

Lamotrigine-induced generalised pustular psoriasis

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Generalised pustular psoriasis (GPP) is a rare form of psoriasis featuring sterile pustules and systemic inflammation.¹ We present a case of GPP secondary to lamotrigine that has not previously been reported.

Case report

A 23-year-old female presented with a 6-week history of an erythematous rash beginning within a week of starting lamotrigine on top of her regular levetiracetam 1g BD, for recalcitrant epilepsy. It began on her feet, then spread cephalically accelerating in extent and degree as the lamotrigine dose was slowly incremented to 100mg BD. She had no personal or family history of dermatological conditions. General practitioner prescriptions including oral antibiotics, topical and systemic steroids, oral antifungals and oral antihistamines failed to help. Public hospital dermatology appointment delays necessitated urgent private dermatology referral. On skin examination, she had an erythematous pseudo-pustular eruption covering 60% of the skin

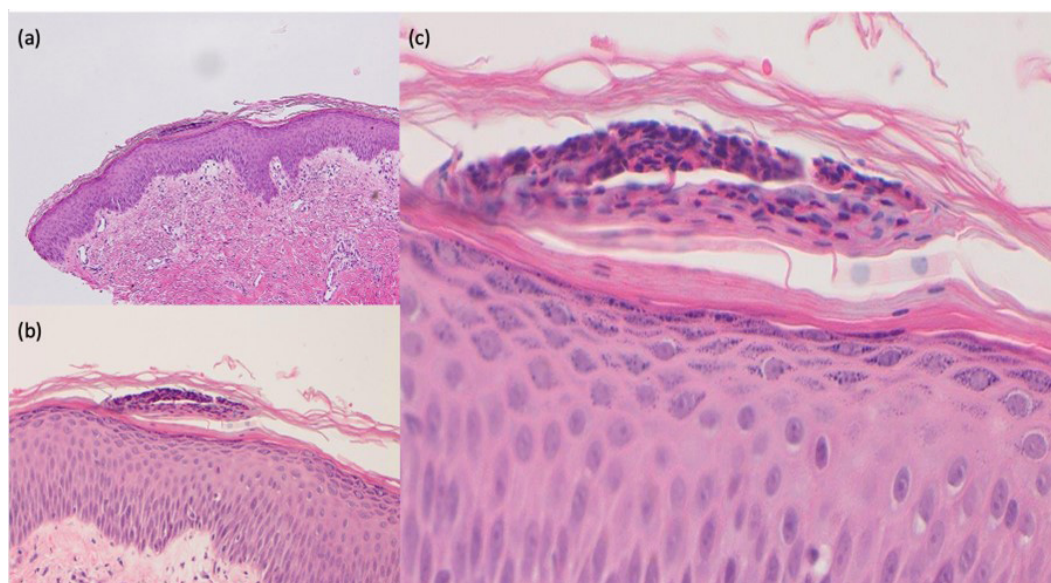
surface, most confluent over the torso where there was confluence, and more classic psoriasis plaques up to 9cm over her anterior shins, sparing her face, palms and soles. The rash can be seen in Figure 2 and 3. The temporal history and cutaneous findings suggested lamotrigine-induced pustular psoriasis as the initial clinical diagnosis.

Lamotrigine was stopped and weekly methotrexate 10mg and folic acid 5mg was prescribed. Levetiracetam was increased to 1.5g BD after consulting an on-call neurologist, to minimise status epilepticus and acute admission arranged to the public hospital for supportive treatment. Oral cyclosporine 100mg BD was added by the inpatient hospital dermatologist.

The skin histology of the pustules can be seen in Figure 1.

One month later significant improvement in the extensive dermatosis was seen and by 4 months, when reviewed in outpatients, it had fully resolved apart from residual anterior shin psoriatic plaques.

Figure 1: Histopathology findings on hematoxylin-eosin staining of the pustules show small plaques of parakeratosis in the keratin layer, as well as neutrophil scale crust. The underlying epidermis was mildly acanthotic and showed a mild degree of basal spongiosis. Neutrophils and lymphocytes are present within the papillary dermis, which shows a mild degree of oedema. a) 100x magnification, b) 200x magnification, and c) 400x magnification.



Discussion

GPP is rare and can be life threatening, as is status epilepticus.^{1,2}

This patient had not been able to seek timely public hospital dermatology clinic review, due to New Zealand health service pressures, resulting in disease progression and subsequent need for admission. Fortunately, she had a favourable (non-fatal) outcome, attributable to timely and collaborative multi specialist care: private dermatology diagnostic expertise identifying and stopping lamotrigine causation, providing appropriate systemic treatment and obtaining immediate neurology expertise, enabling appropriate levetiracetam dose increment to minimise status epilepticus risk.

Naranjo and the WHO-UMC system's standardised causality scales assessment produced a probable or likely causal relationship between lamotrigine and GPP.³ The main differential diagnosis for GPP is acute generalised exanthematous pustulosis (AGEP), which shares similar histopathological findings and clinical features.⁴ However, AGEP is self-limiting and usually settles within a few to 15 days of stopping the

causative agent,⁴ in contrast to our case.

Lamotrigine is a widely used medication in treating epilepsy, bipolar disorder and neuropathic pain.⁵ A cutaneous rash from lamotrigine, appearing within the first 2 to 8 weeks of therapy, has an incidence of approximately 10% and is the most common reason for discontinuation.⁶ More serious rashes including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have an incidence of 0.1%.⁵

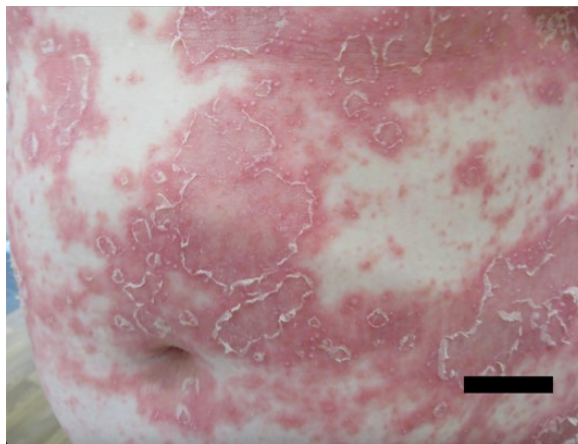
In a recent review on drug-induced psoriasis by Balak et al.,⁵ Google and PubMed literature searches, there have been no previous cases of lamotrigine-induced GPP recorded. On June 2023 there were no reported cases of GPP to the Centre for Adverse Reactions Monitoring (CARM) New Zealand. To the best of our knowledge, lamotrigine-induced GPP has not been previously reported.

This case report serves to raise awareness of life-threatening GPP and severe cutaneous rashes that can be associated with lamotrigine. Access to appropriate specialist care throughout New Zealand to foster prompt diagnosis and management of rare and severe conditions is life-saving.

Figure 2: The posterior trunk with a patchy and confluent erythematous rash studded with fine pseudo-pustulosis and annular peeling.



Figure 3: The anterior side of the abdomen shows a patchy and confluent erythematous rash studded with fine pseudo-pustulosis and peripheral circular peeling.



COMPETING INTERESTS

No conflicts of interest to disclose.

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