Drug Watch

Black hairy tongue with a fixed dose combination of olanzapine and fluoxetine
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ABSTRACT

Black hairy tongue (BHT) is a benign disease characterized by elongated filiform lingual papillae, with a carpet-like appearance of the dorsum of the tongue. It is has been reported to occur with a prevalence ranging from 0.6% to 11.3%. Although its etiology is not fully understood, BHT may be triggered by smoking, excessive coffee or black tea drinking, poor oral hygiene, trigeminal neuralgia, general debilitation, dry mouth as well as certain drugs. We present here a case of a patient with psychosis, depression, and benign prostatic hyperplasia, who developed BHT following treatment with a fixed dose combination (FDC) of olanzapine and fluoxetine and recovered within 3 months after withdrawal of treatment with FDC.

KEY WORDS: Black hairy tongue, filiform papillae, fluoxetine, olanzapine

Introduction

Initially described by Amatus Lusitanus in 1557, black hairy tongue (BHT) is a painless, benign clinical condition characterized by defective desquamation and reactive hypertrophy of the filiform papillae of the tongue. It has also been referred to as hyperkeratosis of the tongue and lingua villosa nigra. It typically affects the dorsum of the tongue. Although the classical manifestation is black in color, the tongue can also appear brown, yellow, green, blue, or unpigmented.

A fixed dose combination (FDC) of olanzapine and fluoxetine is effective for treatment-resistant depression and bipolar depression, particularly for acute-phase treatment and is considered a rational FDC according to the seven-point criteria for assessing the rationality of FDCs. Olanzapine is an atypical antipsychotic drug approved for the acute and long-term treatment of bipolar disorder besides its use in psychosis. The most frequent adverse effects of olanzapine are sedation, orthostatic hypotension, headache, weight gain, and mild hyperglycemia. Common gastrointestinal adverse effects include constipation, dyspepsia, and dry mouth. In addition, olanzapine has also been reported to cause a number of uncommon oral cavity lesions such as stomatitis, glossitis, and oral ulcers. Fluoxetine is a selective serotonin re-uptake inhibitor which, besides important psychiatric adverse effects including suicidal tendency, may cause adverse effects such as headache, nausea, vomiting, abdominal pain, and dry mouth. Thus, both drugs are known to cause dry mouth or xerostomia, which in turn is a predisposing factor for BHT. However, we found no reports of BHT with an FDC of olanzapine and fluoxetine. We came across only one case report of BHT with olanzapine in a 25-year-old woman in whom olanzapine was prescribed for bipolar disorder. We also found two reports of BHT in patients receiving fluoxetine among other drugs.

Here, we present a case of a patient who developed BHT following treatment with an FDC of olanzapine and fluoxetine for psychosis with depression.

Case Report

A 70-year-old male patient, suffering from an unspecified psychotic disorder, was on tablet pimozide 2 mg and tablet procyclidine 2.5 mg, both once daily for 2 years. After 2 years of above treatment and about 5 months prior to presentation, he visited a second private practitioner who diagnosed him to have depression along with psychotic symptoms. The patient was prescribed tablet olanzapine 5 mg and tablet fluoxetine 20 mg, both once daily, and tablet pimozide 2 mg and tablet procyclidine 2.5 mg, both once daily for 2 years. After 2 years of above treatment and about 5 months prior to presentation, he visited a second private practitioner who diagnosed him to have depression along with psychotic symptoms. The patient was prescribed tablet olanzapine 5 mg and tablet fluoxetine 20 mg, both once daily, and tablet pimozide 2 mg and tablet procyclidine 2.5 mg, both once daily for 2 years. After 2 years of above treatment and about 5 months prior to presentation, he visited a second private practitioner who diagnosed him to have depression along with psychotic symptoms. The patient was prescribed tablet olanzapine 5 mg and tablet fluoxetine 20 mg, both once daily, and tablet pimozide 2 mg and tablet procyclidine 2.5 mg, both once daily for 2 years.
patient also complained of increased frequency of micturition. Ultrasoundography of the abdomen showed an enlarged prostate suggestive of benign prostatic hyperplasia. His psychotropic medication was changed to oral escitalopram 10 mg once a day with tablet risperidone 1 mg twice a day. He was also prescribed silodosin 8 mg, tamsulosin 0.4 mg, and dutasteride 0.5 mg for benign prostatic hyperplasia. Procyclidine was stopped as it could worsen urinary symptoms. After another 2 months, he was switched to an FDC of olanzapine 5 mg and fluoxetine 20 mg by the same practitioner. The reason for this change in therapy is not known. Two months after starting the FDC, the patient developed black discoloration of dorsal surface of the tongue. On the assumption of a fungal pathology, he was prescribed oral fluconazole 150 mg daily and clotrimazole 1% mouthwash for 10 days. The discoloration did not subside and continued to worsen. The patient presented at the hospital about 3 weeks after development of tongue discoloration. On examination, there was blackish discoloration with hair-like projections on the dorsum of the tongue [Figure 1]. There were no other physical findings on examination. To rule out a fungal cause of the lesion, potassium hydroxide (KOH) mount was prepared from scrapings from the tongue, which was negative for fungal elements. The patient is not a smoker and uses false dentition which is cleaned by his son once a day. Based on history and clinical presentation, a diagnosis of “BHT” was made. Using the World Health Organization causality assessment criteria, causality was determined as possible with olanzapine and fluoxetine and unlikely with other drugs by the causality assessment committee of the concerned Adverse Drug Reaction (ADR) Monitoring Centre. On the Naranjo ADR probability scale, a causality score was 4 which again indicates that the reaction is possible with olanzapine and fluoxetine. The reaction has been reported to the Pharmacovigilance Programme of India through the in-house ADR Monitoring Centre, with worldwide unique number at Uppsala Monitoring Center 2015-17103.

The FDC containing olanzapine and fluoxetine was suspected to be the causative agent as both are known to cause dry mouth which is a predisposing factor for BHT. Therefore, the FDC was stopped and replaced by pimozide 2 mg. The patient was also advised to brush his tongue with a soft toothbrush two times a day and maintain good hygiene of his oral cavity as well the dentures. Three months after withdrawal of olanzapine and fluoxetine, discoloration of the tongue had resolved almost completely with only a slight yellowish discoloration of the tongue still apparent [Figure 2].

Discussion

BHT is an acquired benign disorder characterized by an abnormal hairy appearance of the dorsal surface of the tongue. The etiology and pathophysiology of BHT are not fully understood. The disorder may be triggered by numerous predisposing conditions such as oncological disorders, smoking, heavy black tea or coffee intake, and poor oral hygiene. BHT also shows clear gender and age predilection.[1,9] According to some reports, BHT is about thrice as common in men as in women. This can be attributed to greater prominence of smoking and higher rates of poor oral hygiene in males. Age is also a predisposing factor, with elderly males being more likely to develop a BHT.

In addition, use of systemic and local medications has been commonly implicated in the development of BHT. Antibiotics including penicillin, erythromycin, doxycycline, neomycin, and linezolid have been associated with this disorder.[1] However, the cause and effect factor between antibiotics and development of BHT needs to be further elucidated. Local or systemic antibiotic use may significantly alter oral flora, which may predispose the patient to develop BHT. On the other hand, anatomical alterations in the filiform papillae may lead to trapping of foreign material and stimulate local microbial overgrowth that results in the color changes seen in patients with this condition.

Besides antimicrobials, drugs, which cause xerostomia or dry mouth, including the antipsychotics such as olanzapine and antidepressants such as fluoxetine have also been associated with BHT. Some other psychotropic drugs, for instance, paroxetine, thiothixene hydrochloride, benzotropine mesylate, clonazepam, and chlorpromazine are also reported to be associated with BHT.[1,10] The pathophysiology of BHT has not been fully understood. It is thought to arise from defective desquamation of the dorsal surface of the tongue.[11] This prevents normal debridement.
leading to accumulation of keratinized layers, hypertrophy, and elongation of the filiform papillae, which appear like hair. The elongated papillae, which are normally <1 mm in length, can be 12–18 mm long and have a diameter of 2 mm. Microorganisms including fungi and bacteria as porphyrin-producing chromogenic organisms may collect in the papillae. Excessive growth of chromogenic bacteria and fungi and desquamating keratin may be responsible for the dark discoloration. In addition, residue from tobacco, coffee, tea, and other foods may also get trapped in the elongated structures.

BHT typically causes only esthetic concerns to the patient. It may, however, be rarely associated with gagging, nausea, dysgeusia, xerostomia, burning mouth syndrome, and halitosis in some patients. Diagnosis of BHT can often be made following visual inspection alone. Management primarily involves mechanical debridement, maintenance of proper oral hygiene, and removal of potential causative agents.

In most cases, elimination of any incriminating factor is usually sufficient to treat the lesions and no drugs are required for treatment. Overall prognosis is excellent as the disease is largely self-limiting.

In our case, at least two of the features of typical patient presenting with BHT were present, an elderly male on antipsychotic medications, that is, olanzapine and fluoxetine. Poor oral hygiene, due to psychiatric condition of the patient and use of false dentition, could also have predisposed to BHT. Although a negative KOH could be explained by prior use of oral fluconazole and topical clotrimazole, there was no relief from tongue condition with antifungal agents. On the other hand, there was resolution of discoloration and hairy appearance after discontinuing olanzapine and fluoxetine.

BHT can be caused by other drugs which lead to dry mouth, especially when used in combination. When therapy with a possible precipitator is required, particularly in a patient with predisposing factors such as age and male gender, such an adverse drug effect can be prevented by patient education about good oral hygiene.

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Conflicts of Interest
There are no conflicts of interest.

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