

Alcohol-induced facial flushing in a patient with atopic dermatitis treated with dupilumab



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Key words: alcohol; atopic dermatitis; dupilumab; eczema; facial flushing.

INTRODUCTION

Atopic dermatitis (AD) is a common, chronic type 2 inflammatory skin disease. Dupilumab (Dupixent; Regeneron, Tarrytown, NY), a fully humanized monoclonal antibody to the alpha subunit of interleukin 4 receptor, is the first and only targeted systemic treatment licensed to treat moderate to severe AD.¹ Here, we report a case of a patient with repeated and clinically significant alcohol-induced facial flushing while taking dupilumab.

CASE REPORT

A 26-year-old white woman presented to an outpatient dermatology clinic with a history of AD since childhood. Her past medical history was significant for asthma and hay fever. Treatment with multiple topical steroids, topical calcineurin inhibitors, oral prednisone, cyclosporine, and light therapy had failed. She was subsequently started on dupilumab for her refractory AD. Her AD rapidly improved and has maintained good control at 1% body surface area, localized to the hands and scalp. For a few years before initiating dupilumab, she was applying a stable dose of topical tacrolimus at least once daily. She continues to use topical tacrolimus on her face and neck once or twice daily and controls flares on her hands and scalp with desonide ointment and clobetasol solution, respectively.

The patient reported that soon after starting dupilumab, she began to experience a unique adverse event. After drinking alcohol, she would

Abbreviations used:

AD:	atopic dermatitis
ALDH2:	aldehyde dehydrogenase 2
CYP2E1:	cytochrome P450 2E1
CYP450:	cytochrome P450

develop periorbital and perioral erythema (Fig 1). The symptoms would spontaneously resolve in 20 minutes, regardless of continued alcohol intake. The reaction did not occur every time she consumed alcohol, but she reported that dark alcohols would make the flushing worse. The patient also reported that the more consecutive days she consumed alcohol, the less severe or less frequent the reactions were. There was no evidence of a different reason for the flushing. She denied any similar flushing symptoms while applying her stable dose of tacrolimus before starting dupilumab.

DISCUSSION

To our knowledge, only 1 case report has discussed similar findings of alcohol-induced flushing provoked by dupilumab treatment.²

Aldehyde dehydrogenase 2 (ALDH2) is responsible for the metabolism of ethanol. Individuals of East Asian descent may have a deficiency in ALDH2, which can lead to a buildup of acetaldehyde, resulting in flushing and erythema of the face after consumption of alcohol.³ According to the package insert, dupilumab is reported to possibly modulate

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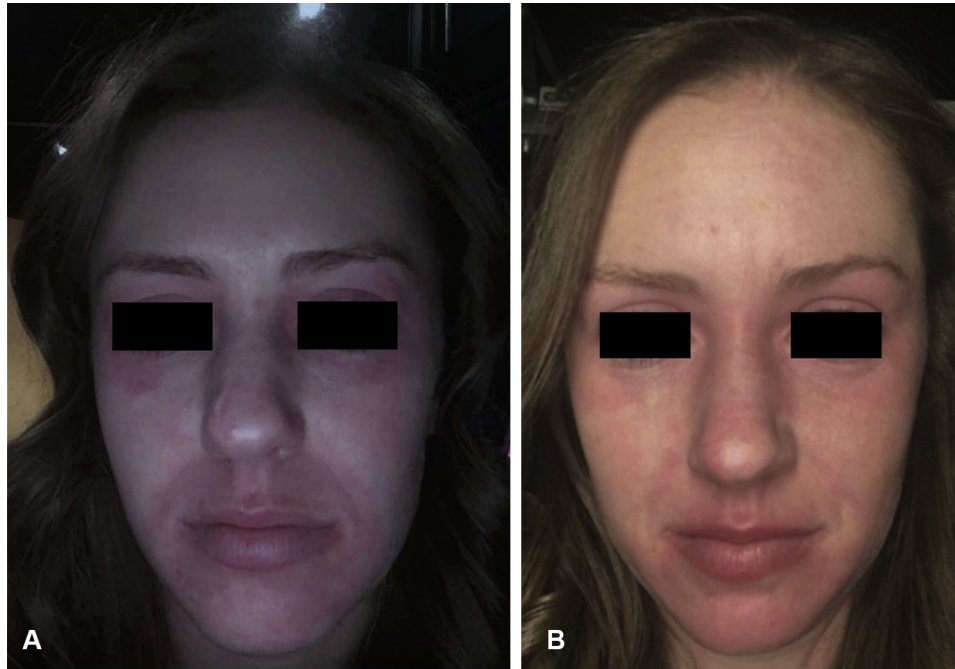


Fig 1. A and B, Distinct periorbital and perioral erythema after alcohol consumption while on dupilumab therapy and tacrolimus ointment.

the formation of cytochrome P450 (CYP450) enzymes and should be used with caution in patients who are using medications that are CYP450 substrates.⁴ Although ALDH2 is a non-CYP450 enzyme, ethanol is also metabolized by CYP450 2E1 (CYP2E1).⁵ One can speculate that dupilumab could modulate the effect of CYP2E1, causing a buildup of acetaldehyde and resulting in facial flush. CYP2E1 accounts for about 10% of the alcohol metabolism at low alcohol concentrations, and its activity increases as the blood alcohol concentration increases.⁶ The degradation of alcohol can also be affected by certain medications that modify hepatic metabolism. Multiple mechanisms exist, including the inhibition of alcohol dehydrogenase, inhibition of acetaldehyde degradation, competitive inhibition at the alcohol binding site on alcohol dehydrogenase, and competition for metabolism by CYP2E1.⁶

A similar reaction to topical tacrolimus has been reported in the literature.⁷⁻⁹ However, we believe this is less likely because our patient had been using topical tacrolimus at least daily for the past few years with no symptoms before starting dupilumab therapy. It may be possible that dupilumab can

potentiate this reaction, although the mechanism is uncertain.

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