A Case of Bupropion-induced Stevens-Johnson Syndrome With Acute Psoriatic Exacerbation

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ABSTRACT

Bupropion is a very popular medication prescribed to millions of patients globally for depression (Wellbutrin®, GlaxoSmithKline, Research Triangle Park, NC) as well as an aid in smoking cessation (Zyban®, GlaxoSmithKline, Research Triangle Park, NC). It has been reported to have some common dermatologic side effects, such as pruritus, urticaria and serum-sickness like reaction. The authors report a case of bupropion-induced Stevens-Johnson syndrome (SJS) with a concomitant acute psoriatic exacerbation in a 56-year-old woman, who began taking bupropion for treatment of depression. While the United States (U.S.) prescribing information for bupropion does include SJS as a rare potential side effect, it does not mention worsening of psoriasis. Physicians should be aware of the potential life-threatening adverse effects of this commonly prescribed medication as well as the risk in patients with known psoriasis.

INTRODUCTION

Bupropion (Wellbutrin®, Zyban®, GlaxoSmithKline, Research Triangle Park, NC) is a popular drug prescribed for both the treatment of major depressive disorder as well as an adjunctive aid in smoking cessation (Zyban). It is believed to inhibit the reuptake of dopamine and norepinephrine, distinct from other commonly used classes of antidepressants such as selective serotonin reuptake inhibitors, tricyclics and monoamine oxidase inhibitors. Dermatologic adverse effects associated with bupropion use are not uncommon. Approximately 1–5 percent of patients taking buproprion have been reported to experience pruritic or urticarial rashes.[1] In a 1995 review, there was a reported 3.7 percent incidence of rash and pruritus associated with buproprion use, compared to one percent or less for other commonly used antidepressants such as fluoxetine, paroxetine, sertraline and venlafaxine.[2] Few cases of more severe dermatologic reactions such as a serum sickness-like syndrome,[3–5] acute psoriatic exacerbation[6] and erythema multiforme[7–9] have been reported.

CASE REPORT

A 56-year-old Caucasian woman with a 25-year history of plaque-type psoriasis began taking 450 mg Wellbutrin XL® for treatment of depressive symptoms. Seven days after she initiated the bupropion, she developed an erythematous circular papule on her right thigh that centrifugally enlarged over the next 48 hours. She also noted soreness of her tongue while eating. On day 10 of bupropion use, she developed widespread erythematous macules, papules and bullae on her trunk and upper and lower extremities and was instructed by her primary care physician to discontinue the bupropion and present to her local emergency room. She was admitted to an outside hospital and started on IV methylprednisolone.

She was subsequently transferred to the authors' facility for further treatment and was found to have diffuse involvement of targetoid patches and plaques, some with resolving central bullae, on her trunk, extremities and palms (Figures 1 and 2). There were superficial erosions on her upper and lower lips, as well as extensive erosions involving her vaginal mucosa. She also had well-demarcated plaques with thick silvery-scale on her scalp, anterior lower legs and upper extremities that were distinctively different from the targetoid lesions and were clinically consistent with her known-diagnosis of psoriasis.

On laboratory evaluation, she exhibited a mild leukocytosis of 13.2, but all of her chemistries were within normal limits. She was also afebrile and had no perioral lesions suggestive of herpes simplex viral infection. Her other medications included topical steroids and Dovonex® (Leo Pharma, Parsippany, NJ) for psoriasis as well as glucosamine, fish oil, vitamins C and E supplements and ibuprofen as needed for chronic back pain, all of which she had been taking for at least eight years. Based on history and clinical appearance, she was diagnosed with bupropion-induced Stevens-Johnson syndrome (SJS). The bupropion was discontinued, and the patient was treated with steroid wet wraps and tapered off of the oral prednisone. She was discharged after seven days in the hospital.

DISCUSSION

SJS is a rare, severe mucocutaneous disease characterized by widespread epidermal necrosis secondary to apoptosis of keratinocytes. SJS lies on a spectrum of disease with toxic epidermal necrolsyis (TEN), which are distinguished from one another by the extent of body surface area involved. SJS involves under 10 percent of body surface area while TEN involves over 30 percent body surface area and is associated with

FIGURE 1. Clinical findings of diffuse erythematous targetoid patches and plaques, some with resolving bullae, involving the trunk and extremities.

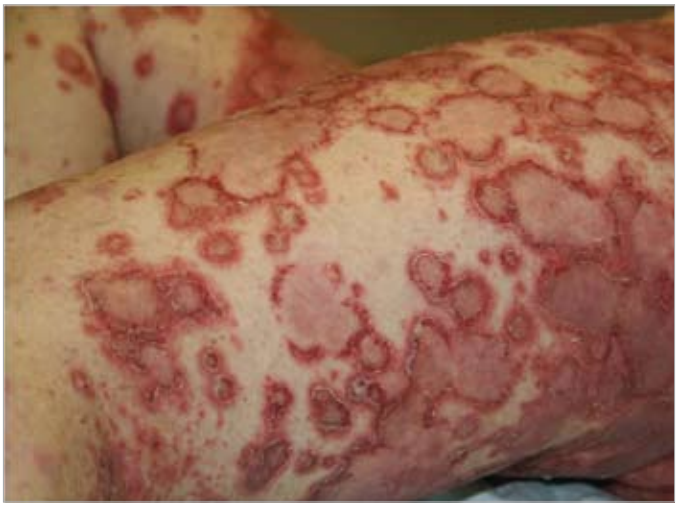
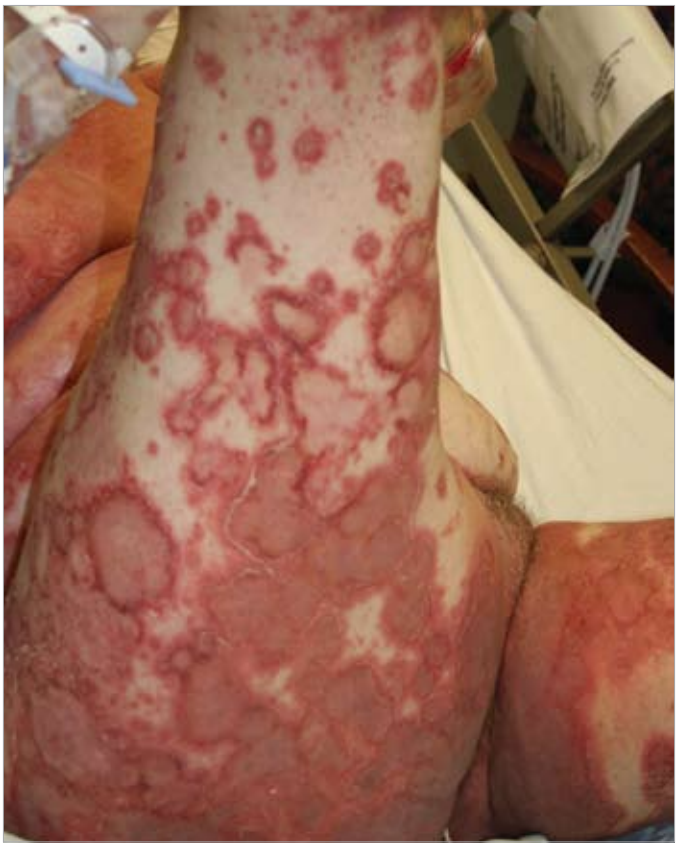


FIGURE 2. Clinical findings of diffuse erythematous targetoid patches and plaques, some with resolving bullae, involving the trunk and extremities.



a much higher mortality rate. The range of 10–30 percent is an overlap between the two entities. Erythema multiforme (EM) major is an acute skin eruption characterized by typical target lesions consisting of three distinct zones of color changes. This entity can affect mucosal surfaces as well as have systemic symptoms such as fever and lethargy, similar to SJS and TEN. However, EM major differs in etiology from SJS and TEN and is more closely linked to infections such as herpes simplex virus and *Mycoplasma pneumoniae*.

While multiple etiologies have been associated with SJS such as various chemicals, *Mycoplasma pneumoniae*, viral infections and immunizations, drugs are the leading cause. Over 100 different drugs have been associated with SJS/TEN, most commonly sulfonamides, allopurinol, antiepileptics and nonsteroidal anti-inflammatory drugs.[10] Although poorly understood, the pathogenesis of drug-induced SJS is thought to involve a cytotoxic immune reaction against keratinocytes expressing drug-related antigens, resulting in apoptosis of epidermal keratinocytes.[11] Apoptosis is thought to be induced by interaction of Fas-Fas ligand, a receptor ligand pair expressed in epidermal keratinocytes.[12]

It is not uncommon for patients taking bupropion to experience mild pruritic or urticarial rashes. However, there have been few reported cases of more serious adverse dermatologic reactions with bupropion use, such as erythema multiforme, SJS and toxic epidermal necrolysis.[9,10] Shortly after its release as Zyban, the Canadian Adverse Drug Reaction Monitoring Program reported two cases of suspected erythema multiforme and one case of SJS secondary to bupropion use.[9] These cases, however, were not discussed in detail in the literature. In 2001, Lineberry et al. reported the first case of erythema multiforme in a 31-year-old woman after taking sustained-release bupropion for 24 days.[7] In the same year, another case was reported by Carrillo-Jimenez et al. in a 38-year-old male after 2.5 weeks of bupropion use for smoking cessation.[8] According to the U.S. prescribing information for Wellbutrin XL, erythema multiforme, SJS and anaphylactic shock are reported as rare reactions.[1] The Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK has recorded 76 cases of erythema multiforme and 20 cases of SJS in patients taking bupropion from January 1963 to May 2006 (MHRA, personal communication). A PubMed search for reports of bupropion and SJS or TEN, however, yielded no results.

This patient's presentation of extensive cutaneous targetoid papules and plaques along with mucosal and genital involvement was consistent with a case of SJS. Based on the patient's history of starting bupropion seven days prior to the onset of symptoms, the authors believe that the drug was associated with the development of SJS. She had not recently undergone any medication changes. Her other medications included topical steroids and Dovonex for psoriasis as well as glucosamine, fish oil, vitamin C and E supplements and ibuprofen as needed for chronic back pain, all of which she

had been taking for at least eight years. No other etiologic agents, such as infections, could be identified.

Additionally, the patient developed slightly erythematous, scaly hyperkeratotic plaques on her upper and lower extremities that were distinctly different from the plaques associated with SJS. These are consistent with an acute exacerbation of psoriasis. Her psoriasis continued to worsen even after her hospitalization, eventuating in treatment with biologic therapy.

The prescribing information for Zyban on GSK's Canadian website reported a rare side effect of worsening psoriasis. The MHRA in the U.K. also reports 45 cases of psoriasis in bupropion users from 1963 to 2006 (MHRA, personal communication). The Zyban patient information leaflet in the U.K. lists worsening of psoriasis as a rare adverse effect.[13] Yet, there is no mention of psoriasis in the U.S. version of GSK's bupropion prescribing information.

In 2002, Cox et al. reported generalized pustular and erythrodermic flares in three patients with previously stable psoriasis shortly after initiating bupropion.[6] They postulated that the rapid worsening of the psoriasis may have occurred as a result of a Koebner reaction from a preceding erythema multiforme. This patient's presentation may additionally support this theory, as SJS lesions may have induced acute formation of psoriatic plaques.

This case is the first detailed report of bupropion-induced Stevens-Johnson syndrome. It is also another example of previously reported cases of psoriatic exacerbation in bupropion users. Because of its unique mechanism of action, bupropion has been marketed as a safer option than other antidepressants with less serious adverse effects. As the use of bupropion for the treatment of depression and smoking cessation is becoming exceedingly popular with 20.1 million retail prescriptions in 2007, physicians should be aware of these as potential severe and life-threatening adverse effects.[14] Additionally, particular care should be taken when prescribing bupropion to patients with a known history of psoriasis as prescribing information available in the U.S. does not mention this potential serious side effect.

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DISCLOSURES

The authors have no relevant conflicts of interest to disclose.

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