



Subject Area : Medical

CLINICAL ANALYSIS OF FOUR PEDIATRIC CASES OF TUBERCULOSIS COMBINED WITH HEMATOLOGICAL MALIGNANCIES

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ARTICLE INFO	ABSTRACT
Received 16 th March, 2025 Received in revised form 25 th March, 2025 Accepted 19 th April, 2026 Published online 28 th April, 2026	Children with B-cell acute lymphoblastic leukemia (B-ALL) present with a compromised immune system, making them more susceptible to various infections. Mycobacterial infections are not frequently recognized in children with ALL or cancer, and the literature detailing tuberculosis (TB) in pediatric oncology from high-incidence regions is limited. We describe three cases of B-ALL and one case of Non-Hodgkin Lymphoma (NHL) that presented with refractory pneumonias ultimately presumed to be TB, as well as one with seizures. Because immunocompromised children commonly exhibit paucibacillary TB, early diagnosis becomes a significant challenge. Paradoxically, the benefits of empirical treatment in this subgroup are substantially greater than the risks, including hepatotoxicity. Given that TB is a severe infection in immunocompromised children, empirical treatment may be initiated when there is strong clinical suspicion after a thorough evaluation of the risks associated with concurrent chemotherapy, especially in children from endemic regions.
Key words:	
Malocclusion, Oral, Respiratory, Cardiovascular, Neurological, Musculoskeletal, Renal, Erectile dysfunction	
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INTRODUCTION

Tuberculosis (TB) has long been a widespread global health challenge, earning its place as one of the oldest and most persistent diseases affecting humanity. Despite major medical advances and coordinated international efforts to control it, TB continues to pose a formidable threat to public health worldwide. The 2024 Global TB Report from the World Health Organization (WHO) recently highlighted a concerning resurgence of TB, identifying it once again as the leading cause of death from a single infectious agent—surpassing even coronavirus disease 2019 (COVID-19). According to the report, in 2023 approximately 10.8 million people became ill with TB, including 8.2 million newly diagnosed cases, resulting in 1.25 million TB-related deaths. This marks the highest figure recorded since the WHO began global TB monitoring in

1995, underscoring the severity of the situation and the urgent need for global action. TB remains one of the leading causes of death from infectious diseases worldwide, surpassing HIV and malaria (Berzosa et al., 2020). The coexistence of TB and acute leukemia presents major diagnostic and therapeutic challenges, especially in endemic regions. This case series explores the clinical characteristics, diagnostic complexities, and treatment outcomes of pediatric patients with concurrent TB and acute leukemia treated at a tertiary-level center.

METHODOLOGY

We retrospectively analyzed data from three pediatric patients diagnosed with acute lymphoblastic leukemia (ALL) and one diagnosed with Non-Hodgkin Lymphoma (NHL) who developed tuberculosis between 2019 and 2024. The diagnosis of TB was considered associated with leukemia if both conditions occurred simultaneously.

CASE 1

A 12-year-old male diagnosed with high-risk B-cell acute lymphoblastic leukemia (based on age, CNS infiltration, tumor

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burden, and iAMP21 alteration), vaccinated according to the national immunization schedule with BCG scar present. The family had a low socioeconomic status and lived in a rural area.

He was treated according to the Total XV protocol with chemotherapy and steroids. During induction, he developed respiratory deterioration with fever and desaturation down to 75%, tachypnea, and decreased bilateral breath sounds. Chest radiograph revealed interstitial thickening and atelectasis (Fig. 1). Given ongoing respiratory distress, a chest CT was requested. Due to a suspected pulmonary abscess, antimicrobial therapy was changed to meropenem and vancomycin.

He experienced worsening respiratory status, requiring a repeat CT scan, which showed increased extension and density of ground-glass opacities associated with multilobar consolidation (Fig. 2). The loculated nodular lesion with hypodense center and peripheral enhancement persisted in the right upper lobe. Bilateral subsegmental atelectasis was noted, along with increased bilateral pleural effusions and passive lung collapse (Fig. 3).

Pleural drainage was performed, and he was evaluated by the intensive care unit. Laboratory tests revealed: hemoglobin 10 g/dL, hematocrit 29.5%, leukocytes 4,800/ μ L, neutrophils 2,110/ μ L, and platelets 151,000/ μ L. With partial clinical and respiratory improvement, he began a second cycle of methotrexate (5 g), intrathecal therapy, bone marrow aspirate, and minimal residual disease (MRD) assessment.

He later developed fever, tachycardia, increased work of breathing, desaturations to 50–60%, and bilateral infiltrates on chest radiograph. Methotrexate level was 0.06. Respiratory deterioration persisted, requiring oxygen flows up to 15 L/min. CT imaging showed further extension of ground-glass and consolidation areas and increased pleural effusions. ICU initiated respiratory support with BIPAP.

Pleural puncture was performed, followed by a transition from BIPAP to high-flow nasal cannula with good tolerance. Gastrointestinal PCR panel returned a positive alarm value for *Clostridium difficile* toxins AB, for which treatment was already underway. However, because of persistent respiratory decline, miliary tuberculosis was suspected, and DOTBAL therapy (ethambutol, isoniazid, rifampicin, pyrazinamide) was initiated.

Oxygen requirements decreased progressively. Quantiferon-TB Gold Plus returned positive. Aspergillus antigen was negative (galactomannan 0.1). High-flow nasal cannula flow

requirements decreased from 18 to 10 L/min. The pleural catheter was removed without complications, and high-flow support was discontinued successfully.

Bronchoscopy was performed, and bilateral bronchial fluid samples were collected. PCR testing confirmed *Mycobacterium tuberculosis*, and anti-TB therapy was continued.

CASE 2

A 12-year-and-6-month-old female with a diagnosis of high-risk B-cell acute lymphoblastic leukemia (based on age), with IKZF1 deletion, IGH rearrangement, and RUNX1 copy number gain, from a low socioeconomic background, and with a maternal history of death due to miliary tuberculosis. She presented for continuation of maintenance chemotherapy under the Total Therapy XV protocol but arrived with clinical features of septic shock, prompting admission to the intensive care unit.

Upon arrival, she was febrile (38.9°C) and tachycardic, with petechiae on the oral mucosa, lips, and distal lower extremities. She reported short episodes of productive cough starting one day prior. Supplemental oxygen was initiated, and a crystalloid bolus of 10 ml/kg was administered. Venous blood gas showed: pH: 7.4, PCO₂: 20.7 mmHg, PO₂: 24.6 mmHg, HCO₃⁻: 18.4 mmol/L, Base excess: -6.2, Lactate: 6.3 mmol/L.

After partial improvement and decreased heart rate, the “golden hour” sepsis protocol was initiated, cultures were obtained, and cefepime 150 mg/kg/day was started. Laboratory tests demonstrated neutropenia and thrombocytopenia. Vasopressor support with norepinephrine was initiated. Procalcitonin measured 17.2 ng/ml, and C-reactive protein was 18.1 mg/dL.

When oxygen support was removed, she desaturated to 87%. She remained tachycardic and febrile. Subsequently, she developed neurological deterioration with a Glasgow Coma Scale score of 9, without an identifiable cause. Endotracheal intubation was performed, and mechanical ventilation was initiated in volume assist-control mode.

A non-contrast cranial CT scan showed no intracranial hemorrhage or cerebral edema. Lumbar puncture was performed, yielding clear cerebrospinal fluid, which was sent for analysis.

Due to persistent fluid overload, mild azotemia, and poor response to diuretics, renal replacement therapy was initiated via veno-venous hemofiltration, starting at a flow rate of 120 ml/hr, increased to 150 mL/hr, with ultrafiltration increased from 90 to 120 ml/hr and no dialysate. A contrast-enhanced

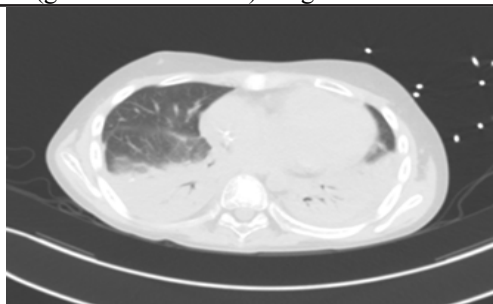


Fig. 1. Chest radiograph revealed interstitial thickening and atelectasis



Fig. 2. Increased extension and density of ground-glass opacities associated with multilobar consolidation



Fig. 3. Bilateral subsegmental atelectasis was noted, along with increased bilateral pleural effusions and passive lung collapse

and non-contrast brain MRI revealed: Parieto-occipital subarachnoid hemorrhage, Changes consistent with vasospasm of the posterior cerebral arteries, Small hyperintense gliotic areas in the semioval centers and left-dominant subcortical frontal regions, Iron deposits in the choroid plexus (Fig. 4)

Despite treatment with meropenem, vancomycin, acyclovir, and fluconazole, she continued to have high fevers. She was eventually extubated electively to high-flow nasal cannula. However, she remained intermittently tachypneic and febrile, with oxygen desaturations to 85–88% off supplemental oxygen. Given persistent fever spikes (one to two daily), the infectious disease team requested: Ubiquitin scintigraphy (Fig. 5) Blood cultures, Inflammatory markers,

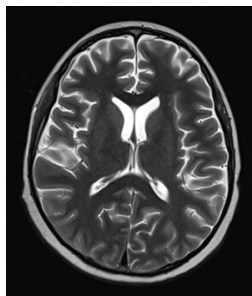


Fig. 4. vasospasm of the posterior cerebral arteries, Small hyperintense gliotic areas in the semioval centers and left-dominant subcortical frontal regions, Iron deposits in the choroid plexus.

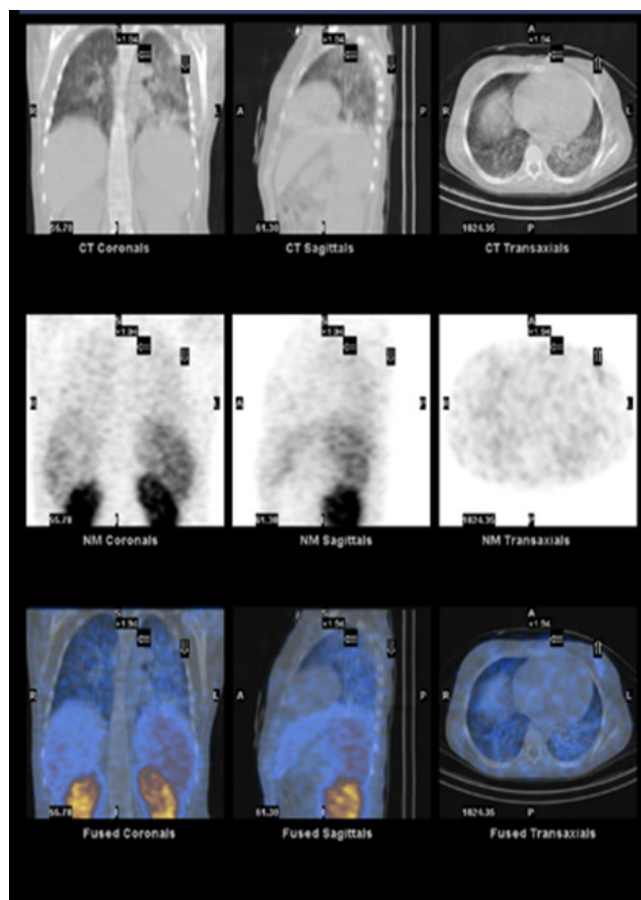


Fig. 5. Bilateral alveolar occupancy areas and ground-glass images.

Quanti FERON, Serum galactomannan. Quanti FERON-TB Gold Plus returned positive. Chest imaging revealed multiple parenchymal and subpleural nodules in both lungs (Fig. 6).



Fig. 6. Multiple parenchymal and subpleural nodules in both lungs

Anti-tuberculosis treatment with DOTBAL (isoniazid, rifampicin, ethambutol, pyrazinamide) was initiated.

Bronchoscopy was performed, and PCR testing of bronchial samples confirmed *Mycobacterium tuberculosis*. She continued receiving both oncologic treatment and anti-TB therapy as an outpatient under combined hematology-oncology and infectious disease follow-up.

CASE 3

A 14 years old male who initially presented with asthenia, adynamia, and lower-extremity weakness, accompanied by temperature instability and fever greater than 38°C. He also reported an oppressive frontal headache associated with photophobia and phonophobia. Laboratory tests revealed tumor lysis syndrome, and he was diagnosed with high-risk B-cell acute lymphoblastic leukemia, based on age, markedly elevated leukocyte count (231,800/ μ L), sex, and the presence of CRLF2/IGH fusion. He came from a low socioeconomic background and had a BCG vaccination scar.

Oncologic treatment was initiated beginning with lumbar puncture and intrathecal chemotherapy, followed by systemic chemotherapy with vincristine, daunorubicin, and pegaspargase. Cytogenetic analysis by FISH showed an abnormal result with the CRLF2/IGH fusion, prompting initiation of imatinib 500 mg.

He developed persistent fever, and as part of the evaluation a chest CT was ordered, showing areas of consolidation and ground-glass opacities. Empirical therapy was started with vancomycin, meropenem, and voriconazole.

A follow-up CT scan of the chest demonstrated persistent encapsulated pulmonary foci (Fig. 7). A non-contrast chest CT was later obtained due to increasing pleuritic pain bilateral pleural effusion with passive lung collapse is observed (Fig. 8). Given poor pulmonary evolution, new cultures were obtained and a lung biopsy was scheduled.



Fig. 7. Persistent encapsulated pulmonary foci

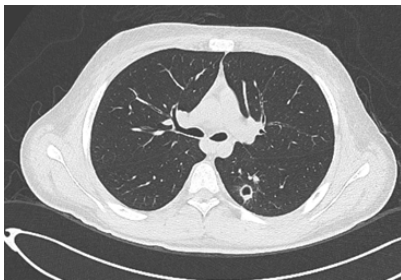


Fig. 8. Bilateral pleural effusion with passive lung collapse is observed

He again developed recurrent fever spikes, and due to the progressive worsening of pulmonary lesions and a positive QuantiFERON-TB Gold test, the infectious disease service recommended initiating anti-tuberculosis therapy with DOTBAL (ethambutol, isoniazid, rifampicin, pyrazinamide).

He continued receiving both oncologic and anti-TB treatment on an outpatient basis under close hematology and infectious disease follow-up.

CASE 4

A 13-year-old male with a diagnosis of Stage III T-cell lymphoblastic Non-Hodgkin Lymphoma, confirmed by mediastinal biopsy, was undergoing chemotherapy. He came from a low socioeconomic background and had a BCG vaccination scar on his arm. He presented to the emergency department with convulsive seizures progressing to status epilepticus, requiring advanced airway protection. Anticonvulsant therapy was initiated with phenobarbital and lacosamide.

From arrival, his abdominal examination was concerning: the abdomen was rigid, tender, and without bowel sounds. He underwent exploratory laparotomy, which revealed: neutropenic colitis, frozen abdomen, intestinal Obstruction, peritoneal granulomatosis

Extensive adhesiolysis was performed, peritoneal fluid was drained, and biopsies were collected.

Given clinical and laboratory evidence of sepsis, broad antimicrobial therapy was initiated, including vancomycin, meropenem, and fluconazole.

Subsequently, *Mycobacterium tuberculosis* was isolated from both bronchial secretions and peritoneal fluid, prompting initiation of first-line anti-tuberculosis therapy with isoniazid, rifampicin, ethambutol, and pyrazinamide (DOTBAL). However, due to the oral route of administration and his poor abdominal condition, adequate absorption of these medications was not possible. Therefore, treatment was escalated to second-line agents, levofloxacin and linezolid.

A lumbar puncture was performed due to worsening neurological status. Cerebrospinal fluid was described as yellow and clear, with the following results: PCR detected *Mycobacterium tuberculosis* DNA, confirming tuberculous meningitis.

Despite therapy, the patient experienced progressive clinical deterioration, developing disseminated tuberculosis, worsening multiorgan failure, and ultimately death.

DISCUSSION

In immunocompromised children, tuberculosis can present in a wide range of forms—from asymptomatic infection to potentially fatal disseminated disease. In children with malignant neoplasms, the decrease in immune function may be related either to the underlying disease itself or to the immunosuppressive effects of chemotherapy. Lancioni et al. reported a known case of precursor B-cell acute lymphoblastic leukemia (ALL) diagnosed with pulmonary tuberculosis after presenting with fever of unknown origin.²

Naidu et al. conducted a study in immunocompromised children to evaluate the incidence of tuberculosis and the usefulness of screening regimens in this population. Their results showed that children with advanced leukemias receiving corticosteroids or immunosuppressive therapy had a higher incidence of tuberculosis. Therefore, the authors recommend initiating empirical therapy in children with known risk factors who present with suggestive symptoms.³

Jain et al. published an important study on the prognosis of pulmonary tuberculosis in three groups of patients with different acute leukemias: ALL, AML, and mixed-phenotype acute leukemia. The authors documented a treatment-induced hepatitis rate of 34.9% as a significant challenge and concluded that continuation of chemotherapy while tuberculosis treatment is administered may reduce mortality rates.⁴

The incidence of tuberculosis in pediatric oncology patients was found to be higher overall, with acute lymphoblastic leukemia being the most common underlying malignancy. Nearly half of TB infections were diagnosed during the intensive phase of chemotherapy, suggesting that ongoing immunosuppression may lead to reactivation of latent infection. Thus, a comprehensive TB screening strategy is recommended in children with malignancies, along with early initiation of empirical treatment for patients from endemic regions.³

Immunocompromised children are 2 to 40 times more likely to develop tuberculosis than healthy children of the same age.¹ Susceptible groups include those with hematologic malignancies, HIV infection, and post-transplant patients. Leukemia, in particular, increases the risk of reactivation of latent tuberculosis as well as progression to active disease, leading to significantly increased morbidity and mortality.¹

Some authors suggest that TB screening should be considered in high-risk children prior to the initiation of chemotherapy, although this is not routine practice—even in endemic countries.

Immunocompromised children commonly present with paucibacillary TB, which poses a significant challenge for early diagnosis.⁵ Because tuberculosis is a severe infection in this population, empirical treatment may be initiated when there is strong clinical suspicion, after a detailed assessment of risks associated with concurrent chemotherapy, especially in en-

demic regions.

Currently, a standard regimen of 3–4 drugs for 9–12 months is recommended for these children.⁵ Given the substantial risk of hepatotoxicity with concomitant anti-TB and chemotherapy drug administration, regular monitoring of liver function is essential.

RESULTS

Four pediatric cases were identified (three ALL and one NHL) with concurrent tuberculosis. TB manifestations included pulmonary involvement (three patients), neurological involvement (one patient), and abdominal involvement (one patient). All four patients developed tuberculosis during either the induction or maintenance phases of chemotherapy. One patient presented with convulsive seizures progressing to status epilepticus, and testing revealed *Mycobacterium tuberculosis* by PCR in both cerebrospinal fluid and peritoneal fluid, consistent with disseminated tuberculosis; this patient experienced clinical deterioration and died. The remaining three patients continued their oncologic and anti-TB treatments on an outpatient basis, with periodic liver function monitoring to detect potential treatment-related toxicity.

CONCLUSION

This case series highlights the complexities of managing tuberculosis concurrently with oncologic disease in pediatric patients. The primary challenges include atypical clinical presentations, diagnostic delays, treatment-related toxicities, and possible drug interactions. A high index of suspicion for tuberculosis in children with hematologic malignancies from endemic regions is essential for timely diagnosis and optimal management. Further research is needed to establish best practices for comprehensive care in this dual-disease population.

Because tuberculosis is a serious infection in immunocompromised individuals, empirical anti-TB therapy may be necessary when clinical and radiologic findings strongly suggest its presence, especially in patients living in endemic areas. In children, oncologic chemotherapy is not a contraindication to initiating tuberculosis treatment.

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