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Disseminated tuberculosis in adolescent systemic lupus erythematosus after negative baseline screening: a case report

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Case Report

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Abstract

Background

Patients with systemic lupus erythematosus (SLE) are at increased risk of tuberculosis (TB) because of disease-related immune dysregulation and prolonged immunosuppressive therapy. Screening for latent TB infection (LTBI) before initiating immunosuppression is recommended, although both the tuberculin skin test (TST) and interferon-gamma release assays (IGRAs) may yield false-negative results in immunocompromised individuals.

Case presentation

A 15-year-old girl with SLE complicated by lupus nephritis presented with fever, progressive dyspnoea, and abdominal pain after approximately eight months of corticosteroid and mycophenolate mofetil (MMF) therapy. Baseline TB screening before immunosuppressive treatment consisted of chest radiography and TST, with a TST induration of 0 mm. IGRA was not performed. During admission, chest radiography demonstrated diffuse miliary nodules with pleural effusion. Laboratory examination showed pancytopenia and markedly elevated transaminases. Repeat TST showed 15 mm induration. GeneXpert MTB/RIF detected rifampicin-susceptible Mycobacterium tuberculosis in sputum, stool, and urine specimens, confirming disseminated TB involving pulmonary, abdominal, and genitourinary systems. Because of severe transaminase elevation, hepatotoxic first-line anti-TB agents were initially deferred, and treatment was started with levofloxacin and ethambutol.

Conclusion

This case demonstrates that negative baseline TST does not exclude LTBI or future TB disease in immunosuppressed patients living in TB-endemic regions. Pre-immunosuppression evaluation should combine clinical risk assessment, chest imaging, and immune-based testing according to national and international recommendations. In high-risk patients requiring prolonged immunosuppression, repeat TB evaluation and consideration of preventive therapy may be warranted despite negative baseline screening.

BACKGROUND

Tuberculosis (TB) remains one of the leading causes of death from a single infectious agent. The World Health Organization (WHO) estimated 10.8 million incident TB cases and 1.25 million TB-related deaths in 2023 [1]. Although pulmonary TB is the most frequent presentation, extrapulmonary TB (EPTB) and disseminated TB are more frequently encountered in children and immunocompromised individuals [2].

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by multisystem inflammation, autoantibody production, and immune dysregulation. Infections remain a major cause of morbidity and mortality in SLE, reflecting both intrinsic immune abnormalities (e.g., complement dysfunction, altered innate immunity, and impaired cellular immunity) and treatment-related immunosuppression [3,4]. In TB-endemic settings, the risk of TB is further amplified in SLE patients receiving prolonged or high-dose corticosteroids and other immunosuppressive agents. [5].

Current recommendations emphasize the importance of latent TB infection (LTBI) screening before initiating prolonged immunosuppressive therapy. Evaluation generally includes clinical risk assessment, chest imaging, and immune-based testing using TST and/or IGRA [6]. However, false-negative results may occur in immunocompromised patients, especially during active immune suppression.

This case is notable because disseminated TB involving pulmonary, abdominal, and genitourinary systems developed in an adolescent with SLE despite negative baseline TST screening prior to prolonged immunosuppressive therapy in a TB-endemic setting.

CASE PRESENTATION

A 15-year-old girl with SLE and lupus nephritis was admitted with progressive dyspnoea, persistent fever, and abdominal pain of two weeks' duration. She appeared generally weak but was conscious and alert. At initial SLE diagnosis, the patient presented with weakness, headache, facial rash, and secondary hypertension. Antinuclear antibody (ANA) testing was positive, and SLE was classified according to the 2019 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) criteria with a score greater than 10. Lupus nephritis was clinically suspected, although renal biopsy had not yet been performed for classification and treatment response evaluation. Induction treatment consisted of methylprednisolone and MMF followed by continuation therapy in the outpatient setting. Before initiation of immunosuppressive therapy, TB screening consisted of chest radiography and TST. The chest radiograph showed no evidence of active or previous TB, and TST induration was 0 mm. IGRA was unavailable and therefore not performed.

At current admission, the patient appeared weak but remained fully conscious. Vital signs showed blood pressure 150/90 mmHg, pulse rate 84 beats/min, respiratory rate 30 breaths/min, body temperature 39.2°C, and oxygen saturation 94% on room air, improving to 98% with low-flow oxygen supplementation. Chest examination revealed bilateral crackles. Abdominal examination demonstrated ascites and severe epigastric tenderness. No known household TB contact or prior household TB treatment was reported. Laboratory examination demonstrated pancytopenia and markedly elevated liver enzymes. HIV serology was negative. Repeat TST demonstrated 15 mm induration. Chest radiography revealed diffuse bilateral miliary nodules with pleural effusion, producing a classic "snowstorm" appearance (Fig. 1). Abdominal ultrasonography demonstrated hepatomegaly and ascites. GeneXpert MTB/RIF assay detected rifampicin-susceptible Mycobacterium tuberculosis (M.Tb) in sputum, stool, and urine specimens. Pulmonary and genitourinary TB were microbiologically confirmed, while abdominal involvement was

clinically inferred from ascites, hepatomegaly, systemic dissemination, and concurrent microbiological confirmation from multiple body specimens.

Differential diagnoses initially considered included lupus flare, macrophage activation syndrome, fungal infection, and hematologic malignancy because constitutional symptoms, pancytopenia, and serositis substantially overlapped with disseminated TB manifestations. Because liver transaminases were elevated to more than five times the upper normal limit, hepatotoxic first-line anti-TB agents were temporarily deferred. The patient was initially treated with intravenous levofloxacin 500 mg once daily and oral ethambutol 750 mg once daily while serial liver function monitoring was performed, with a plan to transition to a standard guideline-based regimen once liver enzymes improved and hepatotoxicity risk was reassessed.

Clinical timeline

- Initial SLE diagnosis: approximately 1 year before current admission
- Baseline TB screening before immunosuppression: chest radiograph normal; TST 0 mm
- Immunosuppressive treatment initiated: corticosteroids and mycophenolate mofetil (MMF)
- Prolonged immunosuppressive exposure: approximately 8 months
- Temporary treatment interruption: approximately 1 month because of suboptimal adherence
- Development of respiratory and abdominal symptoms: 2 weeks before admission
- Disseminated TB diagnosis established during hospitalization

DISCUSSION

This report describes disseminated TB involving pulmonary, abdominal, and genitourinary systems in an adolescent with SLE receiving prolonged corticosteroid and MMF therapy despite negative baseline TB screening.

Patients with SLE are highly susceptible to TB because of combined disease-related and treatment-related immune dysfunction. Disease-related mechanisms include complement abnormalities, impaired opsonophagocytosis, dysfunctional macrophage activity, and altered T-cell responses [3,4]. In addition, prolonged corticosteroid exposure and immunosuppressive medications suppress cellular immunity and impair containment of M.Tb. Protective immunity against M. tuberculosis primarily depends on coordinated macrophage activation and Th1-mediated cellular immune responses. Interferon-gamma and tumor necrosis factor-alpha play essential roles in maintaining granuloma integrity and limiting bacillary dissemination [8–10]. In SLE, both intrinsic immune dysregulation and pharmacologic immune suppression impair these protective pathways, increasing the risk of progression from latent infection to active disease.

The patient had a baseline TST induration of 0 mm before immunosuppressive therapy but later demonstrated a positive TST with disseminated TB. Two possibilities may explain this finding. First,

latent TB infection may have been present initially but undetected because of anergy and impaired cellular immunity. Second, new infection may have been acquired during prolonged immune suppression in a TB-endemic environment.

False-negative TST results are well documented in disseminated and miliary TB, especially in patients with corticosteroid exposure, lymphopenia, or severe systemic illness [11]. Therefore, negative TST alone should not be interpreted as excluding TB infection in immunocompromised patients.

Both TST and IGRA evaluate immune sensitization rather than direct microbial presence. TST specificity may be reduced in Bacille Calmette-Guérin (BCG)-vaccinated populations and in individuals exposed to non-tuberculous mycobacteria [12]. IGRA uses M. tuberculosis-specific antigens such as early secreted antigenic target-6 (ESAT-6) and culture filtrate protein-10 (CFP-10) and therefore provides higher specificity than TST [13]. Several studies also suggest that IGRA may demonstrate improved sensitivity in immunocompromised populations, although indeterminate and false-negative results still occur [6,13,14]. Consequently, neither TST nor IGRA should be used in isolation to exclude TB infection in patients receiving prolonged immunosuppressive therapy.

International recommendations in autoimmune inflammatory rheumatic diseases emphasize comprehensive TB risk assessment before initiating biologic agents, targeted therapies, prolonged corticosteroids, or conventional immunosuppressants [6]. Such evaluation generally includes exposure history, chest imaging, and immune-based testing.

In the present case, baseline screening relied solely on chest radiography and a single TST. In a high-burden setting with anticipated prolonged immunosuppressive exposure, a more robust strategy could have included IGRA testing, closer longitudinal reassessment, and consideration of TB preventive therapy when overall clinical risk was high.

Several studies suggest that repeat testing may be useful during prolonged immunosuppressive therapy, particularly in endemic settings where ongoing TB exposure is likely [16–18]. Although serial IGRA interpretation remains challenging because conversions and reversions may occur, repeat evaluation combined with clinical judgement may help identify patients at increased risk.

This case also highlights the importance of maintaining broad differential diagnoses in immunocompromised patients with fever, cytopenia, respiratory symptoms, and abdominal manifestations. Disseminated TB may clinically mimic lupus flare or other opportunistic conditions, potentially delaying diagnosis and treatment.

Overall, this report underscores the need for structured TB risk assessment before and during prolonged immunosuppressive therapy, awareness of false-negative baseline screening, and prompt microbiological evaluation when new systemic symptoms arise in high-risk patients.

CONCLUSION

A negative baseline TST does not exclude latent TB infection or future TB disease in adolescents with SLE receiving prolonged immunosuppressive therapy. TB risk assessment should be performed before initiating high-dose or long-term immunosuppression and should combine clinical risk factors, chest imaging, and immune-based testing (TST and/or IGRA) according to national and international guidance. In TB-endemic settings, repeat testing during prolonged immunosuppression may be considered when ongoing exposure is likely, and TB preventive treatment should be discussed when overall risk is high.

DECLARATIONS

ETHICAL APPROVAL

The studies were approved by Ethics Committee of Dr. Hasan Sadikin General Hospital, Bandung, Indonesia. The studies were conducted in accordance with the local legislation and institutional requirements.

CONSENT FOR PUBLICATION

Written informed consent for participation in this study was provided by the participant's legal guardians/next of kin.

COMPETING INTERESTS

The authors declare that the research was conducted without any commercial or financial relationships that could potentially create a conflict of interest.

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Author Contribution

DASL: data collection, case analysis, manuscript drafting, and revision, project administration. HMN conceived the report, supervised patient management, and critically revised the manuscript. AW, and RG contributed to case analysis, manuscript revision. All authors approved the final manuscript.

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Figures

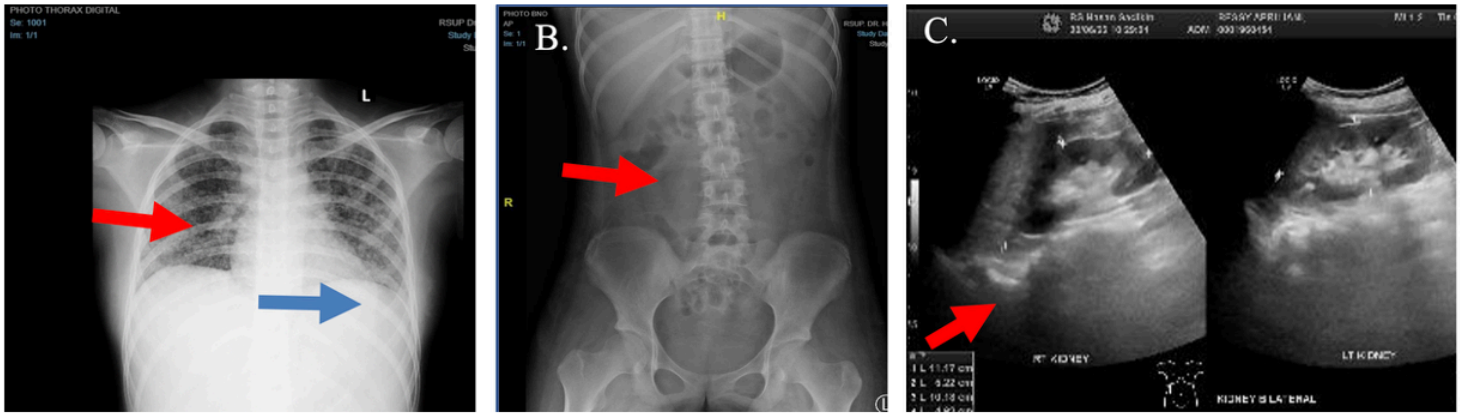


Figure 1

A) Chest radiograph demonstrating a miliary pattern (“snow-storm” appearance) and pleural effusion without cardiac enlargement. B) Lumbosacral radiograph showing mild scoliosis. C) Abdominal ultrasonography showing ascites and hepatomegaly.