CASE REPORT

Cavitary alveolar sarcoidosis complicated by an aspergilloma

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SUMMARY

Cavitation in pulmonary sarcoidosis is rather unusual and even rarer in the alveolar form of the disease. A review of the literature revealed only 13 documented patients with cavitating alveolar sarcoidosis. Of the 13 patients, clinical information was available in only eight cases. Aspergilloma complicating cavitary alveolar sarcoidosis has been documented only once before. A 38-year-old woman with progressive dyspnoea for 3 years presented owing to a bout of haemoptysis. Imaging prior to presentation demonstrated mediastinal lymphadenopathy and coalescent parenchymal alveolar opacities along with air bronchograms, suggestive of alveolar sarcoidosis. On presentation, cavitations were visible in both lungs within the consolidation along with an intracavitary mass in the left upper lobe, which on evaluation was recognised as an aspergilloma. Bronchoscopy disclosed non-caseating granulomas on histopathology confirming pulmonary sarcoidosis. Cavitary alveolar sarcoidosis with aspergilloma formation can result in a diagnostic dilemma, especially in endemic tuberculous areas.

BACKGROUND

A diagnosis of sarcoidosis is still considered to be out of the ordinary in India, as recognition of this disease is often muddled due to the vast pool of patients with tuberculosis.^{1,2} Cavitation in pulmonary sarcoidosis is an unusual phenomenon. In a review of 1254 patients with sarcoidosis, cavitary lesions were found in 3/235 (1.3%) patients.³ A later study⁴ from France estimated the prevalence of cavitary lesions without concomitant morbidities to be 2.2%. However, an appraisal of three large series^{5–7} of pulmonary sarcoidosis from India found no mention of cavitation while discussing radiological features. Alveolar sarcoidosis is an infrequently occurring radiological pattern where large areas of segmental consolidation or scattered, hazy areas of consolidation are seen with irregular borders. Sometimes, air bronchograms can also be seen.⁸ This clinical entity is thought to be a distinct form of the disease.⁹ In a retrospective review of 164 patients with sarcoidosis from India, the alveolar pattern was observed in only 3 (1.8%) and none had cavitary lesions.⁷

Cavitation, if present, complicates the irreversible fibrotic form of the disease;¹⁰ however, cavities seldom occur in the alveolar form of sarcoidosis. Aspergilloma, occurring in cavitary pulmonary sarcoidosis, is rather uncommon and even rarer in alveolar sarcoidosis. In a study¹¹ comprising 427 patients with sarcoidosis, 10 (2.3%) patients were

found to have aspergillomas but none of them had an alveolar pattern. A search of the literature has revealed only 13 patients with cavitary alveolar sarcoidosis (see online supplementary table 1),^{4,12–16} and only one of them was complicated by an aspergilloma.¹⁶ The dearth of literature on the subject prompted this report of a 38-year-old woman who presented with alveolar sarcoidosis with subsequent cavitation and aspergilloma formation.

CASE PRESENTATION

A 38-year-old woman was referred to our institute for evaluation of progressive exertional dyspnoea, persistent cough with scanty mucoid sputum and occasional wheezing for the past 3 years. A bout of haemoptysis 1 month prior to presentation prompted the referral. Physical examination revealed no acute distress. There was no pallor, clubbing or cyanosis. Diaphragmatic excursion was comparable on both sides. On auscultation, vesicular breath sounds of equal intensity along with bilateral basal fine end-inspiratory crackles were audible. Evaluation of other systems, including an ophthalmological and dermatological referral, revealed no abnormalities.

INVESTIGATIONS

Complete blood counts, ECG, urine analyses and renal as well as hepatic functions were within normal limits. A review of the contrast-enhanced CT (CECT) high resolution of the thorax performed one and a half years prior to referral showed bilateral hilar lymphadenopathy and right lower paratracheal mediastinal lymphadenopathy without rim enhancement (figure 1, mediastinal window). Bilateral perihilar consolidation and air

Figure 1 Contrast-enhanced CT high resolution (mediastinal window) prior to presentation, showing bilateral hilar lymphadenopathy along with bilateral perihilar consolidation.

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bronchograms were also visible along with peribronchial beading (figure 2, lung window). Other investigations carried out then included serum ACE levels—66 U/L (normal range: 8–65 U/L), tuberculin testing with 5-TU (no induration) and two samples of sputum for acid-fast bacilli, which were negative. Though the patient continued to be symptomatic, she did not get herself investigated further. However, it appears that the patient had received, during this period, three to four unregulated courses of oral corticosteroids with which she had experienced symptomatic relief.

On presentation, the chest radiograph revealed bilateral perihilar patchy consolidation, but on CECT with high resolution cuts the bilateral consolidation had reduced in size. This could possibly be due to the unregulated courses of corticosteroids which she had received. Regression of the mediastinal lymph nodes was seen (figure 3, mediastinal window), but cavitations had occurred within the consolidation in both lungs. In addition, an intracavitary mass was visible in the left upper lobe, which was not visible on the chest radiograph (figure 4, lung window). Repeated sputum stains and cultures for *Mycobacterium tuberculosis* as well as other aerobic organisms continued to yield negative results. On pulmonary function testing, the forced vital capacity (FVC) was 2.36 L (73% of predicted), forced expiratory volume in 1 s (FEV₁) was 2 L (73% of predicted), and the FEV₁/FVC ratio was 0.84. The total lung capacity was 2.7 L (58% of predicted), and the single-breath diffusing capacity of the lungs for carbon monoxide (DLCO) was 16.5 mL/min/mm Hg (66% of predicted), but diffusion per unit of alveolar volume was normal. This was indicative of mild restrictive ventilatory defect, with reductions in total lung capacity and DLCO. The patient's oxygen saturation at room air fell from 97% to 91% while covering a distance of 440 m during the 6 min walk test. Fibre optic bronchoscopy visualised multiple granulomatous lesions throughout the tracheobronchial tree. Multiple endobronchial and transbronchial biopsies from both the lungs demonstrated non-caseating granulomas consisting of epithelioid cells and multinucleated giant cells. No organisms, including fungi, were cultured from the bronchial aspirate. Tests of tuberculin, serum ACE, serum calcium, rheumatoid factor and 24 h urinary calcium levels performed afresh were within normal limits; antinuclear antibody was not detected. The intracavitary mass, suspected to be a fungal ball, was confirmed as an aspergilloma. The skin prick test with *Aspergillus* antigens demonstrated immediate reactivity to *A. fumigatus* and the serum total IgE level was 114 kUA/L (<64 kUA/L). Specific

Figure 2 Contrast-enhanced CT high resolution (lung window) prior to presentation, showing bilateral perihilar consolidation along with bilateral air bronchograms and peribronchial beading.

Figure 3 Contrast-enhanced CT high resolution (mediastinal window) on presentation, showing regression of the mediastinal lymph nodes.

IgE and IgG, as well as serum precipitins against *A. fumigatus*, were also positive.

DIFFERENTIAL DIAGNOSIS

Pulmonary tuberculosis with concomitant aspergilloma.

TREATMENT

A diagnosis of cavitating alveolar sarcoidosis with aspergilloma was made on the basis of symptoms along with the radiological picture. Imaging demonstrated bilateral hilar lymphadenopathy and right lower paratracheal mediastinal lymphadenopathy without rim enhancement. Bilateral perihilar consolidation was also visible along with bilateral air bronchograms accompanied by peribronchial beading bilaterally. The association of bilateral hilar lymphadenopathy and an alveolar/acinic pattern was suggestive of alveolar sarcoidosis. Subsequently, cavitations occurred in both lungs in the areas of consolidation. This was followed by the appearance of an intracavitary mass in the left upper lobe. The diagnosis of sarcoidosis was confirmed by the demonstration of non-caseating granulomas on histopathology and the intracavitary mass, a fungal ball, on investigation, proved to be an aspergilloma.

The patient was initiated on oral prednisolone in the dosage of 0.5 mg/kg body weight daily, which was reduced to alternate days after 2 weeks and gradually tapered. With this, she experienced marked symptomatic relief.

OUTCOME AND FOLLOW-UP

A chest radiograph conducted after 2 months of therapy showed a marked clearing of the alveolar opacities (figure 5). The patient was largely asymptomatic on treatment and there was no further haemoptysis.

Figure 4 Contrast-enhanced CT high resolution (lung window) on presentation, showing bilateral cavitations along with an intracavitary mass in the left upper lobe.

Figure 5 Chest radiographs (A) on initial presentation; (B) 2 months post-therapy, showing marked resolution of the alveolar shadows.

DISCUSSION

Pulmonary sarcoidosis, on chest imaging, can manifest in many ways. However, cavitory formation is still considered to be rather uncommon and can confound the diagnosis.⁴ While reviewing nine other series of sarcoidosis along with their own series, Mayock *et al*³ analysed 1254 patients and documented cavitory lesions in only 3/235 patients (1.3%) on whom information was available. A retrospective analysis⁴ of 1060 patients with pulmonary sarcoidosis from France, over a period of 17 years, identified 41 (3.9%) patients with cavitory lesions on high-resolution CT (HRCT). The authors excluded 18 patients as they had aspergilloma on initial HRCT and they estimated the prevalence of cavitory lesions without concomitant morbidities to be 2.2%.⁴ However, in three large series^{5–7} describing patients with pulmonary sarcoidosis from India, there was no mention of cavitory lesions while discussing radiological aspects.^{5–7}

Alveolar or acinar sarcoidosis is another uncommon radiological manifestation of pulmonary sarcoidosis and is reported to occur in 1–4.4% patients,^{7 9 17} with one series from India documenting the occurrence of this radiological pattern in 1.8% of patients with pulmonary sarcoidosis.⁷ In a large series of 746 patients with pulmonary sarcoidosis from France,⁹ the authors reported that 33 (4.4%) patients had alveolar sarcoidosis. They observed that this unusual radiological pattern, mostly seen in the younger age group, was inevitably accompanied by mediastinal lymphadenopathy and concluded that alveolar sarcoidosis was a distinct form of the disease.⁹

Cavitation, generally seen in the irreversible fibrotic stage of the disease,¹⁰ is considered to be a rare occurrence in pulmonary sarcoidosis and even less common in alveolar sarcoidosis. A review of the literature revealed only 13 documented patients^{4 12–16} with cavitating alveolar sarcoidosis. Of the 13 patients, clinical information was available in only eight cases.^{12–16} The study from France⁴ mentioned cavitation in five patients with alveolar sarcoidosis but no further description was given.⁴ The conventional tomogram confirmed cavitory lesions in five patients^{12–14} described prior to the advent of CT. Of the eight patients,^{12–16} the proportion of men^{12–14} and women^{14–16} was equal. The men were in the age group of 20–30 years, while the age of women ranged from 25 to 63 years. Six of the eight patients were symptomatic,^{13–16} while two were diagnosed on routine examination.^{12 14} Cough was the predominant symptom in 5/6 symptomatic patients,^{13–16} while dyspnoea was

present in 3/6 patients.^{14–16} No physical abnormality was recorded in 5/8 patients.^{12–15} The Mantoux test was negative in all these eight patients.^{12–16} Bilateral hilar lymphadenopathy was present in 6/8 patients.^{14–16} Solitary cavitory lesions were recorded in four patients^{12 14 16} while the remaining four had multiple cavities.^{13–15}

The first description of an aspergilloma formation in sarcoidosis was by Fougner and Gjone.¹⁸ In a study¹¹ comprising 427 patients with pulmonary sarcoidosis from Detroit, USA, the authors documented 10 (2.3%) patients with aspergilloma and suggested that the incidence of chronic cavitory pulmonary aspergillosis is higher among patients with sarcoidosis. However, there is no mention of alveolar sarcoidosis in their patients. The authors further stated that the major presenting symptom in their patients was haemoptysis.¹¹ Of the eight patients with cavitating alveolar sarcoidosis documented in the literature,^{12–16} one patient had aspergilloma formation during the course of treatment.¹⁶ A bout of haemoptysis led to the diagnosis of concomitant cavitating alveolar sarcoidosis with aspergilloma.¹⁶ A recent study on the global burden of chronic pulmonary aspergillosis complicating sarcoidosis estimated that this phenomenon occurs in 3–12%.¹⁹

In a high tuberculous prevalent area, the occurrence of aspergilloma in a patient with cavitory disease is often presumed to be due to inactive pulmonary tuberculosis. This report serves as a reminder that cavitation can occur in alveolar sarcoidosis and can be complicated by aspergilloma formation.

Learning points

- ▶ Cavitation in pulmonary sarcoidosis is rather uncommon and can confound the diagnosis.
- ▶ Alveolar sarcoidosis, a distinct form of the disease, is a less common manifestation of the disease.
- ▶ Cavitation is rarely seen in alveolar sarcoidosis.
- ▶ Cavitory alveolar sarcoidosis can rarely be complicated by aspergilloma formation.

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drafted the manuscript. AS is the guarantor of the manuscript. All authors have read and approved the final manuscript.

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