Acute localized exanthematous pustulosis (ALEP) caused by lamotrigine

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INTRODUCTION

A case of facial acute localized exanthematous pustulosis (ALEP) secondary to lamotrigine is presented. Upon rechallenge with the culprit medication, the patient had acute generalized exanthematous pustulosis (AGEP). This case highlights lamotrigine as a novel causative agent for this type of drug rash, and the unique progression from ALEP to AGEP upon rechallenge.

Abbreviations used:

ALEP:	acute localized exanthematous pustulosis
AGEP:	acute generalized exanthematous pustulosis
DRESS:	drug reaction with eosinophilia and systemic symptoms
SJS/TEN:	Stevens-Johnson syndrome/toxic epidermal necrolysis

CASE

A 39-year old woman with history of idiopathic intracranial hypertension and severe depression presented to the emergency department with a 1-day history of a tender bullous eruption on her face. She was transferred to the burn unit where the dermatology department was consulted. The patient reported that the blistering eruption was preceded by a burning sensation on the forehead and cheek. She had started lamotrigine, venlafaxine, propranolol, gabapentin, and trazodone 2 weeks prior during a psychiatric hospitalization. Other chronic medications included acetazolamide sumatriptan, lisinopril, diclofenac, and ondansetron.

Physical examination found facial swelling and right-sided facial erythema with numerous non-follicular pustules, some coalescing into lakes of pus and scattered vesicles over the right forehead, cheek, upper lip, jaw line, and neck, as well as on the right dorsal hand (Fig 1, *A*). Mucous membranes were spared. There were no nail changes or lymphadenopathy. She was afebrile with mild leukocytosis (white blood cell count of 12.67 with granulocytosis) and normal liver and kidney function. Blood cultures as well as throat swab for group A streptococcus were negative. Cultures of the exudate from the pustules grew normal skin flora. A biopsy of the right cheek found superficial epidermal and subcorneal collections of neutrophils along with scattered interstitial dermal eosinophils, epidermal spongiosis, and focal acantholysis (Fig 1, *B*). Direct immunofluorescence microscopy of perilesional skin was nondiagnostic. Together, these findings supported ALEP as the most likely diagnosis.

The patient improved rapidly upon discontinuation of all of her medications. During the admission, ondansetron, venlafaxine, and acetazolamide were restarted without relapse of the eruption. Five days after discharge, the patient represented to the emergency department with recurrence of the same rash now involving the bilateral face, chest, axilla, breasts, and abdomen (Fig 2). Symptoms had begun within 24 hours from reinitiating lamotrigine and up-titrating the acetazolamide. Acetazolamide and lamotrigine were discontinued. She improved dramatically over the next day before being discharged home. At her last follow-up, her acetazolamide was reinitiated without incident.

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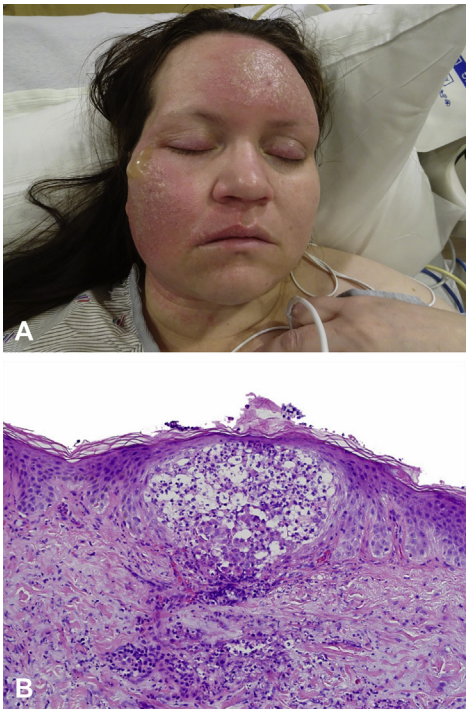

Fig 1. A, ALEP; initial rash presentation consisted of pustules and vesicles on a base of erythema and edema, predominantly on the right side of the face. **B**, Punch biopsy from the right cheek showed spongiosis and subcorneal pustules with neutrophils. (Hematoxylin-eosin stain; original magnification: ×200.) The presentation was consistent with ALEP.

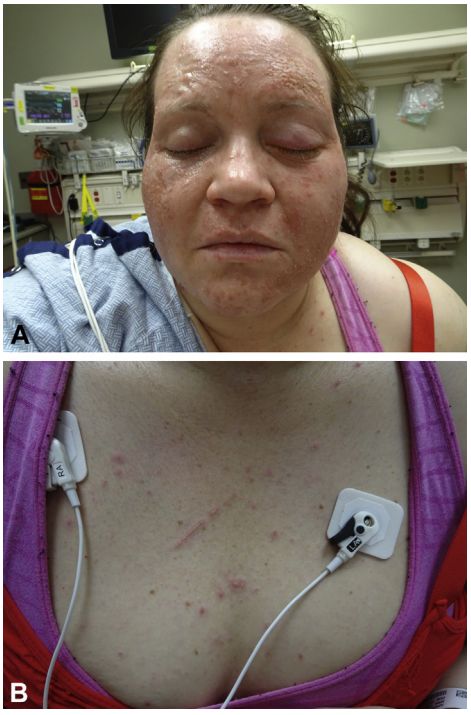

Fig 2. A, AGEP; the rash recurred upon rechallenge with lamotrigine. **B**, Lesions were now widespread and consistent with AGEP.

DISCUSSION

The differential diagnosis for this patient included ALEP, drug reaction with eosinophilia and systemic symptoms (DRESS), pustular psoriasis, and early Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN). Pustular psoriasis was unlikely given the temporal relationship with medications as well as the histologic findings and her lack of a history of psoriasis. The lack of mucosal involvement and limited area of involvement effectively ruled out SJS/TEN. The lack of fever, lymphadenopathy, internal organ involvement, limited skin lesions (<50% body surface area), and rapid resolution of lesions after withdrawal of her medications made DRESS an unlikely diagnosis.[1]

ALEP is a rare, more localized form of AGEP.[2] The most common locations include the face, neck, and chest. Although the presence of vesicles is not common in AGEP/ALEP, it has been reported.[1] The time to onset for ALEP/AGEP is usually within days of starting a medication. We are unsure why the latency period was longer in this case, but time to onset is not part of the proposed diagnostic criteria for this cutaneous reaction.[3] Leukocytosis is common in both AGEP and ALEP, but fever is less common in ALEP.[2] Histologically, ALEP is defined by subcorneal sterile pustules that are usually nonfollicular.[4] Both conditions are known to be caused by medications in most cases, likely through a T-cell–mediated delayed type IV hypersensitivity reaction.[2,5,6] Treatment involves removing the causative agent.

A recent review by Villani et al,[2] summarized all currently reported cases of ALEP and found that β lactam antibiotics were the most common trigger. Notably, lamotrigine has not been described to cause ALEP. The reintroduction of lamotrigine and the more widespread, reemergence of her lesions was unique and helped confirm this as the causative agent. Furthermore, the initial presentation of ALEP, which progressed to AGEP upon reintroduction of the medication, is unique and supports a type IV hypersensitivity mechanism. This case aids in informing the medical community of a novel agent found to cause ALEP and offers further insight into the pathogenesis of this condition.

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