

Chronic Necrotising Pulmonary Aspergillosis: A Rare Complication in a Case of Silicosis

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ABSTRACT

Chronic necrotising pulmonary aspergillosis (CNPA) is a rare complication of silicosis whose diagnosis requires a high index of suspicion as it mimics tuberculosis. We report a case of a 52-year-old male with a long history of silica dust exposure and progressively increasing dyspnoea for the past eight years, productive cough, fever, weight loss for past three months and hemoptysis for preceding three weeks. Based on the clinical, radiological and microbiological evidence, he was diagnosed to be a case of CNPA with aspergilloma complicating silicosis.

Key words: *Silicosis, Progressive massive fibrosis, Aspergilloma, Chronic necrotising pulmonary aspergillosis.*

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INTRODUCTION

Pulmonary aspergillosis may present differently depending largely on the immune status of the patient, the type of exposure, and the presence of underlying disease¹. The various types of aspergillosis may be regarded as constituting a continuous spectrum, ranging from invasive disease in the severely immunosuppressed patients to hypersensitivity reactions, such as allergic bronchopulmonary aspergillosis in the atopic patients². Between these extremes are chronic necrotising disease, seen in mildly immunocompromised hosts, and the non-invasive aspergillosis, which is due to saprophytic growth within a previously diseased area of the lung in an otherwise normal host². In the early 1980s, Gefter *et al*³ and Binder *et al*⁴ independently described "semi-invasive aspergillosis" or "chronic necrotising pulmonary aspergillosis (CPNA)", as a rare

locally destructive form of aspergillosis. In this report we present a case of silicosis with progressive massive fibrosis that developed CNPA with aspergilloma, a complication rarely reported.

CASE REPORT

A 52-year-old male presented to us with complaints of progressively increasing dyspnoea for the past eight years along with productive cough, fever, weight loss and anorexia for the past three months, and hemoptysis for the past three weeks. For the last 32 years his work involved sharpening of metallic instruments on a spinning stone wheel. He had a bout of hemoptysis two years ago and for this he received nine months of antitubercular treatment from a private practitioner though his sputum did not show

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any acid-fast bacilli. He had never smoked, consumed alcohol, or chewed tobacco and had no history of diabetes mellitus, hypertension, or steroid therapy.

On admission, he was ill-looking, with a blood pressure of 118/78 mmHg; pulse rate of 96 beats per minute; respiratory rate of 28 breaths per minute; and temperature of 38.8 °C. The oxygen saturation by pulse oximetry was 86% on room air. Auscultation of the chest revealed bilateral scattered crepitations. The hemoglobin level was 9.6 g/dl, and the total leukocyte count was 11600/cu mm with 84% neutrophils. The blood sugar, the liver function tests and the renal function tests were within normal limits. ELISA for HIV was negative.

The chest radiograph (Figure 1) at presentation revealed bilateral large peripheral masses in the upper and mid zones with areas of breakdown along with fibronodular shadows and scattered parenchymal calcifications in all the lung fields. The left upper zone cavity showed an air crescent surrounding a mass with areas of calcifications. The hilar and paratracheal lymph nodes on both sides showed eggshell calcification. The sputum Gram stain

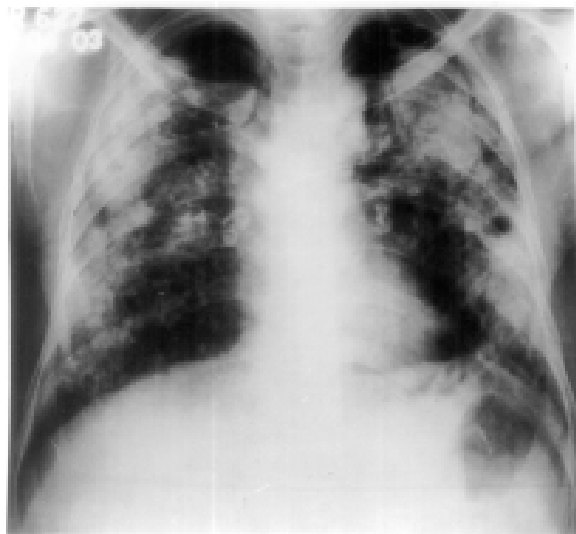


Figure 1. Chest radiograph (postero-anterior view) showing bilaterally extensive disease with large opacities in the upper and mid zones with calcifications. The left upper zone cavity shows an air crescent surrounding a mass with areas of calcifications. The hilar and paratracheal lymph nodes show eggshell calcification.

yielded a mixed respiratory flora. The patient was empirically started on a regimen of intravenous cefuroxime 1.5 g every 12 hours.

The sputum culture for pyogenic organisms was sterile after 48 hours of incubation. The sputum smears for acid-fast bacilli were repeatedly negative and the culture by BACTEC did not grow any mycobacteria. The sputum on fungal culture grew *Candida albicans* and *Aspergillus flavus*. The serum was negative for specific IgG antibodies and precipitins against *Aspergillus* species. The sputum cytology did not reveal any malignant cells. The tuberculin test was negative. Pulmonary function tests revealed a moderate restrictive ventilation defect while the ECG was normal.

The computed tomographic scanning (Figure 2) of the thorax showed large irregular conglomerate masses bilaterally in upper and mid lungs with areas of necrosis and calcification in them. A mass like lesion was seen within a cavity in the left upper lobe with areas of calcification in it. The mass was adherent to the wall of the cavity. Along with this, multiple enlarged calcified nodes were seen in both hilar and bronchopulmonary regions.

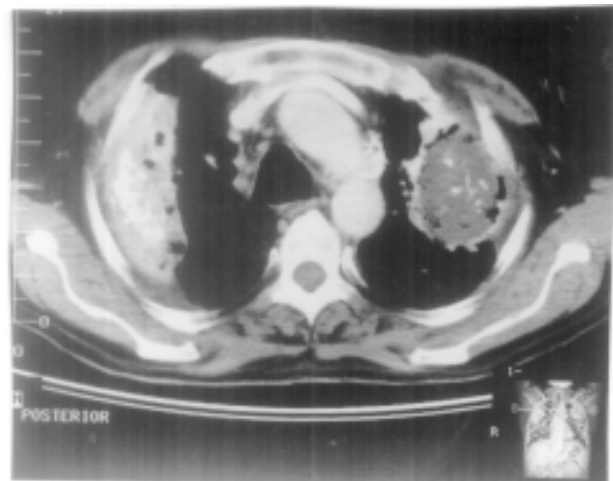


Figure 2. Contrast-enhanced computed tomogram of the thorax showing PMF in the right lung with areas of breakdown and calcifications. A mass like lesion with areas of calcification is seen within the cavity in the left upper lobe. The mass is adherent to the irregular margins of the cavity.

An ultrasound-guided percutaneous needle aspirate of the mass in the cavity revealed

hyphal forms that grew *A. flavus* on fungal culture. The fiberoptic bronchoscopy showed thick purulent secretions coming from both the right and the left upper lobe bronchi. The bronchial aspirate did not reveal any malignant cells and was negative for acid-fast bacilli but showed plenty of fungal hyphae. The pyogenic culture of the aspirate grew *Klebsiella pneumoniae*, sensitive to amikacin and gentamicin. The therapy was modified with addition of injection amikacin 500 mg every 12 hours.

The patient continued to have fever, cough, sputum and mild hemoptysis despite antibiotics. A repeat chest radiograph (Figure 3) taken after five weeks revealed an increase in the size of opacities bilaterally along with new cavity formation in the right lung progressive massive fibrosis (PMF) lesion.



Figure 3. Chest radiograph taken after five weeks reveals increase in the size of opacities bilaterally along with new cavity formation in the PMF lesion on the right side.

A clinico-radiological diagnosis of CNPA with aspergilloma complicating silicosis was made and oral itraconazole 200 mg twice daily

was added. The patient started showing clinical improvement, became afebrile after eight days of itraconazole therapy and the volume and the purulence of sputum reduced considerably. However, sixteen days later he succumbed to an episode of massive hemoptysis.

DISCUSSION

Worldwide, silicosis is the most common occupational lung disease⁵. The major occupational exposure for development of this disease include mining, stone cutting, employment in abrasive industries, foundry work, packing of silica flour, and quarrying, particularly of granite. Most often, progressive massive fibrosis (PMF) occurs in a dose-response fashion after many years of exposure but individual differences in susceptibility to exposure do exist. Host factors that determine susceptibility are poorly understood but probably include both inherited and acquired factors such as diet, and the presence of other lung diseases and exposures⁶. Our patients work involved sharpening of metallic instruments on a spinning stone wheel for the past 32 years, that exposed him to dust containing silica.

Diagnosis of silicosis is largely based on: (1) a history of exposure to silica; and (2) a chest radiograph interpretation showing opacities as per the International Labour Office Classification System for pneumoconiosis or a biopsy of lung tissue showing the characteristic silicotic nodules⁷. Egg-shell calcification of hilar lymph nodes is almost pathognomonic of silicosis⁸. The chest radiograph of our patient showed egg-shell calcification of hilar nodes and PMF in both the lung fields along with reticulonodular shadows and scattered calcification. Some of the PMF areas also had cavitations. Cavitations in the PMF raise the suspicion of complications like infection or malignancy. Tuberculosis and atypical mycobacterial infections are well known in patients of silicosis while fungal infections are rarely reported. Recently, a few cases of chronic necrotising pulmonary aspergillosis (CNPA) have also been reported in patients with silicosis^{3,4,9}.

The CNPA occurs primarily in middle-aged persons who often have underlying pulmonary disease, such as chronic obstructive lung disease, a history of pulmonary tuberculosis, cystic lung disease, previous resectional surgery, or pneumoconiosis. It is also observed in patients with some evidence of mild systemic immunodeficiency including diabetes mellitus, collagen vascular disease, or low dose steroid therapy³.

The patient of CNPA usually presents with fever, cough, sputum production and weight loss of one to six months duration³. Hemoptysis is less common. This presentation can easily be confused with tuberculosis, especially in the high prevalence areas like India. Diagnostic confirmation requires histologic evidence of local lung tissue invasion by septal hyphae, consistent with *Aspergillus* species. However, this is often difficult to obtain. Both transbronchial and percutaneous biopsy have low diagnostic yields for locally invasive aspergillosis when compared with autopsy findings^{3,4}. In a review of 11 published studies, Saraceno *et al*¹⁰ found that a histopathological diagnosis was made in only 49% of the cases and authors had depended on the clinical diagnostic criteria in one-half of the cases. Therefore, Soubani and Chandrasekhar¹¹ have proposed a clinical diagnosis of CNPA using the following criteria: (1) clinical and radiologic features consistent with the diagnosis; (2) isolation of *Aspergillus* species by culture from sputum or from bronchoscopic or percutaneous samples; and (3) exclusion of other conditions with similar presentation, such as active tuberculosis, atypical mycobacterial infection, chronic cavitory histoplasmosis, or coccidioiodomycosis. In such cases, the presence of serum IgG antibodies to *Aspergillus* (is positive in > 90% of patients) is useful to support the diagnosis.

The radiographic changes reported in CNPA are remarkably consistent. The most common findings are progressive upper lobe cavitary infiltrates associated with pleural thickening^{3,4}. Mycetomas are seen in about half of the patients⁴, although pre-existing cavities may not be seen on plain films³. Interestingly, patients with aspergilloma have a similar clinical

profile¹². Nonetheless, some differences are apparent. In contrast to patients with simple mycetoma, CNPA nearly always presents with pulmonary or systemic symptoms. Hemoptysis, the most common symptom in patients with mycetoma, is reported in only 10% of patients with CNPA and is rarely an isolated symptom¹⁰.

In the present case, the chest radiograph and CT scan demonstrated areas of PMF with cavitations along with a mycetoma in the left upper lobe. *A. flavus* was isolated in the ultrasound-guided percutaneous aspirate of the mycetoma. The patient had productive cough, hemoptysis and fever but no evidence of any mycobacterial infection or malignancy. On the basis of the clinico-radiological findings, a diagnosis of CNPA was made. The histopathological confirmation could not be done as the patient was too sick and family of the patient did not give the consent after being informed of the possible complications of the biopsy procedure. The serum IgG antibodies against *Aspergillus* species were negative as has occasionally been observed earlier^{9,11}.

Areas of calcification within the aspergilloma, as seen in this case, are uncommon. In our earlier reported series of 49 cases of aspergilloma, calcification was not reported¹³. Calcification may occur along the cavity rim, scattered through out the fungal mass, or extensively throughout the mycetoma^{14,15}.

Unlike *Aspergillus* fungal ball, in which medical therapy has very little proven benefit^{12,16}, successful treatment of CNPA has been reported^{4,17}. Although initial reports advocated intravenous amphotericin B³, more recently, successful treatment of CNPA has been reported with the use of itraconazole^{10,17}. Advantages of this treatment include oral administration and a benign side effect profile. The dose and duration of therapy is based on clinical response.

The CNPA is associated with considerable morbidity and mortality^{3,4}. Often, the diagnosis is made late in the course of illness⁴. Treatment outcome is likely to be influenced by the severity of co-morbid conditions, the extent of the underlying pulmonary disease, delays in diagnosis, and initiation of effective therapy¹⁰.

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