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Case Report

Disseminated Fungus Balls in Patient with Relapsed/ Refractory Acute Lymphoblastic Leukemia Patient

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- Air crescent

Abstract

Invasive fungal infections, which lead to increased morbidity and mortality, are commonly observed in patients with hematologic malignancies. Pulmonary infiltrates associated with bacterial and fungal infections are often encountered in patients with acute leukemia. Here, we present a 41 year-old male patient with acute lymphoblastic leukemia that developed a disseminated pulmonary invasive fungal infection with halo sign, air crescent and fungus balls. Early initiation of antifungal therapy and antifungal prophylaxis are surviving for patients at high risk in related to acute leukemia.

INTRODUCTION

Pulmonary infiltrates associated with bacterial and fungal infections are often encountered in patients with acute leukemia. Bacterial and fungal infections cause those infiltrates with the high mortality rates [1,2]. The air crescent sign appears as an air that takes a place between ball like mass and the cavity wall on the chest radiographs and computerized tomography (CT) scans. The most common cause of air crescent sign is the fungus ball associated with invasive fungal infections, which often develops in patients with hematologic malignancies. Other causes of air crescent sign include tuberculosis cavity, lung abscess, nocardia infection, carcinoma, hydatid cysts and hematoma [3,4]. Here, we present a 41 year-old male patient with acute lymphoblastic leukemia that developed a disseminated pulmonary invasive fungal infection with halo sign, air crescent and fungus balls.

CASE

A 41 year-old male patient was admitted to our department with spontaneous ecchymoses, intermittent fever, fatigue and bleeding gums. The complete blood count yielded 153000 × 10^9/L of white blood cell count, 4800 × 10^9/L of neutrophil count, hemoglobin 5.7 g/L of hemoglobin, and 23 × 10^9/L of platelet count. Bone marrow examinations revealed bone marrow hyperplasia, decreased megakaryocytes and diffuse proliferation of immature lymphoblasts. Flow cytometry demonstrated the blastic cells expressing T lymphocyte antigens with myeloperoxidase negativity. Acute lymphoblastic leukemia (ALL)-related gene abnormalities were not detected. He was diagnosed with acute lymphoblastic leukemia of T-cell type. Hyper-CVAD (Cyclophosphamide, Doxorubicin, Vincristine, Dexamethasone) plus methotrexate and cytarabine chemotherapy were initiated in addition to supportive treatments with hydration, alkalinization, and anti-emetic therapy. Anti-fungal prophylaxis could not be initiated, as the social insurance system did not reimburse it with the diagnosis of ALL. After two cycles of chemotherapy, ALL-T relapsed and FLAG-IDA (Fludarabine, Cytarabine, Idarubicin) chemotherapy was administered as a salvage regimen. However, remission was not achieved and then EMA (Etoposide, Mitoxantrone, Cytarabine) chemotherapy protocol was administered. Corticosteroid therapy was not administered during chemotherapy. On the 10th day of chemotherapy, the patient had a fever of 39.1°C without an apparent cause and then meropenem and vancomycin were given as an empirical antibiotic therapy. On the first day of antimicrobial therapy, the patient had dispnea and bilateral patchy consolidations by thorax computed tomography scans (Figure 1). Blood cultures did not yield any microorganism and blood procalcitonin value (PCT) was 0.73 ng/mL, while galactomannan (GM) test values were 3.51 (Normal: < 0.5 index value). Bronchoscopy could not be performed due to sever thrombocytopenia. Patient's absolute neutrophils counts were 20 per microliter of blood. The patient was diagnosed with invasive pulmonary aspergillosis in in reltated to GM positivity and pulmonary infiltrates on thorax CT scan. Voriconazole was initiated preemptively with a loading dose of 6 mg/kg, and

subsequently continued with a maintenance dose of 4 mg / kg in line with febrile neutropenia guideline. Chest CT scan showed disseminated fungal balls replacing the previous consolidations after two weeks of treatment (Figure 2). Since new lesions appeared in later images under voriconazole treatment and then antifungal treatment was switched to liposomal amphotericin-B with a dosage of 3 mg/kg. The patient has become stable after that antifungal therapy about probable pulmonary aspergillosis. Thoracic intervention was recommended until remission was achieved, as patient's condition was inappropriate for operation. His bone marrow function recovered after that chemotherapy cycle and he continued to receive chemotherapy. But remission was not achieved and patient died of bleeding after blast crisis.

DISCUSSION

Invasive pulmonary fungal infections are commonly observed in acute leukemia patients, especially in relapsed/refractory patients who need more aggressive salvage therapies compared to induction regimens. When an invasive fungal infection is suspected in those patients, the diagnostic procedures and early appropriate antifungal treatment should be initiated as soon as possible due to the high mortality rates. In our case, we preemptively administered antifungal treatment based on the galactomannan positivity and chest CT scan. However, invasive procedures for sampling carry high risk in those patients due to thrombocytopenia. Radiological investigations, particularly CT,

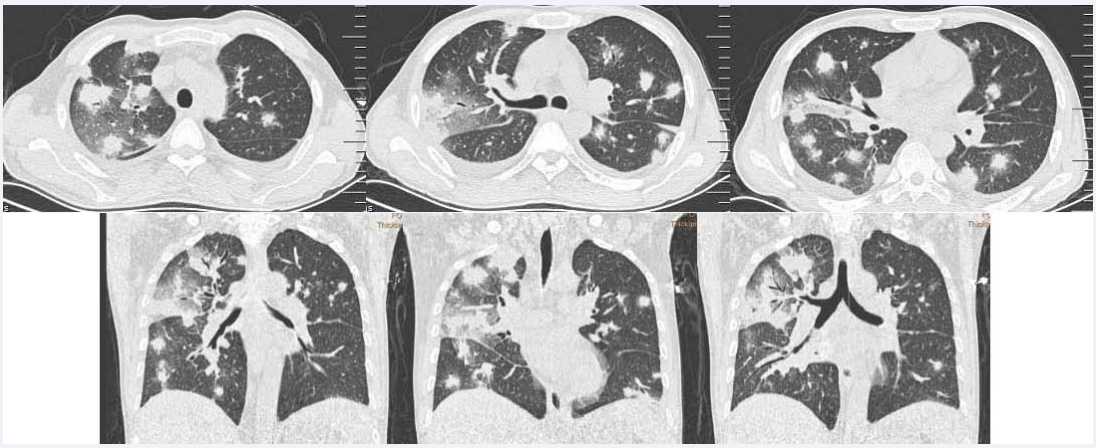

Figure 1 Pulmonary infiltrates of the patient by thorax computed tomography scans.

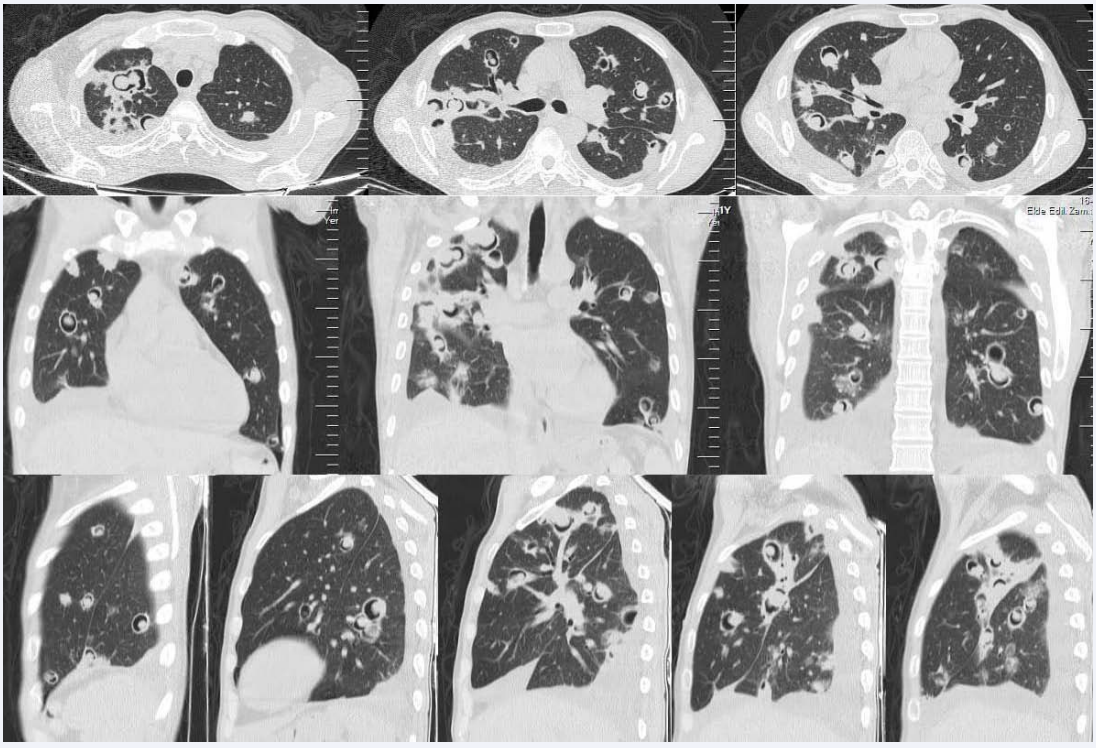

Figure 2 Halo Sign, Air Crescent and Fungus Balls.

provide rapid and earlier diagnosis in severe cases [5]. The halo represents a pulmonary hemorrhage, coagulative necrosis and necrotic nodule as a result of processes that causes pulmonary necrosis. It usually suggests recovery and an increased granulocyte activity. In the angioinvasive fungal infections, the nodules constitutes the infected, haemorrhagic and infarcted lung tissue. Whilst the neutrophil count recovers, an immune response occurs. The peripheral reabsorption of necrotic tissue induces the retraction of the infarcted centre and then the air fills in that space. That constitutes an air crescent within the nodules and suggests a good prognostic finding, as it represents the recovery phase of the infection. This sign is seen in approximately half of patients. This sign is transient and could be seen in the first 10 days [6]. Thus, an empirical or preemptive antifungal treatment should be initiated as soon as possible in those patients with the manifestations implying an invasive fungal infection in any site of body by a radiological imaging or/and laboratory tests [7,8]. A nodular opacity with circular cavitations may indicate a fungal infection, but it is a non-specific sign. It can be seen also in various conditions including metastasis, neoplasms with cavity and pneumonia [9,10]. The fungus ball and the cavity wall could be seen in associated with aspergilloma as well as granulomatous diseases, such as tuberculosis, sarcoidosis etc [11]. In conclusion, the invasive pulmonary fungal infections are commonly seen in patients with the hematologic malignancies with high morbidity and mortality rates. As patients, who receive an induction or salvage chemotherapy for an acute leukemia and have a history of fungal infection, are at a particular risk for an invasive fungal infection, the antifungal prophylaxis and empirical antifungal therapy are administered as soon as possible, when they are needed.

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