

Clinical Image: Halo Sign

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CASE PRESENTATION

A 68-year-old man with no significant past medical history was transferred to our hospital for evaluation of newly diagnosed acute leukemia. His bone marrow biopsy showed acute undifferentiated leukemia. He was initiated on standard induction chemotherapy with cytarabine and idarubicin. His hospital course was complicated by neutropenic fever secondary to *Fusobacterium* bacteremia. He was started on antibiotic therapy with intravenous cefepime and oral metronidazole. Intravenous vancomycin was added in the setting of recurrent intermittent fevers. On hospital day 20, he developed minimal hemoptysis, pleuritic chest pain, and recurrent fevers. A CT scan of the chest showed a right upper lobe band-like opacity. Due to concern for possible invasive aspergillosis, he was started on oral voriconazole. Serum galactomannan was negative. Given the patient's thrombocytopenia, tissue diagnosis was deferred. Repeat CT of the chest two weeks later showed an interval increase in the right upper lobe spiculated mass with surrounding ground glass "halo" (Figure 1). A presumptive diagnosis of pulmonary aspergillosis was made in the setting of prolonged neutropenia, classic symptomatology, and rapid growth of the mass suggestive of an infectious process, as well as the halo sign on CT. He was discharged on voriconazole with plans for repeat imaging in several weeks and possible tissue diagnosis at that time.

DISCUSSION

Members of the fungal genus *Aspergillus* have been implicated as the causal organisms in a spectrum of distinctive pulmonary pathologies in humans, including allergic bronchopulmonary aspergillosis (ABPA), chronic pulmonary aspergillosis, and invasive aspergillosis. The extent of infection is largely determined by differences in the host immunity-microbe interaction. Invasive aspergillosis primarily occurs in the setting of immune compromise, most commonly with acute leukemia, recent hematopoietic stem cell transplant, neutropenia, solid organ transplant on immunosuppression, and chronic granulomatous disease. Pulmonary symptoms typically include dyspnea, cough, and fever unresponsive to broad-spectrum antibiotics. Pleuritic chest pain and hemoptysis can occur due to vascular invasion. If uncontrolled, *Aspergillus* can spread hematogenously and seed all organ systems.

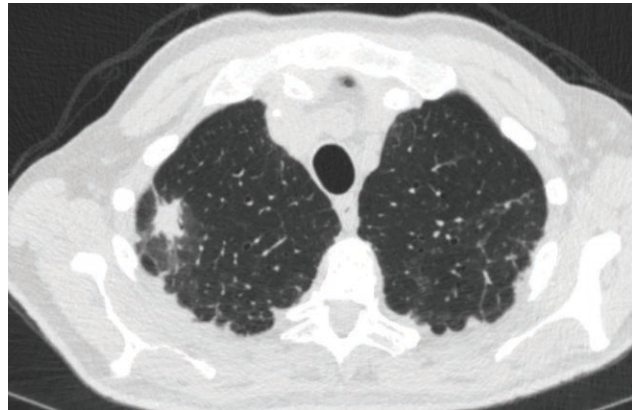


Figure 1: The halo sign, as seen in our patient, is a nodule surrounded by ground glass representing angioinvasive pulmonary infection



Figure 2: A second case of the halo sign, often seen in early pulmonary aspergillosis and aiding in prompt diagnosis in the correct clinical setting.

Diagnosis can be difficult since the only definitive tests are biopsy with positive histopathology or positive cultures from a normally sterile location. Since biopsy is often not performed, infection must often be presumed on the basis of clinical suspicion, respiratory culture data, and biomarkers such as galactomannan. A positive respiratory culture is not sufficient for diagnosis since *Aspergillus* is a common colonizer. In addition, negative cultures do not rule out infection. In immunocompromised or neutropenic hosts, fever may be the only presenting symptom. Patients with persistent fevers despite an appropriate course of empiric antibiotics (10-14 days) should be assessed for potential fungal infection. In patients for whom aspergillosis is suspected, CT scan may help in identifying early invasive disease and, as some studies suggest, lead to earlier initiation of

antifungal therapy and better overall outcomes. The earliest findings on CT are pulmonary nodules and the classic halo sign.

The halo sign is a nodule with surrounding ground glass opacity. It is thought to represent a central area of infarction and coagulative necrosis with surrounding alveolar hemorrhage due to angioinvasion and local pathogen spread. Although statistics vary between reports, one of the largest cohorts included 235 patients with proven or probable invasive disease, of which 94% had a macronodule and 60.9% had a positive halo sign. The halo sign is not pathognomonic for invasive aspergillosis, as it has also been described with other angioinvasive organisms including pulmonary Mucormycosis and Pseudomonas. However, Aspergillus is the most common pathogen in those at risk for invasive fungal infection. Aspergillosis may also present as a bronchopneumonia, which may be indistinguishable from other more common causes. Treatment consists of a 6 to 12 week course of voriconazole.

This article serves to provide several examples of the halo sign as seen in patients with acute leukemia and neutropenic fever (**Figures 1 and 2**). Prompt identification of this characteristic radiographic finding and initiation of early treatment for invasive pulmonary aspergillosis is important as mortality rates from untreated infection range from 29-90% depending on patient characteristics.

REFERENCES

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