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Editorial

Fungal Exacerbations of COPD

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Acute exacerbations of COPD (AECOPD) are important events in the natural history of patients with COPD as they are associated with increased rates of hospitalization, readmissions, disease progression and a negative health status.[1] It has also been shown that AECOPD causes an accelerated decline in lung function, leading to death also.

The key symptom of an exacerbation is increased dyspnoea, which is brought about by increased airway inflammation, increased mucous production and air trapping. The other symptoms include increased frequency of cough, wheeze and increased sputum volume & purulence.

COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy. In turn, it is subdivided into 3 categories – mild, moderate and severe.

The true incidence of AECOPD is difficult to assess since 50% of exacerbations are not reported by patients. AECOPD accounts for 2.4% of acute hospitalizations in the UK.[2] Significantly it also accounts for 50% of the direct costs of COPD treatment.[3]

The most common aetiologies of AECOPD are viral respiratory infections, bacterial infections and non infective environmental factors like pollution and ambient temperature.

Fungal agents causing an exacerbation of COPD though rare, is not uncommon. Although not mentioned in guidelines as a potential

aetiology for AECOPD, these should be kept in mind especially in geographical areas where fungal spores are present abundantly in the ambient air.

Aspergillus species have been described to cause severe exacerbations of COPD.[4] It has been reported that *Aspergillus* species were isolated from sputum in 16.6% of patients with severe AE-COPD.[5] Significantly, a history of AE-COPD in the previous year was reported to be a main risk factor for isolation of Aspergillus species in the sputum samples. In the FUNGICOPD study, filamentous fungi and *Aspergillus* species were identified in 49% and 42% of sputum from patients with stable COPD, respectively, and *Aspergillus* cultures in COPD patients corelate with neutrophilic inflammation, suggesting the presence of a host immune response against the *Aspergillus* organisms.[5]

Normal pulmonary defence mechanisms against Aspergillus, such as the ingestion of conidia by pulmonary macrophages and killing of hyphae by neutrophils, are usually present and preserved in COPD patients. Sructural changes in lung architecture including formation of bullae, predispose to colonization with Aspergillus fumigatus. Also, the common use of long-term steroids (including inhaled steroids) increase host susceptibility by reducing oxidative killing of the organism by pulmonary macrophages and increase its linear growth by 30-40%. Finally, comorbid factors such as diabetes, alcoholism and malnutrition may further enhance the risk of developing fungal exacerbations.

In this edition of Pulmon, Ravindran Chetambath et al have examined the role of pathogenic fungi causing exacerbations of COPD, in Wayanad district, renowned for its coffee plantations. They have also attempted to correlate it with the cropping season of coffee, from October to January. This is because of the fact that branches of the coffee plant as well as the berries carry white flakes which are rich in fungi and hence the fungal spore concentration in the environment is likely to be high during this period. A remarkable aspect of this study is that they have taken meticulous efforts to collect and speciate fungi from five different coffee plantations in the district, in addition to working up all the patients for fungal pathogens.

The results of this study are indeed an eye opener. They have observed that there is a high prevalence of fungal isolation in their cohort of COPD patients with severe AECOPD requiring hospitalization. Diabetes mellitus, expectedly, has been found to be an independent risk factor for fungal isolation. Fungal isolation has been found to be associated with longer duration of hospital stay and an increase in death rate. A large number of pathogenic fungi were isolated including Aspergillus fumigates from samples collected from coffee plants and berries during this period. Aspergillus fumigatus

was the most common fungus to be isolated from patients with AECOPD (16.3%).

This brings into focus the role of biomarkers in diagnosis of AECOPD. Traditionally, C Reactive protein (CRP) has been used to differentiate bacterial from viral exacerbations of COPD. Would fungal biomarkers have a role in future? This is particularly important since fungal exacerbations are severe in nature and are associated with prolonged hospitalisation and even increased mortality. There is some evidence coming up now that elevated levels of serum Aspergillus galactomannan is associated with severe AECOPD.[6] These findings suggest that serum *Aspergillus*-galactomannan antigen is a novel surrogate marker and could potentially be used to evaluate the risk of severe AE-COPD, This might provide new insights in understanding the potential interactions between the fungal microbiome and the pathogenesis of COPD.

In conclusion, it is time that we broaden our outlook, when we attempt to make a search for an aetiological agent causing an acute exacerbation of COPD. Early identification of potential fungal agents in vulnerable population, would help target treatment accordingly, and thereby reduce mortality, morbidity and prevent future exacerbations, which are the goals of COPD treatment as envisaged by the GOLD guidelines.

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Review Article

Airborne Infection Control in Health Facilities

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Airborne transmission of infectious diseases like tuberculosis (TB), H1N1, severe acute respiratory syndrome (SARS), coronavirus, etc is a major public health concern. India continues to have the highest number of tuberculosis (TB) cases in the world.[1] The airborne transmission becomes even more prevalent in health-care settings because of overburdened and overcrowded hospitals and the presence of patients with immunosuppression.[2] Nosocomial outbreaks of air borne infections in many countries have focused attention on the need to control the transmission of the disease in hospital.[3]

Emerging infectious diseases like Nipah virus disease has caused mortality among health care workers and general population with substantial nosocomial transmission.[4] The death of a nurse who treated the patients with Nipah virus disease at recent outbreak in Kerala caught widespread attention.[4]A systematic review of 51 studies conducted in low- to middle-income countries found that TB incidence among health care workers was high, ranging from 69 to 5780 per 100,000.[5] Evidences show that TB is a significant occupational problem among health care professionals. Nosocomial outbreaks of airborne infections like influenza H1N1, drug-susceptible, multidrug-resistant TB (MDR TB), and extensively drug-resistant TB (XDR TB) have been reported and have been linked to the absence or limited application of airborne infection-control strategies in health care facilities.[6-9]

Several factors may facilitate nosocomial transmission in Indian hospitals, although their relative importance in facilitating transmission is unknown. Risk of transmission is highest when there is a high number of cases with poor infection control. Undiagnosed cases especially at medical ICUs and emergency rooms pose great threat for nosocomial transmission.[10] Prevailing infection control practices in India revolve around biomedical waste management and disposal of sharps; while airborne infection control (AIC) measures has not received adequate attention from the health care facilities and practices. National Guidelines on Airborne Infection Control in Health Care and other settings in India were published as the first, formal national guidelines on reducing the risk of airborne infections in health care facilities and special high-risk settings in India.[11]

The guideline involves recommendations categorized into three main components;

I. Administrative controls.
II. Environmental controls.
III. Use of Personnel protective equipment.

I. Administrative controls:

Administrative controls are to classify persons with respiratory symptoms, separate them into appropriate environment, fast-track them through the health care facility to reduce exposure time to others, and diagnose/treat them with minimal delay.

A. Outpatient Setting

a. Screening : Screening for respiratory symptoms need

to occur as early as possible upon patient's entry at the health care institution. A separate screening counter may be placed, patients can be encouraged to first visit this counter if they have suggestive symptoms, by appropriate advertisements, posters or announcements in the registration area. Even if screening at registration is not possible, screening can occur when patients register at specific clinics or when in waiting areas.

b. Education on cough etiquette and respiratory hygiene: This is a physical method that can prove useful for reducing airborne transmission. There should be provision for patient education on cough hygiene and sputum disposal. This education can easily be imparted to patients through posters and other means in the waiting area. Cough etiquette should be reinforced by all staff members. Masks can be provided to all respiratory symptomatics. Simple surgical masks may not help health care worker from getting air borne diseases but are effective when used by the patients to reduce the production of respiratory droplets of all sizes.

c. Patient segregation: Segregation of patients with respiratory symptoms can be achieved by having a separate waiting area for chest symptomatics, within the overall outpatient area. This is particularly important in larger institutions with heavy OPD loads. The outpatient area, more so this segregated area, should be well ventilated to reduce overall risk of airborne transmission.

d. Fast tracking of patients with respiratory symptoms: Those identified as patients with respiratory symptoms can be further fast-tracked in both their clinical and laboratory evaluation. Patients may be allowed to jump the routine queue and be seen earlier than other patients. The other important area where these patients can be given priority is while performing chest radiography.

B. Inpatient areas

a. Minimize hospitalization of TB patients: This is one of the most effective means to reduce the risk of transmission of airborne pathogens such as M. tuberculosis in hospital settings is to manage such patients in the outpatient setting whenever possible.

b. Establish separate rooms, wards, or areas within wards for patients with infectious respiratory diseases: Patients with infectious respiratory diseases should be physically separated from other patients so that others are not exposed to the infectious droplet nuclei that they generate. Policies on patient separation inevitably generate concern about stigma, but with appropriate measures - such as training and public posting of separation rules - stigma can be minimized. Administrative procedures should ensure that separation happens promptly and automatically, similar to the automatic separation of men and women during inpatient admission. The best choice for infectious or potentially-infectious patients is to house and manage them in airborne precaution rooms.

c. Educate inpatients on cough hygiene and provide adequate sputum disposal: Wards housing infectious patients should display sign boards in the ward demonstrating cough hygiene. All patients admitted in the ward/area should be issued surgical masks and counseled on their proper use and adequate measures for safe collection and disposal of sputum.

d. Establish safe radiology procedures: Patients with infectious respiratory disease like TB can have the scheduling of the procedure during non-busy times

II. Environmental Controls:

Ventilation should be prioritized to reduce the number of infectious particles in the air. Effective ventilation may be achieved by natural ventilation where ever possible. When clean or fresh air enters a room, it dilutes the concentration of airborne particles, such as droplet nuclei, in room air.

Unrestricted openings (i.e. those that cannot be closed) on opposite sides of a room provide the most effective natural ventilation. Openings should constitute at least 20% of the floor areas (10% on either side for effective cross ventilations). In existing health-care facilities that have natural ventilation, when possible, effective ventilation should be achieved by proper operation and maintenance of openings, and by regular checks to see that openings remain free of obstruction at all times.

Mechanical ventilation with or without climate control may appropriate where natural ventilation

cannot be implemented effectively, or where such systems are inadequate given local conditions (e.g. building structure, climate, regulations, culture, cost and outdoor air quality). If mechanical ventilation is used, the system should be well designed, maintained and operated, to achieve adequate airflow rates and air exchange. Careful attention must be given to ensuring adequate ventilation when installing air conditioners. Minimum number of air changes per hour need to be ensured while using air conditioners. In OPD and registration areas there should be minimum of 6 air changes per hour while in high risk setting it should be 12.

In high-risk settings where optimal ventilation cannot be achieved through natural or mechanically-aided means, properly designed, placed and maintained shielded ultraviolet germicidal irradiation devices should be considered as a complementary control.

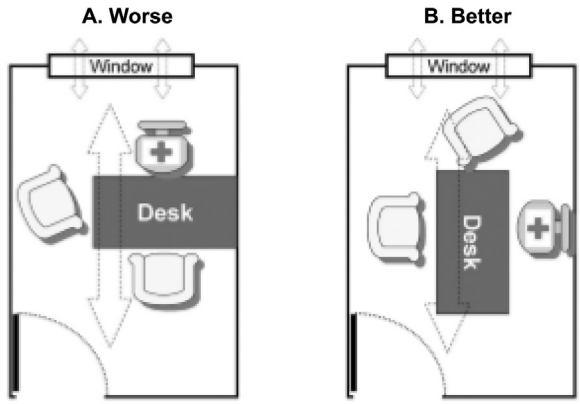

Fig. 1 : Schematic showing seating arrangement for patient and health care worker (red cross)

In (A), natural ventilation would allow potentially infected air to cross health care worker. In (B), with this seating arrangement the chance of such exposure is lessened somewhat. (Picture adapted from NAIC guidelines, 2010).

Other means include UV lamps, air filters, etc. However these have to be placed in the most useful way and need periodic maintenance, in the absence of which they offer no protection. Negatively ventilated rooms also can be constructed, however these require a huge investment on construction as well as regular maintenance.

III. Personal protective equipment:

Simple surgical masks may not help health care worker from getting air borne diseases but are effective when used by the patients to reduce the production of respiratory droplets of all sizes. Personal protective equipment (e.g. particulate respirators certified as N95 or FFP2) should be available as required in high-risk situation, especially during high-risk aerosol-generating procedures such as bronchoscopy or sputum induction. Particular respirators are useful only when worn properly and the health care workers have to be trained on proper use of these.

Conclusion

Numerous studies have shown that implementation of recommended air borne infection-control strategies has been associated with reduced outbreaks of air borne infections and preventing its nosocomial transmissions in health care facilities. It is more important to promote implementation of National Air borne Infection Control guidelines in the hospitals. It has been revealed that most of the countries where a significant reduction of air borne diseases including TB has been observed, air borne infection control practices have played a crucial role.

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Original Article

Pathogenic Fungi in the Environment Causing Acute Exacerbation of COPD and its Link to Coffee Plantations in Wayanad District of Kerala - A Prospective Study

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Abstract

Background : Majority of exacerbations of COPD (AECOPD) are due to infections. Usual agents causingAECOPD are gram negative bacteria, but rarely viruses and fungi are also implicated.Wayanad is a hill district with predominant coffee and tea plantations. Coffee berries ripe in the months of October to January. Branches of coffee plants and berries carry white flakes which are fungi rich. These flakes are dispersed in the environment and we are looking at the possibility of this increased concentration of fungal spores in the environment during this period as a possible cause of fungal infections in AECOPD.

Objectives : 1) To study the prevalence of fungal infection among hospitalized patients with AECOPD during coffee crop season2) To identify a causal relationship with increased fungal spores in the environment during coffee crop season.

Methods : Patients admitted with AECOPD for a period of 4 months from 1st October 2017 to 31stJanuary 2018 are prospectively included from ICU and general ward of Pulmonary Medicine Department of a tertiary care hospital. Clinical, radiological and microbiological data are collected at admission and during the hospital stay. Clinical course and outcome are recorded. A detailed search was made by collecting samples for fungal culture from the surroundings including the plantations to demonstrate growth of fungi.

Conclusion : There is high prevalence of fungal isolation in a cohort of COPD patients with severe AECOPD requiring hospitalization. Diabetes mellitus is found to be an independent risk factor for fungal isolation. Fungal growth is correlated with longer duration of hospital stay and increase in death rate. Many pathogenic fungi were isolated including Aspergillus fumigatus from samples collected from coffee plants and berries during this period. Aspergillus fumigatus is found to be the most common fungi isolated from patients with AECOPD.

Keywords : Coffee Plants, AECOPD, Fungal Spores, Aspergillus fumigatus.

Introduction

Exacerbations of chronic obstructive pulmonary disease (COPD) are frequent events in the natural history of the disease, considerably increasing the morbidity and mortality[1]. Acute exacerbations of COPD (AECOPD) are characterized clinically by worsening of dyspnoea, increased sputum production and/or changes in sputum purulence[2]. There is evidence suggesting that infectious agents, induces AECOPD by increasing bronchial and systemic inflammation[3]. Microbial infections account for the etiology of 75% of AECOPD[4]. However, the role of microorganisms other than bacteria has not been well established. Viral infections causing AECOPD are frequently reported. *Aspergillus*spp. may be responsible for important clinical events from saprophytic colonization of the airways to rapidly invasive and life-threatening disseminated diseases. This is attributed to the reduced immune status of the host due to the presence of underlying lung disease[5], comorbid illnesses such as diabetes and use of broadspectrum antibiotics and corticosteroids[6]. Some retrospective studies have analyzed the incidence of *Aspergillus fumigatus* isolation from lower respiratory tract samples in AECOPD patients and shown that COPD patients are an important group which are affected by either colonization or proven aspergillosis[7]. In one of the largest studies investigating the prevalence, *Aspergillus* was isolated from respiratory samples of 36 patients out of a total of 1756 patients[8]. However, it remains unclear whether COPD patients are colonized by *Aspergillus*spp. or they have invasive pulmonary disease. It is difficult to define the influence of this organism as a causal agent of exacerbations unless invasive infection is proved by histopathological examination.

The state of Kerala has a humid tropical climate with an average annual rainfall of 300 cm. The typical climatic and other physiographic factors offer hostile environment for a large number of microorganisms like fungi[9].Wayanad district in Kerala is a hilly farm land having coffee and tea plantations. Coffee plants and berries show fungal growth which are dispersed during crop season. This may increase the quantities of fungal spores in the environment. Thus, this study was initiated to analyze the prevalence of fungal infection in AECOPD during coffee crop season and to identify the environmental source of fungus. Efforts are made to link the environmental source of fungus to coffee plantation in the district.

Objectives

1) To study the prevalence of fungal infection among hospitalized patients with AECOPD during coffee crop season.

2) To identify a causal relationship with increased fungal spores in the environment during coffee crop season.

Methods

Study design

A : Data are prospectively collected after informed consent from patients hospitalized due to a COPD exacerbation in a tertiary teaching hospital in Wayanad district between 1stOctober 2017 and 31st January 2018. This period is selected because this is the season in which coffee plants flower and berries ripe. Approval from institutional ethics committee (IEC) is obtained for this study.

B : Samples are collected in petri dishes from branches and berries of coffee plants from 5 different coffee plantations within the districts. The white flakes over dry berries and offshoots carrying the berries are selectively collected and sent to microbiology laboratory for processing (Fig-1).

Fig 1 : Coffee plant with dry berries. Black arrow shows white flakes containing fungi

Study protocol

Only known COPD patients as per previous hospital records and on treatment for COPD for more than one year are included. All patients admitted in the pulmonary medicine ward or ICU are evaluated clinically and investigated with complete blood count, X-Ray Chest PA, spirometry, sputum gram stain and culture, fungal smear and culture, bronchoscopy and bronchial washings for bacterial and fungal culture and CT Thorax in selected cases. COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy. Diagnosis of COPD exacerbation, decision to hospitalize, time of discharge and choice of pharmacological therapy were taken by the physician in charge. All the patients are put on standard treatment for exacerbations as per GOLD guideline. Patients in whom fungal growth is detected are subsequently put on itraconazole/ voriconazole in standard adult dose. Patients with active tuberculosis, asthma, renal failure or any other clinical respiratory diseases are excluded. Clinical course and outcome of all patients are recorded. Outcome reported are discharge or death.

Data collection

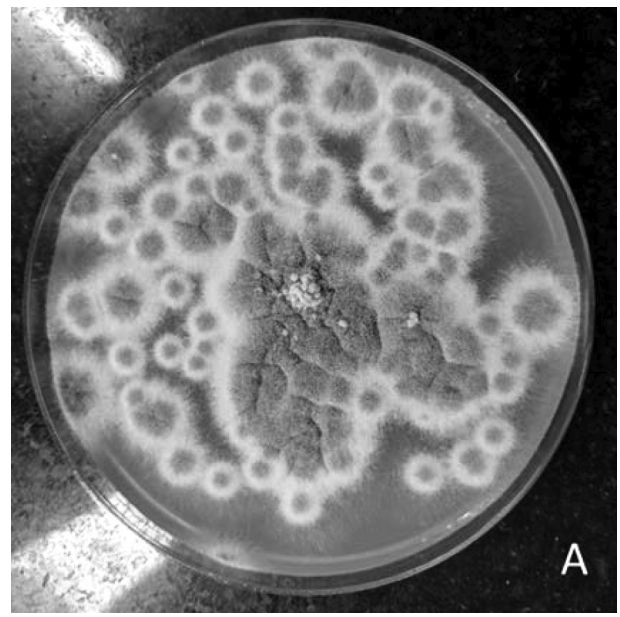
Demographic variables, presence of any comorbid conditions (Hypertension or diabetes), smoking status, use of steroids (Systemic or inhaled) were recorded on admission to hospital. Symptoms/ signs of the AECOPD together with physiological and laboratory data are collected at onset. Other variables such as length of stay (LOS), frequency of patients in whom admission to the intensive care unit (ICU) is needed, requirement of non-invasive mechanical ventilation (NIMV) and death are recorded. The number of AECOPD events in the year preceding hospitalization is assessed based on treatment records. Only exacerbations requiring emergency room visits or admissions are included.

Microbiological analysis

When patients admitted into hospital, their sputum samples were collected in a sterile container with adequate precautions and transported immediately to the microbiological laboratory. Microbiological examinations included direct microscopy(Gram stain & KOH mount), bacterial and fungal culture. All the patients were subjected to fibreoptic bronchoscopy after obtaining written consent. Bronchial washings after saline instillation was recovered and sent for microscopy and culture for bacteria and fungi immediately. All samples were cultured on conventional media, including blood agar, chocolate agar and McConkey agar which were incubated at 37°C for 48 hrs. The samples were also inoculated on Sabouraud's dextrose agar and incubated at 37°C and 25°C for 7 days and observed for growth of fungi each day and the number of visible colonies recorded.

Bronchial biopsy was taken from patients in whom bronchial inflammation is seen. This is subjected to bacterial and fungal culture and histopathological examination. Bacterial infection was confirmed when there is a colony count $\geq 10^5$ cfu/mL. All the fungi grown were subjected to slide culture. The fungal spp. grown was identified based on macroscopic features and microscopic appearance.

33 samples collected in petri dishes from coffee plants and coffee beans from 5 different plantations in the district are transported to microbiology laboratory and one part is processed with KOH mount for fungal elements. Remaining part was inoculated in Sabouraud's Dextrose agar for fungal culture. KOH smear showing fungal mycelia are recorded. Culture is examined after 7 days for colonies and species identified by macroscopic and microscopic methods (Fig-2, Fig-3).



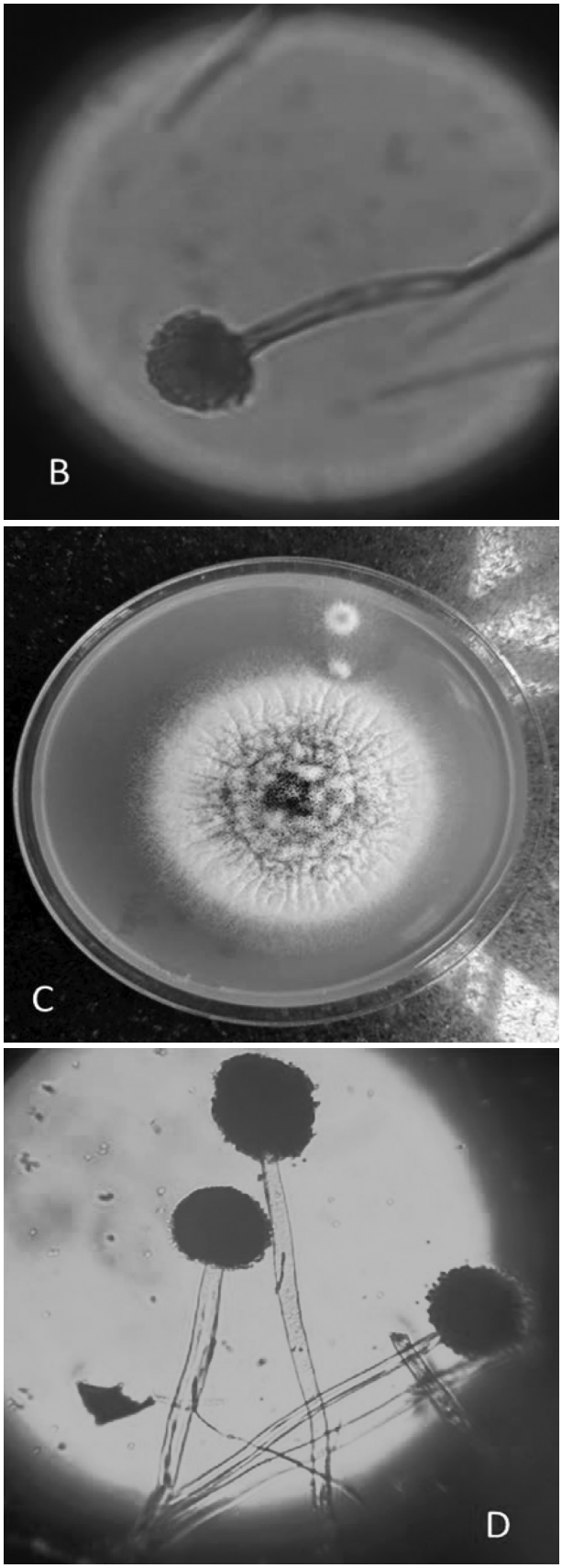


Fig 2 : Growth of fungi in samples collected from Coffee plants. A, B: Aspergillusfumigatus, and C, D: Aspergillusniger

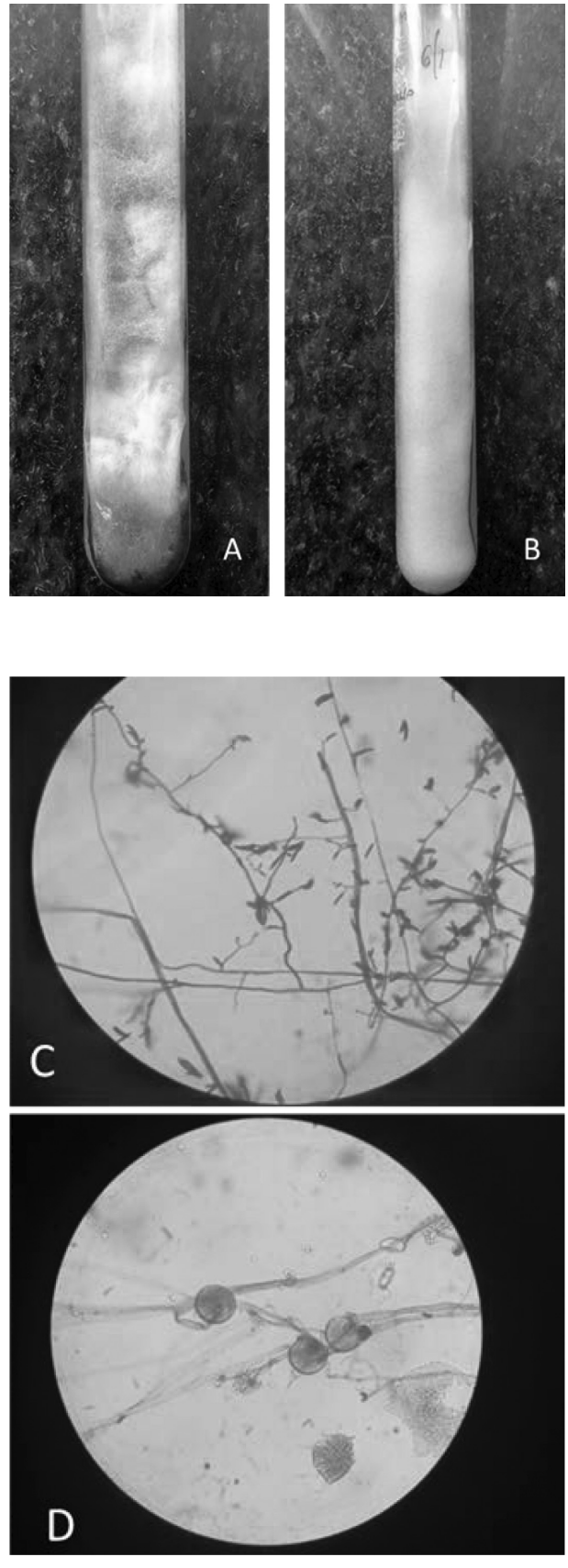


Fig 3 : Growth of fungi in samples collected from Coffee plants. A: Rhizopus spp., B, C: Fusarium spp., D: Mucor spp.

Statistical analysis

Data are analyzed using SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables are presented as absolute numbers and relative frequencies, while continuous variables are presented as the mean, standard deviation (SD) in parametric data, or median with the interquartile (IQR) range in non-parametric data. Categorical variables are compared using the $x2$ test.

Results

Number of subjects treated for COPD exacerbation during the study period was 106. Mean age of the patients were 75.5 years. Study subjects include 97 (93.3%) males and 9 (6.7%) females (Table-1). All the males were reformed smokers and 2 females were smokers. All the female patients had exposure to biomass fuels. Among the study subjects, 17 (16.3%)patients had fungi cultured from sputum or bronchial washings. All the 17 patients had Aspergillus fumigatus and 2 of them were co-infected with Mucor spp. No other fungal species were detected from these subjects. Among those above 65 years 17% had fungal cause for exacerbation and those below 65 years 15% had fungal cause for exacerbations (Fig-4, Table-1). All the patients had treatment with inhaled corticosteroid and antibiotics during previous exacerbation and during the present admission. Hence use of these two agents cannot be attributed to the increased rate of fungal infections. There were 17 diabetic patients in this cohort out of which 35% has fungal infection whereas among the non-diabetic 12.4% only had fungal infection. This is statistically significant (Fig-5, Table-1). When we looked at duration of hospital stay it is found that 95% of patients who had a hospital stay of more than 10 days had fungal infection (Fig-6, Table-2). This is found to be statistically significant. Case fatality among AECOPD patients in this study was 7(6.6%) and death among those having fungal infection was 3 (17.6%) (Fig-7,Table-2).

	AECOPD with fungal Infection, *n*=17	**AECOPD without fungal Infection, *n*=89**	***P*Value**
Demographics			
Age in years	76 ± 7	75 ± 8	0.741
Gender (male/female)	14/3	83/6	0.092
BMI(kg/m2)	23.4 ± 3.1	24.1 ± 3.6	0.266
Smoking history, n (%)	15 (88.2%)	80 (89.9%)	1.000
COPD characteristics(post bronchodilators)			
FEV_1%	42.0 ± 14.0	44.1 ± 12.8	0.261
GOLD grade			
Grade I	2 (11.7%)	15 (16.8%)	
Grade II	4 (23.4%)	23 (25.8%)	
Grade III	10 (58.8%)	44 (49.4%)	
Grade IV	1 (5.9%)	7 (7.9%)	
GOLD grade ≥ 3, n (%)	11 (64.7)	51 (57.3)	0.744
Underlying conditions, n (%)			
Hypertension	7 (41.2%)	24 (27.0%)	0.082
Diabetes Mellitus	6 (35.3%)	11 (12.4%)	0.032
Drug Usage on admission			
Corticosteroids use, n (%)	17 (100%)	89 (100%)	0.000
Broad spectrum antibiotics	17(100%)	89 (100%)	0.000
Long term oxygen therapy	6 (35.2%)	18 (20.2%)	0.353
Times of AECOPD in previous year	1.7 ± 1.3	1.3 ± 1.1	0.186

Table 1 : Basic information of study subjects

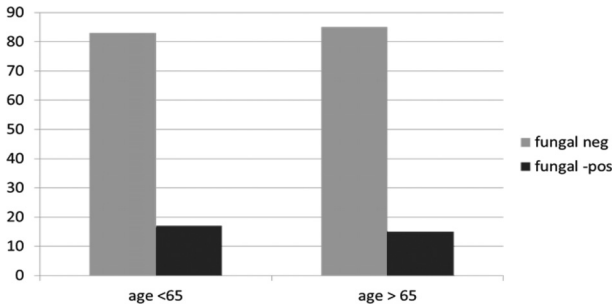


Fig 4 : Characteristics of fungal infection in AECOPD

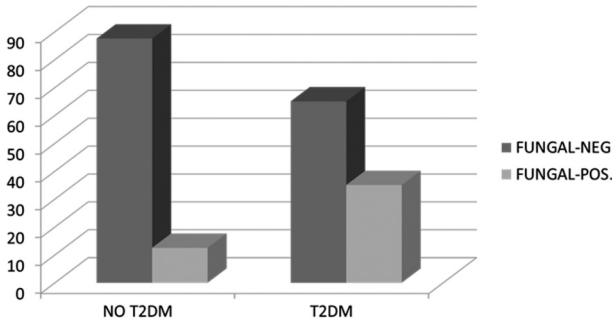


Fig 5 : Fungal infection in relation to T2 DM

	AECOPD with fungal Infection, *n*=17	AECOPD without fungal Infection, *n*=89	*P* Value
Admitted in ICU	4 (23.5%)	16 (18.0%)	0.802
Machanical ventilation	2 (11.8%)	9 (10.1%)	0.906
LOS >10 days	6 (35.3)	8 (9.0%)	0.037
Improved	14(82.35%)	85(95.5%)	0.901
Death	3(17.6%)	4 (4.49%)	0.084

Table 2 : Short-term outcomes in AECOPD patients

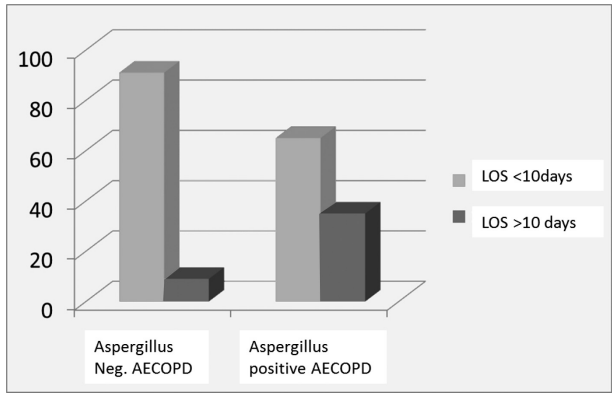


Fig 6 : Relationship between fungal infection in AECOPD and LOS

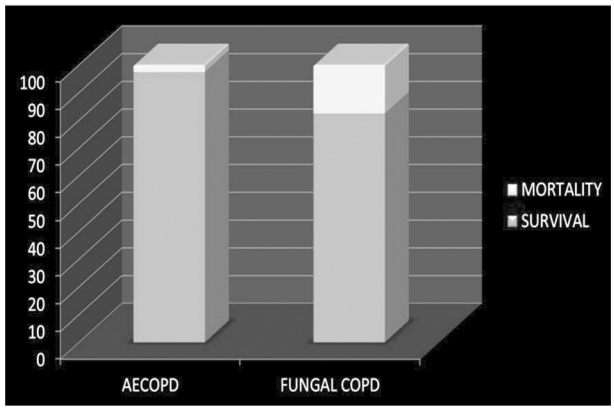


Fig 7 : Outcome due to fungal infection in AECOPD

All samples collected from coffee plantations showed fungal elements in KOH mount. On culture growth was observed in 30 samples (90.9%). On macroscopic cultural characteristics and microscopic features the species identified were Aspergillus fumigatus, Aspergillus niger, Mucor spp., Rhizopus spp and Fusarium spp. (Table-3) (Fig-2&3).

Fungi isolated	Number of isolations, *n*=30	Percentage
Aspergillus fumigatus	25	83.34
Aspergillus niger	2	6.67
Rhizopus spp.	1	3.33
Mucor spp.	1	3.33
Fusarium spp.	1	3.33
Aspergillus fumigatus + Rhizopus spp.	2	6.67
Aspergillus fumigatus + Mucor spp.	2	6.67
Aspergillus fumigatus + Fusarium spp.	4	13.33

Table 3 : Distribution of the various fungi isolated from the coffee beans.

Discussion

Fungi are microorganisms commonly found as both endo and epiphytic symbionts of plants and their products. During the fruit stage and at further steps of coffee bean processing, different species of fungi are seen. This is more important because of the fact that coffee berries are hand plucked by laborers, thus helping in dispersing fungal spores in the environment. Those working in coffee plantations are at higher risk of exposure. From 5,000 sampled coffee beans, 1,433 (28.66%) produced no microorganisms in culture while from the remaining 3,567 (71.34%) beans at least one microorganism was isolated in Petri dishes. A total of 2,525 (70.78%) beans produced strains of fungal taxa in which toxigenic species are commonly found (e.g. Penicillium, Aspergillus, Fusarium)[10].

Moulds growing on food, damp walls or compost piles produce millions of spores that are frequently inhaled by humans and can cause diseases ranging from simple asthma to life-threatening illnesses such as invasive bronchopulmonary aspergillosis (Fig-8). All sampling series show high proportion of Aspergillus and Penicillium species, including potentially pathogenic species such as Aspergillus fumigatus[11].

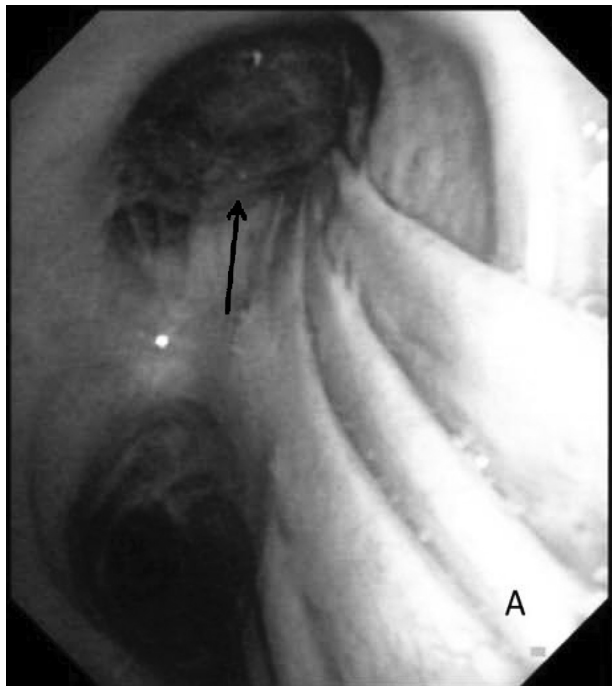


Fig 8 (A)

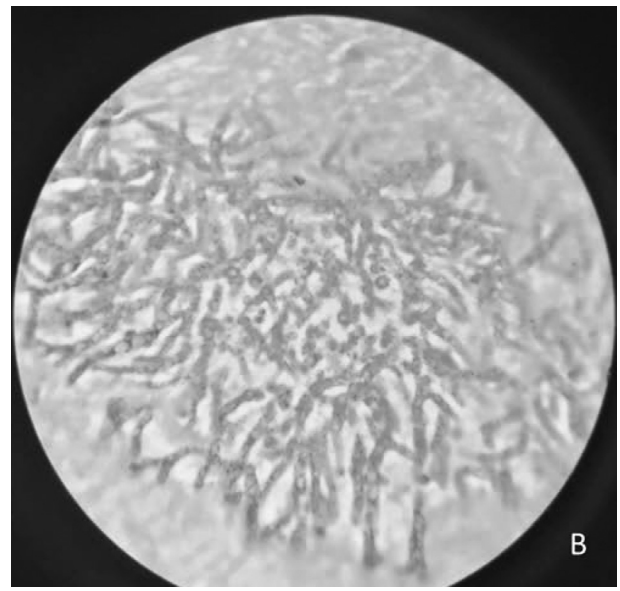


Fig 8 (B)

Fig 8 (A) Aspergillustracheobronchitis in a 79 year old male admitted with AECOPD (Red arrow), Fig-8 (B) Histo-pathological slide demonstrating dichotomous branching mycelia of A. fumigatus[12]

Aspergillus spp. is a ubiquitous fungus in the environment with high sporulation capacity[13]. After Aspergillus sporulates, conidia with a diameter of 2–3 ìm are released into the air, this enters the airway, and reach alveoli[5]. Therefore, the lung is the main organ affected by Aspergillus. Aspergillus spp. causes various diseases in lungs, such as Aspergillus colonization, Aspergillus infection and allergic bronchopulmonary aspergillosis[14]. In COPD patients, impairment of the defense mechanisms of airways facilitates the binding of conidia to epithelial cells, which may cause Aspergillus colonization in the airway[15]. Positive isolation of Aspergillus spp. in LRT samples from COPD patients is common, and a previous study reported that the positive identification rate was nearly 29%[7]. This is the first study in this part of the country to prospectively determine the prevalence of fungal infection, associated risk factors and outcome in a cohort of AECOPD patients requiring hospitalization. We have shown that the prevalence of fungal isolation in this cohort was 16.3% on admission. The independent risk factor associated with fungal infection in this cohort was diabetes mellitus which is clinically and statistically significant with a p value of 0.032. Fungal isolation was associated with clinically and statistically significant outcomes such as increased duration of hospital stay

(p value 0.037) and death (p value 0.084). In a prospective study Auturo et al reported that patients with *Aspergillus* spp. isolation had significantly higher LOS compared to those patients without *Aspergillus* spp. isolation (7.5 ± 5.0 days *versus* 11.8 ± 9.2 days, p = 0.02)[16]. Mortality among these patients was marginally higher when fungal isolation was established.Mortality rate in association with fungal infection in COPD patients is believed to be high because of the difficulty in reaching an early diagnosis. However Auturo et al did not find any significant differences in any of the other clinical outcomes when comparing patients with and without Aspergillus spp. isolation[16].

In a hilly agricultural district of Wayanad where the predominant cultivation is Coffee and tea we were looking for different causal factors leading to AECOPD. This is mainly because during ripening of coffee beans fungal flakes are released to the atmosphere in large quantities. So we thought of looking for fungal infection during this period, that is October to January. The prevalence of fungal isolation is found to be equal or higher in this study when compared to earlier studies. In a study by Pashley et al.[7] the isolation of Aspergillus fumigatus in sputum culture was significantly higher using a research approach compared to the standard method for mycological investigations. There are few previous studies, reporting different prevalence rates of fungal isolation in respiratory samples from patients with COPD[8,17]. Recently, a large, retrospective study conducted by Guinea et al[18], analyzed the incidence of Aspergillus fumigatus isolation from lower respiratory tract samples in patients admitted for AECOPD in a tertiary hospital. They reported 239 isolations of Aspergillus spp. (16.3 per 1000 admissions), and our study shows much higher prevalence (16.3%). It is interesting to note that we could isolate Mucor spp. in two samples among this cohort.

Out of the 33 samples collected from different coffee plantations in the district, 30 showed fungal isolation. All the fungi isolated were pathogenic and the most frequent isolation was that of Aspergillus fumigatus (83.34%). This is the species mostly isolated from respiratory secretions of patients in this cohort. Two patients also had co-infection with Mucor species which is isolated from three of the environmental samples.

Conclusion

There is a high prevalence of fungal isolation in a cohort of COPD patients with severe AECOPD requiring hospitalization. Diabetes mellitus is found to be an independent risk factor for fungal infection. Fungal infection in COPD is correlated with longer duration of hospital stay and increase in death rate. Aspergillus fumigatus is the fungi causing AECOPD in this cohort and this species was isolated from majority of samples collected from coffee plantations.

Conflicts of interest

Authors have no conflicts of interests to declare. This study is not funded by any agency.

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Original Article

Utility of EBUS - TBNA in Mediastinal Lymphadenopathy in a Tertiary Care Centre

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Abstract

Context

Diagnosis of mediastinal lymphadenopathy requires tissue sampling. This can be done by invasive or minimally invasive procedures. The current trend is moving towards less invasive, faster, cheaper and safer procedures.

Aim and objectives

The aim of this study is to assess the usefulness and yield of endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) in patients with mediastinal lymphadenopathy.

Study setting and design

The study is a hospital record-based study conducted in Kerala Institute of Medical Sciences, Trivandrum. The study population included patients with mediastinal lymphadenopathy who were subjected to EBUS-TBNA during the period from March 2015 to September 2018. The results of the study population were analyzed.

Results

In this study, the median age of the study population was 53.27 years with a standard deviation (sd) of 14.02. 78 were males and 45 were females. There was adequate sampling in 109 cases giving a positive yield of 88.61%. Overall, EBUS-TBNA was diagnostic in 87 cases (70.73%). Most common diagnosis was malignancy (38.21%), followed by granulomas (32.52%). Among 36 patients with inconclusive results, 21 patients had atypical cells, reactive lymphoid tissue and fibrinous material whereas in 14 patients the samples were inadequate. 8 patients had necrotizing granulomas typical of tuberculosis out of which only 1 patient came positive for AFB culture and AFB smear and 2 patients had positive CBNAAT. The yield of EBUS in suspected malignancies was 65.08% and suspected sarcoidosis was 86.96%.

Conclusion

EBUS-TBNA is a bronchoscopic procedure with very good yield. In our study, malignancy was the most common diagnosis followed by granulomatous conditions.

Introduction

Mediastinal lymphadenopathy can be due to variety of causes ranging from benign to malignant diseases. The evaluation of mediastinal lymphadenopathy is very important for staging in suspected/proven lung cancer. A definitive diagnosis can only be acquired by tissue sampling which can be done by invasive or minimally invasive methods. Mediastinal nodes are classified basically into anterior, middle and posterior based on the compartment it is located. The current classification of mediastinal nodes is based on IASLC (International association of study of lung cancer) which has divided it into ten groups. Invasive procedures like mediastinoscopy and VATS biopsy are performed by cardiothoracic surgeons. Recent advances in bronchoscopy has allowed pulmonologist to do ultrasound localization of the mediastinal nodes and sampling it with better yield, greater speed and lower rate of complications.

The concept of TBNA (Trans-bronchial needle aspiration) first came in 1949. Dr. Eduardo Schieppati first reported the employment of TBNA without obtaining full attention of clinicians[1]. Then in 1978, Wang et al introduced this technique to North America and promoted it to the whole world by describing TBNA in diagnosing small cell lung cancer[2]. EBUS(Endo-bronchial Ultrasound) is a bronchoscopic technique that uses ultrasound to visualize structures within and around airway and lung parenchyma. Historically, transbronchial needle aspiration done in a blind manner was always under-utilized. Recent advancement with ultrasonography lead to resurgence of TBNA. Endobrochial ultrasound in combination with TBNA was first developed in 2002. By 2007, EBUS-TBNA had been accepted by clinicians as a safe and efficient technique for mediastinal and hilar lymphadenopathy[3,4]. In India, the use of EBUS-TBNA is on the rise for the past few years although, many clinicians across the country are not familiar with the utility and procedure details of EBUS.

Endobrochial ultrasound in combination with TBNA is used to diagnose a new lung cancer and also for staging and re staging a known lung cancer. EBUS is also used for evaluating mediastinal lymphadenopathy of unknown etiology. Using the EBUS-TBNA we can sample the paratracheal lymph node stations (2R & L, 4R & L), subcarinalnode(Level 7), hilar (Level 10 R & L), subaortic (5) and interlobar (11R & L). Mediastino scopy does not have access to the latter two stations[5]. The main advantages of EBUS are cost effectiveness, good yield and acceptable safety profile. The guidelines from American college of chest physicians (ACCP)[6], National Institute of Health and Care Excellence (NICE)[7], and European Respiratory Society (ERS)[8] all recommend the use of EBUS in patients with suspected/proven lung cancer for mediastinal staging. The diagnostic yield of EBUS-TBNA has been found non-Inferior to mediastinoscopy[9]. The diagnostic yield of EBUS-TBNA have been proven previously in different studies conducted in India eg.,Gahlot et al[10] -92%, Dhamija et al[11]- 88% and Srinivasan et al[12]- 62%.

This study was done to evaluate the usefulness and yield of EBUS-TBNA in patients with mediastinal lymphadenopathy in our tertiary care institute.

Methodology

Study design

A hospital record-based study was conducted in the department of Respiratory medicine, Kerala Institute of Medical Sciences Trivandrum. The study population included patients coming mainly from southern parts of Kerala and Tamil Nadu with mediastinal lymphadenopathy. After discussing with the subject experts, a study protocol was made and the needed variables were determined. The study protocol included general baseline characteristics like age and sex, symptoms, initial clinical diagnosis, final pathological and microbiological results and CT chest. Data were collected from Electronic medical records of patients who were subjected to EBUS-TBNA for evaluation of mediastinal lymphadenopathy during the period of March 2015-September 2018.

Procedure

The procedure is done as an outpatient one, either under conscious sedation with Midazolam (2-5 mg IV) and Fentanyl (1-2 mcg/kg IV) or under general anesthesia with LMA(laryngeal mask airway) in few selected patients. The procedure was done with an

EBUS Bronchoscope(BF-UC180F) under ultrasound and color Doppler guidance with either 21 or 22 Gauge needles. The lymph nodes of stations- 2, 4, 5,7, 10 and 11 on either sides are localized using convex ultrasound probe and sampled. Specimens obtained by needle aspiration were made into smears on slides and kept in alcohol based solution for cytopathological examination. Dry smears are also made for AFB staining. Needle core specimen obtained by using suctioning were kept in formalin solution and were sent for histopathological examination. Few core specimens were kept in saline and sent for mycobacterial investigations. Rapid on-site evaluation (ROSE) was not done in our study due to unavailability of on-site pathologist.

The diagnostic yield was studied by pathological and microbiological results of the samples taken by EBUS-TBNA.

Being a record based study, permission of the gatekeeper of information was obtained and patient identifiers were not extracted.

Data storage and analysis

Data collected were entered in Excel spreadsheet and descriptive analytics done with Epi info 7.

Results

The mean age of the study population was 53.27 years with an sd of 14.02. 55 patients were in the age group of 40-60 years and 43 patients were above 60 years. 78 patients were males and 45 were females. The most common presenting symptom was cough which was seen in 77 patients(62.60%) followed by dyspnea and loss of weight. 16 patients were asymptomatic- out of which 9 patients were having known malignancies where EBUS-TBNA was done to rule out mediastinal nodal metastasis and 4 patients had an incidental mediastinal lymphadenopathy during visa medical check-up where EBUS-TBNA was done to rule out tuberculosis. 3 patients presented with symptoms of extra pulmonary tuberculosis and mediastinal lymph nodes were sampled using EBUS TBNA.

Characteristics		Number	Frequency
1. Age	a. Less than 40	25	20.33%
	b. 40 to 60 yrs	55	44.72%
	c. 60 yrs and above	43	34.96%
2. Sex	Male	78	63.41%
	Female	45	36.59%
3. Symptoms	Cough	77	62.60%
	Hoarseness	15	12.20%
	Loss of weight	13	10.57%
	Fever	8	6.50%
	Dyspnoea	17	13.82%
	Hemoptysis	8	6.50%
	Asymptomatic	16	13.01%

Table 1 : Baseline Characteristics of the study population (n=123)

Cytopathological and histopathological examinations revealed definitive diagnosis in 87 (70.73%) patients out of 123, with malignancy seen in 47 patients (38.21%), granuloma seen in 40 patients (32.52%) and inconclusive in 36 patients (29.27%). Among the inconclusive results, atypical cells and reactive lymphoid tissues were seen in 13 patients, fibrinous material was obtained in 9 patients and in 14 patients (11.38%) the specimen was reported as inadequate in which no definite pathology was identified and only scanty material was aspirated.

Among malignancy, most common carcinoma was adenocarcinoma seen in 24 cases, squamous cell carcinoma in 11 patients, neuroendocrine tumors in 10 patients and 1 patient came as B cell lymphoma. Finally, one patient who is a known case of lung carcinoma who was subjected to EBUS TBNA for staging came positive for adenocarcinoma metastasis.

			95% confidence intervals	
H P E	**Frequency**	**Percent**	**Lower**	**Higher**
Adenocarcinoma	24	19.51%	12.92%	27.63%
Squamous cell ca	11	8.94%	4.55%	15.44%
Neuroendocrine tumor	10	8.13%	3.97%	14.44%
Granuloma without features of TB	32	26.01%	18.52%	34.70%
Granuloma suggestive of TB	8	6.50%	2.85%	12.41%
Inconclusive (atypical cells, fibrinous material & inadequate sample)	36	29.27%	21.41%	38.15%
Other malignancy	2	1.63%	0.20%	5.75%

Table 2 : Histopathological examination results (n=123)

Microbiological evaluation was done with AFB smear, CBNAAT and AFB culture. AFB smear was positive in 1 patient (0.81%), AFB culture was positive for mycobacterium tuberculosis in 3 patients (2.44%) and CBNAAT was positive in 2 patients (1.63%).

Comparative analysis was done among different variables which revealed several results. Among 57 suspected TB patients a definitive diagnosis of TB was made with histopathological features (8 patients), AFB culture (2 patients), CBNAAT (2 patients) and AFB smear (1 patient).

	Histopathology		
AFB Culture	**Non Necrotizing granuloma**	**Necrotizing granuloma**	**Inconclusive**
Positive	1	1	1
Negative	31	7	35
AFB smear			
Positive	0	1	0
Negative	32	7	36
CBNAAT			
Positive	0	2	0
Negative	32	6	36

Table 3 : Yield of different tests for Mycobacterium tuberculosis with EBUS

Among 63 suspected malignancy patients, a confirmed malignancy was made in 41 patients and 1 patient turned out to have positive AFB culture and 2 patients had positive CBNAAT. Among 23 suspected sarcoidosis, non-necrotizing granulomatous histo pathology was found in 20 patients (86.96%).

		Number	Percentage
Suspected malignancy (63)	AFB Culture positive	1	1.59%
	CBNAAT positive	2	3.17%
	Histopathology suggestive of Ca	41	65.08%
Suspected sarcoidosis (23)	AFB Culture positive	1	4.35%
	CBNAAT positive		
	Histopathology suggestive of sarcoidosis	20	86.96%

Table 4 : Yield for suspected malignancy and sarcoidosis

Post procedure, only 28 patients (22.76%) had minimal hemoptysis for 24 hours and 52 patients (42.27%) had throat pain. No major complications were reported after procedure.

Discussion

In our record based study based on the data from the last 3 years, most of the study population (n=98) is distributed around the ages of 40-60 and above 60. This is in contradiction to the previous studies done in India- Gahlot et al[10]. (2011) – mean age- 47 years, Madan K et al[13]. (2014)- mean age- 42.1 years.

There was adequate sampling in 109 cases giving a positive yield of 88.61%. Overall, EBUS-TBNA was diagnostic in 87 cases (70.73%). EBUS was diagnostic in 86.96% of sarcoidosis and 65.08% of malignancy. This is comparable to other studies done in India and western countries. GahlotT et al[10] reported a diagnostic yield of 92% whereas Madhan K et al[13] reported a diagnostic yield of 96.1%, Srinivasan et al showed yield of 62.9% and Dhamija et al showed 88%. International studies like Herth et al[14] reported a diagnostic yield of 93.5%, Yasufuku et al[3] reported a diagnostic yield of 100% and YýlmazDemirci N et al[15] showed a diagnostic yield of 96.5%. Yield of EBUS-TBNA in sarcoidosis was evaluated in several studies in India and abroad. Madhan K et al[16] did a study comparing conventional TBNA versus EBUS-TBNA for yield in sarcoidosis and they found that yield with EBUS-TBNA without ROSE was 84% for sarcoidosis whereas in our study, it came as 86.96%.

Most common diagnosis in our study was malignancy with 38.21% followed by granuloma- 32.52%. This is in contrast to other Indian studies where most common diagnosis was granulomas- Tuberculosis and sarcoidosis. Srinivasan et al[12] done in northern part of India reported granulomatous conditions like sarcoidosis and tuberculosis as common results (82.1%) and malignancy only in 17.9% cases. Gahlot T et al[10] done in New Delhi also reported granulomatous diseases (77%) as most common finding with TB as main etiology and malignancy seen in only 17% cases. But western studies likeHerth et al[14] reported malignancy as the most common final diagnosis (98.20%).Gurioli C et al[17]- an Italian case series reported lung cancer as most common final diagnosis (52 out of 94 patients) and granulomatous conditions were seen in 21 patients. The possible reasons could be that the presenting age group in our study is more of 40 years and above and Kerala being a state with low prevalence of tuberculosis comparing other states of the country.

Among malignancies, most common one in our study was adenocarcinoma(n=24) which is consistent with other studies like Herth el[14] reporting adenocarcinoma in 156 out of 502 patients. Second common malignancy was squamous cell carcinoma followed by neuroendocrine tumors.

Regarding mycobacterium tuberculosis diagnosis with EBUS-TBNA in our study, out of 57 suspected TB patients, 8 patients had necrotizing granulomas characteristic of tuberculosis- of which only one had positive AFB culture, two had CBNAAT positivity and one had smear positivity.

Among 63 suspected lung carcinoma patients, 41 patients proved to be malignant whereas, there were CBNAAT positivity in two patients and AFB culture in

one patient. Thus signifying the importance of tissue sampling of mediastinal lymph nodes and proving the diagnosis.

Among 23 suspected sarcoidosis patients, 20 (86.96%) patient had non necrotizing granuloma suggestive of sarcoidosis and one patient turned to be positive for AFB culture.

Conclusion

Our study showed that EBUS-TBNA is a bronchoscopic procedure with high diagnostic yield (88.61%)for evaluation of cases with undiagnosed mediastinal adenopathy. In our study, malignancy was the most common histopathological finding followed by granulomatous diseases with necrotizing granuloma seen only in 8 patients. 3 out of 63 clinically suspected malignancy cases found to be positive for mycobacterium tuberculosis. There were no major complications associated with the procedure and reported complications were throat pain and mild hemoptysis in a small group of patients.

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Case Report

Pulmonary Adenocarcinoma Masquerading as ILD

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Abstract

Pulmonary adenocarcinoma presents in different ways clinically and radiologically. Primary lung cancer presenting as Interstitial Lung disease (ILD) is very rare. Our case presented with manifestation of interstitial lung disease and was initially treated with steroids .Due to non-resolution of clinical symptoms as well as radiological worsening, we went ahead with VATS lung biopsy and the case was finally proved as adenocarcinoma which was confirmed by immunohistochemistry. This case proves that timely referral for lung biopsy is required in selected cases of interstitial lung disease when it is not responding to conventional treatment

Key words

Adenocarcinoma, ILD, VATS lung biopsy

Key Messages

Timely referral for lung biopsy is needed in case of clinicoradiologically persisting or worsening interstitial pattern even with optimal treatment.

Introduction

Pulmonary adenocarcinoma is unique in clinical, radiological and pathological presentations. Association of lung cancer in interstitial lung disease (ILD) is widely reported. But primary lung cancer presenting as interstitial lung disease (ILD) is a rare entity and not widely reported from India. Here we describe a case of primary lung cancer which presented as interstitial lung disease (ILD).

Case History

A 47 year old farmer, reformed smoker, who had significant history of exposure to poultry and pesticides presented to a local hospital with a 4 month

history of non-productive cough and progressive breathlessness. There was no history of fever, hemoptysis, weight loss or joint pain. There were no co morbidities like hypertension, diabetes, COPD or asthma. He was evaluated with routine blood investigations and chest X-ray. Initial chest X-ray (Figure 1) showed bilateral reticulonodular opacities with mid and lower zone predominance with no significant volume loss.

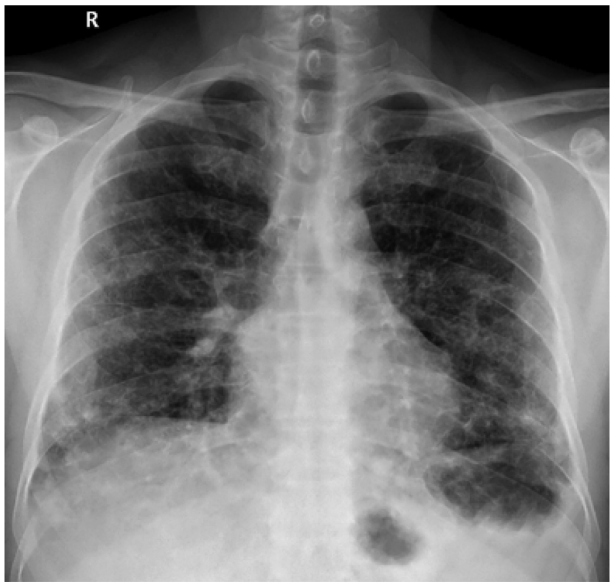

Fig. 1 : Chest Xray showing bilateral reticulonodular opacities with mid and lower zone predominance.

He was further evaluated with CT thorax (Figure 2) which showed bilateral nodular shadows with random and peri-bronchial distribution, associated fibrotic changes in bilateral lungs with traction dilatation of bronchi and mediastinal lymphadenopathy [Largest measuring13 X 10 mm].

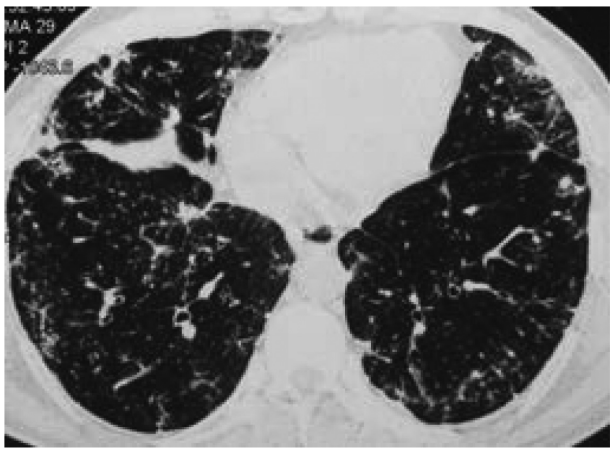

Fig. 2 : CT Thorax showing reticulonodular opacities with peribronchovascular distribution associated with traction bronchiectasis

He was evaluated with spirometry which showed restrictive pattern, however DLCO was 70% predicted. Bronchoscopy was done in the previous centre and BAL AFB smear, Genexpert and cytology were normal. He was started on prednisolone 30 mg once daily on suspicion of subacute hypersensitivity pneumonitis. But as there was no clinicoradiological improvement patient was referred to our centre. When he presented to our hospital, he was afebrile, his vitals were stable and there was bilateral rhonchi on chest auscultation.

He was further evaluated in our centre. His total WBC count was 6300 and CRP was 66 mg/L. Mantoux test was non-reactive. Serum calcium, ANA screening, ANA profile, anti CCP antibody were all normal. Serum ACE was 79 IU/ml. Chest X-ray was repeated from our centre which depicted bilateral reticulonodular opacities with mid and lower zone predominance.

Spirometry showed a restrictive pattern. He could perform a walk distance of 300 meters with no desaturation in six minutes walk test. As there was no clinicoradiological improvement the patient underwent VATS biopsy. Biopsies were taken from visceral pleural nodule and nodule from the right middle lobe. (Figure 3)

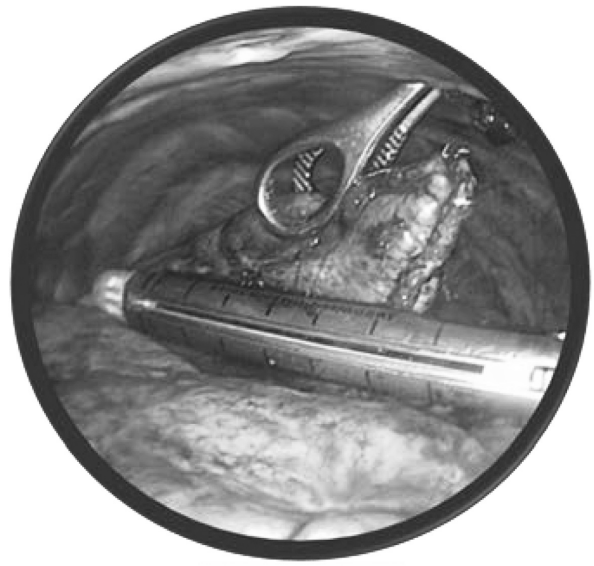

Fig. 3 : Middle lobe wedge biopsy of visceral pleural nodule using Endostapler via VATS

On histopathological examination it was diagnosed as invasive mucinous adenorcarcinoma with tumour infiltration. (Figure 4). Immunohistochemistry examination was positive for CK7, CEA and negative for CK20 (Figure 5) confirming it as primary lung malignancy.

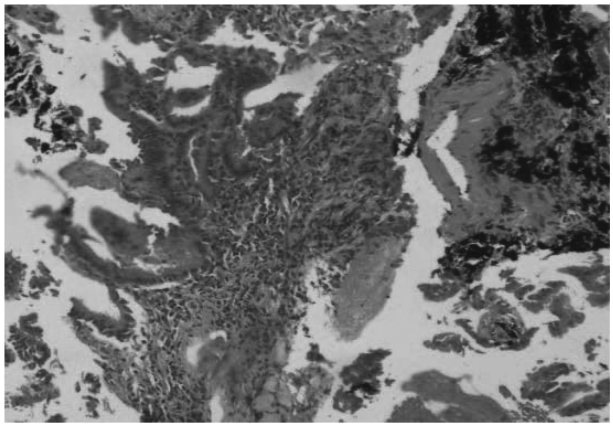

Fig. 4 : Histopathology examination showing invasive mucinous adenocarcinoma with tumor infiltration

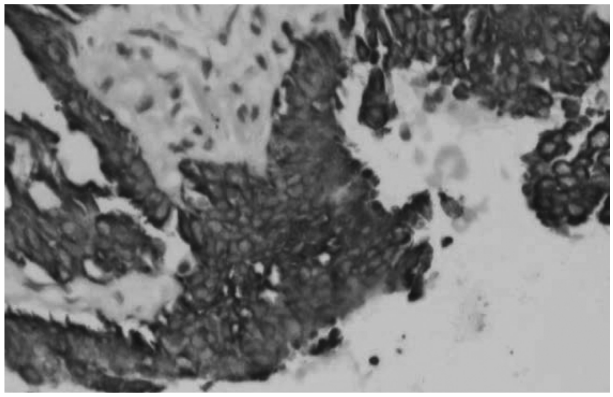

Fig. 5 : Cells are positive for CK7, CEA and negative for CK20.

Discussion

Association of lung cancer in established ILD is well documented. There are reports of higher prevalence of lung cancer in the IPF population, varying from 4.8%-48%[1]. Primary lung cancer presenting as interstitial lung disease is rare. In this case clinico radiologically the features were suggestive of an interstitial pathology.

Pulmonary adenocarcinoma is unique in clinical presentation, epidemiology and radiology. It arise from type 2 pneumocytes. The WHO defines bronchoalveolar carcinoma as a subtype of adenocarcinoma with growth along the alveolar septa and without evidence of stromal, vascular or pleural invasion. Histologically there are three types- mucinous, non mucinous, mixed[2]. The usual clinical presentations are cough, breathlessness and bronchorrhea. Adenocarcinoma has been described previously with presentations like non resolving pneumonia[4] .Though there are diverse presentations, rarely adenocarcinoma can present with interstitial involvement. Very few case reports of similar conditions are available[3,5]. The exact pathogenesis of interstitial shadowing is not known. Most probably intense inflammation and fibrosis may overshadow tumour proliferation and masquerade as ILD[3].

In this case, clinicoradiological and functional evaluation was suggestive of early onset of interstitial lung disease more likely hypersensitivity pneumonitis and the patient was started on oral corticosteroids. Since the response to treatment was poor, we proceeded with surgical lung biopsy which is the gold standard for diagnosing ILD. Surgical lung biopsy being invasive is not preferred usually, but now can be done safely with video assisted thoracoscopic method. In a study by Kayatta et al, surgical lung biopsy provided 88% accurate specific diagnosis of ILD in comparison with 15 % without a surgical lung biopsy[6]. VATS biopsy is a very safe procedure with mortality rate of 0-2 % in low risk patients and 0-11% in patients whose risk was not stratified[6]. So all cases of ILD which has a poor response to steroids or has an atypical presentation would warrant a lung biopsy.

Conclusion

Adenocarcinoma especially bronchoalveolar carcinoma has diverse presentations. It should also be included in differential diagnosis of interstitial lung disease. So all ILD which respond poorly to treatment should be evaluated for alternate diagnosis and this should include bronchoscopic or surgical lung biopsy for obtaining a tissue diagnosis.

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Case Report

Intralobar Sequestration - A Case Report

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Abstract

Intralobar pulmonary sequestration(ILS) is characterized by the presence of nonfunctional parenchymal lung tissue, receiving systemic arterial blood supply. It lacks normal communication with tracheobronchial tree. Most of the ILSs are located in the posterior basal segments of the left lung. Patients with ILS are either asymptomatic or they present with recurrent respiratory infection or hemoptysis. Failure to diagnose and treat this condition can lead to recurrent pneumonia and fatal hemoptysis. A case of recurrent respiratory infection for 20 yrs was investigated and diagnosed as Intralobar sequestration, and is reported due its rarity.

Key Words

Pulmonary sequestration, intralobar, case report.

Introduction

Pulmonary sequestration is a mass of abnormal pulmonary tissue that does not communicate with the tracheobronchial tree and is supplied by an anomalous systemic artery. Bronchopulmonary sequestration is a benign, rare lung abnormality and anatomically it is classified into intralobar and extralobar sequestration.ILS is more common on the left lower lobe.We present a case of ILS on the right lower lobe due to its rarity.

Case Report

35 year old male from Trivandrum district was admitted to Department of Pulmonary Medicine, Medical college, Trivandrum with complaints of fever and cough of two weeks duration. Cough was productive with yellowish sputum that was foul-smelling initially. No postural variation or blood staining was noticed for expectoration. Fever was high grade with chills and rigor, which subsided with medication. There was no history of seizures or loss of consciousness. He did not give history of breathlessness, wheeze, chest pain, loss of

appetite or weight. He gave history of recurrent episodes of cough with purulent expectoration for last 20 years. He gave history of hospital admission 20 years back for Pneumonia. No past history of hemoptysis. For the present episode he had a course of antibiotics from local hospital and was referred to us in view of the persistence of chest x-ray lesion.

The patient did not give history of anti tuberculosis treatment in the past. He is not a known diabetic or hypertensive. He did not give history of episodic breathlessness, wheeze or atopic symptoms. There was no history of recurrent sinusitis or ear infections. Sleep and appetite were normal. There was no change in bowel or bladder habits. He was not a smoker but had passive smoking exposure from co-workers. He was an occasional alcoholic, but did not give history of binge drinking or alcoholic blackouts. No other addictions. No history of exposure to pets. He did tile fixing works for around 15 years. No history of respiratory distress following birth. He was adequately immunized. He was married and had two children.

On examination he was conscious and oriented, moderately built and nourished, He had a BMI of 25.7. General examination revealed grade 1 clubbing. His vitals were stable at the time of examination. There was no pallor, icterus, cyanosis, lymphadenopathy or pedal edema. Pulse rate was 94/min, regular, normal volume and character, no radio femoral or radio radial delay. All peripheral pulses palpable. His Blood Pressure was 110/ 70 mmHg in right upper limb in sitting position, Respiratory rate was 22/min, SpO2 - 99% room air and temperature was normal. His respiratory system examination was normal except for coarse crepitations which were heard in the right infra axillary, infra scapular and lower inter scapular region. The other systems were normal on examination.

His routine blood examination showed Hb 14.2g/dl,TC of 5400 with 62% neutrophils and 45 mm/hr. His blood sugar, LFT and RFT were normal. Sputum AFB smear examination was negative and sputum culture and sensitivity showed normal pharyngeal flora. His viral markers were non reactive.

Chest x-ray showed multiple cystic shadows in the right lower zone (fig 1). HRCT Thorax showed heterogenous attenuation of lung noted in posterior basal segment of right lower lobe with multiple cystic areas and air fluid levels. No obvious communication is demonstrable with right lower lobe bronchus or its segmental branches (fig 2). Contrast study shows systemic arterial supply to the lesion from below diaphragm via a branch from Coeliac trunk. Venous drainage is via pulmonary vein (right inferior). No separate pleural lining identified for the abnormal lung parenchyma. Mediastinal windows revealed subcentimetric prevascular and lower paratracheal

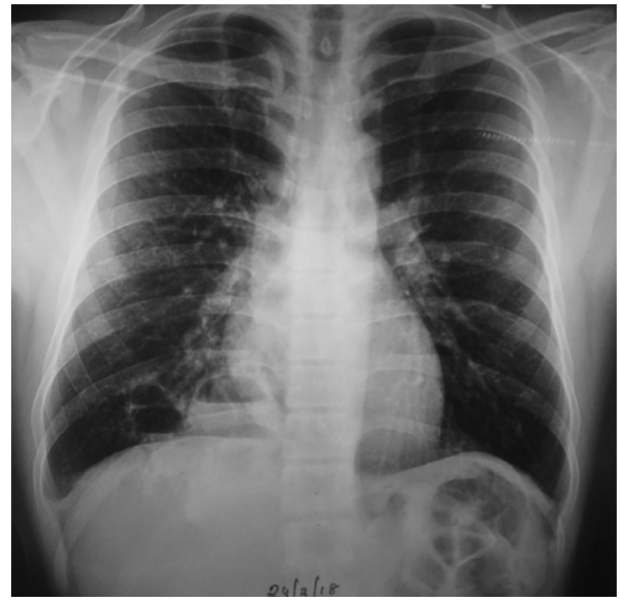

Fig. 1 : Chest x-ray showing multiple cystic shadows with fluid levels in the right lower lobe

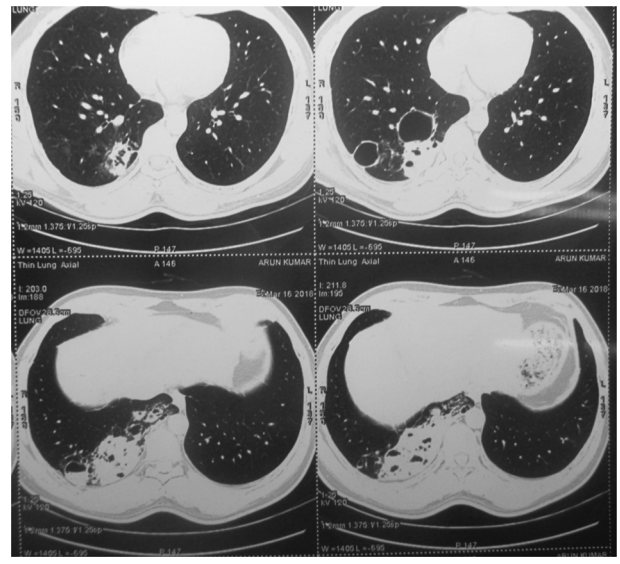

Fig. 2 : Heterogenous attentuation of lung in posterior basal segment of right lower lobe with multiple cystic areas and air fluid levels

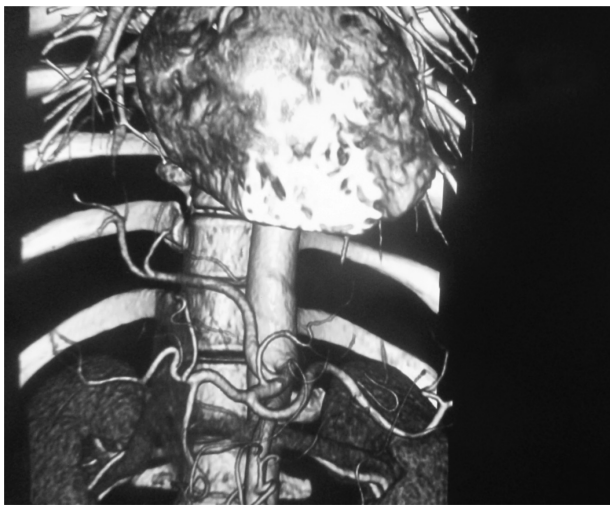

Fig. 3 : Image showing arterial blood supply to sequestrated lung from celiac trunk.

lymph nodes. CECT Chest /aortography showed infected intralobar sequestration in right lower lobe of lung with arterial supply from coeliac trunk and venous drainage into right inferior pulmonary vein (fig 3). A confident diagnosis of Intralobar sequestration was made and the patient was referred to cardiothoracic surgery for right lower lobectomy in view of his recurrent respiratory infections. Right lower lobectomy was done after careful identification and ligation of the feeding vessels. Post operative period was uneventful and the patient remains asymptomatic on follow up.

Discussion

Pulmonary sequestration is a relatively rare entity comprising 0.15-6.4% of all congenital pulmonary malformations [(1)].Pulmonary sequestration was first described by Rektorzik in 1861, as a malformation comprised of dysplastic lung tissue with no normal communication with the tracheobronchial tree and with an anomalous systemic arterial supply[(2)]. There are two types of pulmonary sequestrations: Intralobar sequestration (ILS), which is surrounded by normal lung tissue; and extralobar sequestration (ELS), which has its own pleural investment. Intrapulmonary sequestration is four times more common than the extralobar type. Sequestrations develop because of accessory primordial lung buds,which may be invested with in normal lung tissue in intralobar or external to the normal lungs in extralobar sequestration[(3)].

Patients can present with an incidental pulmonary lesion on imaging and be otherwise asymptomatic. More commonly however, they may manifest varying degrees of pulmonary symptomatology such as pleural effusions or recurrent pneumonia[(4)]. Intralobar sequestration usually presents in the adolescent age. The most common site for intralobar sequestration is posterior basal segment of left lower lobe. The arterial supply is variable with 74% being supplied by the thoracic aorta, while the remainder originates from the abdominal aorta and its branches including the gastric or splenic arteries. Typically, venous drainage from these lung segments is via the pulmonary venous system, although systemic drainage has been noted as well[(5)]. Savic B and colleagues in their analysis found that, the aberrant artery in intralobar sequestration originated in 74% of all cases from the thoracic aorta, and in 14·8% there was more than one anomalous artery. The mean diameter of the aberrant arteries was 6·3-6·6 mm[(1)]. Many theories have been suggested to elucidate the embryologic mechanism responsible for sequestrations. During lung development, an insult to the developing pulmonary arterial blood supply occurs leading to retention and proliferation of the nascent systemic capillary network. Achieving a diagnosis of pulmonary sequestration can range in difficulty depending upon the type of anomaly and presenting symptoms. Computed tomography will typically suffice in most adult cases with the need for angiography to demonstrate blood supply[(6)]. It is important to differentiate sequestration from other congenital malformations specifically, cystic adenomatoid malformation and scimitar syndrome. Definitive treatment involves resection of the affected lung segment. Accurate preoperative identification of the arterial blood supply is crucial since inadvertent injury of these systemic vessels can have a fatal consequence. Endovascular treatment of pulmonary sequestration, with selective embolization of the inflow arteries, is a very attractive minimally invasive therapeutic option, as compared with conventional surgery, and potentially less prone to associated complications[(7)]. Resection via minimal-access procedures such as VATS lobectomy is another option thereby permitting early discharge and a low rate of complications[(8)]. Pulmonary sequestration is a rare entity especially in the adult population and early surgical resection should continue to be the standard of care in both adolescent and adult patients with this disease process. Although intralobar sequestration is more

common on left side, our patient had right sided sequestration. His surgery and postoperative period were uneventful. He was totally asymptomatic on follow up.

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Case Report

Intrapulmonary Teratoma - Bronchoscopic Visualisation

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Abstract

Mediastinal teratomas are among the third common type of teratomas after ovary and testes. Primary or Intrapulmonary teratomas are extremely rare and it is said that intra pulmonary teratomas are one of the rarest tumours encountered by pathologists (Spencer)[1]. The diagnosis is usually made after surgery. A pre operative diagnosis by bronchoscopy is extremely rare[2]. We report this case where the diagnosis was established pre operatively by bronchoscopic visualisation of hairs in the bronchus.

Key Words

Bronchoscopy, Intrapulmonary, teratoma, visualisation.

Case Report

A 22 year old girl presented to the Department of Respiratory Medicine with a chronic cough with mucoid and at times purulent expectoration since childhood. She also had occasional haemoptysis She had 2 courses of anti tuberculous drugs three years apart as the treating doctors suspected tuberculosis from her X rays. Her sputum was never positive for AFB and she was told that her X rays had not cleared even after complete course of the drugs. Drug resistance was suspected and she was referred.

Examination showed a moderately built and well nourished young girl who was coughing off and on but was not dyspnoeic. She was afebrile, had no clubbing or lymphadenopathy. Respiratory system examination revealed diminished breath sounds on the left side, dull percussion, bilateral wheezes and crackles predominantly on the left side.

Blood investigations showed polymorpho nuclear leucocytosis, ESR of 80mm/hr, polycythemia with Hb of 18 gm%,and normal hepatic and renal function. The Chest x ray showed opacification of the left lung with the presence of irregular calcifications near the centre of the opacity. As the diagnosis was not definite, bronchoscopy was planned.

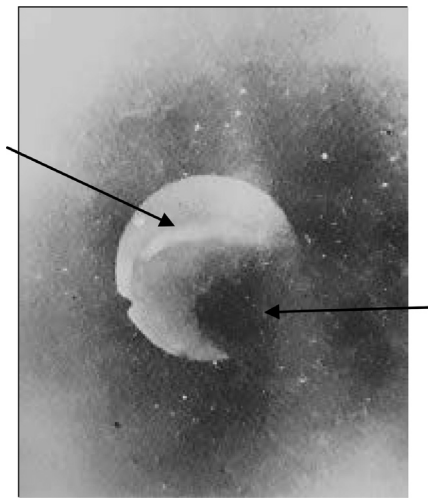

Fig. 1 : Bronchoscopic photograph showing single and tuft of hairs (arrows)

Fibre-optic bronchoscopy was done under local anaesthesia. During the procedure, the girl had cough inspite of adequate amount of local anaesthetic and pre medication. The vocal cords could be negotiated fairly easily but the carina and the bronchial tree on the right side had chronic inflammatory changes with ulcerations and sloughing. The left main bronchus looked black with hairs 'waving' in the air flowing through. Pus exuded from the distal end and the bronchoscope could not be moved into the left main bronchus. The patient had immediate relief after suctioning out pus. The visualisation of hairs through the bronchoscope made it possible to diagnose 'intra-pulmonary teratoma'. The pus did not show AFB, culture was negative and there were no malignant cells.

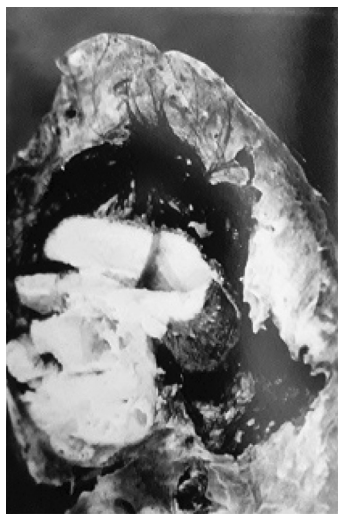

Fig. 2 : Cut section of left lung - post pneumonectomy showing hairs & skeletal tissue

The patient had very good symptomatic improvement after bronchoscopy. After making a diagnosis of intrapulmonary teratoma, she was referred to thoracic surgeon. She underwent left pneumonectomy. Post procedure patient was asymptomatic.

The histopathological examination of the resected specimen showed the mass to be well encapsulated with the presence of hair, teeth, bone etc.

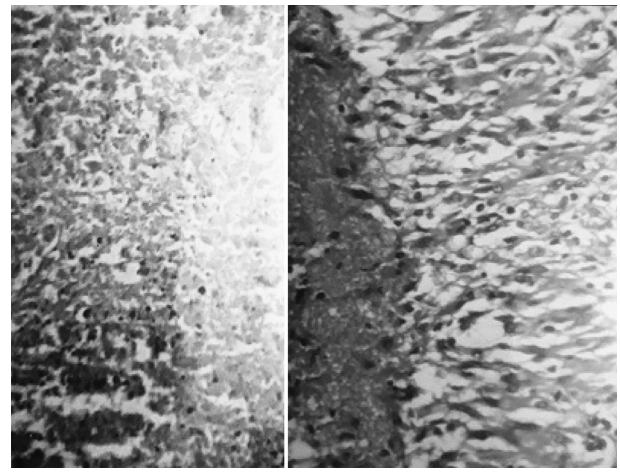

Fig. 3 : Histopathology specimen showing different types of tissues in Teratoma.

Discussion

Intrapulmonary teratomas are rare; only 44 cases have been reported in the world literature till 2007.[7] These tumors are thought to originate from the third pharyngeal pouch. They occur equally in men and women and usually are diagnosed in the second to fourth decade of life. They are more often benign than malignant. Malignant lesions have a better post operative prognosis. Benign lesions may exhibit high morbidity and mortality because of their size and location[8]. These tumors present radiographically as lobulated masses that may contain calcification or peripheral collections of air. They most often occur in the upper lobes.

There are very few case reports of bronchoscopic visualisation of the intrapulmonary teratoma pre operatively in world literature. M.Y. Ali and P.K. Wong[1] reviewed 15 cases of intrapulmonary teratoma in Thorax in 1964. Most of these cases were diagnosed post operatively as bronchoscopy was not common place. Again in 1983 a case of recurrent

teratoma, initially mediastinal and later intrapulmonary, was reported by Präuer et al[2] from Munich. The intra pulmonary teratoma in this case was seen through the bronchoscope as a tuft of hair. From India, Dr. Sushama et al[5] from Calicut, Kerala, South India reported a case in which whitish material could be seen coming out from the involved bronchus during bronchoscopy. Our case is unique in that the diagnosis could be established by bronchoscopic visualisation of hairs in the bronchi and the presence of a mass with calcifications inside. But the patient never had trichoptysis which is mentioned in many cases. A similar case is reported in a male patient where pre operative diagnosis was made.[9] A high index of suspicion is required in such cases especially when there are calcific spots inside the mass. CT thorax will be helpful for a pre operative diagnosis in most of the cases. Because of its potential for rupture or malignancy, surgical removal is the curative treatment.

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The merit of the publication lies in its quality and content. Contributions are invited on any aspect of Pulmonary and critical care medicine. Articles are accepted on the basis of significance, scientific perfection and practical applicability. Authors are requested to base their papers on the basis of original work carried out by themselves or their groups. Manuscripts should not be submitted to more than one journal at a time.

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2. Organization as author

The Cardiac Society of Australia and NewZealand. Clinical exercise stress testing. Safety and performance guidelines. Med J Aust 1996; 124:282-4.

3.Books and other Monographs

Ringsven MK, Bond D. Gerontology and leadership skills for nurses. 2nd ed. Albany (NY): Delmar Publishers; 1996.

4. Editor(s), compiler(s) as author

Norman IJ, Redfern SJ. editors. Mental health care for elderly people. New York: Churchill Livingstone; 1996.

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Philips SJ, Whisnant JP Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis, and management. 2nd ed. New York: Raven Press;1995.p.465-78.

6. Unpublished Material In press

LeshnerAl. Molecular mechanisms of cocaine addiction. N Engl J Med. In Press 1996.

7. Journal article in electronic format

Morse SS. Factors in the emergence of infectious diseases.Emerge Infect Dis [serial online] 1995 Jan-Mar (cited 1996 Jun 5); 1 (1): [24 screens]. Available from: URL: http://wwwcdc.gov/ncidod/EID/eid.htm.

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