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Case Report

Radiologic–Pathologic Correlation of the CT Halo Sign in Invasive Pulmonary Aspergillosis

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Abstract: Invasive pulmonary aspergillosis in the immunocompromised host is difficult to diagnose. Early therapy with amphotericin B improves survival. We correlated early pathologic findings with high-resolution CT of a fixed-inflated air-dried lung obtained from an autopsied patient with invasive pulmonary aspergillosis. Two distinct types of lesions were found radiologically. A large zone of air space consolidation was shown to be a confluent bronchopneumonia, and small halo-like lesions were shown to correspond to a central fungal nodule surrounded by a rim of coagulative necrosis. The halo lesion may represent an early specific sign by which invasive pulmonary aspergillosis can be diagnosed. **Index Terms:** Aspergillosis—Computed tomography—Lungs, infection.

Invasive pulmonary aspergillosis (IPA) is characterized by a necrotizing bronchopneumonia associated with blood vessel invasion, vascular occlusion, and hemorrhagic infarction (1–3). Invasive pulmonary aspergillosis is a common, often fatal disease in the immunocompromised host, and its clinical manifestations and radiologic findings are nonspecific (4–8). More sensitive techniques are needed to establish the diagnosis of IPA early so that effective antifungal therapy can be initiated (7).

High-resolution CT has recently been advocated in the early diagnosis of IPA (9). Kuhlman et al. reviewed CT of nine immunocompromised patients with IPA and in two cases found a distinctive radiologic abnormality consisting of a nonspecific pulmonary mass surrounded by a zone of low attenuation (9). They proposed that this halo sign was an early clue to the diagnosis of IPA.

We applied high-resolution CT to a fixed-inflated air-dried lung. The lung was obtained from an autopsied patient who died from IPA following steroid therapy for sarcoidosis. An excellent one-to-one pathologic–radiologic correlation was obtained, and the validity of the CT halo sign confirmed.

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CASE REPORT

A 50-year-old woman developed dyspnea and cervical lymphadenopathy. Supraclavicular lymph node biopsy revealed noncaseating granulomas, and a diagnosis of sarcoidosis was made. She was treated with corticosteroids for 6 months with good response. Four years later, she developed a recurrence of her dyspnea and was admitted with severe weight loss and fever. A liver biopsy showed an extensive granulomatous hepatitis. Steroid therapy was reinstated with transient symptomatic improvement. Despite therapy she developed progressive pancytopenia, and a bone marrow aspirate was remarkable for hypocellularity and erythrophagocytosis. Chest radiography revealed bilateral lung infiltrates. She died from multiorgan failure 4 days later. Autopsy, performed 1 h after death, revealed IPA in the right lung, and an extensive proliferation of histiocytes with noncaseating granulomas in the spleen, liver, bone marrow, and lymph nodes. A perforated gastric ulcer with 1.5 L of associated intraluminal blood was also present. The left lung was taken for fixation and air drying.

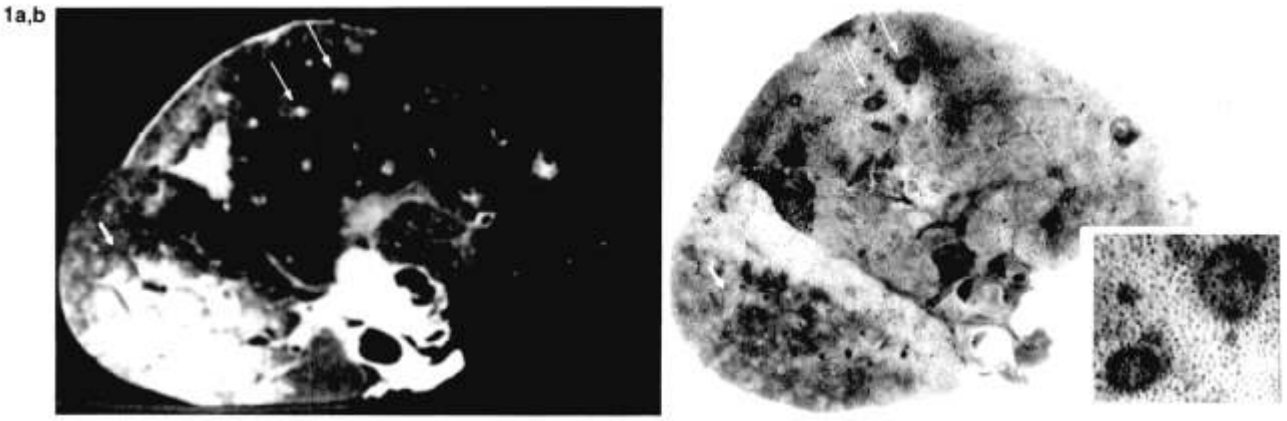

FIG. 1. A CT-pathology correlation. **a:** Postmortem CT scan of fixed and air-dried left lung. Nonspecific focal infiltrate is present in the lower lobe (short arrow), and numerous small nodules with a surrounding zone of low attenuation (halo sign) are scattered throughout the lung parenchyma (long arrows). **b:** Cross section of fixed left lung at level of CT scan shown in (a) demonstrates one-to-one correlation both of the lower lobe infiltrate with a large area of necrosis and consolidation (short arrow), and of the halo sign with target lesions (long arrows). The wedge-shaped lesion in the upper lobe is an area of typical aspergillus bronchopneumonia. Close-up of two target lesions designated by arrows (insert).

LUNG FIXATION

The lung was fixed and inflated by the method described by Markarian and Dailey (10) as modified from Sills (11). Briefly, the lung was removed with 2 cm of mainstem bronchus intact, and the pulmonary artery and vein tied off. The bronchus was cannulated, and the lung distended with a fixative. After fixation of the lung, it was air dried for 48 h. The resulting specimen was dry and inflated and, therefore, suitable for radiologic study. The specimen was scanned in a Siemens DR-3 unit using 2 mm slices with 0.3 × 0.3 mm pixels and targeted reconstruction (7 s, 780 mAs, 125 kVp). The lung was sectioned so that each slice corresponded directly to a CT scan. Sections were then taken for histologic study from areas of interest.

RESULTS

Computed tomography revealed two distinct types of lesions. First, a large zone of typical air space consolidation was present in the lower lobe. Second, multiple small 1 cm diameter nodules with a thin corona of low attenuation were scattered throughout the remainder of the lung parenchyma (Fig. 1a). Sectioning of the fixed lung specimen showed the large lesion to correspond to an area of consolidation and necrosis. Microscopically, extensive bronchopneumonia with marked coagulative necrosis and multiple fungal forms morphologically consistent with *Aspergillus* were present. The smaller nodules with coronas (halos) corresponded to target lesions seen grossly (Fig. 1b). These target lesions have been described in IPA and are characterized grossly by a dense tan center and a hyperemic rim (3,12). Histologically, (Fig. 2), the center of the target lesion corresponded to a dense fungal ball with associated coagulative necrosis, and the corona or halo to a surrounding area of hemorrhagic infarction. Small necrotic vessels were occasionally associated with these nodules. The wedge-shaped lesion seen in the upper lobe was histologically similar to the typical necrotizing bronchopneumonia seen in the lower lobe.

DISCUSSION

The radiographic findings in IPA have been extensively studied (2–4,12,13), and the CT halo sign has recently been proposed by Kuhlman et al. as a specific early finding in this disease (9). They reviewed CT of nine immunocompromised patients

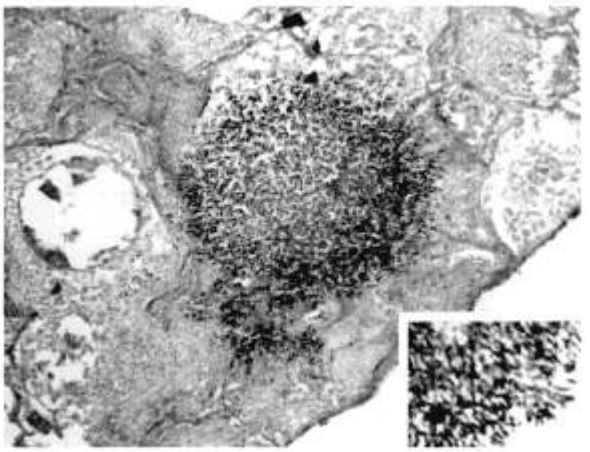

FIG. 2. Histologic section of one of the target lesions designated by long arrows. Target lesion consists of a core of densely packed fungi surrounded by a corona of coagulative necrosis. Close-up (insert) of fungi shows characteristic septate hyphae with branching at approximately 45°. Hematoxylin/eosin. ×65. Insert: methenamine silver. ×160.

with IPA and in two cases found a distinctive radiologic abnormality consisting of a mass-like infiltrate surrounded by a halo of low attenuation. These nodules frequently progressed to larger pulmonary consolidations. Kuhlman et al. hypothesized that this halo sign corresponded to a nodule frequently seen at autopsy in these patients. This nodule consisted of a core of necrosis surrounded by a rim of hemorrhage or hemorrhagic necrosis.

Using postmortem fixed and air-dried lung specimens, we have been able to demonstrate that the CT halo sign is indeed a small *Aspergillus* nodule (target lesion). As shown in Fig. 2, this lesion consists of a central dense fungal ball with coagulative necrosis surrounded by a rim of hemorrhagic infarction. The discovery of a thrombosed necrotic vessel associated with some of these nodules also offers a clue to their pathogenesis. *Aspergillus*, unlike most other pathogens, is angiotropic and often invades blood vessels. The resulting microinfarct is usually spherical and not wedge shaped because of the dual circulation of the lungs. The surrounding rim of hemorrhage is most probably a result of disruption of this vessel. The pathogenesis of the target lesions explains the specificity of the CT halo sign for IPA. Most infectious causes of pulmonary disease, with the possible exceptions of *Pseudomonas* and *Staphylococcus*, are not angiocentric and, therefore, would not cause this type of lesion.

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