Lichenoid Drug Eruption in the Setting of Lamotrigine and Amoxicillin: A Case Report

Nina H. Cheng, BS¹, Shaymaa Ashi, MD², Giuseppe Militello, MD³, Douglas Degler, MD⁴

¹ Drexel University College of Medicine, Philadelphia, PA
² Department of Dermatology, St. Luke’s University Health Network, Bethlehem, PA
³ Dermatology Private Practice, Greenvale, NY
⁴ Department of Medicine, St. Luke’s University Health Network, Monroe, PA

ABSTRACT

A 43-year-old female with a 5-week history of lamotrigine use presented with a rash over the neck and torso following 2 days of amoxicillin for acute pharyngitis. Despite antibiotic discontinuation, the rash progressed to confluent erythematous papules across the face, trunk, extremities, palms, and soles. Persistent fever, severe lymphadenopathy, and angioedema ensued, with leukocytosis, thrombocytosis, neutrophilia, elevated ESR and CRP. Punch biopsy revealed lichenoid drug eruption with prominent histiocytic components and rare eosinophils. Patient improved after lamotrigine discontinuation with prednisone 80 mg to 20 mg tapered over 8 days. This is the first report of a lichenoid drug eruption in the setting of lamotrigine. Lamotrigine is associated with many cutaneous reactions; this risk may be potentiated in the setting of antibiotic therapy.

INTRODUCTION

Lichenoid drug eruption, or drug-induced lichen planus, is a medication-induced cutaneous reaction characterized by symmetric, erythematous or violaceous papules over the trunk and extremities¹. Its name derives from its clinical resemblance of lichen planus but is distinguished by the absence of Wickham striae. A variety of drug classes have been reported to cause lichenoid drug eruptions, including thiazide diuretics, angiotensin-converting enzyme inhibitors, NSAIDs, and tumor necrosis factor-a antagonists.

Lamotrigine is known to have cutaneous adverse effects ranging from urticaria to Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and DRESS. Amoxicillin is also independently known to cause adverse drug reactions (ADR), especially in the setting of infectious mononucleosis. However, little is known about amoxicillin’s ability to either independently cause cutaneous ADR outside the setting of infectious mononucleosis or to potentiate the risks of ADR in the setting of antiepileptics such as lamotrigine. Here, we present a unique case of lamotrigine-induced lichenoid drug eruption that began only after the patient started taking amoxicillin for acute pharyngitis and persisted for 4 weeks after drug discontinuation.

CASE REPORT

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A 43-year-old Caucasian female with a history of depression on lamotrigine for 5 weeks received amoxicillin-clavulanate for acute pharyngitis with fever, cough, cervical lymphadenopathy, and myalgias. Lamotrigine dosage had been increased from 50 to 100 mg 2 weeks prior.

After 2 days of starting amoxicillin, the patient developed an erythematous macular rash over the neck and torso. Despite immediate antibiotic discontinuation, the ADR progressed to erythematous papules with confluence across the body involving the face, torso, palms, and soles (Figure 1). Persistent daily fevers up to 101°F, severe lymphadenopathy, and angioedema followed. Rapid Strep, COVID, CMV, varicella zoster, rubeola, syphilis, coxsackie A, and coxsackie B workup, were negative. EBV testing was positive for historical but not active infection. Complete blood count with differential revealed leukocytosis with absolute neutrophilia, thrombocytosis, and slight basophilia. Of note, no peripheral eosinophilia was noted. ESR and CRP were elevated.

A punch biopsy from the right upper back skin was performed to reveal a lichenoid inflammatory pattern with broad band-like lympho-histiocytic inflammation with degeneration of the epidermal basal layer and scattered apoptotic keratinocytes. Of note, few eosinophils were identified (Figures 2 and 3).

Lamotrigine was tapered and discontinued, and the patient improved with a course of prednisone tapered from 80 mg to 20 mg over 8 days, combined with hydroxyzine 25 mg and triamcinolone 0.5% cream for symptomatic management. Clinical follow up after 6 months confirmed complete resolution without recurrence.

**DISCUSSION**

Cutaneous drug eruptions can pose a challenge to clinical diagnosis and often require the assistance of histologic analysis for accurate identification. In this clinical setting, the histopathologic differential diagnosis was broad including MDE, DRESS,
early SJS/TEN, and viral exanthem. On histologic grounds, the lack of significant epidermal necrosis militated against SJS/TEN. Likewise, our findings were not supportive of DRESS, which is most frequently associated with the presence of atypical lymphocytes and interface dermatitis with or without spongiosis, superficial perivascular infiltration, and eosinophils.

Clinically, the patient’s lack of eosinophilia, transaminitis, or desquamation did not favor SJS or DRESS.

Consistent with the findings of this case is lichenoid drug eruption, which is characterized by lichenoid interface dermatitis and basal keratinocyte apoptosis, with or without eosinophils, plasma cells, or
perivascular infiltrate. Lichenoid drug reactions have been previously reported in association with carbamazepine\textsuperscript{2-4} but not lamotrigine. This may be the first case report of a lamotrigine-induced lichenoid drug eruption.

Lichenoid drug reactions should be distinguished from morbilliform drug eruptions (MDE), which are far more common and comprise an estimated 95\% of adverse cutaneous drug reactions\textsuperscript{1}. Classically, MDE patients present 1-3 weeks following drug exposure with a diffuse symmetric eruption of erythematous macules and papules, usually over the trunk and extremities without mucosal involvement. Features suggestive of MDE include epidermal spongiosis and perivascular and interstitial lymphocytic infiltrate with or without neutrophils and eosinophils.

Considering that this patient’s ADR worsened despite amoxicillin discontinuation and given her short history of total lamotrigine therapy (5 weeks), her recent lamotrigine dose escalation, and her symptomatic improvement following lamotrigine discontinuation, the most plausible trigger for this patient’s ADR is lamotrigine. Whether this patient’s ADR was caused by recent increase in lamotrigine dosage, or secondary to antibiotic potentiation of lamotrigine toxicity is difficult to prove. We believe the latter is more likely as the patient had no adverse cutaneous effects until after starting amoxicillin, with no other history of amoxicillin or lamotrigine intolerance. Three case reports have described adverse effects secondary to the concomitant use of lamotrigine and amoxicillin\textsuperscript{5-7}. In each case, drug reactions occurred only after the patient began taking amoxicillin; these patients had been tolerating lamotrigine without complication. Adverse drug-drug interactions between antiepileptics and antibiotics generally manifest within 2-5 days of initiation, and the risk may be exacerbated by the narrow therapeutic index of most anticonvulsants. Antibiotic potentiation of anticonvulsant toxicity has been previously noted to varying extents in phenytoin and carbamazepine in relation to fluoroquinolones, macrolides, and trimethoprim/sulfamethoxazole\textsuperscript{8-10}; however, the pharmacokinetic interactions between lamotrigine and amoxicillin remain to be explored. Continued research in this realm may have important clinical implications for choice of antimicrobial therapy in patients on antiepileptics to mitigate adverse effects.

To our knowledge, this is the first case report of a lichenoid drug eruption in the setting of lamotrigine use. Adverse cutaneous reactions are a known side effect of lamotrigine; this risk may be potentiated in the setting of antibiotic therapy.

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Corresponding Author:
Nina H. Cheng
2900 W Queen Lane, Philadelphia, PA, 19002, USA
Phone: 732-983-1468
Email: nina.cheng@drexel.edu

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