Lithium-Induced Rash:

Unveiling the Dermatological Dilemma

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Bipolar affective disorder (BPAD) is a chronic episodic psychiatric illness with a lifetime prevalence of 1%–5%.[1] Treatment includes antipsychotics and mood stabilizers, among which lithium has shown remarkable therapeutic benefits.[2] First reported by John Cade in 1949 and approved by the US Food and Drug Administration in 1970 for acute mania and in 1974 for maintenance therapy,[3] lithium offers significant benefits despite a narrow therapeutic index. Cutaneous adverse effects of lithium are less studied, with reported prevalence of 3.4%–45%.[4–6] Cutaneous reactions include acneiform eruption, exfoliative dermatitis, pityriasis versicolor, dermatitis herpetiformis, hyperpigmentation, follicular keratitis, rash, urticaria, alopecia, and hidradenitis suppurativa.[7] Acute rash is rare, with only a few case reports.[8–11] Here, we report the case of a BPAD patient who developed a lithium-induced rash that did not recur on rechallenge.

Case Report

A 32-year-old woman, with no past psychiatric history or drug allergies, presented with 2 weeks of low mood, decreased interaction, decreased interest, and fatigue, followed by 1 week of elevated mood, overtalkativeness, and increased activity. Olanzapine 10 mg daily was initiated and increased to 20 mg, but mood fluctuations persisted. A diagnosis of BPAD, current episode mixed, was established. Lithium carbonate 300 mg was started. Within 12 hours, she developed maculopapular rash on her neck, chest, and axilla, later spreading to the flexor aspects of her arms, forearms, and medial sides of her thighs (Figure 1). Initially nonpruritic, the rash later became pruritic, without fever, myalgia, breathlessness, or mucosal involvement.

She continued lithium for 48 hours before presentation, after which it was discontinued. The complete blood count, absolute neutrophil count, and systemic examination were within normal limits. The dermatology team recommended continuing olanzapine; no additional treatment was given. The rash resolved spontaneously after 2 days.

The Naranjo Adverse Drug Reaction Probability Scale[12] score was 8 (probable). Due to persistent mood fluctuations, olanzapine-related weight gain, and sedation, she was cross-tapered to aripiprazole, which worsened symptoms, necessitating a mood stabilizer. Lithium was rechallenged 2 weeks later and titrated to 750 mg (serum level = 0.9 mmol/L). No rash recurred, and she achieved remission. Over 12-month follow-up, she remained stable.

Discussion

Psychotropics can cause dermatological reactions ranging from mild urticaria to severe, life-threatening conditions such as Stevens-Johnson syndrome, erythema multiforme, and drug reaction with eosinophilia and systemic symptoms. Other effects include angioedema, pigmentary disorders, alopecia, psoriasiform eruptions, acne, and seborrhoeic dermatitis.[13] Lithium-induced acute rash is uncommon and may be pruritic or asymptomatic.[14]

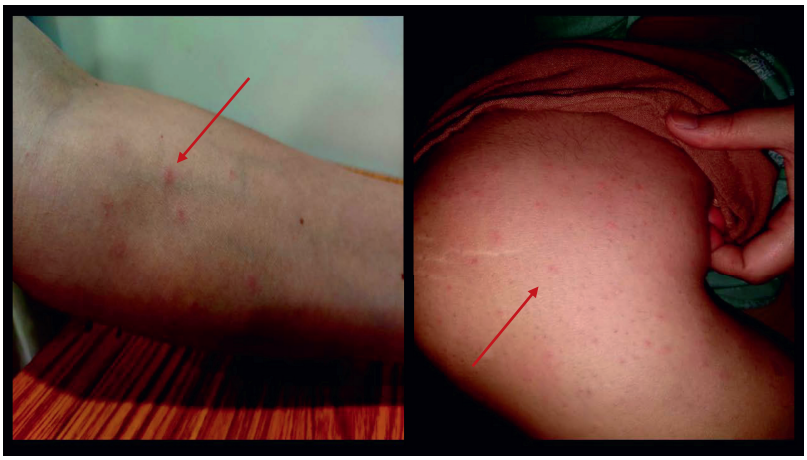
Few cases are reported. Callaway et al[8] first documented 5 cases: 4 patients had pruritic skin rashes (2 cases also with leg ulcers), and 1 patient had a leg ulcer alone. One patient's rash recurred on rechallenge, while 2 patients' did not.[8] Kusumi[9] reported 2 cases: 1 rash resolved despite continued lithium; the other resolved after discontinuation, with no recurrence on rechallenge. Sharma and Padala[10] described a maculopapular rash resolving within 2 days of stopping lithium. Wang and Yang[11] reported a nonitchy erythematous maculopapular rash resolving within 3 days after discontinuation. Our patient's presentation and spontaneous resolution were similar, and she tolerated rechallenge without recurrence.

The mechanism of lithium-induced rash is unclear; type IV hypersensitivity is suspected. Lithium inhibits the phosphatidylinositol system and G-protein signaling, lowering inositol and cyclic adenosine monophosphate levels, which promote keratinocyte proliferation and neutrophil chemotaxis.[14] Lithium inhibits glycogen synthase kinase-3, activating hypoxia-inducible factor-1 and increasing neutrophil, platelet, and CD-34+ cell production.[15]

Female sex and increased age are risk factors.[5] Genetic variability in chemotaxis and neutrophil activity may influence susceptibility.[11] Most rashes are self-limiting and respond to supportive care; lithium discontinuation may be required in some cases.[14] Whether rechallenge is appropriate remains debated.

Figure 1.

Rashes on Different Body Parts After Initiation of Lithium on the (A) Dorsum of Forearm and (B) Medial Side of Thigh



This case highlights that lithium-induced rash, though rare, can occur soon after initiation and resolve rapidly upon discontinuation. In selected patients, rechallenge may be feasible without recurrence, allowing continued use of lithium's well-established mood-stabilizing benefits under close monitoring.

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