Periorbital Dermatitis Induced by Apixaban

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ABSTRACT

Introduction: Periorbital dermatitis can be due rarely to an adverse drug reaction. We present a case of a patient whose periorbital dermatitis was caused by apixaban.

Case Presentation: A 76-year-old female presented with severe periorbital dermatitis 3 weeks after starting apixaban. Varying potencies of antihistamines, topical steroids, calcineurin inhibitors, and emollients were used over a 20-month span with no relief of symptoms. Upon discontinuing apixaban and switching to rivaroxaban, she experienced complete resolution of her symptoms.

Discussion: Periorbital dermatitis is a lesser-known adverse effect of apixaban. To our knowledge, there has only been 1 other reported case of periorbital dermatitis induced by apixaban.

Conclusions: We report this case to increase awareness among clinicians of adverse effects of apixaban and to encourage consideration of drug side effects as part of the differential diagnosis for new skin complaints.

INTRODUCTION

Adverse drug reactions, including drug hypersensitivity reactions, are common in the primary care setting and affect up to 20% of outpatients. In 1 meta-analysis, cardiovascular drugs were found to be the most common cause of adverse drug reactions.[1] Cutaneous manifestations are the most common drug hypersensitivity reactions. In 2017, Vu and Gooderham reported a variety of cutaneous drug reactions associated with direct oral anticoagulants.[2] However, at the time of that study, there were no reports of dermatologic eruptions associated with apixaban. More recent research has linked apixaban to lichenoid eruption, vesicular urticarial dermatosis, hypersensitivity reactions, and periorbital edema.[3-6] These reactions usually are diagnosed clinically; thus, it is essential for clinicians to maintain a high index of suspicion to avoid prolonged symptoms as occurred in this case.

CASE PRESENTATION

A 76-year-old female with a medical history significant for congestive heart failure, atrial fibrillation, gastroesophageal reflux disease, myelofibrosis, prior stroke, and pulmonary hypertension presented to outpatient primary care clinic with ongoing severe periorbital dermatitis. Twenty months prior, she had been admitted to the hospital due to pneumonia and recurrent atrial fibrillation. Apixaban was prescribed on discharge.

One month after discharge, the patient presented to urgent care with a 3-week history of eyelid irritation, redness, edema, and itchiness. She was using multiple over-the-counter creams (including antibacterial and anti-itch creams) to treat this and, thus, was diagnosed with contact dermatitis and told to use only 0.1% triamcinolone cream. Symptoms did not improve with cessation of all over-the-counter treatments and triamcinolone cream alone. She sought care multiple times from several specialists, including dermatology, ophthalmology, optometry, and allergy. She had been using makeup (foundation, mascara, rouge, eyebrow pencil) and was advised to stop all makeup, nail polish, and facial products/creams. Doing so for months did not resolve her symptoms. She denied any new exposures to laundry detergents, household products, hobby related products, etc. Various treatments were tried for periorbital dermatitis, including a daily antihistamine (fexofenadine and cetirizine), topical steroids of varying potencies (hydrocortisone 2.5% cream, triamcinolone

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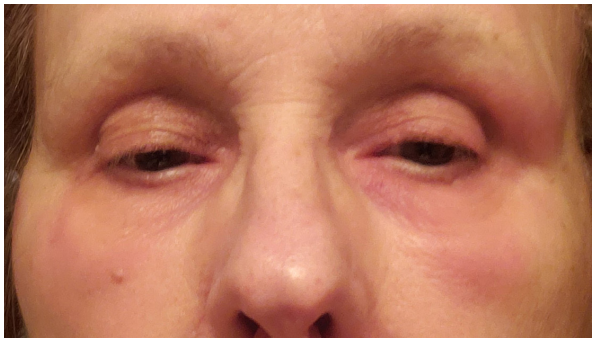
Figure 1. Periorbital Dermatitis



0.1% cream), calcineurin inhibitors (pimecrolimus, tacrolimus), and emollient creams (chilled petroleum jelly, La Roche-Posay Toleriane eye cream, Cetaphil cream), none of which resolved her symptoms. She also was treated for possible seborrheic dermatitis with ketoconazole 2% cream, which did not resolve her symptoms. A skin biopsy was not done. Standard allergy patch testing was negative. She improved briefly with a 7-day course of oral prednisone prescribed in urgent care, but symptoms reoccurred after cessation.

Twenty months after her symptoms began, the patient saw her primary care physician and reported that she was having ongoing extremely bothersome symptoms. She reported that the skin around her eyes was itchy, burning, red, and swollen every day (Figure). She said that her symptoms started after her hospitalization, and the physician identified that she was started on apixaban at that time. Literature review found 1 case report of a similar patient who had "periorbital swelling and pruritus limited to her eyes" after starting apixaban.[3] All of this patient's other medications were reviewed and no other possible drug reactions were identified. Apixaban was discontinued and she was started on rivaroxaban. She reported complete resolution of her symptoms at her follow-up visit 2 weeks later, and symptoms did not recur over the next 2.5 years.

DISCUSSION

Using the Naranjo scoring system[7] for adverse drug reactions, this patient's reaction scores a 7, rating it as a "probable" reaction. Points were given for previous reports of this reaction (+1), the adverse event appearing after the suspected drug was given (+2), resolution of the reaction when the drug was discontinued (+1), no known alternative causes of the reaction (+2), and objective evidence (physical exam, +1) of the reaction.

Direct oral anticoagulants are prescribed increasingly over vitamin K antagonists due to their wide therapeutic window and fixed dosage without need for monitoring.[8] In product information literature, apixaban was reported to have a hypersensitivity rate of <1%.[9] In addition to the previously mentioned periorbital edema case, several other apixaban-induced cases of cutaneous hypersensitivity reactions have been identified in the literature. Isaq et al reported 4 cases of hypersensitivity reactions, including possible drug-induced lupus, 2 cases of IgA vasculitis, and 1 case with palpable purpura and acute kidney injury.[4] An additional case report describes a woman who "developed a vesicular-urticated erythematous rash initially located on her right upper extremity, progressing to her face" from apixaban.[5] Our case, along with recent case reports, indicates that cutaneous reactions from apixaban have a wide range of presentations, and it is important to be aware of these risks.

CONCLUSIONS

Apixaban is a frequently prescribed drug and, increasingly, adverse cutaneous effects are being reported. Early recognition of cutaneous side effects will allow for improved medication management. We hope that presenting this case will help physicians consider the possibility of cutaneous adverse effects from apixaban in future cases and maintain a high index of suspicion for other drug-induced cutaneous side effects.

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