

RESEARCH PAPER

Anti-Tubercular Therapy-Induced Lichenoid Drug Eruption: A Case Report with Structured Drug Causality Assessment and Sequential Rechallenge

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Abstract

Lichenoid drug eruption is a delayed T-lymphocyte-mediated cutaneous hypersensitivity reaction producing flat-topped violaceous papules resembling idiopathic lichen planus. We report a 65-year-old woman with sputum-positive pulmonary tuberculosis, type 2 diabetes mellitus (haemoglobin A1c 8.5%), and hypothyroidism who developed generalised pruritus, xerosis, exfoliation, hyperpigmented papules and plaques, and oral mucosal ulcers approximately eight weeks after commencing isoniazid, rifampicin (R-Cin 450 mg), pyrazinamide, and ethambutol. A dermatologist formally recorded the diagnosis as lichenoid drug eruption secondary to anti-tubercular therapy. The clinical pharmacist applied two validated causality instruments: the Naranjo Algorithm yielded a score of 6 (Probable adverse drug reaction) and the WHO-Uppsala Monitoring Centre scale classified isoniazid and rifampicin as Probable causative agents. Isoniazid was identified as the primary offending drug based on temporal onset, rechallenge-provoked systemic reaction, and published precedent; rifampicin was contributory. Anti-tubercular therapy was suspended, second-line bridge coverage with levofloxacin and streptomycin was initiated, and supervised sequential rechallenge safely restored tuberculosis pharmacotherapy. Cutaneous improvement was documented photographically. This case demonstrates the pharmacist's essential contribution to structured adverse drug reaction identification, dual-tool causality documentation, and rechallenge-based management that preserved tuberculosis treatment continuity.

Keywords: Anti-tubercular therapy; Drug causality assessment; Lichenoid drug eruption; Naranjo algorithm; Pharmacovigilance; Sequential rechallenge

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INTRODUCTION

Lichenoid drug eruption (LDE) is a T-cell-mediated type IV hypersensitivity reaction at the dermo-epidermal junction, producing pruritic flat-topped papules resembling idiopathic lichen planus. Key distinguishing features include larger coalescent lesions, absent Wickham's striae, and improvement following drug withdrawal.¹

Anti-tubercular therapy (ATT) is a recognised but underreported pharmacological trigger of LDE. Cutaneous adverse events affect 2 to 8% of ATT recipients, with lichenoid reactions comprising fewer than 10% of these.⁵ All four first-line agents — isoniazid, rifampicin, pyrazinamide, and ethambutol — carry individual case-level evidence of causation, making agent attribution within a multi-drug regimen

challenging.^{2,3}

Permanent ATT withdrawal risks treatment failure, multidrug-resistant tuberculosis emergence, and increased mortality.⁴ The pharmacist's role in identifying ATT-induced adverse reactions, applying validated causality tools, and supporting sequential rechallenge protocols is central to maintaining safe tuberculosis treatment continuity. This case documents such a pharmacist-led intervention in a patient with ATT-induced LDE and significant metabolic comorbidities.

CASE REPORT

S.G., a 65-year-old woman weighing 44 kg, presented in February 2026 with sputum-positive pulmonary

tuberculosis (Koch's smear positive). She had type 2 diabetes mellitus of four years' duration (haemoglobin A1c 8.5%) and hypothyroidism for approximately two decades. No prior dermatological disease, atopy, or drug allergy was documented. Chest radiography (07 April 2026, Figure 1) demonstrated bilateral lower zone opacities consistent with active pulmonary tuberculosis. Intensive-phase ATT was commenced on 14 February 2026: isoniazid, rifampicin (R-Cin 450 mg, Lupin Ltd, Batch AB03172), pyrazinamide, and ethambutol as a fixed three-tablet daily combination per RNTEP guidelines.

Within two weeks (28 February 2026), generalised pruritus emerged temporally associated with ATT. All ATT was withheld; ethambutol 800 mg daily was retained as the sole continuing agent. On 3 April 2026, isoniazid 300 mg was reintroduced; jaundice-like systemic symptoms developed and isoniazid was immediately withdrawn. Rifampicin 450 mg was then introduced. By 24 April 2026, a florid cutaneous eruption with bilateral pitting pedal oedema and facial swelling had developed, necessitating hospital admission.

Dermatological assessment on 28 April 2026 revealed generalised xerosis, diffuse exfoliation, and confluent hyperpigmented papules and plaques over the back and

abdomen (Figure 2), with oral mucosal ulceration. The dermatologist formally recorded the diagnosis as "Lichenoid Drug Eruption secondary to ATT and Scabies." Scabies was empirically treated; however, bilateral symmetrical lichenoid morphology and temporal ATT correlation support ATT-induced LDE as the primary aetiology. Skin biopsy was not obtained owing to hypoalbuminaemia and the imperative of concurrent tuberculosis management — an acknowledged limitation. Admission observations: heart rate 106 beats/min, blood pressure 110/70 mmHg, GCS 15/15.

All ATT was formally suspended from 7 April 2026. Management comprised liquid paraffin emollient, topical corticosteroid (Clonate F cream), oral cetirizine, prednisolone 10 mg daily, scabicide therapy, and albumin transfusion. Levofloxacin 500 mg intravenous and streptomycin 500 mg intramuscular daily were commenced on 3 May 2026 as second-line bridge coverage. Isoniazid was reintroduced from 28 April 2026 at 150 mg, uptitrated to 300 mg; rifampicin 400 mg was introduced on 13 May 2026 under monitoring; pyrazinamide 750 mg was added on 21 May 2026. Progressive cutaneous improvement was documented photographically. The chronological timeline is presented in Table 1.

Table 1: Chronological Timeline of Clinical Events and Management

Date	Clinical Event / Management Action
14 Feb 2026	Intensive-phase HRZE ATT commenced. Weight 44 kg. K/c/o T2DM (HbA1c 8.5%), hypothyroidism.
~28 Feb 2026	Generalised pruritus emerged (~2 weeks post-ATT). ATT withheld; ethambutol 800 mg OD retained as single agent.
3 Apr 2026	Isoniazid 300 mg reintroduced → jaundice-like systemic symptoms → immediately withdrawn. Rifampicin (R-Cinex 450 mg) introduced. Empirical scabies treatment commenced.
7 Apr 2026	Chest radiograph (Figure 1): bilateral lower zone opacities consistent with active PTB. All ATT formally suspended.
28 Apr 2026 (Admission)	Dermatologist diagnosis: "LDE secondary to ATT and Scabies." Xerosis, generalised exfoliation, hyperpigmented plaques and papules over back and abdomen. Prednisolone 10 mg OD, cetirizine, Clonate F cream, liquid paraffin commenced.
28–30 Apr 2026	Isoniazid 150 mg cautiously reintroduced. Albumin transfusion for hypoalbuminaemia. Antidiabetic and thyroid medications continued.
3 May 2026	Second-line bridge: Levofloxacin 500 mg IV OD + Streptomycin 500 mg IM OD commenced to maintain anti-TB coverage during rechallenge interval.
13 May 2026	Rifampicin 400 mg OD reintroduced under dermatological monitoring.
21 May 2026	Pyrazinamide 750 mg added. Full ATT coverage progressively restored. Progressive cutaneous improvement documented.



Figure 1: Chest radiograph (PA view, acquired 07 April 2026) demonstrating bilateral lower zone opacities with right-sided haziness consistent with active pulmonary tuberculosis. Combined with sputum microscopy (Koch's positive), this confirms the PTB diagnosis for which HRZE therapy was commenced. All patient-identifying information removed.



Figure 2: Peak disease presentation — confluent hyperpigmented macules, papules, and diffuse exfoliation over the entire dorsal trunk following approximately eight weeks of HRZE anti-tubercular therapy. Patient S.G., 65 years, female. Documents dermatologist-confirmed generalised lichenoid drug eruption.

DISCUSSION

Diagnostic Validity Without Histopathology

The primary limitation of this report is the absence of histopathological confirmation, acknowledged explicitly at the outset. Histological interface dermatitis — bandlike lymphohistiocytic infiltrate, basal keratinocyte apoptosis, perivascular eosinophilia — constitutes the diagnostic gold standard for LDE.¹ Biopsy was clinically imprudent owing to hypoalbuminaemia requiring albumin replacement and the competing priority of managing active tuberculosis. In its place, five independently verified clinical pillars support the diagnosis: (1) pruritus onset within two weeks of ATT — within the established latency window; (2) a formal dermatologist written diagnosis with institutional seal confirming lichenoid morphology; (3) photographic documentation of positive dechallenge; (4) jaundice-like systemic reaction specifically on isoniazid rechallenge; and (5) systematic exclusion of six differential diagnoses. Idiopathic lichen planus was excluded by drug-temporal onset and dechallenge improvement. DRESS syndrome was

excluded by absence of eosinophilia, lymphadenopathy, fever, and systemic organ involvement, with GCS 15/15 throughout. Erythema multiforme was excluded by absence of targetoid iris lesions and acral predominance. Psoriasis was excluded by absence of silvery scaling, Auspitz sign, and nail involvement. Chronic eczema was excluded by absence of prior eczematous history. Scabies, while empirically treated, cannot produce bilateral symmetrical lichenoid plaques and ichthyosiform exfoliation over the trunk.

Agent Attribution

Isoniazid is the primary suspect on three grounds: pruritus onset at two weeks coinciding with isoniazid as the first reintroduced agent; a distinctive rechallenge-provoked jaundice-like reaction on 3 April 2026; and its established predominance in published ATT-induced LDE literature.^{2,8} Rifampicin is contributory based on cutaneous exacerbation on R-Cinex introduction.^{3,9} Ethambutol was excluded by its tolerance as a sole agent after initial ATT suspension. Pyrazinamide-induced LDE classically presents with photodistribution, not

seen in this case.

Drug Causality Assessment

On the WHO-UMC causality scale,⁶ both isoniazid and rifampicin fulfilled Probable criteria: temporal plausibility, positive dechallenge, rechallenge response, no alternative aetiology, and prior published reports. Neither fulfilled Certain criteria owing to absence of controlled single-drug rechallenge and histopathology. The Naranjo Algorithm⁷ applied to isoniazid yielded a score of 6 (Probable): prior reports (+1); ADR after drug (+2); improved on withdrawal (+1); partially recurred on rechallenge (+1); no convincing alternative (+1); drug level not measured (0); dose-response not assessed (0); no prior history (0); biopsy absent (0). This dual-tool pharmacovigilance assessment applied simultaneously to two agents within a multi-drug regimen constitutes the primary scientific contribution of this report — an approach notably absent from most published ATT-induced LDE cases.

Sequential Rechallenge and Bridge Therapy

Permanent ATT withdrawal was avoided because LDE carries no absolute rechallenge contraindication unlike Stevens-Johnson syndrome or DRESS, and treatment interruption risks drug resistance selection.⁴ Levofloxacin and streptomycin provided bacteriological bridge coverage during the rechallenge interval. Pathave et al.² confirmed corticosteroid-managed ATT-induced LDE in five patients who completed tuberculosis treatment without permanent withdrawal — fully concordant with this clinical trajectory.

Role of the Clinical Pharmacist

The pharmacist's contribution encompassed three documented domains: temporal recognition of the two-week pruritus-isoniazid correlation during ward rounds; structured dual-tool causality scoring providing objective pharmacovigilance evidence; and participation in rechallenge protocol sequencing with second-line bridge coverage rationale. These interventions collectively preserved tuberculosis treatment continuity and reduced the patient's MDR-TB risk.

CONCLUSION

ATT-induced lichenoid drug eruption requires early clinical recognition, structured pharmacovigilance assessment, and rechallenge-based management. In the absence of histopathology, a five-pillar clinical diagnostic framework is valid. Isoniazid was the primary offending agent and rifampicin contributory. Naranjo score 6 and WHO-UMC Probable classification provide validated pharmacovigilance documentation. Sequential rechallenge under second-line bridge coverage restored tuberculosis treatment continuity without permanent ATT withdrawal. Pharmacists must maintain vigilance for lichenoid reactions in ATT recipients, apply dual-tool causality assessment, and advocate for sequential rechallenge over permanent drug discontinuation.

PATIENT'S PERSPECTIVE

"The itching was very severe and I could not rest at night. I was frightened that stopping the tuberculosis medicines would mean the chest disease would return. The pharmacist students and doctors explained that the skin reaction was caused by one of the medicines and

that both problems would be treated together. They restarted the medicines slowly, one by one, and watched me carefully at every step. The itching lessened and the skin healed. I am grateful that my tuberculosis treatment was not stopped permanently." — Paraphrased account of patient S.G., documented by the treating team with informed consent.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest with respect to the research, authorship, and publication of this article.

ETHICAL APPROVAL

This case report was conducted in accordance with the Declaration of Helsinki. Ethics Committee approval was not required for a de-identified single case report per ICMR guidelines. Written informed consent for publication of clinical details and photographs was obtained from the patient (referred to as S.G. throughout). The consent form is retained at the Department of Pharmacy Practice, BVV's H.S.K. College of Pharmacy, Bagalkot, and is available for inspection on request.

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