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Case Report

Pulmonary tuberculosis in a child with acute lymphoblastic leukemia – role of empirical therapy

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ABSTRACT

Children with B-cell acute lymphoblastic leukemia (B-ALL) are immunocompromised, making them more prone to various infections. Mycobacteria are not commonly known to cause infections in children with ALL or cancer, and literature detailing tuberculosis (TB) in childhood cancer from high-burden areas is limited. We describe a case of B-ALL presenting with refractory pneumonia, which was finally presumed to be TB. As immunocompromised children typically present with paucibacillary TB, early diagnosis becomes a significant challenge. Paradoxically, the benefits of empirical ATT in this subpopulation are significantly higher than the associated risks such as hepatotoxicity. As TB is a serious infection in immunocompromised children, an empirical ATT regimen can be commenced in the setting of strong clinical suspicion after detailed assessment of the risks associated with concurrent chemotherapy, especially in children hailing from endemic regions.

Keywords: Pulmonary tuberculosis, Child, Acute lymphoblastic leukemia, Empirical therapy

INTRODUCTION

Children with acute lymphoblastic leukemia (ALL) are immunocompromised, making them more prone to various infections.[1] Several opportunistic pathogens are known to cause systemic, life-threatening infections in immunocompromised children. These infections often have atypical presentations due to the underlying immune dysregulation, making a clinical diagnosis extremely challenging. Mycobacteria are not commonly reported to cause infections in children with ALL or cancer. We describe a case of B-ALL presenting with refractory pneumonia, which was finally presumed to be tuberculosis (TB).

CASE REPORT

A six-year-old boy presented to our hospital with fever, cytopenia, pallor, hepatomegaly, elevated lactate dehydrogenase and uric acid levels. Bone marrow biopsy revealed B-ALL and he was started on chemotherapy as per institution protocol.

A year later, the child presented with complaints of fever and cough. Complete blood count and other blood investigations were within normal limits. He was started on first-line antibiotic (piperacillin-tazobactam), antifungal (azoles) and antiviral (oseltamivir) therapy. Blood cultures were sterile. Bone marrow biopsy was done in view of hepatosplenomegaly to rule out a relapse and showed reactive marrow.

Chest X-ray revealed consolidation of the left upper lobe (Figure 1a). A high-resolution computed tomography (HRCT) scan showed the presence of multifocal consolidations with surrounding ground-glass opacities in bilateral lung fields, radiologically suggestive of fungal pneumonia (Figure 1b). However, serum galactomannan was negative. Workups for cytomegalovirus, adenovirus, influenza A and B, and gastric aspirate tested for acid-fast bacilli (AFB) were all negative. Bronchoalveolar lavage (BAL) cytology showed the presence of non-specific inflammatory cells. GeneXpert, AFB smear, fungal smear and BACTEC culture from BAL were all negative. In view of persistent fever and pneumonia, the antibiotics were escalated to meropenem and teicoplanin with empirical cotrimoxazole therapy.

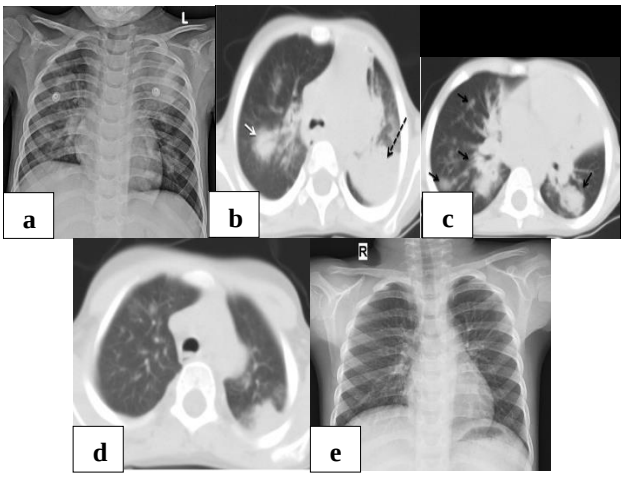

Figure 1: (a) Chest radiograph (AP view) showing patchy air space opacities in both lungs, largest in the left upper zone; (b) and (c) axial section of HRCT lung showing multiple nodules (black arrows) in both lungs with a mass-like lesion in the left upper lobe (dotted arrow); some of the nodules show surrounding halo of ground glass opacity (white arrow); (d) axial section of HRCT lung showing reduction in the size of the left upper lobe opacity (taken after one month of ATT); and (e) chest radiograph (AP view) showing resolution of the lung opacities with normal appearance of the lungs (taken after completion of full course of ATT).

Repeat HRCT showed progression of the consolidation in the left lung with few enlarged mediastinal lymph nodes (Figure 1c). A CT-guided biopsy was done, and histopathological examination revealed a necro-inflammatory lesion that was negative for malignancy (Figure 2a and b). As none of the investigations were confirmatory but clinical and radiological features raised the suspicion of TB, the child was started empirically on anti-tubercular therapy (ATT) 2HRZ+4HR (isoniazid + rifampicin + pyrazinamide) after consultation with the infectious disease expert. A week later, the child became afebrile and improved clinically with an increase in appetite and weight gain. He completed the full 6-month course of ATT. Repeat CT showed significant resolution of the consolidation (Figure 1d). He is 1-year post treatment now, continued on chemotherapy and is doing well with disease in remission.

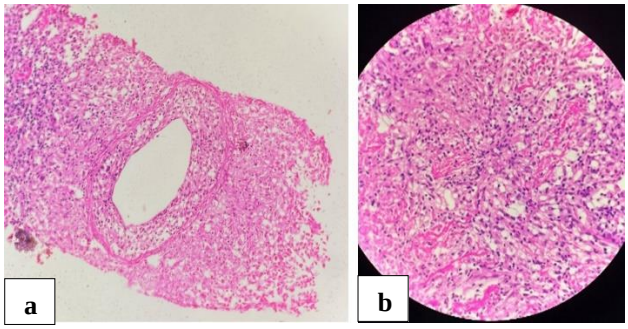

Figure 2: HPE 400x (a) vessel with features of vasculitis, and (b) ill-defined epithelioid granuloma surrounded by lymphocytes.

DISCUSSION

In immunocompromised children, TB may have a wide range of presentations from being asymptomatic to producing disseminated life-threatening disease. In children with malignancy, the decrease in immunity may be due to the underlying disease process per se or may be chemotherapy-induced. Lancioni et al reported a known case of precursor B-cell ALL diagnosed with pulmonary TB after presenting with pyrexia of unknown origin.[2]

Naidu et al conducted a study in immunocompromised children to study the incidence of TB and evaluate the role of screening regimens in this subpopulation. The study results showed that children with advanced leukemias receiving corticosteroids/immunosuppressive drugs had a higher incidence of TB. The authors hence advocate empirical ATT in children with known risk factors presenting with symptoms suggestive of disease.[3]

Jain et al have published a significant study on the outcome of pulmonary TB in three study groups with various acute leukemias – ALL, AML and APML. The authors document the incidence of ATT-induced hepatitis (seen in 34.9%) as a significant challenge and conclude that continuation of chemotherapy while administering ATT can decrease mortality rates.[4]

The incidence of tuberculosis in pediatric oncology patients was found to be more with ALL as the most common underlying malignancy. Moreover, nearly half of

the infections were confirmed during the intensive phase of chemotherapy, indicating that the ongoing immunosuppression had caused reactivation of latent infection, hence suggesting a thorough TB screening regimen in children with malignancy and advocate early commencement of empirical ATT in patients presenting in endemic areas.[3]

Immunosuppressed children are 2 to 40 times more likely to develop TB as opposed to a healthy child of the same age.[1] Susceptible children include those with hematological malignancies, HIV infection, and post-transplant patients. Moreover, leukemias increase the risk of reactivation of latent TB as well as its progression to active infection, as a result of which the morbidity and mortality is significantly high in these children.[1]

Some propose that screening for TB in susceptible children could be considered before initiating chemotherapy, which is not a common practice even in endemic countries. Commonly used screening techniques of TB include Mantoux test (tuberculin sensitivity testing) which could be expected to show poor response, interferon gamma release assay (IGRA) and lipoarabinomannan assay, which has a good sensitivity in immunocompromised patients.[4]

Immunocompromised children present with paucibacillary TB, posing a significant challenge to early diagnosis.[5] As TB is a serious infection in this population, in the setting of strong clinical suspicion, an empirical ATT regimen can be commenced after detailed assessment of the risks associated with concurrent chemotherapy, especially in endemic regions.

A standard regimen with 3–4 drugs for 9–12 months is currently recommended in these children.[5] As there is substantial risk of hepatotoxicity with concurrent administration of ATT and anticancer drugs, the children must be monitored regularly.

CONCLUSION

Literature detailing TB in childhood cancer from high-burden areas is limited. This raises the necessity of formulating appropriate screening regimens to aid early diagnosis and improve clinical outcomes in children with leukemias.

The benefits of starting empirical ATT are significantly higher than associated risks such as hepatotoxicity and other drug toxicities. Therefore, even in the absence of definitive proof of infection, in the setting of strong clinical and/or radiological suspicion of TB in a child hailing from an endemic area, we strongly advocate commencing empirical ATT.

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