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Burning Mouth Syndrome: Case Report

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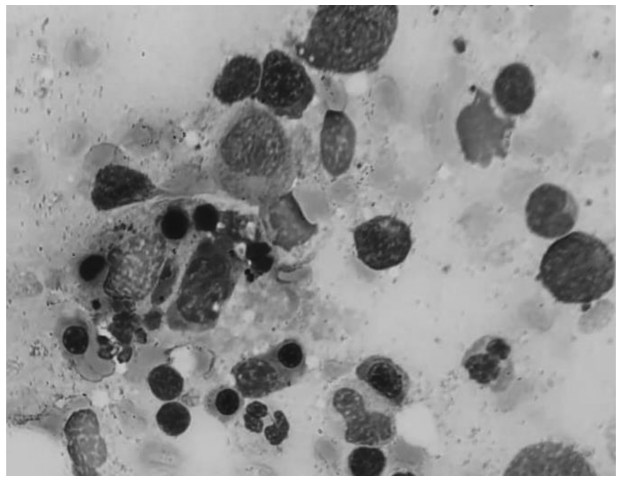

FIGURE 1. Histiocyte showing phagocytosis of numerous erythrocytes. Color image is available online only at www.psychopharmacology.com.

The patient received only supportive care during his admission. Interestingly, halving of ferritin levels was observed in 1 day after cessation of lamotrigine, which corresponds to the half-life of ferritin,[5] clearly supporting HLH as serious adverse event of lamotrigine. Venlafaxine was restarted on the second day after admission. Six days after admission, the patient had made a full clinical recovery, and his biochemical parameters had largely normalized and continued to do so during the next few weeks of outpatient follow-up.

Hemophagocytic lymphohistiocytosis has sporadically been described after initiation of lamotrigine. With an increasing number of reports surfacing in recent years, the association with this nontrivial condition is becoming more clear.[6–11] Nevertheless, only a handful of detailed reports are currently available in the literature. Such scarcity provides little guidance to the clinician confronted with this adverse event when it comes to treatment decisions. For example, our report indicates that early cessation of the drug enables patients to make a full recovery without treatment and that disease markers fall very quickly upon cessation of lamotrigine. Such observations may help forestall aggressive treatment of the HLH where this is not strictly necessary.

Antiepileptic drugs are known to modulate immune system activity and alter the production of cytokines. Through these mechanisms, immunogenic adverse effects have been well documented for this class of drugs, although newer agents have been less extensively described.[12] Therefore, reports like this one should prompt clinicians to close monitoring of the patient in the weeks after the first prescription of lamotrigine or other antiepileptic drugs.

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Burning Mouth Syndrome

Case Report

To the Editor:

Burning mouth syndrome (BMS), also known as glossodynia or stomatodynia, is characterized by burning oral pain in the absence of an identifiable lesion.[1] The prevalence of BMS is estimated to be between 0.7% and 4.5%.[2–4] This condition is more common in postmenopausal women[5] and often co-occurs with other symptoms, such as parageusia and xerostomia.[4]

There are no laboratory tests to establish a definitive diagnosis of BMS.[6] As BMS is associated with somatization, anxiety, depression, dissociation, and personality disorders,[7,8] a patient's description of these symptoms may be overlooked. Herein, we present the case of a patient with bipolar disorder who developed BMS after the initiation of quetiapine.

CASE PRESENTATION

The patient is a 65-year-old White woman with a longstanding history of bipolar 1 disorder with mixed features. The patient's symptoms were relatively controlled with 10-mg aripiprazole and 0.25-mg clonazepam daily. In May 2020, she reported increasing jaw tightness, and therefore, aripiprazole was cross-titrated with quetiapine. Concurrently, clonazepam was discontinued. By June 2020, the cross-titration was completed, and she was no longer taking aripiprazole, which was replaced with 300-mg quetiapine nightly. She reported resolution of her facial extrapyramidal symptoms and denied any adverse effects from quetiapine.

Throughout July 2020, she began to experience worsening xerostomia. She used sugarless gum and lemon drops/mints, but these did not alleviate symptoms. At this time, she demonstrated a weakly positive antinuclear antibody titer of 1:320. By August 2020, her symptoms had significantly intensified; she reported a constant burning sensation on her hard palate accompanied by a sore throat. The symptoms were severe enough to cause her distress during the day and interfere with sleep.

Subsequently, the patient underwent an extensive medical workup. Electrolytes were within normal limits, as were renal and liver functions. Anti–Sjögren syndrome A/anti–Sjögren syndrome B, anti–double-stranded DNA, C3 and C4 complement, and extractable nuclear antigen/anti-Smith/antiribonucleoprotein antibodies were all negative. Complete blood cell count with differential, iron level, and hemoglobin/hematocrit level were within normal limits. Biopsy of her lip showed squamous mucosa, and biopsy of minor salivary gland showed focal fibrosis, focal atrophy, and minimal chronic inflammation. The focus score of 0 to 4 mm^2 was not consistent with Sjögren syndrome.[9,10]

Considering her negative medical workup, we suspected that she developed BMS secondary to quetiapine. In October 2020, quetiapine was cross-titrated with olanzapine over 4 weeks. Subsequently, while on olanzapine 5 mg daily, her BMS fully resolved by December 2020. She continued to report occasional xerostomia, which she differentiated from BMS.

DISCUSSION

The exact etiology and pathogenesis of primary BMS have not been well delineated.[1] It has, however, been linked with central and peripheral neuropathic disturbances, including dopamine pathway dysfunction.[5] Specifically, patients with BMS demonstrate disruption in striatal dopamine regulation.[11,12] Local and systemic factors, including autoimmune diseases, nutritional deficits, infections, and medications, may contribute to the development of secondary BMS.[8] Medications that have been implicated in BMS include angiotensin-converting enzyme inhibitors, efavirenz, fluoxetine, L-thyroxine, levodopa, nevirapine, sertraline, and topiramate among others.[3,8,13,14]

Our patient's symptoms remitted after quetiapine was discontinued. Quetiapine's mechanism of action is through blockade of dopamine D_2 and serotonin $5HT_2A$ receptors; it also has serotonin $5HT_{1A}$ partial agonistic, serotonin $5HT_{2C}$ and $5HT_7$ antagonist, histamine H_1 antagonist, M_1 antimuscarinic, and $\alpha 1$ adrenergic antagonist properties.[15] One, or multiple, such receptor modulations may be implicated.

Although we speculate that our patient's symptoms were caused by quetiapine, she may have already had BMS before quetiapine's initiation—she was previously taking clonazepam and aripiprazole, both of which have been cited in the improvement of BMS symptoms.[6,16–18] Moreover, BMS is a diagnosis of exclusion, and we felt that our patient's negative medical workup was sufficient to explain her diagnosis. However, a variety of local and systemic disorders may mimic BMS symptoms,[5] which potentially may have confounded her presentation. There may also exist some correlations between iron deficiency states and BMS[4]; however, our patient's iron level was normal.

To the best of our knowledge, there are no other reported cases of BMS secondary to quetiapine. Although our patient responded well to olanzapine as has been described previously,[19] treatment options for BMS are limited and are largely based on cessation of the presumed offending agents. Further literature on psychopathological explanations for BMS, along with randomized controlled trials for potential therapeutics, would be welcomed contributions.

AUTHOR DISCLOSURE INFORMATION

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Patient's verbal consent was obtained to develop and to publish this case report. Information has been deidentified to protect anonymity.

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