Clinics in Diagnostic Imaging (64)

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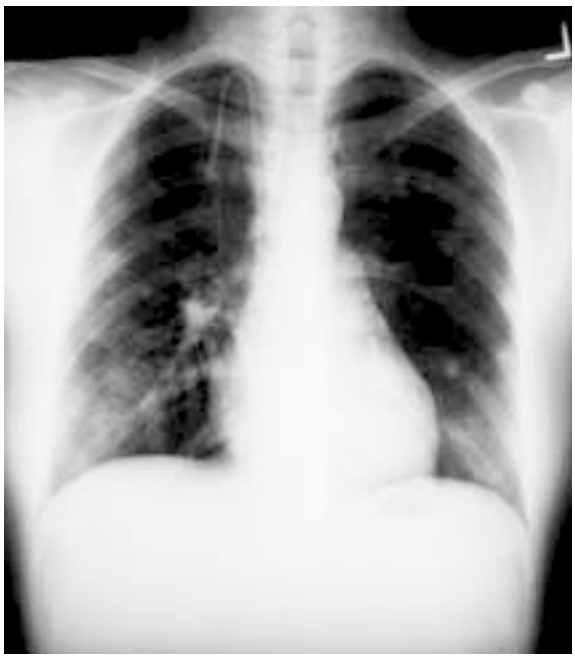

Fig. 1 Frontal chest radiograph.

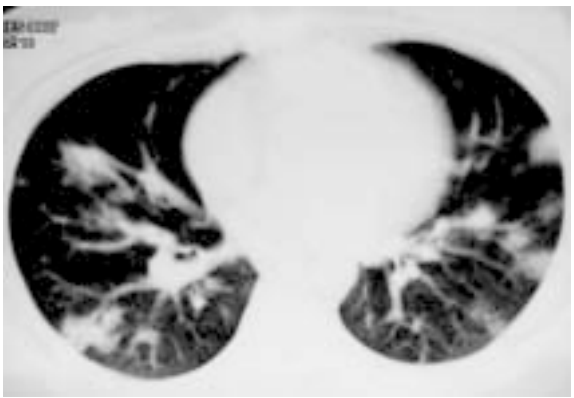

Fig. 2 CT of the thorax taken at the level of the basal segments of the lower lobes.

CASE PRESENTATION

A 30-year-old woman was admitted for chemotherapy following a relapse of acute myeloid leukaemia after bone marrow transplantation. Two weeks after the commencement of chemotherapy, she developed fever with no localising symptom. Her total leucocyte count was not raised at 4.2 X 10^9/L (normal range 4.0-10.0 X 10^9/L). A chest radiograph performed as part of a septic workup was interpreted as being normal. Empirical treatment with broad spectrum antibiotics was commenced despite negative growth in repeated specimens of blood, sputum and urine cultures. There was no clinical improvement and a repeat chest radiograph was obtained. What does the chest radiograph (Fig. 1) show? Computed tomography (CT) of the thorax was then performed (Fig. 2).What is the diagnosis ?

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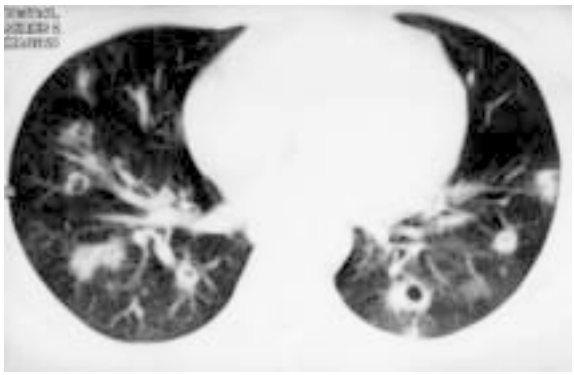

Fig. 3 Follow-up CT of the thorax taken at the same level as Fig. 2 shows bilateral cavitating nodules.

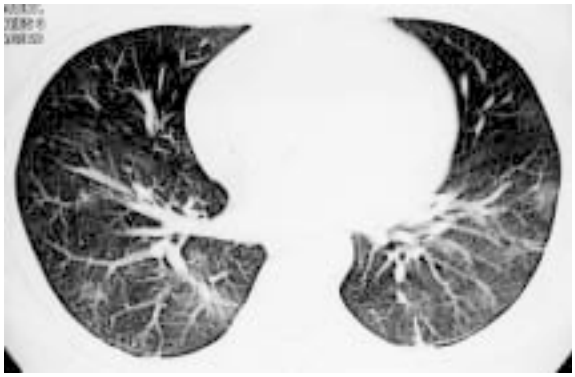

Fig. 4 Follow-up CT of the thorax taken at the same level as Figs. 2 & 3 shows complete resolution of the nodules with residual pulmonary scarring.

IMAGE INTERPRETATION

The chest radiograph (Fig. 1) shows ill-defined nodules bilaterally, with a mid and lower zonal predominance. A central venous catheter for the delivery of chemotherapy is present. The CT of the thorax (Fig. 2) shows nodules in both lungs and surrounding ground-glass changes which represent haemorrhage around the pulmonary nodules.

DIAGNOSIS

Invasive pulmonary aspergillosis.

CLINICAL COURSE

The patient was immediately started on intravenous anti-fungal therapy with resultant clinical improvement. Subsequent sputum and blood cultures still did not reveal any growth of organism. Repeat CT of the thorax (Fig. 3) performed two weeks after commencement of anti-fungal therapy showed cavitation of the previously documented nodules. In addition, the lung parenchymal ground-glass changes were also less obvious. The leucocyte count was then 6.1 X 10^9/L. She showed continued clinical improvement and was subsequently discharged. A follow-up CT of the thorax (Fig. 4) performed one month after commencement of anti-fungal therapy showed complete resolution of the pulmonary nodules. There were residual pulmonary scars.

DISCUSSION

Aspergillus fumigatus (*A. fumigatus*) is a common commensal of the human airways. Its clinical presentation depends on the immune status of the host[1]. In a person with intact immunity, it colonises pre-existing pulmonary cavities and manifests as an aspergilloma. In the immunocompromised patient (especially those with severe neutropaenia), there is transbronchial vascular invasion of the pulmonary arteries with subsequent haemorrhage and pulmonary infarct. This results in invasive pulmonary aspergillosis (IPA). In the hyperimmune host, hypersensitivity reaction to the A. fumigatus antigen results in complement-mediated damage to the central airways producing allergic bronchopulmonary aspergillosis (ABPA). The imaging features of these manifestations are reviewed.

Patients with haematological malignancy, those who have had solid organ and bone marrow transplant, as well as patients with acquired immunodeficiency syndrome (AIDS) are at risk of developing IPA[2]. The clinical manifestations of IPA include fever, cough and haemoptysis[3]. Fatal haemoptysis from IPA has been reported although it is a rare complication[4]. On the chest radiograph, IPA should be suspected when pulmonary airspace consolidation that does not improve with broad spectrum antibacterial therapy. Nodules with ground-glass changes relating to haemorrhage around the nodules is a fairly typical early CT finding[5] (Fig. 2). Although obtaining tissue by biopsy is ideal, it is too invasive, has low yields, and hence diagnosis is often based on typical CT findings[5-7]. Following anti-fungal therapy with recovery of neutropaenia (usually two to three weeks later), the appearance of cavitation within the pulmonary nodules heralds a better prognosis[5,8] (Fig. 3). This is however not invariable as a case of pulmonary cavitation following appropriate therapy for IPA that progressed to fatal pneumothorax and haemothorax[9] has been reported. The outcome following anti-fungal therapy and immunotherapy for IPA is dismal, with cure rate of only 10% - 26%[2,10]. Surgical resection with anti-fungal therapy has been advocated in selected cases[3].

Semi-invasive aspergillosis manifests in mildly immunocompromised patients and is intermediate in severity between mycetoma and invasive pulmonary aspergillosis. There is extensive lung destruction with no vascular invasion. This combination of findings is not typically found in mycetoma and invasive pulmonary aspergillosis. Radiologically, semi-invasive

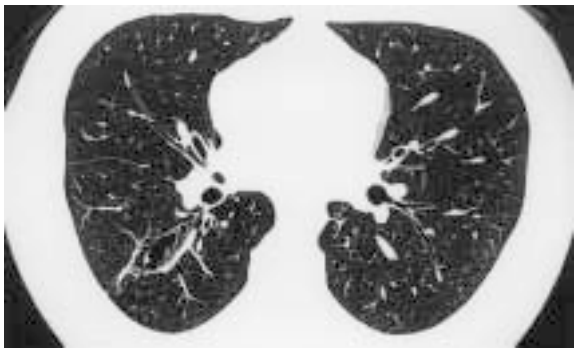

Fig. 5 24-year-old man with ABPA who presented with recurrent pneumonia and wheezing. He had elevated A. fumigatus antibodies (> 10,000) and a positive skin prick test. CT of the thorax shows dilated bronchial airways with thickened walls that are centrally distributed. Diagnosis of ABPA was confirmed on bronchoalveolar lavage and bronchial biopsy. The patient improved on anti-fungal drugs and steroids.

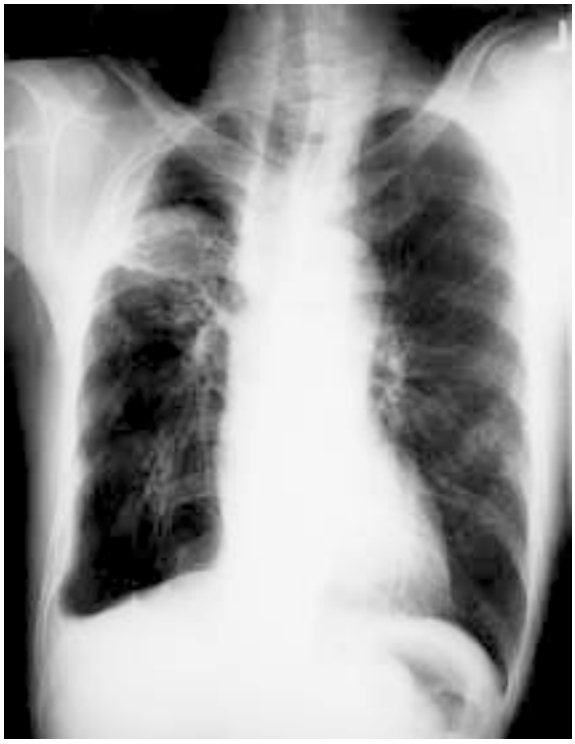

Fig. 6a 65-year-old woman with aspergilloma who presented with cough. Chest radiograph shows a right upper zone nodule with a surrounding cleft (air-crescent sign).

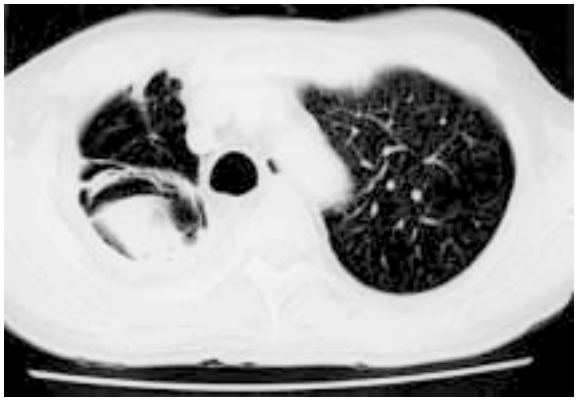

Fig. 6b Same patient as in Fig. 6A. CT of the thorax shows a crescent-shaped cleft of air surrounding a well-defined pulmonary nodule. There is adjacent lung scarring.

aspergillosis appears as persistent or progressive consolidation that may cavitate[11]. Clinical progression is usually over a period of months as opposed to invasive aspergillosis which progress over weeks and, it also takes a less malignant clinical course[12,21].

Allergic bronchopulmonary aspergillosis (ABPA) usually affects young patients with asthma or cystic fibrosis. In a study utilising the Epidemiologic Registry of Cystic Fibrosis criteria of ABPA, 10% of the patients with cystic fibrosis over six years old were found to be affected[13]. ABPA should be considered in adult-onset asthma although it may affect patients of any age[14]. Eaton et al studied 255 consecutive patients with asthma and found 20% to be skin prick positive for *A. fumigatus* of which 20%-40% satisfied the criteria for ABPA[15]. The primary diagnostic criteria includes symptoms of asthma, chest radiographs showing pulmonary inflitrates (IgE mediated acute manifestation due to eosinophils filled alveoli), central bronchiectasis (IgG mediated late manifestation due to chronic inflammation of the large airways), peripheral eosinophilia, elevated serum specific IgE and IgG, as well positive skin test (early wheal and flare reaction)[14]. The presence of A. fumigatus in the sputum is of secondary diagnostic importance as it is a common commensal of the airways. Early radiological findings is mainly airspace consolidation that may be fleeting. Late changes include bronchiectasis (dilated thickened airways with bronchocoeles) (Fig. 5), fibrosis and respiratory failure[14]. Treatment options include steroids and anti-fungal therapy[7,14]. Long-term steroids may be needed for multiple asthmatic exacerbations[7].

On imaging, aspergilloma manifests as a gravity-dependent soft tissue nodule within a pre-existing cavity, most commonly secondary to pulmonary tuberculosis (Fig. 6a-b). This manifests as the air-crescent sign that is well-demonstrated on CT performed in the supine and prone position[16]. The air-crescent sign is however non-specific and has been reported with bronchogenic carcinoma, haematoma, chronic abscess and pulmonary haemangioma[16]. The other CT finding is that of irregular sponge-like air-spaces within the pulmonary cavity[16]. Adjacent pleural thickening is also a common association. Besides tuberculosis, aspergilloma also occurs within any any kind of lung cysts e.g. sarcoidosis, bronchiectasis and pulmonary fibrosis. The patient usually presents with haemoptysis and sputum production[7]. Anti-fungal therapy is often ineffective[17]. Surgical resection for medically-fit patients and cavernostomy for medically-unfit patients may be considered[7,18,19,20] in those with massive haemoptysis. The majority of aspergillomas however do not cause life-threatening haemoptysis and should be followed-up.

SUMMARY

Aspergillus fumigatus is a common commensal of the human airways with myriad clinical manifestations. Invasive pulmonary aspergillosis (IPA) occurs in the severely neutropaenic patients (e.g. patients on chemotherapy for haematologic malignancy) with high fatality. Allergic bronchopulmonary aspergillosis (ABPA) occurs in asthmatics and if undetected may lead to pulmonary fibrosis. Aspergilloma occurs within pre-existing lung cavities. It uncommonly presents with massive haemoptysis for which surgical intervention may be considered. Imaging is useful in affected patients.

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ABSTRACT

A 30-year-old woman undergoing chemotherapy for acute myeloid leukemia developed fever. Chest radiograph showed ill-defined nodules in the mid and lower zones. CT showed multiple nodules that cavitated with commencement of anti-fungal therapy. Follow-up CT showed complete resolution of the pulmonary nodules, confirming the diagnosis of invasive pulmonary aspergillosis. Aspergillus fumigatus presents clinically as aspergilloma, invasive pulmonary aspergillosis or allergic bronchopulmonary aspergillosis depending on the immune status of the host. The different manifestations are discussed and imaging features of representative clinical case studies are illustrated.

Keywords: Aspergillus, aspergilloma, allergic bronchopulmonary aspergillosis, Pulmonary aspergillosis, invasive bronchopulmonary aspergillosis, Computed tomography

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