall of trachea 4 cm proximal to carina. As she desaturated during the procedure, further evaluation or biopsy was not possible. A tentative diagnosis of Chronic TEF was made.

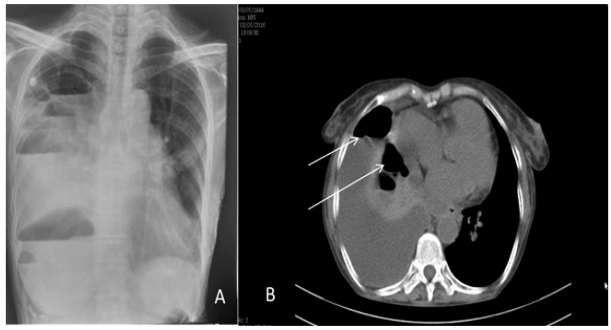

Fig-1 A: X-Ray chest PA view showing multiple air fluid levels on the right side. 1 B: CT scan thorax showing right pleural effusion. White arrows points to air fluid levels in the pleura and parenchyma.

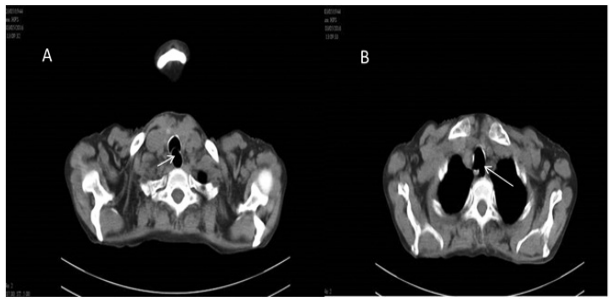

Fig 2 A & B showing dilated esophagus at different levels. White arrows point to the open esophagus sign of trachea-esophageal fistula.

Discussion

Aspiration is defined as the misdirection of oropharyngeal or gastric contents into the larynx and lower respiratory tract [3]. Aspiration pneumonia comprises two pathological conditions such as inflammation of the lung affecting primarily the alveoli and dysphagia-associated mis-swallowing. Matsuse et al described a distinct entity called diffuse aspiration bronchiolitis (DAB), secondary to chronic bronchiolar inflammation due to recurrent aspiration [4].

A recent large-scale cross-sectional study in Japanese elderly people showed that the risk factors for aspiration pneumonia were sputum suctioning, dysphagia, dehydration, and dementia [5]. The incidence rate for dementia increased with age, mostly occurring in the seventh and eighth decades of life [6]. Another recent study has shown that patients with senile dementia inevitably develop dysphagia and have a high risk of death due to pneumonia from aspiration [7].

Tracheo-esophageal fistula (TEF) can be congenital or acquired. The common etiologies of acquired TEF are iatrogenic, malignant and traumatic. Approximately 50% of acquired TEFs are secondary to mediastinal malignancy[8]. Tumours arising from the oesophagus, trachea, lungs, larynx, thyroid and regional lymph glands can all lead to the formation of an acquired TEF[9]. Of the non-malignant causes of acquired TEF more than 75% are the result of endotracheal cuff-related trauma in patients subjected to prolonged mechanical ventilation. Secondary erosion of the tracheal and oesophageal walls occurs in mechanically ventilated patients[10]. Reported mechanisms of injury include traumatic intubation, airway suctioning, and vascular compression of the tracheal wall resulting in ischaemia and subsequent ulceration. An acquired TEF should be considered in any ventilated patient who has unexplained weight loss, recurrent chest infections and repeated failures to wean. Although rare, acquired TEF can occur as a consequence of tuberculosis, HIV infection and mediastinitis. Infection as an aetiological factor in acquired TEF has declined in recent years [9-11]. In countries where tuberculosis is highly prevalent, necrotizing mediastinal lymph nodes should be considered as an important cause of acquired TEF.

Endoscopy is the best diagnostic method available for diagnosis. Esophagoscopy will enable the diagnosis of tumours as well as fistulae. Flexible or rigid bronchoscopy identifies the TEF orifice better on the smooth posterior membranous wall and facilitates biopsies. Accurate identification of the site of the TEF is central to successful intervention. X Ray Chest and CT Thorax can better delineate pneumonia and pleural complications. Sometimes the fistulous track may be missed unless there is high index of suspicion. At the same time looking at the esophageal lumen may give additional information. Usually the lumen is not visualized or minimally open during peristaltic movement. If a large segment of esophagus remains open and filled with air (not food particles), it suggests communication with airway. Thus an open lumen of esophagus should raise the suspicion of TEF. This "open esophagus sign" in CT Thorax can be considered as a diagnostic sign in trachea-esophageal fistula.

Conclusion

Tracheo-esophageal fistula is an important cause for aspiration pneumonia and pleural complications in the elderly. Endotracheal intubation is an important predisposing factor for TEF in the elderly apart from malignancy. Early diagnosis and appropriate intervention are required for good outcome. Persistently open esophagus on CT scan provides an important clue for the diagnosis. Here we report a case of an elderly debilitated female having tracheoesophageal fistula and severe pneumonia with pleural complications. We would like to highlight that visualization of the lumen of esophagus in CT thorax(open esophagus sign) may be used as a diagnostic sign in debilitated, demented patient in whom all investigations may not be always possible.

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Case Report

A Case of Takayasu Arteritis Presenting as Hemoptysis

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Abstract

A Twenty seven year old female patient presented with recurrent hemoptysis since the age of 14 years. Clinical examination was normal except for a difference in pulse volume and blood pressure between right and left upper limbs. In X-ray chest there was no lung field abnormality other than a dilated aorta. On detailed evaluation it was found to be a case of Takayasu Arteritis with bronchiectasis which is a very rare presentation.

Key words : Takayasu Arteritis, Bronchiectasis, Hemoptysis

Introduction

Takayasu Arteritis (TA) is a rare granulomatous large vessel vasculitis. It is also called as pulseless disease. The disease mainly involves aorta and its major branches, pulmonary and coronary arteries [1,2] . Incidence of Takayasu Arteritis is between 1.2 and 2.6 cases/million/year and mostly affects young women of East Asian ancestry [3]. The first description of the disease was in 1908 by an Ophthalmologist Mikito Takayasu, and so the disease was named after him [4,5] That was a case of 21 year old woman with characteristic fundal micro aneurysm formation and arteriovenous anastomosis [4,6] . It is a difficult disease to manage as clinical presentation can vary from those who are asymptomatic to death from stroke [3,5,7,8] . Early diagnosis and assessment of treatment efficacy remain a problem as the conventional blood tests are unreliable and vascular inflammation persists even in the phase of disease remission.

The common symptoms of presentation are claudication of limbs, stroke and hypertension due to occlusion of various branches of aorta. It may be preceded with constitutional symptoms, fever or arthralgia during pre-pulseless phase[9] .Pulmonary artery stenosis can cause pulmonary artery hypertension. It is quite rare for the disease to present with hemoptysis. Also only very few cases have been reported on lung involvement as bronchiectasis in TA [10,11].We are reporting this case because of the rare presentation of TA as recurrent hemoptysis in the absence of vascular symptoms and the rare association of bronchiectasis in TA.

Case History

27year old female presented with recurrent hemoptysis since the age of 14 and most of the episodes were during her menstrual cycles. Usually she had scanty hemoptysis and there was only one episode of moderate hemoptysis which was 2 months prior to hospital admission. No other significant illness in the past. Attained menarche at 13years and had regular cycles.

On general examination, she was pale. Pulse rate was 140/min, low volume in left carotid and radial pulse. Blood pressure in Right Upper Limb was 130/70mm of Hg where as in Left Upper Limb was 80 mmHg systolic. In both lower limbs systolic BP was 130mmHg. Carotid bruit on right and bilateral femoral bruit was present.

Cardiovascular system examination revealed an ejection systolic murmur of 2/6 grade in aortic and pulmonary Area. There was no abnormal physical finding on respiratory system examination.

Her Hemoglobin was 9.8 gm% and ESR was 100 mm/hr. Bleeding parameters were within normal limit.

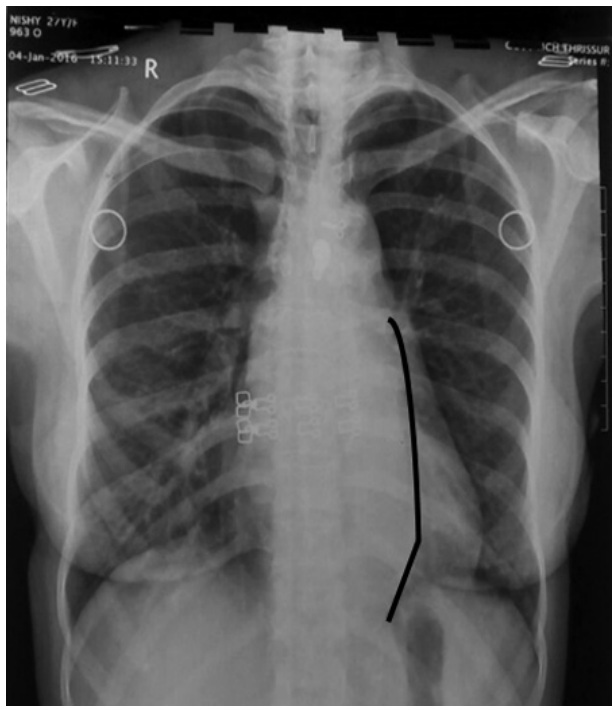

Fig 1 : Chest X-Ray Lung field appears normal Dilated aorta is marked

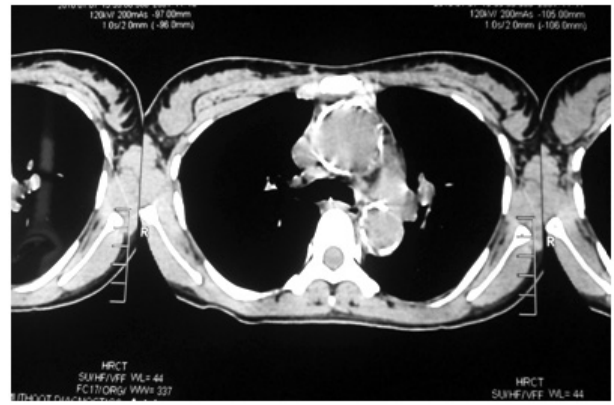

Fig 2 : CT thorax Thickened aortic wall with calcification

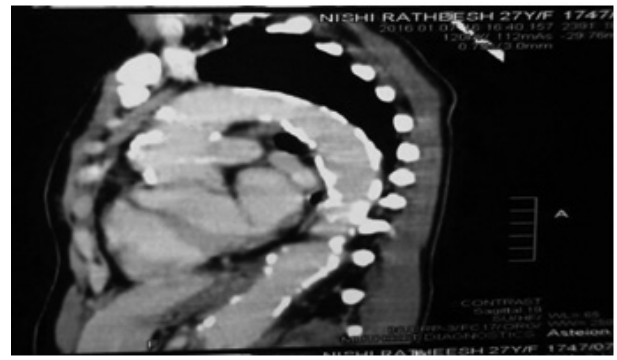

Fig 3 : Continuous Mural Calcification from Aortic Root up to Supra Renal Portion

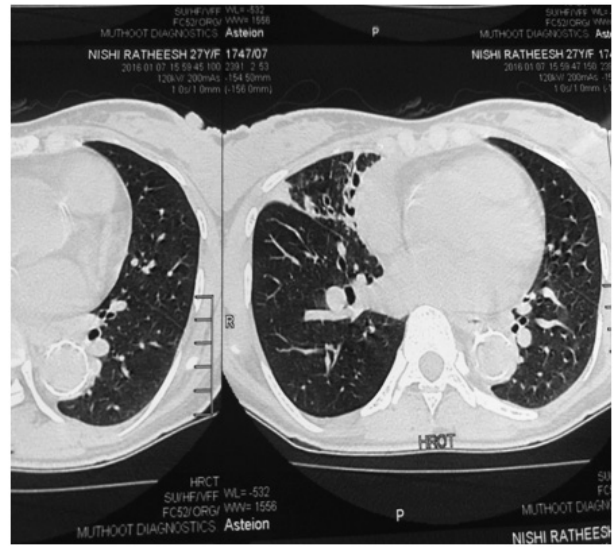

Fig 4 : Bronchiectatic areas mainly involving middle lobe

Thoracic CT showed fusiform dilatation of ascending aorta and aortic root with maximum diameter of 5.1cm suggestive of aneurysm. There was continuous mural calcification from aortic root up to supra renal portion with mild intermittent wall thickening noted in lower descending and supra renal portion of aorta. Heart

was enlarged. In lung window the right middle lobe showed partial collapse with dilatation of segmental bronchi suggestive of bronchiectasis.

Cardiology consultation was done. Echo scan showed no RWMA, good LV function. Clinical and radiologic features were suggestive of TA

Discussion

Takayasu Arteritis is a granulomatous panarteritis of medium and large vessels affecting predominantly the aorta and its branches, coronary arteries and pulmonary arteries [12]. It is also known as aortic arch syndrome or pulseless disease [10,12]. The aetio-pathogenesis of the disease has not been clearly defined yet. Infections, auto immunity and genetic factors have been the proposed aetiologic factors. There will be inflammation in vessel wall resulting in mural thickening, fibrosis and subsequent stenosis and thrombosis. It is ten times more common in females than males of 10–40 years of age with a higher incidence in Japan and in the Asian continent.[10]

TA has an initial pre pulseless systemic phase and a later occlusive phase [10]. Pre pulseless stage is an early inflammatory phase where patients present with constitutional symptoms, fever, and arthralgia. Diagnosis in this stage is difficult as it is highly non specific. Symptoms of presentation are mainly limb claudication, neurological symptoms, hypertension due to arterial ischaemia during the occlusive stage of the disease. The differential diagnosis are other inflammatory conditions like Gaint cell arteritis, Behcet's disease, sarcoidosis and infections like tuberculosis and syphilis [13].

We report the case of a patient with an unusual initial presentation. She had recurrent hemoptysis mimicking catamanial hemoptysis and bronchiectasis. Literature search revealed two case of bronchiectasis with TA [10,11]. Clinical examination showed marked difference in pulse and blood pressure in upper limbs which lead to a high degree of suspicion of Takayasu arteritis. Later the radiological investigations and elevated ESR was supporting the diagnosis.

The diagnostic criteria established in 1990 by the American college of Rheumatology is sensitive in diagnosing TA in the occlusive stage of the disease but in the early stages of the illness it has got less value [5]. No definite serological tests were identified to diagnose Takayasu arteritis. Elevated serum CRP and ESR are supportive markers but not at all specific or sensitive. By the time of diagnosis patients often have extensive vascular disease. The diagnosis of TA is made on the basis of clinical signs together with radiological evidence of large vessel arteritis. Imaging modalities include X-Ray, angiography, CT, MRI and 18 F-fluorodeoxyglucose positron emission tomography (18 F-FDG-PET). Angiography was considered as the gold standard to evaluate the disease extent and was used to identify the type of vascular involvement [14-18] . Non-invasive imaging methods FDG-PET & MRI provide important additional information about disease activity and progression of vessel wall thickening when compared with conventional imaging. So they are useful for treatment outcome assessment and follow up[19,20]. Color Doppler ultrasonography plays an important role for screening, detection and follow-up of carotid and subclavian arteries [21-25].CT may show areas of low attenuation in lungs as a result of regional hypo perfusion, sub pleural reticulolinear changes, and pleural thickening.

Therapy primarily is immunosuppression with glucocorticoids. Cyclophosphamide, azathioprine or methotrexate may be needed to achieve remission and to taper off corticosteroid treatment. Mycophenolate mofetil, leflunomide, tumor necrosis factor (TNF)-α antagonists and tocilizumab have been reported as beneficial in patients who are refractory to standard therapy [26-29].Surgical revascularization techniques have been used with success for critical vessel narrowing. Vascular bypass or stenting procedures may be beneficial [30,31]. In studies the overall mortality was low over a follow-up period of 5 years, with the course of the disease "quite stable" in approximately 50% of patients. In the Indian study, cumulative survival at 5 years after disease onset was 91% and 84% at 10 years, whereas event-free survival figures were 75 and 64%, respectively.

It is now well recognized that vascular inflammation may persist, although the patient has achieved remission by clinical and biochemical criteria. In a review of surgical aortic biopsy specimens from patients with clinically inactive disease, 44% showed

histological evidence of continuing vascular inflammation [32]. There are also criteria defined for assessing disease activity in TA. According to the Kerr criteria, the presence, recent occurrence or deterioration of at least two of the following four criteria shows active disease: (i) systemic features like fever and arthralgia that cannot be explained by other reasons, (ii) elevated ESR, (iii) findings of vascular ischaemia and inflammation and (iv) typical angiographic findings.[33]

Our patient responded to a combination of prednisolone and azathioprine. Her left radial pulse reappeared. Though there was a clinical improvement and the radiological progression was halted, repeat imaging failed to show significant radiological resolution. Currently her disease activity is monitored by the inflammatory markers and improvement in clinical symptoms.

Bronchiectasis with hemoptysis is a rare presentation of Takayasu arteritis. In the absence of vascular occlusive symptoms, it is difficult to identify patients with these atypical presentation and to differentiate from diseases with similar manifestations. Proper clinical examination and elevation of inflammatory markers may help the physician to suspect Takayasu Arteritis and to search for evidence of the disease with other appropriate radiological investigations.

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Case Report

Pulmonary Arterial Hypertension and Primary Lymphedema : A Rare Association

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Abstract

Only two cases of primary lymphedema associated with primary pulmonary hypertension were reported so far. 36 year old male presented with 3 weeks history of increased leg swelling and haemoptysis. He had a past history of gradually progressive swelling of left lower limb from 16 years of age. He also gave history of progressive dyspnoea on exertion for the past 5 years. Examination revealed enlarged left lower limb with skin thickening and non-pitting oedema and features of pulmonary hypertension. CT angiogram showed dilated pulmonary trunk with no evidence of chronic or acute thromboembolism. Lung parenchyma was normal. Spirometry was normal. Serum filarial antibody analysis was negative. So pulmonary arterial hypertension associated with primary lymphedema of the leg was diagnosed.

Introduction

Unilateral lymphedema in the context of pulmonary disease usually occurs in association with filariasis which can be associated with tropical pulmonary eosinophilia or Loffler's syndrome or deep vein thrombosis associated with pulmonary thromboembolism. Primary lymphedema is another rare cause of chronic oedema of extremities. It is usually associated with various other organ system involvements.

Case Report

Here we report the case of a 36 year old male who presented with increased swelling of left leg, dyspnoea on exertion and haemoptysis of 3 weeks duration. The swelling was noted in the left lower limb predominantly below the knee. There was no redness or pain. Exertional dyspnoea was of grade 2 to 3 MMRC. Patient did not complain of orthopnoea, paroxysmal nocturnal dyspnoea or chest pain. Haemoptysis was streaky in nature. He gave a past history of gradually progressive swelling of left leg since around 16 years of age. The swelling of limb became persistent for around the last 15 years. There was no associated redness pain or dyspnoea associated with the leg swelling. There was no associated wheeze cough or haemoptysis. He also noted insidious onset of dyspnoea on exertion which has been gradually progressive over last 10 years . There were no joint symptoms, eye or ear symptoms. There was no history of surgery, trauma or abdominal tumours. No similar illness in the family. He was married with three children. He was a barber by profession.

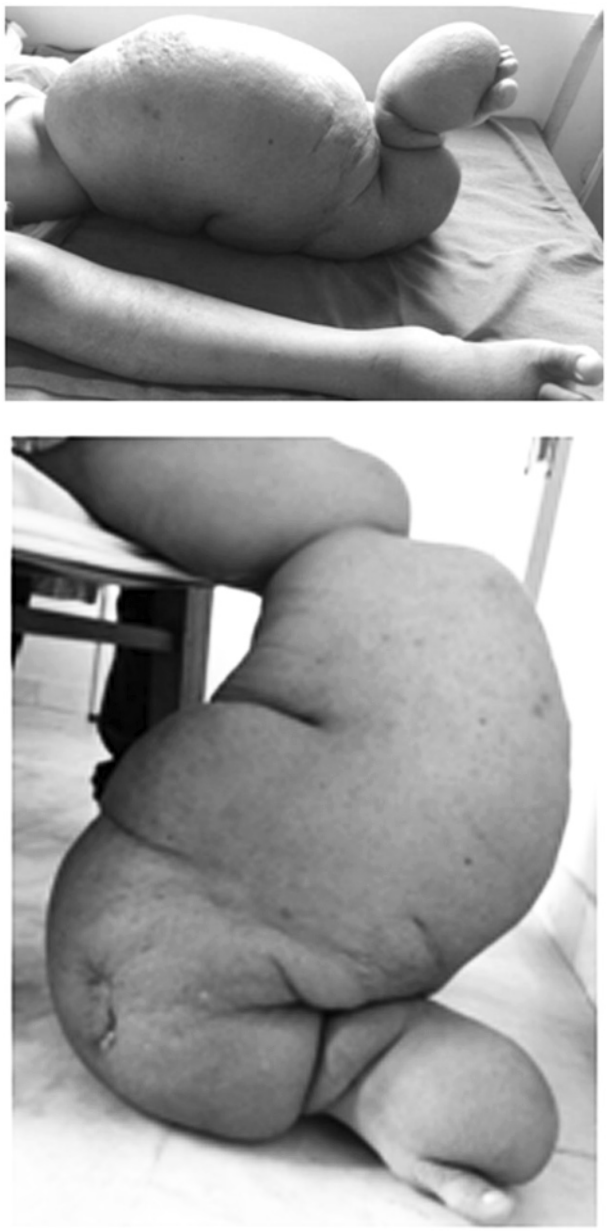

Fig 1 : Non pitting edema of left lower limb with thickened skin

General examination revealed non pitting oedema of left leg without local rise in temperature or tenderness. Skin of the left leg was thickened with areas of hyperpigmentation.There was no regional lymphadenopathy. Respiratory system examination was within normal limits. CVS examination revealed loud P2.

CBC, RFT, LFT were within normal limits. Sputum AFB was negative, D dimer - 289, absolute eosinophil count was 410. ECG showed poor R wave progression. Chest X ray showed normal lung parenchyma with bilateral hilar prominence probably due to pulmonary hypertension (fig 2).

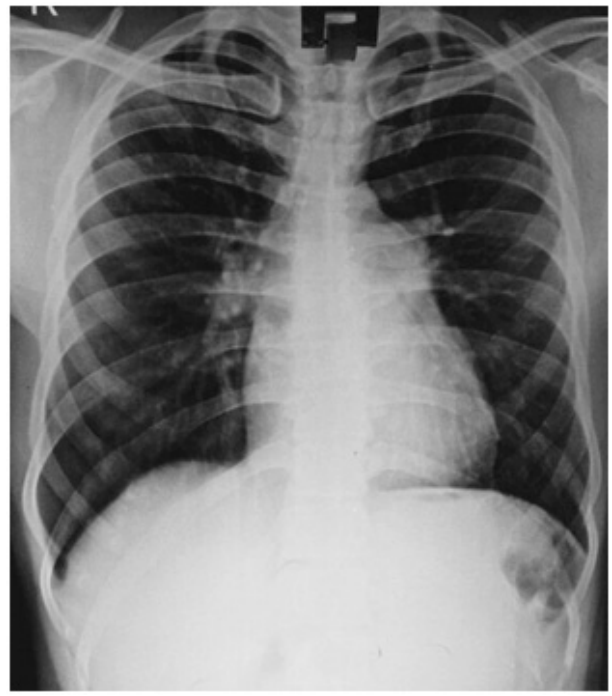

Fig 2 : Chest xray showing prominent main pulmonary artery and bilateral dilated pulmonary arteries

Bilateral lower limb venous doppler revealed hyperechoiec, thickened and oedematous skin. There was no evidence of DVT. ECHO finding were mildly dilated RA/RV with moderate pulmonary hypertension and good LV function. Contrast ECHO showed no intracardiac shunt.

CT pulmonary angiography (fig. 3) showed dilated main pulmonary (44mm), right (21.5mm) and left (25mm) pulmonary arteries. There was no filling defects in pulmonary arteries to suggest thromboembolism.

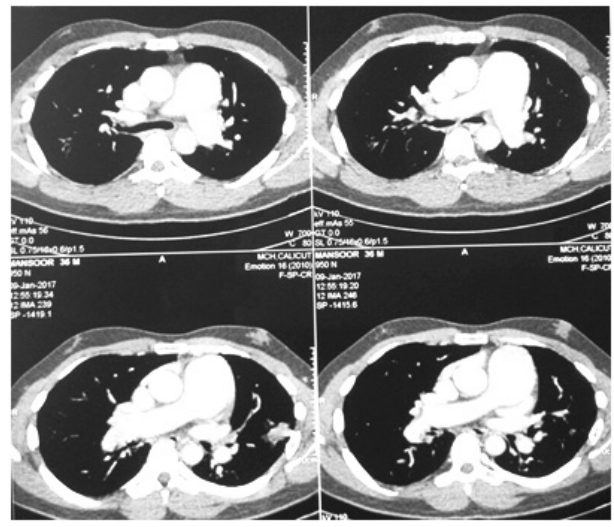

Fig 1 : CTPA showing dilated main, right and left pulmonary arteries

RA factor and ANA were within normal limits. Thick smear for microfilariae, filarial antigen test and DEC provocation test were negative.

There was no evidence suggestive of repeated filarial infection causing filariasis in this case and the typical skin changes associated with filariasis were absent. There was no evidence to suggest active or previous filarial infection. Pulmonary hypertension in filariasis is usually secondary to tropical pulmonary eosinophilia which may be denoted by fibrotic lung disease in CT thorax. But in this case lung parenchyema was normal. Spirometry with post bronchodilator testing revealed a normal lung function. There was no evidence to suggest thromboembolic pulmonary hypertension. The association between primary lymphedema and pulmonary arterial hypertension has been described. This case could be considered as an association between lymphedema praecox and pulmonary arterial hypertension.

Discussion

Primary lymphedema is a form of lymphedema which is not directly attributable to another medical condition. Primary lymphedema is usually classified[1] as

Congenital lymphedema (Milroy disease)

Lymphedema praecox (Meige disease)

Lymphedema tarda

The age of onset of these are different. Congenital lymphedema (at birth), lymphedema praecox(onset at puberty) and lymphedema tarda (onset after 35 years). Primary lymphedema is thought to be due to congenital lymphatic dysplasia. Congenital lymphedema is associated with mutations that inactivate VEGFR3[2]. Primary lymphedema is associated with various other congenital anomalies like distichiasis lymphedema syndrome[3], Yellow nail syndrome, Noonan's syndrome, Turner's syndrome, Klinefelter's syndrome, neurofibromatosis type I, haemangiomas, xanthomatosis[4,5] etc. Some forms of primary lymphedema can be associated with abnormalities in cardiovascular system (heart, arteries, veins). For children and some adults, diagnosed with primary lymphedema, it is important to evaluate for other vascular abnormalities.

Avasthey and Roy (1968) reported a family with lymphedema associated with primary pulmonary hypertension and vascular anomalies[6]. The mother had lymphedema of feet and legs since adolescence, as well as a cerebrovascular anomaly that caused a bruit detectable by auscultation. Three out of her four sons also had lower extremity lymphedema. One of them had a large extracranial AVM over the parietal region, whereas the other two had primary pulmonary hypertension.

This case is reported due to the rarity of association of primary pulmonary hypertension and primary lymphedema.

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Case Report

Non-resolving Dense Consolidation

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Abstract

Metastatic pulmonary calcification (MPC), a rare clinical entity, occurs in normal healthy lung and is usually described in chronic renal failure patients undergoing haemodialysis. Here, we describe a case of 37 year old post renal transplant patient who presented with sub-acute onset of dyspnoea and cough and chest radiograph showing acino-nodular shadows. Further evaluation with CT thorax revealed focal areas of hyper intense attenuation predominantly in the right lung and biopsy confirmed the diagnosis of metastatic calcification. The case had many atypical clinical and radiologic features.

Introduction

Metastatic calcification refers to the deposition of calcium in healthy tissues; one of the most susceptible sites being pulmonary parenchyma. Pulmonary metastatic calcification is most commonly observed in chronic kidney disease patients on haemodialysis. Even though diagnosed rarely during lifetime, it is described in 60- 80 % of autopsy specimens of such patients[1]. Clinically it is either asymptomatic or can present with severe respiratory failure. Routine chest radiograph have low sensitivity in detection whereas CT offers a promising solution. Findings might mimic air space disease, requiring histopathological study for diagnostic conclusion.

Case Report

A 37 year old non-smoker, non-alcoholic male patient was referred from nephrology department with exertional dyspnoea of grade 2 to 3 severity, cough with scanty mucoid expectoration and low grade intermittent fever of nearly 3 weeks duration. He was having chronic kidney disease and hypertension detected 11 years ago, treated with multiple haemodialysis initially and underwent living donor kidney transplantation ten years ago. The post-transplant period was uneventful and was asymptomatic until three weeks ago. The patient was initially treated as a case of community acquired pneumonia from nephrology department but because of poor radiologic resolution referred to our side for

further workup. At the time of presentation patient's vitals were stable, general examination revealed pallor and a surgical scar on the right side of the abdomen and lower respiratory system examination was consistent with minimal pleural effusion on the right side.

Routine haematological investigations showed anaemia (Hb–7.2 g/dl), deranged renal function and electrolyte abnormalities (Blood urea -104 mg%, Serum creatinine - 3.4mg%, sodium - 134 mEq/l, potassium - 4.2 mEq/l, serum calcium -8.6mg%, phosphorous -8.7 mg%, Uric acid -6.1 mg%). LFT and blood counts were within normal limits. Chest radiograph (Fig.1) showed dense alveolar shadows predominantly in the right mid and lower zones extending to upper zone and left mid and lower zones with blunting of right costophenic angle.

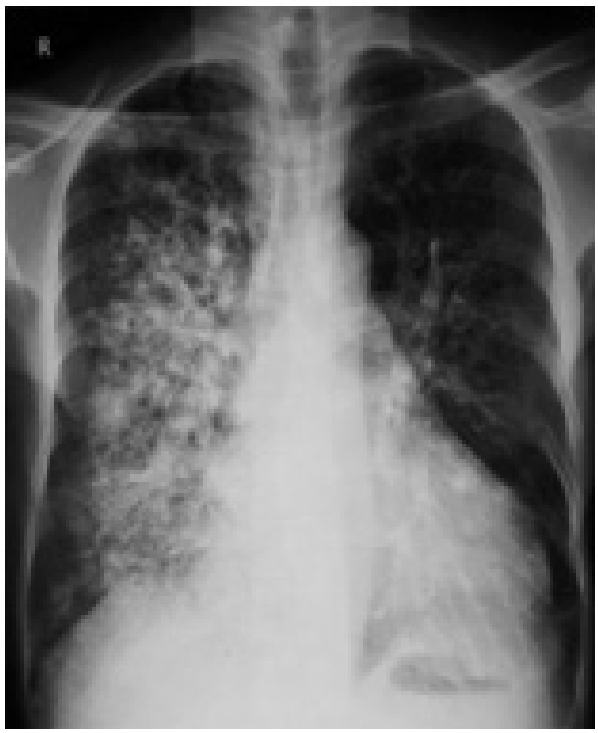

Fig 1 : Chest Radiograph PA view showing asymmetrical dense alveolar shadows

Further evaluation with CT Thorax (Fig 2) showed patchy areas of consolidation, ground glassing predominantly along peribronchovascular distribution in right lung and lingula. Mediastinal window showed areas of heterogeneous enhancement with focal hyper intense attenuation and right pleural effusion.

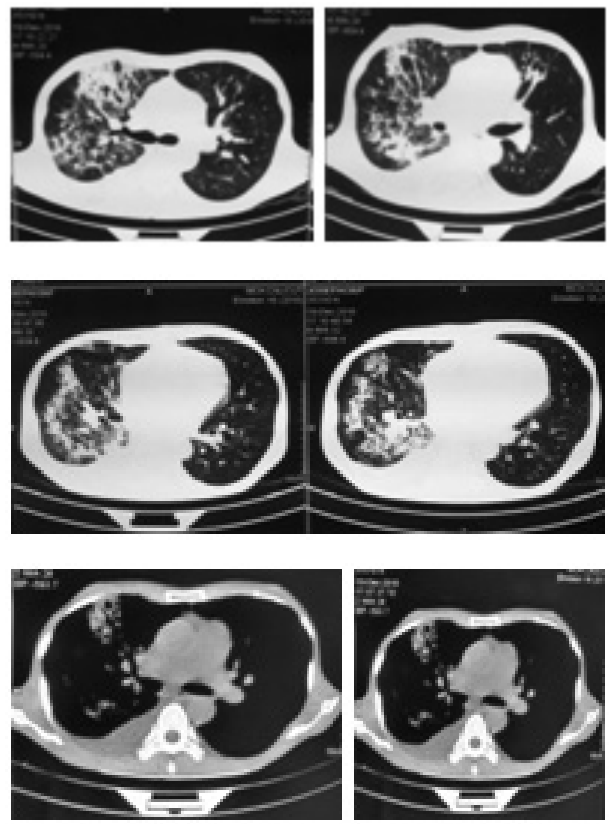

Fig 2 : CT Thorax showing patchy consolidation with focal hyper attenuation and pleural effusion

Spirometry was normal. Patient was subjected to bronchoscopy which revealed normal bronchial tree. Brochoalveolar lavage (BAL) obtained from middle lobe for relevant investigations and transbronchial lung biopsies (TBLB) taken from posterior basal segment of right lower lobe. BAL cultures for bacterial, fungal and tuberculous organisms were sterile; similarly AFB staining, gene expert and PCP staining were negative. No malignant cells were identified in BAL fluid cytology. TBLB specimen showed foci of calcification in interstitium with no evidence of inflammation, necrosis or atypical cells suggestive of metastatic calcification

The calcium phosphorous product was 74.8(8.6 ×8.7) well above the cut off of >55 which increase the risk of calcification in soft tissues as per the NKF- KDOQI guidelines for CKD patients. Serum parathyroid hormone level was 167.9 pg/ml (10-60 pg/ml). Vitamin D3 assay, USG neck and CECT neck ruled out primary parathyroid abnormalities. Hence we came to the final diagnosis of pulmonary metastatic pulmonary calcification in a post renal transplant patient with CKD recurrence and secondary hyperparathyroidism.

Discussion

Depending on the pathophysiologic mechanism involved, ectopic calcification can be either dystrophic or metastatic. Dystrophic calcification is the deposition of calcium salts in previously injured tissues while metastatic calcification is deposition of calcium salts in previously healthy tissues. Metastatic calcification can occur widely throughout the body but principally affects the interstitial tissues of the vasculature, kidneys, lungs and gastric mucosa. Metastatic pulmonary calcification (MPC) commonly occurs in conditions that produce an elevated calcium-phosphate product and result in the deposition of calcium salts in the alveolar and vessel walls of normal lungs.

So factors influencing metastatic calcification include increased serum calcium and phosphate concentrations, alkaline phosphatase activity and local physicochemical conditions such as pH. It is described in 60–80% of autopsied haemodialysis patients, although rarely recognized during life. Severity is highly variable – while majority of patients will be completely asymptomatic, a minority of patients will develop hypoxia, restrictive pulmonary function tests and may progress to respiratory failure and death.[2] It has been associated with several other conditions including primary and secondary hyperparathyroidism, hypervitaminosis D, malignancy (including multiple myeloma and parathyroid carcinoma) and milk-alkali syndrome.[3] However it is most commonly described in chronic renal failure with secondary hyperparathyroidism.

Being mostly asymptomatic, the condition is rarely diagnosed ante mortem and occasionally can present with slowly progressive dyspnoea and chronic non productive cough. But our patient had a rather sub acute presentation which may be partly due to super added infection in the setting of recurrence of chronic renal failure. Standard chest radiograph frequently fails to detect calcification since the amorphous calcium salts deposited in lung parenchyma in this condition are less radio opaque. Sometimes can be seen as nodules or airspace opacities or simulating pulmonary oedema. It can be unilateral or bilateral and most frequently involves upper zones,even though can occur in all lung zones. Upper zone predilection may be due to increased alkalinity at the apices which encourages deposition of calcium salts. This can be explained by the higher ventilation–perfusion ratio at the apices producing a lower $PaCO_2$ and higher blood pH. HRCT is the most efficient method for detecting MPC. Three common parenchymal patterns are described, namely, diffuse or irregular opacities with groundglass attenuation, dense consolidation with frequent lobar distribution and multiple nodules with diffuse or localized distribution. Such patterns are not mutually exclusive and a combination of patterns can co-exist.[4] The most common parenchymal HRCT finding is the presence of poorly defined centrilobular nodules with groundglass opacity measuring approximately 3-10 mm in diameter. Despite the histologically interstitial nature of the infiltrate, the HRCT finding may mimic nodular alveolar filling. The radiology of our case was also atypical with predominant involvement of right mid and lower zones. Recently, MRI and nuclear medicine imaging using technetium-99m methylene disphosphonate (MDP) demonstrating increased uptake in the lungs of patients with metastatic pulmonary calcification were also described.[5] PFT is usually normal and can be restrictive sometimes.

Spontaneous resolution of changes has been described in patients with metastatic pulmonary calcification and although the optimal treatment for this condition is not known, attempts to normalise calcium and phosphate biochemistry have been the mainstay of therapy.[6] Clearly, the large number of patients with renal failure and non-progressive asymptomatic disease do not require any intervention but, for patients with symptomatic disease, treatments such as parathyroidectomy, adequate dialysis or bisphosphonates have been suggested and used with some success.[7]

MPC is classically described in CRF patients undergoing haemodialysis as dialysis fluid cause increased alkalinity of blood. But our patient was not on maintenance haemodialysis. Hence in chronic renal failure patients presenting with diffuse parenchymal opacities, pulmonary metastatic calcification should be considered as one of the differentials eventhough not encountered frequently.

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