Monoarthritis Induced by Bupropion Hydrochloride

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ABSTRACT ~ Bupropion hydrochloride is an inhibitor of dopamine and norepinephrine, which is commonly prescribed for major depression, smoking cessation, and bipolar depression. Here we report a highly unusual case of bupropion induced knee monoarthritis in a bipolar depression patient. With bupropion XL 150 mg for 2 weeks, her left knee began to swell; at the third week, this condition was worsening. The aggravation of the left knee effusion stopped after the discontinuation of bupropion XL. The effusion and swelling disappeared after 15 ml of synovial fluid was drawn out and the effusion has never returned. Analysis of the synovial fluid showed noninflammatory effusion. Her left knee swelling was most likely due to angioedema caused by bupropion XL.

INTRODUCTION

Bupropion hydrochloride (Wellbutrin, Aplenzin or Zyban) is an antidepressant of the aminoketone class, and its structure closely resembles that of diethylpropion. Bupropion can inhibit the presynaptic uptake of dopamine and norepinephrine and therefore boost neurotransmitters dopamine and norepinephrine. It also inhibits the uptake of serotonin and has moderate anticholinergic activity.

Bupropion is commonly prescribed for major depression, smoking cessation, bipolar depression, seasonal affective disorder, sexual dysfunction, and attention deficit hyperactivity disorder, with low incidences of somnolence, sexual dysfunction and weight gain. The extended-release preparation has been shown to be effective for treating geriatric depression, depression characterized by reduced energy, pleasure and interest, and the prevention of the recurrence of seasonal affective disorder. The common side effects of bupropion XL are agitation, anxiety, and insomnia, caused by the activity of norepinephrine and dopamine in

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several brain areas. It is also reported to cause anorexia, nausea, dry mouth, constipation, and weight loss by the activity of norepinephrine in the periphery. In this report, we described an angioedema case presenting with highly unusual knee monoarthritis caused by bupropion.

CASE REPORT

A 51 year old Caucasian lady with history of bipolar I disorder, anxiety disorder and hypothyroidism presented with a complaint that she had had left knee swelling for one week. She was diagnosed with Bipolar I at 30 years. She was treated with Risperdal 1 mg qhs and Lamictal 50 mg qd for bipolar disorder, Klonopin 2 mg bid for anxiety and levothyroxine 25 mg qd for hypothyroidism. Because her depression was out of control, bupropion XL 150 mg qd was administered. After two weeks, her left knee began to swell. The swelling was getting worse by the third week of taking bupropion XL. She complained of mild pain while walking and warmness of her left knee. Considering an adverse effect of bupropion, bupropion was discontinued. The left knee remained swollen, but has not aggravated since then. The right knee was normal. She denied any rash, fever, sore throat, or other systemic manifestations. She has had no known drug allergy or recent traumatic events. She denies any substance abuse or alcohol abuse. She smokes one pack of cigarettes per day.

Her physical examination revealed that her vital signs were normal. No rash was visible on her body. Her left knee revealed significant effusion and mild warmness without redness, tenderness or erythema. There was no effusion over her right knee. The range of motion in both knees was normal. The pulse on both feet was normal. On mental status examination: The patient was alert and oriented × 3, elevated in her affect and mood. Perceptions were grandiose and paranoid. She had pressured speech, loose associations, tangentiality and flights of ideas. She denied suicidal and homicidal thoughts. Judgment and insight were poor.

Lab tests: CBC, ESR, BNP (B-type natriuretic peptide), and D-dimer were normal. Echocardiogram and venous Doppler of the left lower extremity were performed and results were normal. After informed consent, around 15 ml yellow and hazy synovial fluid was drawn out from her left knee. After the fluid drainage, the effusion and swelling on her left knee disappeared and the effusion has never come back. Analysis of the aspiration from her left knee revealed: white cell 430/mm³, red cell 900/mm³, polynuclear: 5/100 cells, mononuclear 95/100 cells and no gout/pseudogout crystals seen, suggesting non-inflammatory effusion.
DISCUSSION

This patient’s clinical course and features were consistent with drug-induced acute knee effusion. Synovial fluid analysis showed noninflammatory effusion. The event occurred two weeks after the addition of 150 mg bupropion XL to her treatment regime, and this was the only change during that period. The swelling increasingly worsened over 3 weeks’ treatment with bupropion XL. The aggravation of the left knee effusion stopped after the discontinuation of bupropion XL, and the effusion and swelling went away after 15 ml of synovial fluid was drawn out, never to reoccur. Other causes of knee swelling were ruled out, such as osteoarthritis, osteoporosis, rheumatoid arthritis, deep vein thrombosis, gout, pseudogout, and lupus. Her left knee swelling was mostly like due to angioedema caused by bupropion XL.

It has been reported that bupropion XL induced angioedema and serum sickness-like reaction.5–7 In the product labeling, angioedema is documented as a possible, but rare, with symptoms usually developing between 10 and 20 days after initiation of the drug. But monoarthritis caused by bupropion was highly uncommon. Angioedema is nonpitting edema of the deep dermal and subcutaneous tissues. Metabolites of the drugs might bind with tissue proteins inappropriately, eliciting an acute inflammatory response that typically develops 7–14 days after initiation of the offending agent. The edema is thought to be because of the release of immunoglobulin-E causing inflammation that results in fluid leakage and leads to vascular dilation and increased vascular permeability.

Monoarthritis ascribed to bupropion XL seems rare.7 The authors wish to make readers aware of bupropion as a possible cause of this kind of angioedema and to educate patients accordingly. The treatment for this adverse reaction is to discontinue bupropion XL and administer steroid and antihistamine for manifestations resolution. However, the limitations of this single case report must be acknowledged. Further investigations with a larger sample are needed.

REFERENCES