HISTOPLASMOSIS – CASE REPORT

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INTRODUCTION

Histoplasmosis is one the chronic pulmonary diseases which can present just like pulmonary tuberculosis[1,2]. Acute pulmonary histoplasmosis is usually asymptomatic. Cough, fever and malaise with chest radiological findings of hilar adenopathy are typical features. Sometimes erythema nodosum or erythema multiforme may occur. Perinodal fibrosis may occur in rare circumstances if hilar nodes go through caseation and granuloma formation. In this manner progressive mediastinal fibrosis may occur.

Clinical manifestations are of three types [3]. The most common presentation in the vast majority of the patients is of acute pulmonary histoplasmosis, which is a mild infection. The other two manifestations are that of chronic pulmonary histoplamosis and the acute disseminated infection - these are progressively fatal and serious in outcome.

The acute disseminated form occurs usually in immunocompromised, especially in AIDS. A wide spread of features may be found - fever, lymphadenopathy, hepatomegaly, splenomegaly, jaundice, leukopenia, chronic meningitis, endocarditis, granulomatous hepatitis, Addison's disease and GIT ulceration. Some of the features overlap with chronic pulmonary histoplasmosis, which is usually localized as the main differentiating point.

Chronic pulmonary histoplasmosis mimics tuberculosis of the lungs [1-3]. Night sweats, weight loss and productive cough with chest radiology showing uni- or bilateral hilar adenopathy with fibronodular shadows in the upper zones of the lungs are the hallmark features. 33 percent of the cases improve spontaneously but the rest undergo cavitation of upper lobes or emphysematous bulla formation develops. The resultant cor pulmonale and recurrent bacterial infections kill the patient eventually.

Histoplasma capsulatum is a dimorphic fungus that causes infection when a person inhales it [1, 3]. It prefers to grow on moist surfaces and in soils especially having droppings of birds and bats. Infectivity can occur within 5-18 days after exposure to dust contaminated with its hyphae during raking, bulldozing, cave exploring and by cleaning the soiled floor of chicken droppings.

The pathogenesis involves the inhalation of the small spores of this fungus into the alveoli and proliferation by budding. With the passage of time there is a granulomatous reaction leading to caseation necrosis and calcification that can produce a mass of scar tissue known as **histoplasmoma** [3]. The pathology resembles the chronic process of granuloma formation in tuberculosis.

Treatment of the disease includes intravenous amphotericin B (0.6 mg/kg daily) for the initial phase for acute dissemination in patients who are severely ill. The patient can be switched over to Itraconazole (200 mg twice daily) once improvement is evident [3, 4].

Similarly chemotherapy can be given for chronic pulmonary fibronodular histoplasmosis but no treatment is required for acute pulmonary histoplasmosis.

CASE REPORT

A 60-year-old man, resident of Battagram, with long standing diabetes mellitus type II presented with left sided chest pain, weight loss and a left sided pleural effusion in July 1999. His dry cough had been persistent for the last 4 years, but a history of productive mucopurulent sputum had been present for almost 8 months.

Management included drainage of pleural fluid and the routine examination showed exudative fluid with neutrophilia.

A high ESR (62mm / 1st hour), with three consecutive negative sputum samples for Acid Fast Bacilli (AFB) and a clinical history of night sweats, weight loss and chronic cough with deteriorating health had convinced us to commence anti-tuberculous therapy on 25 July 1999. Radiology showed a large left sided pleural effusion shifting the mediastinum to the right and small fibronodular opacities in right upper zones with slight right hilar engorgement

Six weeks after commencing anti-tuberculous therapy, a left hydropneumothorax occurred. This time chest intubation was done to drain the massive pleural effusion and for the expansion of the lung. The bronchopleural fistula took four weeks to heal despite continuous efforts with negative suction. A CT-Scan of the thorax was performed during the expansion process of the lung as a prerequisite for any surgical intervention being considered at that time for the delay in expansion of the lung. It showed a left hydropneumothorax with a consolidation in left lower lobe.

Anti-tuberculous therapy (ATT) ended after 8 months on 25/2/2000. The patient's condition was not satisfactory upon completion of therapy. The dry cough was still persistent during the last month of therapy and the weight had reduced by 3 kilograms at the end of the 8-month ATT. Also the left sided chest pain worsened. At this moment the ESR had risen to 94mm / 1st hour. Radiology at this stage showed a consolidation at the left lower lobe. Ultrasound chest confirmed it to be a loculated pleural effusion.

A pleural biopsy was arranged but it was not informative at all and the loculated pleural effusion could not be drained with the Abram's needle.

Bronchoscopy was arranged which revealed a grapelike lesion in the basal segment of the left lower lobe. There was no endobronchial lesion visible on the right side of the lung. Bronchoalveolar lavage (BAL) specimen was sent for pathological examination and showed numerous yeast forms of *Histoplasma capsulatum* with background respiratory epithelial cells with features of mild dysplasia and superimposed infection with streptococci and staphylococci (Figs. 1 & 2).

The microscopic appearance of the fungus showed typical rounded to oval yeast forms (with occasional budding), with a surrounding clear halo, representing the capsule (Fig. 1 a & b).

Figure-1: Typical appearance of *H. capsulatum* spores at low and high magnification (H&E and Giemsa stain). Respiratory cells, yeast forms and capsules are visible.

a- Low power **b- High Power**

Morphological identification was possible with the Haematoxylin and Eosin (H&E) stain, Giemsa stain and the PAS stain [5]. The latter stain was particularly good for staining the walls of hyphae and conidial (yeast) structures (Fig. 2).

Figure-2: *H. capsulatum* stained with the PAS stain, showing both hyphae and spores.

There was little background inflammatory cellular exudate, although some respiratory epithelial cells did show evidence of chronic irritation and mild dysplasia.

Bronchial biopsy revealed chronic inflammation with polypoid changes.

A confirmed histological diagnosis of chronic pulmonary histoplasmosis had been established. The patient was commenced on itraconazole (200 mg twice daily) for 6 months. The patient is on regular follow up.

DISCUSSION

Our patient presented with a usual presentation of histoplasmosis mimiciking pulmonary tuberculosis [1-3]. The productive cough, night sweats, weight loss, fever and chest pain are typical symptoms of pulmonary tuberculosis. The unusual feature in this case of histoplasmosis was the presence of a large pleural effusion. This is a rare presentation for histoplasmosis [6].

This patient presented with chronic pulmonary histoplasmosis, which is more common in individuals >40 years, especially those who are smokers with preexisting lung diseases [1, 3]. Being a nonsmoker, this case should not have been at risk for infection with histoplasmosis, but the age of 60 years and having chronic bronchitis correlates with the risk factors. The patient also denies living in any endemic area of poultry farms or dealing with poultry manure, bird droppings etc. He had also neither travelled to any other country abroad endemic with histoplasmosis. This would have supported the evidence for risk of exposure to histoplasmosis spores. Such was the case with eight male Japanese

who travelled overseas and presented with pulmonary nodule and mediastinal lymphadenopathy upon their return to Japan [7].

Thus, high suspicion is required to diagnose histoplasmosis and other fungal infections, especially for those patients who do not live in endemic areas [8]. In this case, the nonresponsiveness of ATT therapy and persistence of symptoms created the doubt regarding the diagnosis of tuberculosis. Therefore, pleural biopsy and bronchoscopy were performed to reach a conclusion. Had the pathologist not been suspicious of the histoplasmosis capsulatum microconidiae, the diagnosis would have been missed. BAL examined in 10% KOH showed large yeast cells, but slide stained by PAS, Giemsa and cellufluor methods were superior to KOH preparations [9]. In the future, the differential diagnosis must include histoplasmosis, which is thought to be uncommon in our region, Abbottabad.

The pleural fluid in the early stages should have been examined carefully for fungal spores. Also the culture of the pleural fluid would have revealed the diagnosis. The loculated pleural effusion at the end of ATT treatment could not prove beneficial for culture, because it could not be drained even during pleural biopsy done under ultrasound guidance. This would require surgical intervention to see any granulomatous process in the left lower lobe. This case has certain resemblance with the presentation of multiple loculi and a large pleural effusion with chest pain, fever and chills of a patient with histoplasmosis reported by Richardson JV in a chest journal in 1997 [10].

Thus it is recommended that cytology of sputum or pleural fluid by an expert pathologist to locate especially fungal spores / hyphae with great scrutiny be considered a crucial step for approaching a diagnosis, particularly in cases suspected to be nonresponsive pulmonary tuberculosis.

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