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Case Report Open Access

Pulmonary Cryptococcosis Secondary to Bronchial Asthma Presenting as Type I Respiratory Failure- A Case Report with Review of Literature

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Introduction

Cryptococcus spp, was first isolated and described in 1894 by Sanfelice F in Italy from peach juice and named it as Saccharomyces neoformans, is an yeast like fungus [1], first isolated from a clinical specimen by Busse in the same year from Germany [2]. Cryptococci are a saprophytic fungi present in soil contaminated with bird droppings mainly of pigeons, roosting sites and decaying vegetables [3]. Previous reports have also showed the presence of *Cryptococcus spp* colonized in the nasopharynx and on skin of healthy individuals [4]. Belonging to Basidiomyctes group of fungi *Cryptococcus spp* primarily infects central nervous system causing meningoencephalitis mostly in immunocompromised individuals. Classical and molecular genetic studies have revealed that *Cryptococcus spp* are closely related to ascomycetes group (*Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*) and basidiomycetes pathogens and mushrooms (*Ustilago maydis*,*Coprinus cinereus*, *Schizophyllum commune*) [5]. *Cryptococcus spp* have a defined sexual cycle which decides the species and its virulence. From being a saprophyte to opportunistic pathogen, *Cryptococcus spp* is now recognized as a potential pathogen which is having the ability to cause superficial as well as systemic disease. Though meningitis is considered as the most common manifestation of Cryptococcal infection, recent studies have implicated *Cryptococcus spp* in lung disease which may be asymptomatic, pneumonia or leading to respiratory failure [6,7]. *Cryptococcus spp* being an encapsulated yeast, can evade defense mechanism of intact immune system and lead to dissemination mostly from lungs and central nervous system to blood, skin, eyes, skeletal system and urinary tract [8]. *Cryptococcus neoformans* and *Cryptococcus gattii* are the two species that are frequently associated with infections in immunocompromised and immunocompetent individuals respectively. Infection in humans by *Cryptococcus* laurentii has also been reported. Molecular studies have confirmed the presence of five capsular phenotypes of *Cryptococcus spp*. *Cryptococcus neoformans* includes serotype A (*Cryptococcus neoformans var grubii*), D (*Cryptococcus neoformans var neoformans*) and AD hybrids and serotypes B and C are designated as *Cryptococcus gattii*. Evolutionary studies have revealed that each species of *Cryptococcus neoformans* (VNI-VNIV) and *Cryptococcus gattii* (VGI-VGIV) contain four molecular types. More than 90% of human infections are attributed to serotype A (*Cryptococcus neoformans var grubii*) and geographical prevalence showed *Cryptococcus neoformans* var neoformans as common cause of cryptococcosis in Europian countries and USA and *Cryptococcus gattii* is prevalent in southern Asia, central Africa and tropical and sub tropical regions of America including Brazil [9].

Pulmonary cryptococcoisis in immunocompetent individuals usually remains as asymptomatic where *Cryptococcus spp* remain colonized in the tracheobronchial tree or cause benign pulmonary cryptococcosis. Previous reports have suggested that HIV-negative patients (30-70%) suffer from pulmonary cryptococcis more frequently as compared to AIDS(2%) patients who suffer from disseminated cryptococcal disease [10-12]. Clinical disease of the lungs by *Cryptococcus spp* was reported in pulmonary disorders like tuberculosis of lungs, pneumothorax and allergic bronchopulmonary Aspergillosis. Pulmonary cryptococcosis was also reported in pregnancy, diabetes mellitus, pleuritis, systemic lupus erythematus, cushings syndrome, Continous Ambulatory Peritoneal Dialysis (CAPD), liver cirrhosis, cancer, organ transplants, spleenectomy, malnutrition, leprosy, pulmonary tuberculosis and those on cortico steroid therapy [13-20]. Pulmonary Cryptococcosis may be presenting as pleural effusions, solitary or multiple masses, glass-ground interstitial opacities, dense consolidations, patchy, segmented or lobar air space consolidation (*cryptococcal pneumonia*) and nodular and reticulonodular cavities. Differential diagnosis of pulmonary cryptococcosis should be done with pneumonia [21,22]. Review of literature showed only two previous reported cases of pulmonary cryptococcosis presenting as acute respiratory failure [7,23,24]. We report a case of Acute respiratory failure due to pulmonary cryptococcosis in the presence of bronchial asthma in an otherwise immunocompetent individual.

Case Study

A 35-yearold male patient presented with mild fever, severe cough, breathlessness and night sweats on 09-03-12 to the casualty of Prathima Institute of Medical Sciences, Karimnagar, Andhrapradesh, India. Patient gave a history of white scanty sputum with severe cough with no history of hemoptysis and orthopnea. He was a non smoker and occasional alcoholic. Patient had no similar complaints in the past and was not suffering from either diabetes mellitus or hypertension. Patient was an agriculturist and gave a history of residing near poultry farm since his birth. Patient's previous history revealed that he was treated for pulmonary tuberculosis 10 year back. The details of therapy and previous reports were unavailable with the patient. History of bronchial asthma since 2 years and was on corticosteroid therapy (Hydrocortisone 100mg BD) since then. Hematological investigations revealed mild leucocytosis (13,200cell/mm^3), slightly raised ESR (10mm) and normal serum creatinine(0.7) and random blood glucose levels (148g). X-ray revealed bilateral parenchymal fibrosis with secondary infection as shown in figure 1. 2D echo and color Doppler studies revealed pulmonary arterial hypertension. A provisional diagnosis of bronchial asthma with acute exacerbation with type I respiratory failure was made. Voluntary HIV test for detection of antibodies was non reactive. Serum Interferon gamma was not performed as the patient was not able to afford. Sputum was sent for routine and fungal culture along with acid fast staining for *Mycobacterium tuberculosis*. Routine culture showed normal flora after overnight incubation and fungal culture revealed large spherical budding cells (as shown in Figure 2), later identified as *Cryptococcus*

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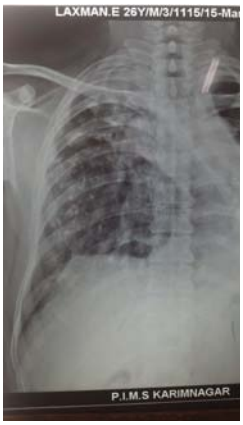

Figure 1: chest radiograph showing extensive bilateral air spaces.

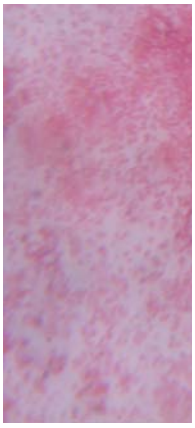

Figure 2: Gram's stain of culture of *Cryptococcus spp* clearly showing a halo surrounding cells indicating presence of a capsule.

spp by using standard lab procedures. No acid fast bacilli were seen ruling out tuberculosis. Blood culture showed no growth ruling out the possibility of cryptococcemia. Patient was advised back rest and oxygen inhalation of 2.4L/min. Nebulization using duolin 3hourly and budate 8 hourly was advised. Treatment with fluconazole 400mg/day for at least 3 months was initiated once sputum culture showed the presence of *Cryptococcus spp*. The patient has gradually recovered and at the time of discharge on 20th march 2012, was found to be a febrile, with SPO_2 of 90%, an ESR of 5mm. A review after one week showed no growth of *Cryptococcus spp* in sputum.

Discussion

The cryptococcal disease is also known as Busse Buschke's disease, European blastomycosis or Torulosis. Previously considered as a sleeping disease has now become an awakening giant [25]. *Cryptococcus* is a ubiquitous fungus present as a normal flora of man and animals, plants being other habitats where cryptococci can be isolated [26,27]. Cryptococcosis in human can be seen mainly as cerebromeningeal cryptococcosis, pulmonary cryptococcosis, visceral cryptococcosis, osseous cryptococcosis, cutaneous cryptococcosis and mucocutaneous cryptococcosis [28]. In the present case what is interesting to note is that the patient was previously treated for pulmonary tuberculosis, now suffering from bronchial asthma and has given a history of living near poultry farm and basically is a farmer. The patient would have been exposed to *Cryptococcus* by inhalation and was carrying the organism asymptomatically. Because of the bronchial asthma and chronic airway obstruction and due to prolonged corticosteroid therapy the cryptococci may have taken the advantage of disturbed pulmonary function and responsible for acute exacerbation leading to respiratory failure. The pulmonary infection here was differentially diagnosed against Mycobacterium tuberculosis infection keeping in mind its prevalence. Pulmonary cryptococcosis was suspected considering the prolonged corticosteroid therapy, chronic airway obstruction and close contact with poultry farms all of which could have predisposed the patient to cryptococcal infection. In the present case, due to prolonged corticosteroid therapy the immune system could have been compromised although patient was otherwise immunocompetent. We also suspected pulmonary cryptococcosis due to its frequency in recent times and increased reports of cryptococcal infection in both immunocompromised as well as immunocompetent individuals. Previous studies have shown 29% incidence of pulmonary cryptococcosis in HIV- negative patients [23]. Basically a saprophyte and an opportunistic pathogen, *Cryptococcus* has got complex virulence factors that can make it a potential pathogen [29]. Transmitted to humans by respiratory route, studies have confirmed its presence in respiratory tract without symptoms [30]. Pulmonary cryptococcosis and disseminated cryptococcosis including cryptococcemia has been reported in immunocompetent and immunocompromised individuals respectively [31]. Pulmonary cryptococcosis either asymptomatic or with symptoms can resolve even without treatment in immunocompetent individuals [32]. Reports of dissemination to other organs from lungs in immunocompetent individuals, though rare are available in literature [33]. Studies have indicated that there is a 12.5% chance of dissemination in untreated pulmonary cryptococcosis and recommended fluconazole therapy which is less toxic as compared to other reports who do not prefer therapy [34,35]. Risk factors for Cryptococcal infection include Medical and environmental factors [36]. Asthma, pregnancy, diabetes mellitus, pleuritis, systemic lupus erythematus, cushings syndrome, Continuous Ambulatory Peritoneal Dialysis (CAPD), liver cirrhosis, cancer, organ transplants, spleenectomy, malnutrition, leprosy, pulmonary tuberculosis and those on cortico steroid therapy are some of medical risk factors. Environmental risk factors include trees, dust arising from cutting or chopping wood, digging earth, repairing/building house, gardening, and pruning. In all, compromised pulmonary function could well be a compounding risk factor acquiring cryptococcal infection. There are reports of nosocomial spread and occupational risk of acquiring cryptococcosis. Clinical diagnosis of pulmonary cryptococcosis relies on radiological findings and studies have observed typical radiological presentation both in immunocompetent and immunocompromised [37,38]. Confirmation of Cryptococcal infection of lungs is traditionally done by isolation of *Cryptococcus* in sputum or other respiratory secretions and identification by using standard laboratory methods like Gram's stain, India ink staining for capsule and latex agglutination tests. In the current perspective we try to focus light on the increasing reports of cryptococcal disease in immunocompetent individuals, possible predisposing factors for infection [21,33,34,37]. Since only few reports have suggested colonization of *Cryptococcus spp* on normal healthy individuals, studies should be encouraged on epidemiology of *Cryptococcus spp*, its prevalence as colonized in healthy, asymptomatic and in the environment [39, 40,41]. Though cryptococcosis is hard to eliminate, effective measures should be taken to prevent its spread to susceptible population [42]. Recent reports on outbreaks of cryptococcal infection should be considerd as an alarming signal [43,44,45]. Epidemiology of Cryptococcal infections is unclear in India, where an increase in incidence of cryptococcosis was observed in AIDS patients in a study from north India (1992-2004). Recent

reports have suggested an increase in cryptococcal disease in north India where HIV seroprevalence is low when compared to south and western India that show high prevalence of HIV [46]. Isolated reports give an impression probably of misdiagnosis or under reporting as the cryptococcal infections are not notifiable.

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