Case Report

Unraveling sickle cell anemia with widespread lymphadenopathy

S M Preetham[1], G Balachandra[2], Sumedha Swamy[3]

From [1]Post Graduate, [2]Head, [3]Assistant Professor, Department of General Medicine, ESIC MC and PGIMSR, Bengaluru, Karnataka, India

ABSTRACT

Tuberculosis (TB) remains highly prevalent in India, with extrapulmonary forms comprising 15–20% of cases. Among these, tuberculous lymphadenitis is the most frequent manifestation. Sickle cell disease (SCD) predisposes patients to infections due to functional asplenia and impaired immune responses. The coexistence of TB and SCD presents diagnostic and therapeutic challenges. We report the case of a 25-year-old female with known SCD, status-post allogeneic hematopoietic stem cell transplant, who presented with progressive right cervical lymphadenopathy evolving over 10 months. She later developed a fever and productive cough. Clinical examination revealed multiple cervical lymph nodes and mild hepatomegaly. Imaging and biopsy confirmed necrotizing granulomatous lymphadenitis with acid–fast bacilli, establishing the diagnosis of tuberculous lymphadenitis. The patient was initiated on first-line anti-tubercular therapy with isoniazid, rifampicin, pyrazinamide, and ethambutol at standard weight-based doses. She demonstrated symptomatic improvement and regression of lymphadenopathy on follow-up. This case highlights the atypical and often indolent presentation of TB in SCD patients. The overlap of two geographically co-endemic diseases may contribute to underdiagnosis. Awareness of this association and early consideration of TB in the differential diagnosis of chronic lymphadenopathy in SCD is essential. Tuberculous lymphadenitis should be strongly suspected in immunocompromised patients with SCD presenting with persistent lymphadenopathy. Early diagnosis and treatment can prevent morbidity and misdiagnosis.

Key words: Case report, Extrapulmonary tuberculosis, Immunocompromised host, Sickle cell disease, Tuberculous lymphadenitis

Tuberculosis (TB) continues to be a major public health problem in India, accounting for nearly one-quarter of the global burden of disease. According to the World Health Organization, extrapulmonary TB constitutes approximately 15–20% of all TB cases, with tuberculous lymphadenitis being the most common form, representing about 30–40% of extrapulmonary presentations [1,2]. Cervical lymph nodes are the most frequently affected sites, particularly in young adults and women.

Sickle cell disease (SCD) is one of the most common inherited hemoglobinopathies, characterized by recurrent vaso-occlusive crises, hemolytic anemia, and progressive multi-organ involvement. Functional asplenia and defects in both innate and adaptive immunity predispose these patients to severe infections [3]. The geographic overlap of SCD prevalence with TB-endemic regions increases the likelihood of co-existence.

Although TB is commonly encountered in clinical practice, its manifestation in patients with SCD is often atypical. Instead of the classical pulmonary involvement, extrapulmonary TB, such as tuberculous lymphadenitis, is more frequently observed, which may contribute to underdiagnosis [4,5].

Access this article online	
Received - 07 July 2025 Initial Review - 23 July 2025 Accepted - 13 October 2025	Quick Response code
DOI: ***	

CASE PRESENTATION

A 25-year-old woman, known case of SCD diagnosed at the age of 12 years, presented with a history of a progressively enlarging swelling in the right side of the neck. The swelling initially appeared as a pea-sized nodule approximately 10 months before presentation and gradually increased in size to about 5 × 5 cm. Over the subsequent months, additional swellings developed in the right cervical region, as well as the right axilla. Three days before admission, she developed a fever associated with a productive cough. Her past medical history was significant for an allogeneic hematopoietic stem cell transplant performed in December 2016 and osteonecrosis of the right hip and knee joint secondary to SCD. She was not on any immunosuppressive medications at the time of presentation. There was no

Correspondence to: S M Preetham, Room No 304 PG Boys Hostel 2 BHK, ESIC MC and PGIMSR, Rajajinagar, Bengaluru - 560010, Karnataka, India. E-mail: preetham.sm@gmail.com

history of weight loss, night sweats, or contact with a patient with pulmonary TB.

On general physical examination, she was febrile (temperature 38.3°C), pulse rate was 98 beats/min, blood pressure was 108/70 mmHg, respiratory rate was 20 breaths/min, and oxygen saturation was 97% on room air. She was mildly pale, but there was no icterus, cyanosis, clubbing, or pedal edema. Local examination revealed multiple enlarged, discrete cervical lymph nodes, more pronounced on the right side. The nodes were firm, rubbery in consistency, and non-tender. Right axillary lymphadenopathy was also noted. Systemic examination revealed mild hepatomegaly on abdominal palpation. Cardiovascular and respiratory examinations were unremarkable.

Initial laboratory investigations showed a hemoglobin level of 9.6 g/dL, leukocyte count of 8,900/µL, and platelet count of 2.4×10^5/µL. Erythrocyte sedimentation rate (ESR) was markedly elevated at 100 mm/h, and C-reactive protein was positive. Ultrasound of the abdomen confirmed hepatomegaly with evidence of asplenia. Ultrasonography of the neck revealed multiple enlarged lymph nodes. The Mantoux test was positive with an induration of 15 mm.

The patient was initially managed as a case of lower respiratory tract infection and received empirical first-line intravenous antibiotics. However, sputum smear microscopy for acid–fast bacilli (AFB) and cartridge-based nucleic acid amplification test (CBNAAT) were both negative. Given persistent symptoms and high ESR, further evaluation was undertaken. A positron emission tomography-computed tomography scan revealed metabolically active cervical lymph nodes more consistent with TB than lymphoma. Cervical lymph node biopsy was performed, which showed necrotizing granulomatous lymphadenitis. Staining for AFB was positive, although CBNAAT was negative. These findings confirmed a diagnosis of tuberculous lymphadenitis.

After confirmation of tuberculous lymphadenitis, the patient was initiated on standard first-line anti-tubercular therapy (ATT) under the National TB Elimination Program guidelines [6]. The regimen included isoniazid (5 mg/kg/day), rifampicin (10 mg/kg/day), pyrazinamide (25 mg/kg/day), and ethambutol (15 mg/kg/day). This intensive phase (HRZE) was planned for 2 months, followed by a continuation phase with isoniazid, rifampicin, and ethambutol (HRE) for 4 months, making a total treatment duration of 6 months. Supportive care included adequate hydration, nutritional supplementation, folic acid, and monitoring of liver function tests, given the hepatotoxic potential of ATT. The patient was counseled about adherence, possible side effects, and the importance of regular follow-up.

At the end of 2 months, she reported marked improvement in systemic symptoms with complete resolution of fever and cough. Cervical lymph nodes had significantly regressed in size on clinical examination. Liver function tests remained within normal limits. She is currently continuing on the continuation phase of ATT and is being monitored monthly.

DISCUSSION

SCD is associated with profound immune dysfunction that predisposes patients to infections. Functional asplenia, which develops in the majority of patients by adolescence due to repeated splenic infarctions, results in impaired clearance of encapsulated organisms and reduced splenic opsonization capacity [5]. In addition, abnormalities in complement activation, reduced memory B cell function, and impaired T cell–independent antibody production further compromise both innate and adaptive immunity [3]. These immunological defects, combined with frequent transfusions and possible post-transplant immunosuppression, increase the vulnerability of SCD patients to infectious diseases, including TB.

TB remains endemic in India, with extrapulmonary forms comprising 15–20% of all cases [1]. Tuberculous lymphadenitis is the most common extrapulmonary manifestation, representing approximately one-third of these cases [2,4]. In SCD patients, TB often presents atypically as indolent extrapulmonary disease rather than classic pulmonary involvement. This diagnostic challenge may contribute to underdiagnosis and treatment delays [6].

Jha *et al*. reported that cervical tuberculous lymphadenitis accounted for 63.8% of lymph node TB cases in their series from Chandigarh [4]. Okar *et al*. described a patient with SCD who developed active pulmonary TB, highlighting the risk of TB in this population [7]. More recently, Arliny *et al*. reported tuberculous lymphadenitis in a young woman with systemic lupus erythematosus, another immunocompromised state, underscoring the predisposition of such patients to extrapulmonary TB [8].

CONCLUSION

This case emphasizes the importance of recognizing TB as a significant cause of chronic lymphadenopathy in patients with SCD. The immunocompromised state associated with functional asplenia and defective immune responses in SCD increases susceptibility to extrapulmonary TB, which often presents in an indolent manner. Early consideration of TB in the differential diagnosis, timely use of imaging and histopathological evaluation, and prompt initiation of ATT are crucial to ensure favorable outcomes. Reporting such cases adds to the clinical understanding of overlapping endemic conditions and highlights the need for heightened clinical suspicion in similar scenarios.

REFERENCES

1. Sharma SK, Mohan A. Extrapulmonary tuberculosis. Indian J Med Res 2004;120:316-53.

2. Golden MP, Vikram HR. Extrapulmonary tuberculosis: An overview. Am Fam Physician 2005;72:1761-8.
3. Booth C, Inusa B, Obaro SK. Infection in sickle cell disease: A review. Int J Infect Dis 2010;14:e2-12.
4. Jha BC, Dass A, Nagarkar NM, Gupta R, Singhal S. Cervical tuberculous lymphadenopathy: Changing clinical pattern and concepts in management. Postgrad Med J 2001;77:185-7.
5. Pearson HA, Spencer RP, Cornelius EA. Functional asplenia in sickle-cell anemia. N Engl J Med 1969;281:923-6.
6. Dasgupta S, Chakrabarti S, Sarkar S. Shifting trend of tubercular lymphadenitis over a decade-a study from eastern region of India. Biomed J 2017;40:284-9.
7. Okar L, Rezek M, Abdelhamid MT, Yassin MA. Case report of active pulmonary TB in a sickle cell disease patient. Ann Med Surg (Lond) 2021;72:103073.
8. Arliny Y, Yanifitri DB, Utami WA, Geraldine S. Case report: Tuberculosis lymphadenitis with systemic lupus erythematosus in a young woman: A case report. F1000Res 2023;12:763.

Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Preetham SM, Balachandra G, Swamy S. Unraveling sickle cell anemia with widespread lymphadenopathy. Indian J Case Reports. 2025; October 21 [Epub ahead of print].