BUPROPION HYDROCHLORIDE INDUCED SERUM SICKNESS-LIKE REACTION

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Sustained-release bupropion is commonly used for the symptomatic relief of depressive disorders and as an adjuvant in smoking cessation therapy. The frequency of adverse reactions with bupropion has been estimated to be more than 1%. Hypersensitivity reactions to bupropion are fairly common and include rare cases of serum sickness-like reaction. Here we report a case of bupropion hydrochloride induced serum sickness-like reaction. Complete resolution of symptoms was achieved on discontinuing bupropion and instituting therapy with glucocorticoid and a non-steroidal antiinflammatory drug.We report this case to notify clinicians of potential serious multisystem complications that can occur with sustained-release bupropion therapy.

Key words: Bupropion; adverse reactions; arthritis; serum sickness-like reactions

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INTRODUCTION

Bupropion, first developed as an antidepressant, is a selective inhibitor of neuronal reuptake of dopamine and noradrenalin. It shares structural similarities with amphetamine derivates such as amfepramone and diethylpropion (1). Bupropion was found to reduce nicotine withdrawal symptoms and the urge to smoke. Beginning in 2000, sustained release preparations of bupropion has been used as an aid to smoking cessation in combination with psychological support. Its mechanism of action in reducing nicotine dependency is not understood. A drammatic increase has been observed in the prescripition of this drug with the particular aim of smoking cessation in recent years. In this case report we describe a patient who develeoped serum-sickness like reaction induced by bupropion therapy.

CASE

A 28-year-old man had an unremarkable medical history and was in good general health when he was admitted to our rheumatology outpatient clinic in June 2004 due to inflammatory joint pain involving his ankles. The pain had started 15 days after bupropion therapy which had been prescribed for smoking cessation. A diffuse pruriginous eruption with erythematous and papuler lesions and fever had occured concomitantly. He had been treated with intramuscular long acting glucocorticoid (betamethasone acetat) in the emergency unit of another hospital. Although fever and eruptions resolved promptly, the inflammatory joint pain persisted, and the patient had been referred to our clinic. On physical examination, his body temperature was 36.5 °C, the pulse rate 84/min, and the blood pressure 112/74 mmHg. He had no edema of the oral cavity or pharynx. Auscultation of the heart and lungs was normal. There were no skin eruptions. Swelling and tenderness involving both ankles were noted. Laboratory test results were as follows: erythrocyte sedimentation rate (ESR), 62 mm/h; C-reactive protein, 3.8 mg/dl (normal, <0.8 mg/dl); white blood cell count, 7260/mm^3; haemoglobin, 14.7 g/dl; platelets, 270.000/mm^3; kreatinin ,0.9 mg/dl; AST, 23 U/l; ALT, 67 U/l and GGT, 72 U/l. Rheumatoid factor, antinuclear antibodies, serologic tests for hepatitis B and C were all negative. Serum uric acid, lactate dehydrogenase, ferritine, C3, C4 and IgE levels were in the normal range. The urinalysis was normal. Radiographs of the

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ankles were unremarkable. A nonsteroidal anti-inflammatory drug in combination with analgesics were given and bupropion was stopped. Arthritis resolved completely within two weeks after which the ESR was 19 mm/h, and CRP was 0.5 mg/dl. Liver and kidney function tests were in the normal range. There were no recurrences during the one-year follow-up.

DISCUSSION

Zyban, a sustained-release formulation of bupropion hydrochloride, is a useful oral and non-nicotine form of pharmacotheraphy for smoking cessation. Efficacy has been demonstrated in published trials and its efficacy was found to be superior to nicotine patch (2).

Adverse events have been reported in more than 1% of patients on bupropion therapy(3). Minor adverse effects such as insomnia, tremor, asthenia, headache, dry mouth and nausea are common. Serious adverse effects are rare and include seizures and hypersensitivity reactions. The latter can manifest with a variety of eruptions and as a semi-delayed (type III) reaction (4-8). Bupropion SR is contraindicated in patients with a current seizure disorder or history of seizures.

Serum sickness-like reactions (SSLRs) following bupropion ingestion appear to be rare. Between May 1998 and May 2001, GlaxoSmith Kline received 172 reports of seizures and only 37 reports of serum sickness-like reactions (9). However, SSLRs may be underrecognized or underreported. The onset of symptoms of SSLRs typically begins 6 to 21 days after administration of the causative agent. Patients with SSLRs present with urticaria, arthralgia or athritis with or without fever, which are usually self-limiting symptoms usually resolving without long-term sequela following discontinuation of bupropion and instituting therapy with glucocorticoid and antihistamines.

SSLRs are examples of immune-complex mediated disorders. Soluble circulating immune complexes can deposit on the vessel walls, where they trigger a local inflammatory response, which is usually mediated by complement activation. Mastocyte degranulation with histamine release and an influx of polymorphonuclear cells occur, producing the clinical manifestations; fever, urticaria, edema, arthralgia, lymph node enlargement, vasculitis and glomerulonephritis (10).

The present case suggests a role for bupropion in the development of acute oligoarthritis. Non-steroid antiinflammatory treatment allowed prompt resolution of the symptoms. Joint symptoms ascribed to bupropion are uncommon but fairly severe particularly when serum sickness occurs. Given the possibility that bupropion might induce arthritis, we suggest that physicians should be careful concerning a history of bupropion use in patients presenting with acute oligoarthritis.

In conclusion, we suggest that severe hypersensitivity reactions should be born in mind when prescribing bupropion as a smoking cessation aid and patients should be educated about this potential side effect at the onset of treatment.

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