Superior vena cava thrombosis and haemorrhagic mediastinitis as manifestations of angioinvasive aspergillosis
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Technique: CT
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Case Type: Clinical Cases
Authors: E. Parlorio, G. Ortuño*
Patient: 23 years, male

Clinical History:

Persistent fever and severe right chest pain after chemotherapy for acute myeloid leukaemia.

Imaging Findings:

The patient was admitted for therapy of acute myeloid leukaemia in the first haematological relapse. On day 4 he developed fever and severe right chest pain. Blood cultures were negative, and the first chest radiograph and CT revealed no lung pathology. Empirical treatment with broad-spectrum antibiotics was instituted. One week later he also developed abdominal pain, profuse diarrhoea and rectal bleeding. Laboratory examinations showed severe pancytopenia: haemoglobin 8g/dl, neutrophils 0%, and platelets 20,000/mm³.

Chest radiography and CT of the thorax were performed. The chest film revealed an infiltrate in the right upper lobe. The CT scan (Figs 1,2) demonstrated multiple nodules in both lung fields, a mass lesion anteriorly in the right upper lobe, bilateral pleural effusion, and diffuse infiltration of mediastinal fatty tissue.

Based on the clinical data and imaging findings, a diagnosis of mediastinitis and invasive pulmonary aspergillosis (IPA) with multiple infarcts was suggested, and empirical therapy with amphotericin B was added.

On day 27 the fever persisted, and the patient developed a gradual superior vena cava syndrome. Despite intensive therapy he died in respiratory failure a few days later. Autopsy revealed a disseminated angioinvasive aspergillosis involving the kidneys, lungs, pleura and mediastinum, with haemorrhagic infiltration of the mediastinal fat (Fig. 3). Biopsy specimens (Fig. 4) showed septated hyphae that branched at 45° angles and were highlighted with silver and PAS stains. Autopsy also revealed a thrombus of Aspergillus occluding the superior vena cava.

Discussion:

We illustrate a patient who developed IPA, superior vena cava (SVC) thrombosis and haemorrhagic mediastinitis due to Aspergillus. To our knowledge, this is the first case reported of the coexistence of SVC thrombosis and haemorrhagic mediastinitis complicating invasive aspergillosis, and the third reported case of SVC thrombosis caused by Aspergillus (1,2).
Aspergillus fumigatus is the most common cause of infection by Aspergillus in humans. This is a ubiquitous dimorphic fungus that primarily affects the lungs, causing a variety of pulmonary diseases. These can be divided into three groups: aspergilloma, invasive and semi-invasive aspergillosis, and allergic forms of aspergillosis (3). Invasive pulmonary aspergillosis (IPA) is a serious infection that requires severe impairment of host defense mechanisms, usually due to acute leukemia and granulocytopenia from chemotherapy. Other risk conditions include corticosteroid use, allogeneic bone marrow transplant, solid organ transplantations (kidney, liver, heart), increased use of immunosuppressive regimens for autoimmune diseases, late-stage HIV infection, thoracic surgery and chronic obstructive pulmonary disease (9%).

Pathologically IPA is characterised by the invasion and thrombosis of small to medium-sized pulmonary arteries by fungal hyphae, which leads to haemorrhagic infarction with necrosis and cavitation. In tissue, Aspergillus forms septated hyphae that branch at 45° angles. IPA typically manifests with fever, cough, pleuritic chest pain, dyspnoea and haemoptysis. The diagnosis is difficult and should be suspected when airspace consolidation does not improve with broad spectrum antibacterial therapy.

Computed tomography (CT) may be useful in certain circumstances, particularly in cases of fever despite intensive therapy with antibiotics, and it plays an important role in early diagnosis. Characteristic findings correspond to haemorrhagic infarcts and consist of nodules or pleura-based, wedge-shaped areas of consolidation, surrounded by a halo of ground-glass attenuation.

Histologically the "halo sign" represents haemorrhage around a focal area of lung infarction and it is best seen with high-resolution CT (3,4). This early sign is nonspecific and a similar appearance has been described in tuberculosis, mucormycosis, candidiasis, herpes simplex and cytomegalovirus pneumonias, Wegener granulomatosis, Kaposi sarcoma and haemorrhagic metastases. However, in the appropriate clinical setting, the CT halo sign is highly suggestive of IPA.

Cavitation in the nodules or masses is a late finding that occurs with recovery from neutropenia, and it is associated with a better prognosis. It typically results in a distinctive radiographic appearance, the "air crescent" or "meniscus" sign. This finding is an air crescent near the periphery of a lung nodule formed by contraction of infarcted tissue, trapping air between the necrotic lung and the healthy surrounding parenchyma. Aspergillus may disseminate beyond the lung by haematogenous spread to the central nervous system, kidney and gastrointestinal tract (25-50%). Chest wall or mediastinal invasion can occur, but pleural and pericardial involvement and the presence of adenopathy are rare. Mortality may exceed 90%, and has not changed significantly over the past decades, despite the introduction of itraconazole and lipid formulations of amphotericin B. At present, invasive aspergillosis is the leading cause of infection-related mortality in many immunocompromised hosts.

Differential Diagnosis List: Superior vena cava thrombosis and haemorrhagic mediastinitis caused by Aspergillus

Final Diagnosis: Superior vena cava thrombosis and haemorrhagic mediastinitis caused by Aspergillus

References:
4. Logan PM, Müller NL. High-resolution computed tomography and pathologic findings in pulmonary aspergillosis: a
**Figure 1**

**a**

*Description:* Multiple ill-defined nodular opacities (arrows) in both lung fields, some with the halo sign. A right perihilar infiltrate and mediastinal widening are shown. *Origin:*

**b**

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Figure 2

a

Description: Soft tissue attenuation mass (m) in the anterior aspect of the right lung adjacent to the mediastinum, corresponding to a large pulmonary infarct at autopsy. Diffuse infiltration of mediastinal fatty tissue (white arrows) and bilateral pleural effusion are also seen. A Hickman catheter positioned in the superior vena cava is marked (hollow arrow). Origin:

b

Description: Soft tissue attenuation mass (m) in the anterior aspect of the right lung adjacent to the mediastinum, corresponding to a large pulmonary infarct at autopsy. Diffuse infiltration of mediastinal fatty tissue (white arrows) and bilateral pleural effusion are also seen. A Hickman catheter positioned in the superior vena cava is marked (hollow arrow). Origin:
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**Figure 3**

**a**

*Description:* An axial slice of the mediastinum shows the trachea (T), and the superior vena cava (outlined in blue), almost totally occluded by a thrombus of *Aspergillus*. Note two foci of venous lumen not invaded by fungi (white hollow arrows) and the haemorrhagic appearance of the mediastinum surrounding the superior vena cava. **Origin:**

**b**

*Description:* Dorsal view of the lungs. The pleural surface shows multiple nodules (arrows), some of them umbilicated. Note the hyperaemic rim surrounding some of the nodules (left lung). **Origin:**
Figure 4

Description: Haematoxylin-eosin stain. Inflammatory exudate consisted of lymphocytes and histiocytes and coagulative necrosis. Note hyphal elements among the necrotic tissue. A pulmonary vessel (black arrows) full of fungi is shown. This phenomenon is associated with intraluminal thrombi, tissue ischaemia, and infarction. Origin:

Description: Methenamine silver stain. Section of the same vessel shows branching fungal hyphae that invade the vessel wall (red arrows) from the lung parenchyma into the lumen. Origin: