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Literature Review

Pancytopenia in Pediatric Tuberculosis – A Case Series and Literature Review from North India

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Abstract

Background: *Pediatric tuberculosis (TB) remains a major public health challenge in India, where malnutrition and immune immaturity increase vulnerability. While anemia and isolated cytopenias are frequent hematological manifestations, pancytopenia is rare and often mimics hematological malignancies or syndromes, delaying diagnosis. This case series from North India highlights clinical diversity, diagnostic challenges, and therapeutic outcomes of TB-associated pancytopenia.*

Objectives: *To describe the clinical spectrum, hematological findings, diagnostic pitfalls, and treatment responses in children with pancytopenia due to disseminated TB, supported by a literature review.*

Methods: *Five children who presenting with fever, pallor, constitutional symptoms, and hepatosplenomegaly and Pancytopenia from Jan to July 2025 in pediatric IPD were evaluated. Investigations included blood counts, micronutrient assays, bone marrow studies, imaging, and microbiological confirmation by GeneXpert/AFB. All received first-line anti-tubercular therapy (ATT) with nutritional and supportive care; one child required corticosteroids for hemophagocytic lymphohistiocytosis (HLH). Outcomes were monitored for 3–6 months.*

Results: *All patients had disseminated or extrapulmonary TB with pancytopenia:*

Case 1: Bone marrow granulomas with hematological recovery after ATT.

Case 2: Splenic lesions and vitamin B12 deficiency improved with ATT and supplementation.

Case 3: TB-associated HLH responded to ATT with steroids.

Case 4: Severe malnutrition with abdominal TB showed recovery after ATT and nutritional therapy.

All children recovered clinically and hematologically within 3–6 months of treatment.

Discussion: *Pancytopenia in TB may result from marrow infiltration, hypersplenism, nutritional deficiencies, or immune dysregulation. Recognition is critical to avoid misdiagnosis as leukemia or aplastic anemia. Literature supports timely ATT with correction of nutritional deficiencies and, in selected cases, adjunctive immunomodulation.*

Conclusion: *Pancytopenia, though uncommon, may signify disseminated pediatric TB. Early diagnosis, comprehensive evaluation, and prompt therapy ensure favorable outcomes in endemic settings.*

Keywords: *Bone marrow, Disseminated TB, Pediatric tuberculosis, Pancytopenia, HLH.*

Background

Pediatric tuberculosis (TB) remains a significant health concern in endemic countries like India, where malnutrition and immunological vulnerabilities exacerbate disease severity. Although anemia of chronic disease is well documented, pancytopenia is an uncommon and under-recognized hematological manifestation of pediatric TB. This case series from North India presents multiple children with disseminated TB and pancytopenia, highlighting their clinical profiles, diagnostic challenges, therapeutic responses, and outcomes. A consolidated discussion, enriched with literature review, explores the underlying mechanisms, diagnostic pitfalls, and management implications.

Introduction

Tuberculosis (TB) remains a major global health challenge, with children contributing substantially to its associated morbidity and mortality. According to the Global Tuberculosis Report 2021, children accounted for nearly 8.75% of all treated TB cases between 2018 and 2022, amounting to approximately 3.5 million cases worldwide. India bears the highest burden of pediatric TB, where children represent a particularly vulnerable subgroup due to factors such as malnutrition, incomplete immune maturation, and frequent exposure to infectious household contacts.

National surveillance data reflect a worrisome trend, with notified pediatric TB cases rising by 38% in the past

five years, from 102,090 in 2020 to 141,182 in 2024 (India TB Report 2024). Several factors likely contribute to this increase, including widespread malnutrition, post-COVID-19 immune vulnerabilities, intensified active case-finding under the National Tuberculosis Elimination Programme (NTEP), and the growing prevalence of drug-resistant TB.

Although pulmonary TB remains the most common clinical presentation, extrapulmonary forms are also frequently observed in children, with manifestations ranging from lymph node involvement to disseminated disease affecting the bone marrow, liver, spleen, and even reproductive organs. Hematological abnormalities are not uncommon in TB and may present as anemia, leukopenia, or thrombocytopenia. However, the occurrence of pancytopenia is relatively rare and often indicates disseminated or severe disease. Importantly, in TB-endemic regions, pancytopenia can closely mimic hematological malignancies, genetic conditions and syndromes posing a diagnostic challenge.

This case series describes children with TB-associated pancytopenia managed at a tertiary care centre in North India and presents a discussion integrating current literature to highlight diagnostic considerations and clinical implications.

Case Series

Case 1

A 5-year-old girl presented with persistent fever, weight loss, generalized weakness, and progressive pallor for two months. Clinical examination revealed hepatosplenomegaly and generalized lymphadenopathy. Laboratory investigations demonstrated pancytopenia, with hemoglobin of 6.8 g/dL, leukocyte count of 2,500/µL, and platelets at 85,000/µL. Bone marrow aspiration revealed caseating granulomas consistent with tubercular infiltration. Chest radiograph suggested hilar lymphadenopathy. Gastric aspirates sent for GeneXpert came positive with rifampicin sensitivity. The child was started on first-line ATT, following which hematological parameters gradually normalized, and she showed significant clinical improvement.

Case 2

A 7-year-old girl presented with recurrent fever, abdominal pain, and progressive pallor for one month. On examination, she had hepatosplenomegaly, ascites, and signs of malnutrition. Investigations revealed pancytopenia with vit B12 deficiency and severe anemia. Abdominal ultrasonography showed mesenteric lymphadenopathy and splenic lesions. Bone marrow evaluation demonstrated macrocytic RBCs with no evidence of malignancy or granulomas. Biochemical parameters of ascetic tap were suggestive of tuberculosis and ZN stain of the same was positive for Acid Fast Bacilli. She was treated with ATT and blood (pack cell

volume) transfusions and other supportive supplementation leading to progressive resolution of symptoms and recovery of blood counts over three months.

Case 3

A 9-year-old girl presented with low-grade fever, significant weight loss, anorexia, and generalized weakness for three months. She had pallor, mild hepatosplenomegaly, and poor nutritional status. Investigations confirmed pancytopenia. Her triglyceride and LDH. Bone marrow biopsy showed cellular marrow with increased histiocytic activity along with histophagocytic cells. These findings were consistent with HLH (hemophagocytic lymphohistiocytosis). Imaging revealed mediastinal lymphadenopathy. She responded well to systemic steroids, ATT combined with vitamin supplementation, showing marked symptomatic as well as hematological recovery and weight gain within three months.

Case 4

A 10-year-old girl presented with fever, cough, abdominal distension, progressive pallor and generalized weakness. She was having constitutional symptoms of Urinary Tract Infections with blood culture proven acinobacter sepsis. She was severely malnourished with wasting and stunting. Clinical examination revealed hepatosplenomegaly and free fluid in the abdomen. Laboratory evaluation showed pancytopenia, hypoalbuminemia, transaminitis and multiple micronutrients deficiencies mainly vit B12, Iron, vit D. Bone marrow aspiration showed hyper cellular marrow mainly with macrocytic RBCs , and abdominal CT revealed multiple tubercular abscesses in mesenteric nodes, omental thickening, ileocecal thickening along with ascites. Gastric aspirates came positive for mycobacterium. She had a history of abdominal surgery one year back in view of small intestinal strictures. Biopsy at that time was suggestive of chronic granulomatous disease; microbiological evidence of TB was not there hence was kept under the diagnosis of inflammatory bowel disease at that time. This time, after gaining microbiological, biochemical as well as well as clinical evidences of TB, she was initiated on ATT along with nutritional rehabilitation and supportive care. Over 4 months, she showed remarkable clinical improvement, resolution of cytopenias, and catch-up growth.

Case 5

A 12-year-old girl presented with Turner syndrome-like morphological features including short stature, a shield-like chest, and a short neck. She had progressive pallor, generalized weakness, and persistent abdominal pain. Laboratory evaluation revealed pancytopenia with coexistent iron deficiency. Imaging studies revealed distorted ovarian anatomy along with abdominal and pulmonary TB. Interestingly, karyotyping was normal,

ruling out Turner syndrome. The ovarian involvement was attributed to disseminated TB causing ovarian dysfunction. The patient was started on ATT and nutritional supplementation, following which she gained height and weight, her ovarian dysfunction improved, and pancytopenia resolved gradually.

Comparative Summary of Cases

All five children presented with pancytopenia in association with disseminated or extrapulmonary TB, yet each case illustrated distinct clinical features. The youngest children (Cases 1 and 2) primarily presented with constitutional symptoms, hepatosplenomegaly, and bone marrow involvement. The mid-childhood cases (Cases 3 and 4) demonstrated the added contribution of nutritional deficiencies, sequelae of chronic disease mainly effects of inflammatory response (HLH) and multi-organ involvement, further complicating the hematological profile. The oldest child (Case 5) uniquely mimicked Turner syndrome due to ovarian involvement, underscoring TB's ability to imitate genetic and endocrine disorders. Despite these varied presentations, all children showed hematological and clinical recovery after initiation of ATT and supportive care. This reinforces the importance of considering TB in the differential diagnosis of pancytopenia in children, especially in endemic regions.

Table 1. Summary of Hematological and Diagnostic Findings in Reported Cases

Case	Hb (g/dL)	TLC (×10⁹/L)	Platelets (×10⁹/L)	Microbiology	ZN stain	Radiology	Vit B12 (pg/mL)	Folate (ng/mL)	Iron (µg/dL)	Bone Marrow Findings
1	6.8	2.5	85	Gastric aspirate positive for mycobacterium by geneXpert	AFB in marrow aspirate	CXR: hilar lymphadenopathy	Normal	Normal	70	Caseating granulomas
2	4.2	1.3	56	Gastric aspirate negative	AFB in ascitic fluid	USG: mesenteric lymphadenopathy, splenic lesions	<159	Normal	50	Hypercellular marrow with macrocytosis
3	3.2	1.1	8	Gastric aspirate positive for mycobacterium by geneXpert	AFB in gastric aspirate	CXR: mild hilar changes	570	Normal	82	Hypocellular marrow with histiocytosis (HLH)
4	2.8	1.53	10	Gastric	AFB	CT: abdominal	<159	1.5	28	Hypercellular

Case	Hb (g/dL)	TLC (×10⁹/L)	Platelets (×10⁹/L)	Microbiology	ZN stain	Radiology	Vit B12 (pg/mL)	Folate (ng/mL)	Iron (µg/dL)	Bone Marrow Findings
				aspirate positive for mycobacterium by geneXpert	in gastric aspirate	abscesses, ileocecal thickening, ascites				marrow with macrocytosis
5	6.0	2.8	97	Gastric aspirate positive for mycobacterium by geneXpert	AFB in gastric aspirate	CXR: pulmonary TB; CT: ovarian granulomas, ascites	Normal	Normal	<10	Normocellular, no granulomas

Discussion

The present case series highlights the protean manifestations of pediatric TB when associated with pancytopenia. All children demonstrated features of disseminated TB, suggesting that pancytopenia is often a marker of advanced disease. The spectrum of manifestations ranged from growth failure and endocrine dysfunction to HLH, underscoring the diverse pathophysiology.

Pathophysiology

Pancytopenia in TB results from multiple mechanisms: direct invasion of bone marrow by granulomas, marrow fibrosis, hyperspleenism, nutritional deficiencies (folate, vitamin B12), and immune-mediated destruction. Bone marrow involvement may present with granulomatous infiltration, sometimes mimicking leukaemia or aplastic anaemia [3,4]. Disseminated TB affecting the ovaries, as seen in one of our cases, has rarely been reported and can lead to endocrine dysfunction and syndromic mimics [6,7].

Literature Review within Discussion

Several studies have described hematological manifestations in TB. Sharma et al. (2021) reported granulomatous lesions in bone marrow aspirates of children with unexplained cytopenias, many of whom responded to anti-tubercular therapy [3]. Liu et al. (2022) presented a case of TB with pancytopenia and coagulopathy that closely mimicked hematological malignancy [4]. Disseminated TB involving bone marrow, spleen, and ovaries is associated with severe nutritional compromise, which further contributes to anemia and pancytopenia [5–7].

Nutritional deficiencies are important compounding factors. Iron deficiency and megaloblastic anemia due to

vitamin B12 and folate deficiency have been frequently documented in TB, particularly in children with poor dietary intake and chronic infection [10,11]. These deficiencies worsen marrow suppression and can delay hematological recovery if not corrected alongside ATT.

The immunological dimension is equally important. Chronic TB infection results in dysregulated cytokine responses, particularly TNF-α and IFN-γ, which suppress erythropoietin activity and impair marrow proliferation [8,9]. Furthermore, TB-associated HLH, though rare, represents a life-threatening hyper-inflammatory state characterized by uncontrolled macrophage activation. Rajagopala et al. (2014) systematically reviewed TB-associated HLH, emphasizing its recognition in cases of fever with pancytopenia and hepatosplenomegaly [8]. One of our patients manifested TB-associated HLH and improved with adjunctive steroids along with ATT, consistent with reported cases [12].

Our series also highlights the unique case of a girl with Turner syndrome–like phenotype due to ovarian TB. Reports have described ovarian tuberculosis mimicking ovarian malignancy and causing reproductive dysfunction in adolescents [6,7]. In our case, ovarian involvement led to growth retardation and Turner-like features, but recovery after ATT and nutritional support confirmed the reversible nature of these manifestations.

Diagnostic Challenges

The major diagnostic challenge lies in differentiating TB-associated pancytopenia from hematological malignancies. In endemic settings, high suspicion for TB is essential when pancytopenia is accompanied by organomegaly, chronic symptoms, nutritional deficiencies and suggestive imaging. Bone marrow biopsy remains invaluable, as demonstration of granulomas or positive PCR can establish diagnosis [3,4,12]. Advanced molecular diagnostics, including GeneXpert and TB PCR, improve diagnostic yield.

Therapeutic and Prognostic Considerations

Timely initiation of ATT is crucial and often results in complete hematological recovery within 3–6 months. Correction of micronutrient deficiencies (iron, folate, vitamin B12) is essential for sustained hematological response. In cases of HLH, steroids or immunomodulators may be required alongside ATT. Prognosis is generally favourable with appropriate therapy, as reflected in our patients who demonstrated recovery of blood counts and clinical improvement.

Programmatic Implications

Pediatric TB programs must incorporate hematological evaluation into case management, particularly in

severe or disseminated TB. Strengthening laboratory services for bone marrow studies, PCR-based diagnostics, and nutritional assessment is essential. Raising awareness among pediatricians about pancytopenia as a manifestation of TB can prevent misdiagnosis and unnecessary interventions such as chemotherapy.

Conclusion

Pancytopenia in pediatric TB, though rare, is a significant manifestation of disseminated and severe diseases. The present case series from North India underscores its varied clinical spectrum, including Turner-like phenotypes, nutritional deficiencies, and HLH. Early recognition, appropriate investigations, and timely initiation of ATT, along with nutritional and supportive therapy, are vital for favourable outcomes. A high index of suspicion is warranted in endemic regions to avoid misdiagnosis as hematological malignancies.

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