

Case Report

Tuberculous lymphadenitis presenting with Coombs-negative hemolytic anemia, vasculitic rash: A rare association

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ABSTRACT

Tuberculosis (TB) is a widespread infectious disease that primarily affects the lungs but can manifest in extrapulmonary forms, such as lymphadenitis. The occurrence of severe anemia, direct Coombs test-negative hemolysis, and vasculitic rash in a patient with tuberculous lymphadenitis is an uncommon and challenging clinical scenario. We report the case of a 21-year-old male presenting with scattered petechiae, lower limb swelling, and fatigue, ultimately diagnosed with tuberculous lymphadenitis. This case report highlights the importance of considering TB in atypical presentations to ensure timely diagnosis and treatment.

Keywords: Coombs negative, Hemolytic anemia, Lymphadenitis, Tuberculosis

INTRODUCTION

Tuberculosis (TB) continues to be a significant global health concern, affecting millions annually, with extrapulmonary TB accounting for 15–20% of TB cases.^[1] Tuberculous lymphadenitis, the most common form of extrapulmonary TB, is often characterized by insidious onset and non-specific symptoms such as lymph node enlargement, fever, or weight loss.^[2] Rarely, TB presents with atypical systemic manifestations, such as hemolytic anemia or vasculitic rash, which complicate the diagnostic process. Hemolytic anemia in TB is typically associated with immune mechanisms, including direct Coombs test (DCT)-positive hemolysis; however, DCT-negative hemolysis remains exceedingly rare and poorly understood.^[3] Vasculitic rashes in TB are hypothesized to result from hypersensitivity reactions or immune complex deposition, adding another layer of diagnostic challenge.^[4] Here, we present a rare case of tuberculous lymphadenitis in a young immunocompetent patient, manifesting with DCT-negative hemolytic anemia and petechiae, underscoring the diverse and atypical presentations of TB.

CASE REPORT

A patient in their 20s presented to the emergency department with complaints of scattered petechiae over their extremities and face, bilateral lower limb swelling, and generalized fatigue for the past 2 weeks. The patient denied any history

of chronic illness, prior hospitalizations, or similar symptoms in the past.

On examination, the patient appeared pale and icteric, with scattered petechiae over the extremities and face. There was bilateral pitting lower limb edema. There was no significant hepatosplenomegaly. Examination of the neck revealed palpable bilateral cervical lymphadenopathy.

The patient presented with severe anemia (hemoglobin [Hb] 3.5 g/dL on day 1) and mild thrombocytopenia, with a normocytic normochromic anemia. Neutrophilia and lymphopenia were noted (Neutrophils: 72.3% and lymphocytes: 19% on day 1). Biochemical parameters [Table 1] revealed hyperbilirubinemia, predominantly unconjugated (Bilirubin: 3.1 mg/dL and unconjugated: 2.7 mg/dL on day 1). Liver enzymes were elevated, with a notable rise in serum glutamate pyruvate transaminase (alanine aminotransferase: 267 U/L on day 15), serum glutamic-oxaloacetic transaminase (aspartate aminotransferase: 136 U/L on day 15), and gamma-glutamyl transferase (159 U/L). Serum albumin levels were reduced (2.8 g/dL on day 1), consistent with systemic inflammation or chronic disease. Electrolytes showed hyponatremia (Sodium: 123 mmol/L), with potassium and chloride levels within normal limits. Serum electrolytes were corrected. Renal function was preserved. Creatinine: 1.0 mg/dL on day 1, and serum ferritin was within range -198 ng/

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Table 1: Investigations.

Tests	Day 1	Day 5	Day 20	Follow-up after 2 weeks	Reference values
Hemoglobin (g/dL)	3.5	5.6	9.6	11	13.0–17.0
WBC (/cumm)	4400	3500	5700	4500	4,000–11,000
Neutrophils (%)	72.3	76.9	79.8	70	44–68
Lymphocytes (%)	19.0	16.7	10	20	25.0–48.0
Platelet (10 ³ /uL)	229	150	234	255	150–400
Bilirubin (mg/dL)	3.1		2.8	1.4	0.2–1.3
Conjugated bilirubin (mg/dL)	0.00		1.00	0.40	0.00–0.30
Unconjugated bilirubin (mg/dL)	2.70		1.70	1.00	0.00–1.10
SGOT (AST) (U/L)	28		136	60	17–59
SGPT (ALT) (U/L)	33		267	45	4–50
Alkaline phosphatase (U/L)	54		218	134	38–126
GGT (U/L)	22		159	90	15–73
Total protein (g/dL)	6.10		7.5	8.0	6.30–8.20
Albumin (g/dL)	2.80		3.3	4.0	3.50–5.00
Creatinine (mg/dL)	1.0			1.2	0.8–1.5
Serum sodium (mmol/L)	123			134	137–145
Serum potassium (mmol/L)	3.6			3.7	3.5–5.1
Serum chloride (mmol/L)	95			99	98–107

WBC: White blood cells, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, GGT: Gamma-glutamyl transferase

dL, though serum iron -16 µg/dL (49–181 µg/dL) and total iron binding capacity (TIBC) -241 µg/dL (261–462 µg/dL). Fecal occult blood was negative. Coagulation studies revealed a prolonged prothrombin time (PT)-18.5 s (Ref 11–16 s), elevated international normalized ratio (INR)-1.59 (Ref 1.0–1.3), and normal partial thromboplastin time (PTT), which we believe are due to underlying liver dysfunction. Direct and indirect Coombs tests performed using glass bead technology were also negative. Peripheral blood smear demonstrated reticulocytosis (corrected reticulocyte count: 5.3%; ref 0.5–2.5%) without spherocytes, which are characteristic of warm autoimmune hemolytic anemia. The absence of spherocytes, together with a negative Coombs test, suggests that the findings are more consistent with low-grade hemolysis likely masked by concurrent anemia of chronic disease. Hemolytic anemia was suggested based on laboratory findings, including elevated lactate dehydrogenase (LDH), indirect bilirubin, and reticulocyte count. No hemoparasites were identified. Serologies for viral hepatitis, dengue, malaria, autoimmune markers (anti nuclear antigen [ANA], anti neutrophil cytoplasmic antibodies [ANCA], Anti mitochondrial antibody [AMA], anti smooth muscle antibody [ASMA], and anti-liver kidney muscle-1 [LKM-1]), Epstein-Barr virus, and HIV were negative. Pleural fluid analysis findings are summarized in Table 2.

The pleural fluid analysis demonstrated turbid fluid, straw-colored suggesting high protein content and cellular

Table 2: Pleural fluid findings.

Test	Patient's value	Reference value
Appearance	Turbid	Clear, straw-colored
Protein	7.0 g/dL	<1.5 g/dL
Lactate dehydrogenase	2149 U/L	30–140 U/L
Glucose	32 mg/dL	Similar to plasma glucose levels
White blood cell count	200 cells/cumm	0–150 cells/cumm

presence. Protein levels were elevated at 7.0 g/dL consistent with an exudative process. LDH was increased at 2149 U/L. Glucose was markedly low at 32 mg/dL, reflecting high metabolic activity from infection. The white blood cell count was elevated at 200 cells/cumm (reference: 0–150 cells/cumm), further supporting the presence of an inflammatory or infectious process. Hemoglobin electrophoresis and G6PD levels were normal. Urinalysis showed the presence of RBCs and protein. Imaging studies included a neck ultrasound, which revealed multiple enlarged cervical lymph nodes, and an abdominal ultrasound, which identified gallbladder sludge but no gallstones in the cystic duct. A contrast-enhanced computed tomography of the chest demonstrated a loculated right pleural effusion [Figure 1]. Histopathological examination of the cervical lymph node biopsy showed caseating granulomatous lymphadenitis with necrosis [Figure 2] and granulomas composed of epithelioid cells and

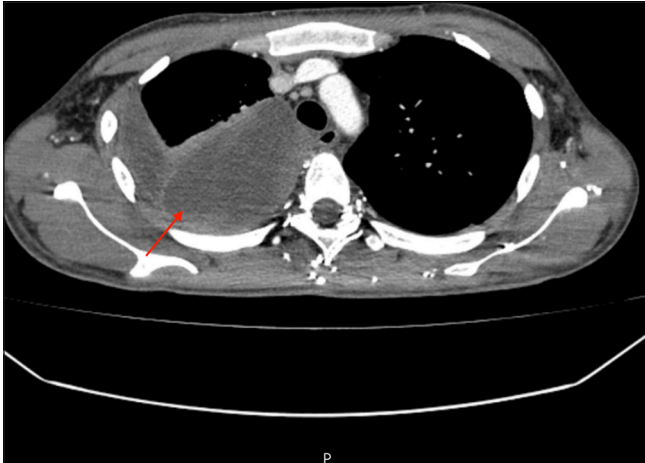


Figure 1: High-resolution computed tomography chest showing loculated pleural effusion (red arrow).

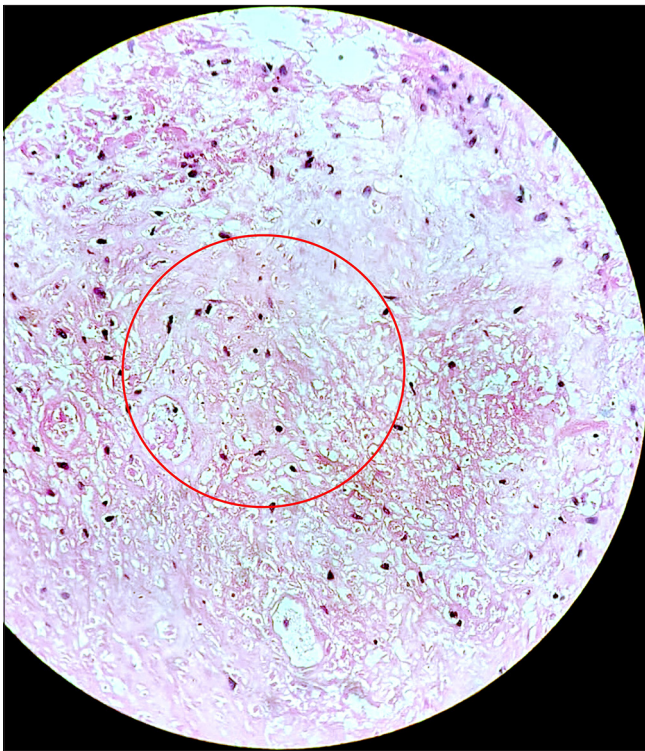


Figure 2: Histopathology of lymph node showing caseous necrosis (red circle). Stain- Hematoxylin and Eosin (H&E); Magnification-100x

lymphocytes [Figure 3]. While acid-fast bacilli were not seen on Ziehl–Neelsen staining, TB-polymerase chain reaction of the lymph node confirmed a diagnosis of TB.

Clinical course

The patient was initially treated with packed red blood cells (PRBC) transfusions to stabilize their Hb. Methylprednisolone was administered to control hemolysis

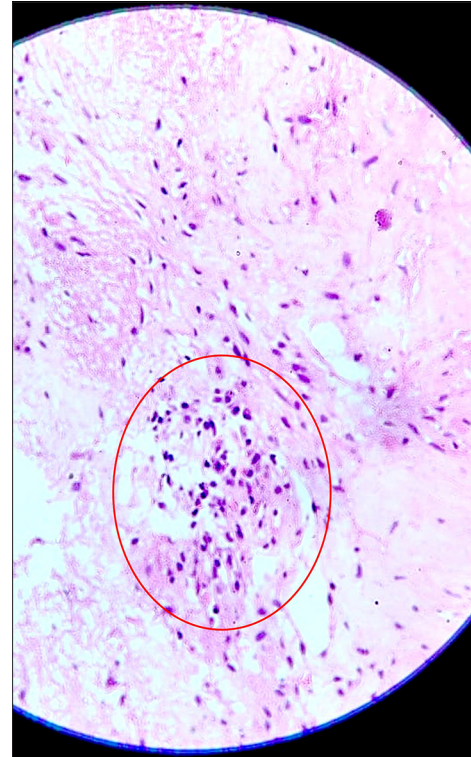


Figure 3: Histopathology of lymph node showing granuloma formation (red circle). Stain- Hematoxylin and Eosin (H&E); Magnification- 100x

and the vasculitic rash. Vitamin D deficiency was corrected with calcitriol. Modified anti-TB therapy (ATT) for liver function was started with ethambutol, levofloxacin, and streptomycin. The cause for elevated liver enzymes was attributed to gallbladder sludge, causing cholestasis.

Over the course of treatment, the patient's hemoglobin has increased, indirect bilirubin has decreased, and the reticulocyte count has normalized, suggestive of resolving hemolysis and response to steroid therapy. Petechiae and lower limb swelling subsided, and pleural effusion showed significant regression. DCT remained persistently negative throughout.

DISCUSSION

Tuberculous (TB) lymphadenitis is the most common extrapulmonary form, often presenting with painless lymphadenopathy.^[5] The immune dysregulation associated with TB can trigger rare hematological manifestations. Anemia affects around 16–94% of TB patients, which could be due to either anemia of chronic disease, vitamin deficiencies, hemolytic anemia, and bone marrow involvement.^[6] Autoimmune hemolytic anemia (AIHA) is a rare manifestation of TB, and Coombs-negative hemolytic anemia is seen in around 5–10% of patients with AIHA.^[7] The causes of Coombs'-negative DCT could be immunoglobulin

G (IgG) levels below the threshold of detection of low affinity of IgG.^[8] Hemolysis may also result from cytokine-mediated destruction. Persistent systemic inflammation promotes oxidative damage to red blood cells, leading to their destruction independently of antibody-mediated pathways.^[9] The underlying iron deficiency combined with anemia of chronic inflammation may have precipitated the severe anemia due to hemolysis in our patient.

Vasculitic rash is another rare TB manifestation, likely caused by immune complex deposition in small vessels.^[10] Our patient presented with palpable purpura affecting the legs, and face. A recent study from Korea has found an increased risk of systemic vasculitis in extrapulmonary TB (adjusted hazards ratio 4.28, 95% confidence interval 3.52–5.21).^[11]

Standard ATT is effective for tuberculous lymphadenitis and its associated manifestations.^[12] The use of corticosteroids in cases with immune-mediated complications, such as hemolytic anemia and vasculitis, may provide additional benefit. Corticosteroids were previously shown to be beneficial in reducing mortality in tuberculous meningitis.^[13] However, it is not clear if corticosteroids are beneficial for TB-induced vasculitis.

Our patient was started on modified ATT with levofloxacin 750 mg once daily, ethambutol 800 mg once daily, and streptomycin 0.75 mg I.M. once a day due to the underlying cholestasis and elevated liver enzymes. Over 2 weeks, liver function and coagulation studies improved. Streptomycin was discontinued, and rifampicin, isoniazid, and pyrazinamide were introduced on a follow-up visit.

Our patient showed significant improvement in a vasculitic rash after initiating methylprednisolone, which was administered intravenously at 40 mg and gradually tapered down over 2 weeks. On follow-up in the outpatient department after 2 weeks of prednisolone therapy at 20 mg once daily and anti-tubercular therapy, the patient reported improvement in rash. The patient also reported significant improvement in fatigue and weight gain, with no symptoms of fever. The prednisolone was further tapered down over the next 2 weeks to 5 mg once daily.

CONCLUSION

This case highlights the rare presentation of tuberculous lymphadenitis with DCT-negative hemolytic anemia and vasculitic rash. A clinical vigilance and thorough diagnostic approach were critical in confirming the diagnosis. Early initiation of ATT and supportive care, including corticosteroids, led to a favorable outcome.

Further studies are required to identify the etiology of tuberculous-induced cutaneous vasculitis, Coombs' negative hemolytic anemia, and the role of corticosteroids in TB vasculitis.

Ethical approval: Institutional Review Board approval is not required.

Declaration of patient consent: The authors certify that they have

obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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