Delayed Onset of Bupropion-Induced Urticaria

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Bupropion, a norepinephrine and dopamine reuptake inhibitor, is commonly used to treat depression. Potential adverse side effects include urticaria, angioedema, erythema multiforme, Stevens-Johnson syndrome, and anaphylactic shock, but these allergic reactions are not commonly reported with bupropion. To date, there are only case reports[1–4] and 1 large-scale study[5] describing bupropion-induced allergic reactions, and a delayed onset of an allergic reaction was associated with a significant majority of these cases. It has been hypothesized that allergic reactions from bupropion may be underrecognized due to patients receiving care for these allergic reactions from other physicians.

Case Report

A 17-year-old male was admitted to a psychiatric inpatient unit for suicidal ideations, with the only recent stressor being breaking up with his girlfriend. He had no previous psychiatric hospitalizations. While an inpatient, he was started on bupropion for depressive symptoms. He had not taken antidepressants prior to this time. During admission, blood work results including complete blood count, comprehensive metabolic panel, and thyroid-stimulating hormone were within normal limits. The patient denied any alcohol, tobacco, or illicit substance use, and his urine drug screen was negative. The patient was discharged 4 days later and was compliant with bupropion after discharge. Eighteen days after the patient started bupropion, he presented to the medical emergency department for urticaria. He complained of multiple episodes of diffuse urticaria on his bilateral upper and lower extremities that were not relieved by diphenhydramine. There were no systemic manifestations.

The patient denied recent exposures to substances and had discontinued bupropion 1 day prior to his arrival to the emergency department. During his initial emergency department visit, he had received prednisone and 1 dose of intramuscular epinephrine, which alleviated his symptoms, and he was sent home. Two days later, he went to his primary care physician and complained of persistent urticaria. He was given another epinephrine injection and a prescription for prednisone. The next day, the patient again presented to the emergency department, continuing to complain of urticaria in his bilateral upper extremities, which had only mildly improved. In the emergency department, he was given intravenous methylprednisolone. He was instructed to continue his oral prednisone and was sent home. His symptoms appeared to alleviate the next day, and he reported no further episodes of urticaria.

The patient has a history of severe urticarial reactions to mangoes but did not report a similar reaction to medications or other exposures. He was unsure of any family history of urticaria. After he discontinued bupropion, he was started on escitalopram, which he tolerated well for 2 months.

Discussion

To date, there is only 1 large-scale study[5] assessing the delayed onset of urticaria associated with bupropion use in patients with depression. This study[5] found that urticaria occurred significantly more often in days 15–28 compared to days 1–14 after starting bupropion and that it occurred significantly more often in male subjects under 40 years of age. Similar to this large-scale study,[5] the delayed urticarial reaction occurred in a young male 18 days after starting bupropion.

It should be noted that it is possible to develop an allergic reaction to any of the ingredients of bupropion. Ingredients of bupropion include bupropion hydrochloride, D&C Yellow No. 10 Lake, FD&C Yellow No. 6 Lake, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, polyethylene glycol, talc, and titanium dioxide.[6] Thus, it is possible that the patient may have developed an allergic reaction to one of these ingredients instead of to bupropion as a whole.

Current first-line treatment of acute urticaria includes histamine H_1 blockers such as loratadine and fexofenadine. Addition of histamine H_2 blockers such as ranitidine to histamine H_1 blockers may provide some benefit. Corticosteroids may be added in patients with more severe symptoms.[7] The patient in this report had trialed a histamine H_1 blocker, which had not alleviated his urticaria, and afterward was administered prednisone. However, symptoms continued to persist despite this treatment. Further research must be done to investigate why this patient's urticaria persisted despite treatment with both an H_1 blocker and corticosteroids.

Overall, this case study emphasizes the importance of consistently monitoring patients for adverse medication side effects of bupropion and serves to promote awareness among

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clinicians of the delayed phenomenon of allergic reactions associated with bupropion use. In addition, the patient's initial refractoriness to treatment for urticaria highlights the need for further investigation as to why initial treatment was ineffective. Other potential future areas of research include investigating the cause of the delayed urticarial reaction to bupropion and examining if there is a delayed allergic reaction to other classes of antidepressants.

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