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Erythema Multiforme as a Rare Adverse Reaction to First-Line Anti-Tuberculosis Therapy: A Case Report

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Abstract
Cutaneous adverse drug reactions (CADRs) due to anti-tuberculosis therapy (ATT) are uncommon but clinically significant, ranging from mild rashes to severe hypersensitivity reactions. We report the case of a 55-year-old woman diagnosed with pulmonary tuberculosis, initiated on fixed-dose ATT under the National Tuberculosis Elimination Program (NTEP). After one month of therapy, she presented with high-grade fever, generalized rash, dyspnea, and respiratory failure. Skin biopsy confirmed erythema multiforme. The patient improved upon withdrawal of ATT and administration of corticosteroids. Erythema multiforme, though rare, should be considered in patients presenting with systemic symptoms and cutaneous manifestations during ATT. Early recognition and prompt dermatologic evaluation are critical.

Keywords: *Anti-tuberculosis therapy, Erythema multiforme, Cutaneous adverse drug reaction, Skin biopsy, Tuberculosis*

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I. INTRODUCTION

Anti-tuberculosis therapy (ATT), while highly effective, is associated with a spectrum of adverse effects. Cutaneous adverse drug reactions (CADRs) are among the less common but potentially serious complications. Erythema multiforme is a rare manifestation in this context. Early diagnosis and timely withdrawal of the offending agent are key to patient safety. This report highlights a rare presentation of erythema multiforme in a patient receiving first-line ATT.

II. CASE REPORT

A 55-year-old female presented with a 2-month history of productive cough and breathlessness. Sputum smear for acid-fast bacilli was negative; however, bronchial washings tested positive for Mycobacterium tuberculosis via CBNAAT. She was diagnosed with pulmonary tuberculosis and started on a weight-based fixed-dose combination of first-line ATT under NTEP.

After 30 days of therapy, the patient returned with complaints of generalized rash, pruritus, high-grade fever (102°F), weakness, and worsening dyspnea. Oxygen saturation on room air was 88%. Laboratory evaluation showed a markedly elevated total leukocyte count (21,000/mm³), with normal liver function tests. Renal function was impaired, with serum urea at 67 mg/dL and creatinine at 2.5 mg/dL. She had not received any medications other than ATT.

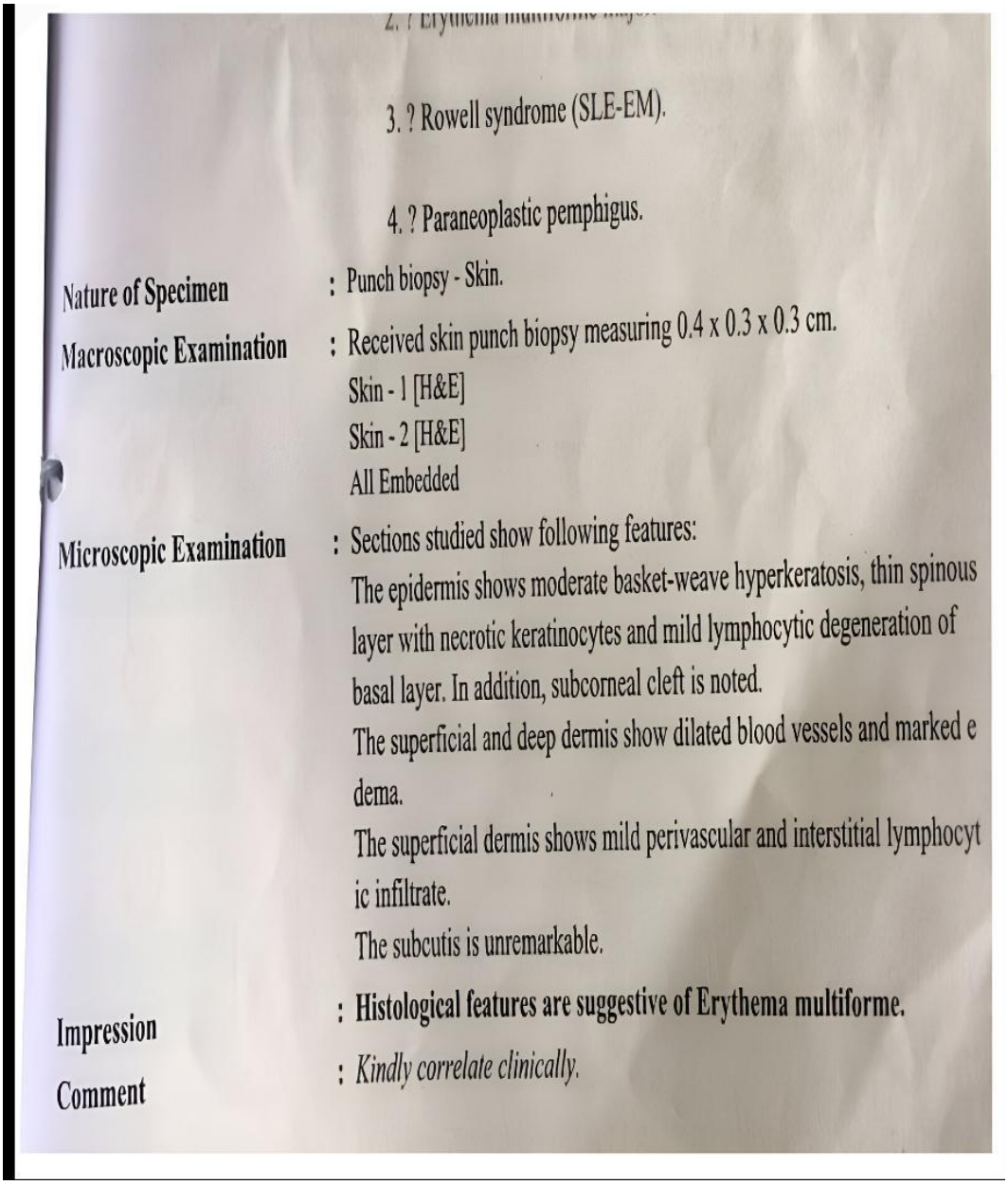
ATT was withheld, and dermatologic consultation was obtained. Skin examination revealed erythematous eruptions over the hands, legs, back, and face. A 4mm punch biopsy of the lesions confirmed the diagnosis of erythema multiforme. The patient received supportive treatment including oxygen therapy and corticosteroids. Over the next two weeks, her symptoms resolved, and oxygen saturation returned to normal.

Although a stepwise drug rechallenge is standard in confirmed TB cases to identify the offending agent, the patient and her family declined this approach. As such, the specific drug responsible for the reaction could not be determined.

III. FIGURES

Figure 1: Erythematous and hyperpigmented macular lesions over the lower limbs.

Figure 2: Close-up view showing extensive bilateral involvement of lower limbs.



2. ? Erythema multiforme major.

3. ? Rowell syndrome (SLE-EM).

4. ? Paraneoplastic pemphigus.

Nature of Specimen : Punch biopsy - Skin.

Macroscopic Examination : Received skin punch biopsy measuring 0.4 x 0.3 x 0.3 cm.
Skin - 1 [H&E]
Skin - 2 [H&E]
All Embedded

Microscopic Examination : Sections studied show following features:
The epidermis shows moderate basket-weave hyperkeratosis, thin spinous layer with necrotic keratinocytes and mild lymphocytic degeneration of basal layer. In addition, subcorneal cleft is noted.
The superficial and deep dermis show dilated blood vessels and marked e dema.
The superficial dermis shows mild perivascular and interstitial lymphocyt ic infiltrate.
The subcutis is unremarkable.

Impression : **Histological features are suggestive of Erythema multiforme.**

Comment : *Kindly correlate clinically.*

Figure 3: Histopathology report showing features consistent with erythema multiforme.

Figure 4: Generalized skin lesions involving the upper limbs and trunk.

IV. DISCUSSION

Erythema multiforme is an immune-mediated skin condition, often triggered by infections or drugs. While ATT-induced CADRs are well documented, erythema multiforme remains a rare occurrence. The typical onset is within 72 hours of exposure, but in this case, symptoms appeared after three weeks, a finding also observed in previous reports.

Common dermatologic reactions to ATT include maculopapular rash, pruritus, and flushing. Skin biopsy remains the gold standard for confirmation. Our patient responded well to ATT cessation and steroid therapy, supporting the diagnosis.

Previous literature, including a report by Sameer Gulati et al., has documented pyrazinamide as a culprit in similar cases. However, without drug rechallenge, causality remains presumptive.

V. CONCLUSION

This case underscores the importance of vigilance in monitoring ATT patients for rare but potentially severe cutaneous adverse reactions. Prompt dermatological referral and biopsy can expedite diagnosis and management. Rechallenge remains essential for drug identification but requires patient consent and clinical stability.

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