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Lung nodules in an immunocompromised patient

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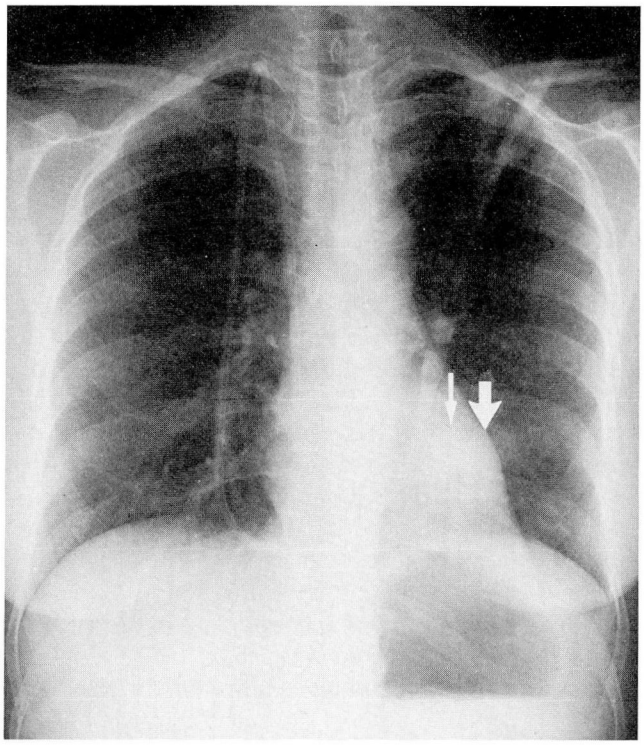

FIGURE 1. Chest radiograph reveals two ill-defined left lower lung nodules. The more medial nodule was present 1 week earlier (thin arrow). A second nodule (thick arrow) developed subsquently. A right Hickman catheter is in place.

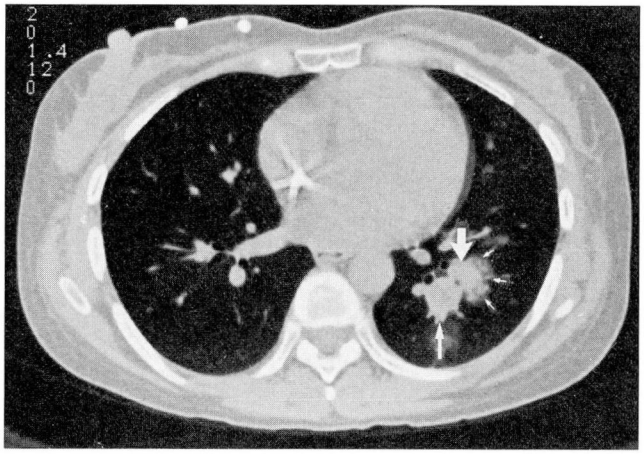

FIGURE 2. High-resolution CT scan through the lung bases reveals two soft tissue nodules in the left lower lobe (top and bottom arrows) with the newer lesion displaying a central dense nodule (top arrow) surrounded by a halo of lower attenuation (small thin arrows).

CHRONIC MYELOGENOUS leukemia was diagnosed in June 1987 in a 31-year-old white female. In January 1989 she received an allogenic bone marrow transplant and was started on immunosuppressive therapy with cyclosporine and prednisone. A chest radiograph, obtained in April 1989 because of persistent fever (99.2° F for 2 weeks), pleuritic chest pain, and dyspnea on exertion, revealed a 2-cm, well-defined new nodule in the left lower lobe. A repeat chest radiograph 1 week later revealed a new left lower lobe nodule appearing lateral to the first nodule (*Figure 1*). A high-resolution computed tomographic (CT) scan *(Figure 2)* obtained

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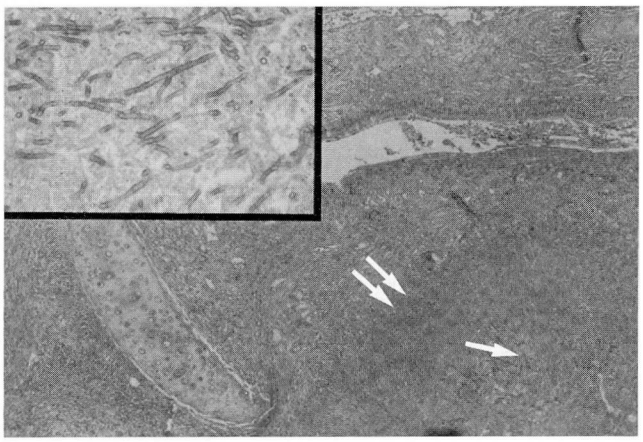

FIGURE 3. A broad rim of necrotic debris and organizing pneumonia (double arrows) surrounds a collection of *Aspergillus* organisms (single arrow) in the lower right corner (hematoxylin and eosin, magnification × 5).[3] The hemorrhagic necrosis often seen around these lesions is responsible for the "halo sign" seen on the CT scan. The inset (magnification × 40) illustrates the characteristic morphology of *Aspergillus*. The hyphae are 3 to 6 microns in diameter and exhibit repeated dichotomous branching at a 45° angle. The hyphal septa are usually easy to see.

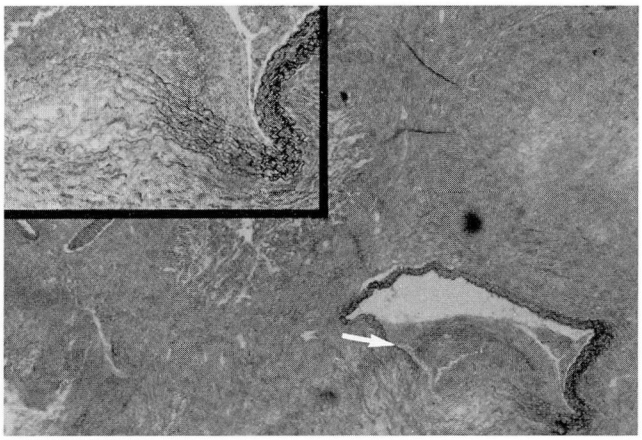

FIGURE 4. Invasion and disruption of a blood vessel by *Aspergillus* is seen (arrow, magnification × 2.5). The elastic van Gieson's stain highlights the elastic fibers. The splaying and destruction of these fibers is visible in the inset (magnification × 10).

through the lung bases the same day showed two soft tissue nodules in the left lower lobe. The newer lesion displayed a central dense nodule surrounded by a halo of lower attenuation.

DIAGNOSIS: INVASIVE PULMONARY ASPERGILLOSIS

Aspergillus was first identified in two cytology specimens: a transthoracic fine needle aspiration and a bronchial washing. *Figures 3* and *4* are photomicrographs of tissue obtained from a subsequent resection of the left lower lobe, illustrating invasive pulmonary aspergillosis (IPA).

DISCUSSION

With few exceptions, invasive pulmonary aspergillosis is a disease of the severely immunocompromised patient. It is especially common in patients who have leukemia with prolonged granulocytopenia. The respiratory tract is the most important entry site.[1]

The clinical presentation of IPA is varied and nonspecific, and mimics bacterial infection. Dyspnea, tachypnea, persistent fever, and the presence of pulmonary infiltrates despite broad-spectrum antibiotic therapy in the immunocompromised patient suggest the diagnosis. Early pulmonary radiographic findings may reveal single or multiple nodules that may progress to larger nodules; early findings also may demonstrate alveolar infiltrates that can progress to widespread parenchymal consolidation.

High-resolution lung CT has been advocated recently for early diagnosis of IPA.[2] In the clinical setting of the immunocompromised host, the demonstration on CT of a pulmonary mass or nodule surrounded by a distinctive halo of infiltrates of lower attenuation (*Figure 2*) is highly suggestive of IPA. Hruban and associates correlated these radiographic findings with pathologic findings, and demonstrated that the central pulmonary mass is a dense fungus ball; the halo of low attenuation is a surrounding area of hemorrhagic infarction and coagulative necrosis.[3]

When IPA is suspected because of the halo sign on CT, tissue invasion can be confirmed on histologic studies (*Figures 3* and *4*). Inhaled hyphae migrate through the bronchi and surrounding tissue, causing an acute, pyogenic necrotizing pneumonia. *Aspergillus* also invades the blood vessels, causing thrombosis with pulmonary infarction and necrosis. However, cultures and histology cannot diagnose IPA unless the specimen is obtained directly from infected tissues by invasive procedures such as transthoracic needle aspiration or open lung biopsy. These procedures may be risky for some patients because of their deteriorating clinical status and the increased chance of bleeding. Because of the toxicity of amphotericin B, which is the treatment of

choice, tissue diagnosis may be necessary to confirm the suspicions of IPA raised by the CT scan findings. Clinical judgment is needed to weigh the risks of therapy against the risk of tissue diagnosis.

Early and specific recognition of IPA and prompt treatment with amphotericin B limit the dissemination of the disease and increase the chances of survival.

In addition to the invasive form of *Aspergillus* described here, aspergillosis can manifest as a noninvasive form or a semi-invasive form. The noninvasive form of the disease may present as an aspergilloma or fungus ball colonizing a pre-existing cavity; as allergic bronchopulmonary aspergillosis in patients with asthma; or as extrinsic allergic alveolitis in reaction to overwhelming aspiration of organisms. A semi-invasive form occurs as chronic necrotizing or cavitary pulmonary aspergillosis in debilitated patients.

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