Brain Zygomycosis in a Patient with High Risk Myelodysplastic Syndrome after Initiation of Chemotherapy

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Introduction
Zygomycetes are a group of fungi that can cause a variety of life-threatening infections particularly in immunocompromised patients. Zygomycosis manifests as a spectrum of diseases including stroke.1-3 We present a case of disseminated zygomycosis with central nervous system (CNS) involvement in a patient with myelodysplastic syndrome (MDS) after initiation of chemotherapy.

Case report
A 46-year-old female with a history of diffuse large B-cell lymphoma status post autologous stem cell transplantation developed high risk MDS, which was thought to be secondary to her treatment. She had received induction chemotherapy with idarubicin, cytarabine and vorinostat (suberoylanilide hydroxamic acid) and was discharged. She was then readmitted to the hospital after developing fevers and diarrhea. After admission, she continued to be febrile despite broad-spectrum antibiotics and antifungal drugs. She had been on fluconazole prophylactically and it was subsequently switched to posaconazole upon admission. While on the floor, she developed hemiplegia, hemineglect, dysarthria, mental status changes, and respiratory distress and was transferred to the intensive care unit. The chest x-ray showed bilateral pulmonary infiltrates and CT of the brain revealed multiple hypoattenuated lesions with associated marked edema scattered throughout the brain. Follow-up CT of the brain showed a mild midline shift. MRI of the brain reported multiple supratentorial and infratentorial masses producing ring-enhancing lesions that are centrally...
hemorrhagic, suspicious for high-grade tumor or an ischemic process (Figure 1). The patient was started on liposomal amphotericin B in addition to voriconazole. A lumbar puncture was not performed for fear of causing uncal herniation. Her condition continued to deteriorate and she died in the ICU. Autopsy revealed multiple hemorrhagic areas in the cerebrum and diencephalon along with a 1 cm hemispheric lesion in the cerebellum. Microscopic examination identified fungal hyphae involving cerebral vessels with extension into the parenchyma of the cerebrum and cerebellum. The lungs, liver, spleen and kidneys showed disseminated intravascular fungal infection consistent with zygomycosis.

Discussion

Infection with zygomycetes is usually acquired through inhalation of spores and can cause aggressive rhino-orbital-cerebral and pulmonary disease in diabetic or immunocompromised individuals. Risk factors include diabetes mellitus, hematologic malignancies, neutropenia, drug-induced immunosuppression, solid organ or bone marrow/stem cell transplantation, and intravenous drug use.4 The patient had iron overload secondary to repeated blood transfusions for underlying MDS and some reports have suggested that iron overload might be a risk factor for Zygomycetes.1-8

There have been several reports of disseminated zygomycosis in patients with leukemia, lymphoma, intravenous drug abuse and HIV.9-11 The disease should be suspected in high-risk individuals who present with sinusitis, altered mentation and/or necrotic tissue in the nose or palate. A high index of suspicion is essential for early diagnosis and treatment. Endoscopic evaluation of the sinuses should be performed to look for tissue necrosis and obtain specimens. Cultures often yield no growth and histopathological identification of zygomycete may provide the only evidence of infection.

The CNS is typically involved as a direct spread from infected paranasal sinuses, or rarely through hematogenous spread in disseminated disease in immunocompromised patients. Zygomycosis of the CNS can present in three distinct clinical forms: rhinocerebral zygomycosis, disseminated zygomycosis with CNS involvement, and isolated cerebral zygomycosis. Zygomycosis fungus has a high affinity for blood vessels, particularly for the elastic membranes.

Fatal ischemic strokes caused by major artery occlusion by zygomycosis have been reported previously.1,2 A few cases have reported intracranial hemorrhage in patients with zygomycosis.3,12,13 We present a case of disseminated zygomycosis with CNS involvement presenting clinically as stroke and radiographically as a hemorrhagic mass. Although the patient received posaconazole and amphotericin B, she succumbed to the disease in the ICU and the definitive diagnosis was made on autopsy.

The diagnosis is often difficult to make because of the often vague clinical presentation and nonspecific radiographic findings. Histological identification of the fungus provides the definitive diagnosis, however cultures are often negative.14 A high degree of clinical suspicion is crucial for timely diagnosis and treatment.

References