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CASE REPORT | STOMACH

A Case of Lansoprazole-Induced Bullous Pemphigoid After Zantac Recall

Minh Tran, MD[1], Andrew M. Armenta, MD[2], Michael G. Wilkerson, MD[2], Marjan Afrouzian, MD[1,3], and Kashif Khan, MD[4]

[1]*Department of Internal Medicine, University of Texas Medical Branch, Galveston, TX*
[2]*Department of Dermatology, University of Texas Medical Branch, Galveston, TX*
[3]*Department of Pathology, University of Texas Medical Branch, Galveston, TX*
[4]*Department of Gastroenterology and Hepatology, University of Texas Medical Branch, Galveston, TX*

ABSTRACT

Proton pump inhibitors (PPIs) are the mainstay of treatment for many gastric acid-related diseases with a relatively safe drug profile. One of the rare side effects is PPI-induced bullous pemphigoid. We describe a case of new-onset bullous pemphigoid on initiation of lansoprazole for esophagitis after a nationwide Zantac recall. This condition can improve with the cessation of PPI and the use of corticosteroids. However, it poses a significant challenge to the management of gastroesophageal reflux disease by limiting available pharmacologic options. In addition, this case highlights the negative effects of a drug recall.

INTRODUCTION

Drug-induced bullous pemphigoid (BP) is an acquired autoimmune disease that is associated with the use of many drugs such as certain diuretics, antibiotics, anti-inflammatory, and biologic medications. Proton pump inhibitor (PPI) is a common medication class used in gastroesophageal reflux disease (GERD) with a relatively safe profile. Acquired BP is a rare side effect of PPI, and there is a paucity of literature on this condition. Our report will serve to inform physicians about this rare side effect associated with PPI use and our approach in managing this condition.

CASE REPORT

A 50-year-old woman with a medical history of obstructive hydrocephalus and oropharyngeal dysphagia requiring a gastrojejunostomy (GJ) tube for feeding presented to the outpatient dermatology clinic with persistent pruritic rash of 3-week duration. Her mother noticed the initial rash on her left arm, which gradually spread to her other arm, trunk, groin, and both lower extremities. She was prescribed diphenhydramine and a short course of methylprednisolone tablets, which did not improve her symptoms. On examination, there were psoriasiform plaques with scattered erosions and blistering throughout her trunk and extremities (Figure 1). A few months earlier, she underwent esophagogastroduodenoscopy to evaluate for worsening dyspepsia, nausea, and vomiting. Esophagogastroduodenoscopy revealed LA grade D esophagitis. She was prescribed pantoprazole, ranitidine (Zantac), and sucralfate. However, there was difficulty in administering pantoprazole through the GJ tube, so she was taking only Zantac and sucralfate with notable improvement in gastrointestinal symptoms. When Zantac was recalled after the discovery of carcinogenic chemical N-nitrosodimethylamine in the medication, her mother requested a different medication to treat esophagitis. Lansoprazole (Prevacid) was prescribed in the compounded form to be delivered via the GJ tube.

One month after the initiation of lansoprazole, she developed the rash. A punch biopsy was performed, which revealed a subepidermal bullous lesion accompanied by abundant eosinophils (Figure 2). A shave biopsy was subsequently obtained for immunofluorescence microscopy, which showed moderate (++) linear IgG and C3 deposition along the dermoepidermal junction (Figure 3). The linear pattern of IgG and C3 antibody deposition was suggestive of BP. Pemphigoid panel was positive with markedly

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Correspondence: Minh Tran, MD (minhtran@utmb.edu).

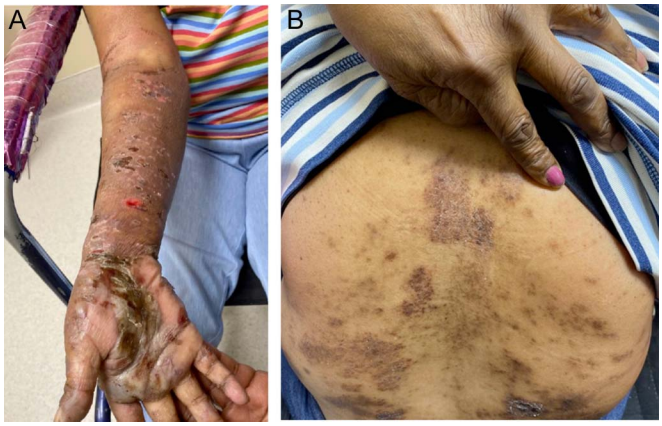

Figure 1. Psoriasiform plaques with scattered erosions and blistering observed on (A) her right arm and (B) back.

elevated BP 180 and BP 230 IgG antibodies, confirming she had developed antibodies to the basement membrane antigens. Pemphigus vulgaris panel was negative. Her skin condition was thought to be related to the proton pump inhibitor, given its recent prescription. Lansoprazole was discontinued, and she was treated with topical triamcinolone. One week later, the patient was admitted to the hospital because of increasing dyspepsia and started on intravenous pantoprazole. On reintroduction to a PPI, her rash flared with a marked increase in the number of blisters. All PPIs were discontinued, and systemic steroids were given over the next few months, followed by a gradual taper. She demonstrated improvement with remarkable regression of blisters and rash. Her reflux symptoms were also better controlled by famotidine and sucralfate.

DISCUSSION

PPIs have been the mainstay of treatment for many acid-related diseases, including esophagitis and GERD, over the past 30 years. Many antisecretory agents provide suppression of gastric acid secretion, including PPIs, H2-receptor antagonists (H2-RA), antacids, sucralfate, anticholinergics, and others. Two notable and commonly used classes of medication are PPIs and H2-RAs (ex. ranitidine, famotidine, cimetidine). Both are safe and effective in the treatment of GERD and reflux esophagitis. However, PPIs have been shown to be more effective than H2-RA in relieving reflux symptoms, esophageal healing, and maintaining remission of esophagitis.[1–3] H2-RAs have a shorter duration of action, less postprandial antisecretory effect, and a tendency to build tolerance within 2 weeks of use, making them less effective over time.[4,5] Therefore, PPIs remain the drug of choice for the management of GERD and different grades of esophagitis. Despite an excellent safety profile, PPIs have many short- and long-term side effects, including malabsorption of calcium, magnesium, vitamin B12, and increased risk of pneumonia and enteric infection.[6–8] Acquired BP is a rare and under-reported side effect of PPIs.

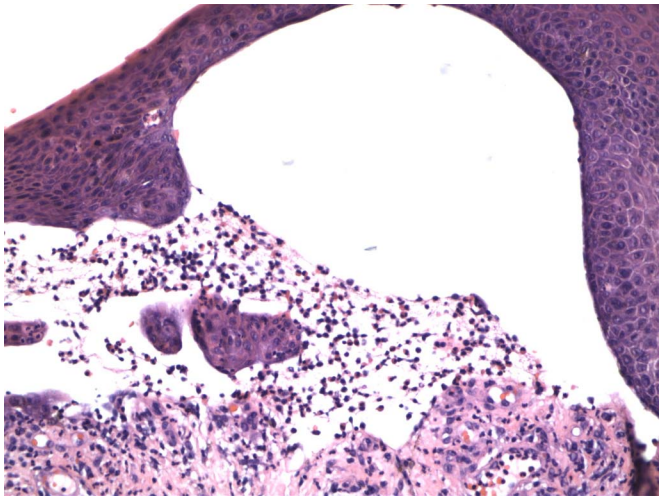

Figure 2. Left inferior arm, punch biopsy showing subepidermal blister with abundant eosinophils (hematoxylin and eosin stain, 200× magnification).

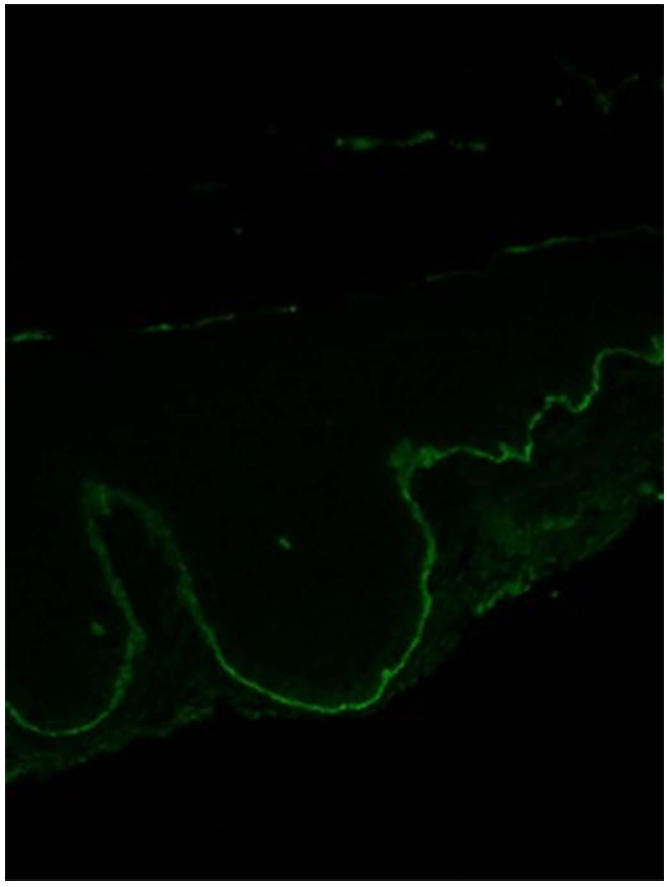

Figure 3. The presence of linear C3 along dermoepidermal junction (C3 antibody, 200× magnification).

Drug-induced BP is an acquired autoimmune blistering disease that is characterized by the appearance of tense bullae on normal skin. It may take up to 3 months after administering the culprit medication for an eruption to begin.[9] There are currently 50 different medications that are reported to be associated with BP.[9] PPIs have been reported

to cause BP, but this side effect is rarely observed. Diagnosis is both clinical and histological. Histologic finding in most patients consists of IgG antibodies and C3 deposited linearly along the basement membrane under direct/indirect immunofluorescence.[10] Clinically, after the inciting drug is withdrawn, symptoms can either respond quickly or have a more prolonged and persistent course of healing. The pathogenesis for PPI-induced BP is currently unexplainable. In the "2-step" theory, 2 drugs in the same class can work together to induce immunologic changes.[11] The patient could have been sensitized to PPIs from previous pantoprazole use. Cross-reactivity could have then occurred with lansoprazole leading to the skin eruption. Molecular mimicry can also explain PPI-induced BP. The misidentification of PPIs as foreign agents by the immune system could lead to the activation of the autoimmune cascade involved in skin blistering.[12]

There are currently no official guidelines on the treatment of drug-induced BP.[9] Discontinuation of the suspect medication and the use of corticosteroids are essential in the treatment of drug-induced BP. Most patients achieve improvement in skin blistering with the combination of low-dose oral and topical corticosteroids within 6 weeks.[9] Although her gastrointestinal symptoms are currently well controlled, H2-RAs are not a permanent solution for reflux esophagitis because of the severity of the condition and other limits of this drug class. In patients with a history of drug-induced BP, there is currently no literature exploring whether it is appropriate to rechallenge the patient on the suspect medication. In cases of refractory GERD, a nonpharmacologic approach including endoscopic or surgical intervention can be considered to adequately control acid reflux and disease progression.[13]

DISCLOSURES

Author contributions: M. Tran and AM. Armenta wrote the manuscript. MG. Wilkerson, M. Afrouzian, and K. Khan revised the manuscript for intellectual content. M. Tran is the article guarantor.

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