The Importance of Radiological Findings in Disseminated (Rhinocerebral and Pulmonary) Invasive Fungal Infection with Childhood Acute Lymphoblastic Leukemia: Case Report.

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ABSTRACT

The diagnosis of invasive fungal infection (IFI) is particularly difficult in immunocompromised patients. Clinical and radiological findings supporting the diagnosis of IFI are very important. We presented a case report to emphasize the radiological findings of IFI as a diagnostic tool in an acute lymphoblastic leukemia (ALL) patient with rhinocerebral and pulmonary IFI.

Key words: Invasive fungal infection, leukemia, radiological diagnosis, childhood

Approximately one third of neutropenic patients who remain persistently febrile on standard antibiotic therapy have invasive fungal infections (IFI) (1). The diagnosis of IFI is particularly difficult in immunocompromised patients. Although hematogenous dissemination of fungi has occurred, blood cultures can be negative. The detection of specific antibodies in patients with IFI reveals poor sensitivity and specificity (2). Therefore, tissue biopsy and histologic identification of fungi remain the gold standard of diagnosis. Still diagnosis of IFI has been done post-mortem (3). Although the overall prognosis of rhinocerebral IFI has improved in recent years, survival is rare in intracranial diseases or cerebral abscesses (4,5). At
Radiological findings of invasive fungal infection

this point, clinical and radiological findings supporting the diagnosis of IFI are very important. Here we report the importance of radiological findings of IFI in childhood malignancies.

Case
A 16 year-old male patient diagnosed with ALL was admitted to the Pediatric Oncology clinic with a nose lesion. Enduration on the tip of his nose, a dense purulent discharge and a necrotic lesion with a dimension of 0.5x0.5 cm on the left side of nose were seen, other system findings were normal on his physical examine. White blood cell (WBC) count was 1900/mm³ and absolute neutrophyl count (ANC) was 760/mm³. On contrast enhanced computed tomography (CT), a thick walled lesion with peripheral ring-enhancement and significant vasogenic edema, consistent with abscess formation at the right temporal lobe, were reported. Abscess diameter was 11x13 mm. Sulcal and temporal ventricular horns were effaced, accompanied with Pansunsitis (figure 1). Serum C-reactive protein (CRP) and procalsitonine (PCT) levels were 120 mg/L and 0.5 μg/L, respectively. Meropenem (80 mg/kg/day) and liposomal amphotericine B (5 mg/kg/day) were started for medication. Surgery was planned but on the following days fever continued, WBC was decreased to 1100/mm³ (ANC: 550/mm³) and rales were auscultated in the lung. Since neutropenia and fever continued Vancomycine and acyclovir were added to the therapy. On posterior-anterior chest film, a reticulonodular pattern was seen. Diffuse reticulonodular infiltration and ground-glass appearance were reported in bilateral lung parenchyma on contrast enhanced axial thoracic CT scan (figure 2). The patient was transported to the intensive care unit because of acute respiratory distress syndrome (ARDS). On the third day, the patient was intubated and mechanical ventilation was started. Increased CRP and PCT values were found as 392 mg/L and 39.7 μg/L, respectively. Donor granulocyte was given once as full match HLA tissue groups with his brother. WBC value increased to 2600/mm³. In the following days WBC decreased again. On the 14th day of therapy, a non-enhanced cerebral CT scan was repeated and significant regression of abscess wall, edema, sulcal and temporal ventricular horn effacement were seen. Since tachycardia and hypotension developed, positive inotropic therapy was started. On follow up, acute renal failure developed. Neutropenia persisted during the therapy (the last ANC: 520/mm³). Trombocytopenia and coagulation abnormalities occured. In spite of the medical therapies there was no improvement and on the 20th day of therapy, the patient died.

Discussion
Tissue biopsy and histologic identification of fungi remain the gold standard in diagnosis of IFI. Since our patient’s clinical status deteriorated quickly and ARDS developed, surgery could not be done. Therefore sample material for diagnosis could not be taken. Depending on clinical and radiological findings, treatment was done presumptively.
Sino-nasal form of IFI presents as sinusitis and then rapidly progresses to involve neighboring tissues like the orbit, eye and optic nerve. The involvement of these sites can result in brain metastasis. Aspergillusosis and mucormycosis are the most common types of mycosis caused by filamentous fungi in sino-nasal IFI patients. Maxillofacial CT findings of IFI are sinusitis, opacification of sinuses, mucosal thickening and bony erosion. Pansinusitis and mucosal thickening were seen on our patient’s maxillofacial CT.

According to the literature, histopathologically three patterns of fungal infection in the CNS are found (6). The first pattern is generally seen with Aspergillus and Zygomycetes. When intracerebral blood vessels were blocked by hyphal elements, commonly hemorrhagic infarction occurred (6). Therefore the fungus begins to erode through the vessel wall into the ischemic brain parenchyma and causes a mixed inflammatory reaction and necrosis. The erosion of the vessel wall may even result in mycotic aneurysms. Aspergillus infection is more commonly seen than other fungal infections. Diffuse or localized leptomeningitis is uncommon (7). In our case, the hyphal form was the predominant form in the brain parenchyma. The CT findings of the first pattern were infarction, diffuse or localized lucency and intraparenchymal abscess formation.

The second pattern is characterized by intraparenchymal granulomatous lesions in association with diffuse leptomeningitis (6). This type of fungal infection is generally seen with Cryptococcus, Histoplasma, and Blastomycetes. The yeast phase is the predominant form in the brain parenchyma. The CT findings of this pattern are enhancing nodular lesions (7).

The third pattern, most commonly seen with Candida, reveals small abscesses, typically in the middle cerebral artery distribution and is not associated with diffuse meningitis or infarction (6).

In our patient’s radiological findings there was a cavitating mass with a 2 cm diameter, 3-4 mm wall thickness and accompanying circumscribed edematous area at the medial part of the temporal lobe on the right. These findings are compatible with the first pattern of IFI in the central nervous system.

Pulmonary CT findings of IFI are various. Early radiological findings are often normal or non-specific. Single or multiple nodular infiltrates, segmental or subsegmental consolidation, a diffuse ground-glass pattern (often progressing to consolidation) and cavitation (air-crescent sign) are seen (8). In our patient’s thoracic CT scan findings there were bilateral diffuse reticulonodular infiltration and a ground-glass pattern.

The diagnosis of possible IFI was determined according to the Criteria for Diagnosis of Invasive Fungal Infection developed by the European Organisation for Research and Treatment of Cancer (EORTC) and the Mycoses Study Group of the National Institute of Allergy and Infectious Diseases (9). In our case, serological studies of fungal infections could not be performed in our hospital. In conclusion, we aim to emphasize the importance of radiological findings of IFI in childhood malignancies due to the difficulty of diagnosis.

References