

Lithium-Induced Cutaneous Pseudolymphoma

Dear Editor,

Lithium, an effective drug for mood disorders, may cause kidney- and thyroid-related adverse reactions.¹ A meta-analysis reported that the association between lithium and skin disorders was not significant.² However, cases of acne, psoriasis, and rash have been reported.³ Herein, I report a lithium-induced cutaneous pseudolymphoma case in a patient with no previous cutaneous disease. Ethical committee approval was obtained from the Institutional Review Board of Kosin University Gospel Hospital in South Korea (approval number: KUGH 2022-10-020).

A 40-year-old woman with major depressive disorder was hospitalized in a psychiatric ward due to suicide attempt. She had repeated depressive episodes since she was 16 years old and had been treated at psychiatric clinics since she was 34 years old. This was her third hospitalization due to a major depressive episode. Laboratory examination and brain magnetic resonance imaging revealed unremarkable findings. On admission, she had a Beck Depression Inventory (BDI) score of 34. She was managed as a case of treatment-resistant depression because no improvement was noted despite the use of 3 antidepressants. Her antidepressant was switched to sertraline on hospital day (HD) 1 and lamotrigine was initiated on HD 3. Her symptoms partially improved (BDI 22) on HD 19. However, due to persistent symptoms, lithium was initiated. She was discharged and was prescribed sertraline (150 mg), lamotrigine (50 mg), lithium (300 mg), quetiapine (300 mg), doxepin (6 mg), trazodone (50 mg), methylphenidate (20 mg), and diazepam (5 mg). One week post-discharge, the development of pruritic erythematous morbilliform papules and patches (Supplementary Figure 1) with an itching sensation over the whole body prompted a consultation. Considering previous studies and the increase in lamotrigine dosage 12 days prior, lamotrigine was deemed most likely to have caused her symptoms. Lamotrigine was discontinued, and her lithium dose was increased to 600 mg for persistent depression. She was referred to a dermatologist and was managed for 3 days but was hospitalized due to the persistence of symptoms. Skin biopsy revealed a perivascular lymphocytic infiltration as a pathological finding (Supplementary Figure 2), and the lesion was clinically diagnosed as a pseudolymphoma. Lithium was discontinued to minimize the potential risks. The patient received oral methylprednisolone, antihistamines, methylprednisolone cream, and narrowband ultraviolet B treatment. She was discharged from our institution on HD 7. Her lesions mostly improved after 1 month, and she was advised to avoid lamotrigine and lithium. Her depression improved with 500 mg of valproate, 500 mg of quetiapine, 20 mg of methylphenidate, and 25 mg of trazodone. Five months later, she accidentally took lithium and experienced the same eruption the next day. She was advised to discontinue lithium, and the lesion improved after 2 weeks of treatment. It may be concluded that lithium was the most likely cause of her eruptions.

Cutaneous pseudolymphoma is a benign dermatologic lymphocytic proliferation that is histologically and clinically similar to lymphomas.⁴ Pseudolymphoma may be caused by several factors, including anticonvulsants and antidepressants.^{4,5} Lithium causes lymphocyte proliferation by inhibiting the inositol-1 phosphate of monocytes.⁵ Since a drug's effect on pseudolymphoma is relatively long-term and cumulative, it may be challenging to consider the temporal relationship between medication and skin lesions.⁵ Additionally, in clinical practice, drugs such as lamotrigine, which often causes drug eruptions, are commonly used in combination with other drugs. Lymphocyte function may also be affected by drug interactions,⁵ necessitating particular attention. Cutaneous adverse events reduce treatment compliance and may cause significant inconvenience and risk if the causative drug is not identified



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Received: September 15, 2022

Accepted: November 7, 2022

Publication Date: January 6, 2023

Cite this article as: Lee Y. Lithium-induced cutaneous pseudolymphoma. *Alpha Psychiatry*. 2023;24(1):34-35.



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Supplementary Figure 1. Skin lesions on the back. Pruritic erythematous morbilliform papules and patches are shown.

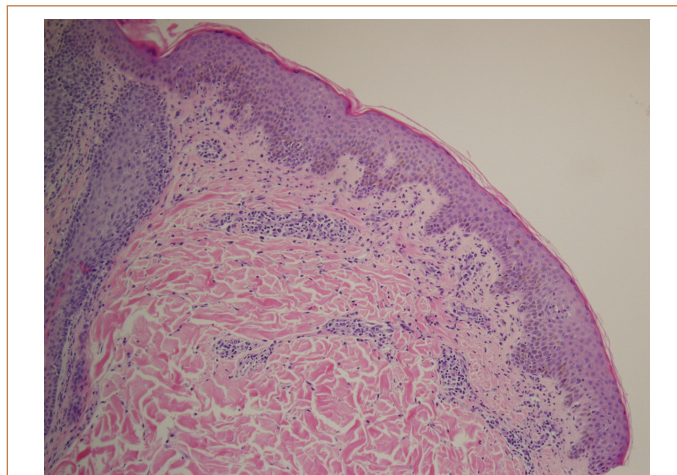
immediately. Even if other drugs are suspected as the cause of eruptions, lithium should be considered and carefully assessed as a potential cause.

A limitation of this study was that a drug-induced lymphocyte stimulation test was not performed on this patient. Therefore, the additives in the lithium tablets cannot be excluded as a possible cause of the skin lesions. Clinicians should also carefully determine whether a drug should be discontinued by considering the effects of drug additives.

Ethics Committee Approval: Ethical committee approval was obtained from the Institutional Review Board of Kosin University Gospel Hospital in South Korea (approval number: KUGH 2022-10-020).

Peer-review: Externally peer-reviewed.

Acknowledgments: The author would like to thank the staff of the dermatology, pathology, and psychiatry departments of the Kosin University Gospel Hospital.



Supplementary Figure 2. Pathological findings of the back skin. The skin shows a dermal perivascular lymphocytic infiltrate (hematoxylin and eosin stain, ×100).

Declaration of Interests: The author has no conflicts of interest to declare.

Funding: The author has declared that this study had received no financial support.

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