Oral Entomophthoramycosis: A Rare Fungal Infection

KD Shah*, RA Bradoo**, UV Warwantkar***, AA Joshi****

Abstract
Entomophthoramycosis is a rare fungal infection which primarily affects the nose and can later spread to involve the paranasal sinuses, nasopharynx, oropharynx, palate and the cervical region. It usually has a nodular appearance with infiltration of the underlying tissues and no clear demarcation from the surrounding tissues. We present the case of a 28 year old man, who presented with entomophthoramycosis affecting the palate, oropharynx and nasopharynx without involvement of the nose. The diagnosis was confirmed by histopathology, which showed invasive mycotic inflammation, and the fungal culture revealed entomophthoramycosis. The patient was treated with oral Itraconazole (400 mg / day) for a period of one year. He responded very well to this single-drug therapy with clinical resolution of the lesion within 6 months. Further, the patient was kept under a regular follow-up for a period of one year, without any recurrence. This case is reported due to the absence of a nasal lesion of a rare fungal infection which usually originates in the nose.

Introduction
Entomophthoramycosis is a fungal infection which affects individuals with an apparently intact immunological status and occurs primarily in tropical areas. Two zygomycetes belonging to the order Entomophthorales are the aetiologic agents of subcutaneous entomophthoramycosis, viz., Basidiobolus ranarum (= B. haptosporus) and Conidiobolus coronatus.1,2 Infection with C. Coronatus usually begins in the inferior turbinate, and spreads in the submucosa through the natural ostia to the paranasal sinus, and to the subcutaneous tissue of the face (forehead, periorbital region and upper lip).3 Infection by B. ranarum manifests itself as a subcutaneous tumefaction located on the trunk, buttocks or proximal portion of the limbs or as an invasion of the thoracic or abdominal cavities.

The disease is essentially chronic, evolving over the course of years. No incubation period or cases of spontaneous involution are known. Diagnosis is made by clinical, histopathological, and mycological examination.4 A review of medical literature indicates that the condition can be treated with potassium iodide, amphotericin B, and ketoconazole. However, the literature provides little information on details of long-term follow-up and occurrence of relapses. We present a case of oral entomophthoramycosis where a single-drug, i.e., Itraconazole, has been used for a period of 1 year to achieve complete remission.

Case Report
A 28 year old male, residing in Mumbai and a labourer by occupation, presented with chief complaints of intra-oral growth since three months. The growth was insidious in onset and had gradually increased in size over the last three months. He had history of odynophagia and dysphagia. On enquiry, he also had a history of change in voice and nasal blockage.

*Senior Registrar; **Professor and Head; ***Registrar; ****Associate Professor, Department of ENT, LTMG Hospital, Sion, Mumbai.
Examination revealed a diffuse inflammatory submucosal lesion involving the soft palate, uvula, both the anterior pillars and extending up to the posterior pharyngeal wall [Fig. 1]. On diagnostic nasal endoscopy, the lesion was seen to be involving the nasopharynx also. Examination of the larynx, neck and the ears was unremarkable.

A CT scan of the neck showed a diffuse, submucosal, non-enhancing mass involving the nasopharynx, the oropharynx and soft palate bilaterally [Fig. 2].

A punch biopsy of the lesion was taken from the soft palate which was suggestive of vascular proliferative tissue. A nasal endoscopy was performed and a biopsy was taken from the nasopharyngeal lesion. This tissue was reported to be non-specific chronic inflammatory tissue.

The patient was treated empirically with antibiotics but he showed no response. A short course of intravenous steroids (dexamethasone) was also given. The lesion showed partial regression; however, it increased in size on discontinuing steroid therapy. An incisional biopsy was repeated again from the lesion on the soft palate. The tissue was sent for KOH mount and fungal culture in addition to histopathology. This biopsy was positive for an invasive mycotic inflammation and the fungal culture was suggestive of entomophthoramycosis. The patient was started on oral Itraconazole 200 mg twice a day.

The patient responded well to this treatment protocol. All lesions on the soft palate, in the oropharynx and in the nasopharynx had resolved after...
6 months of treatment [Fig. 3].

A CT scan of the neck done at the end of 10 months showed complete resolution of all the lesions [Fig. 4].

Itraconazole was continued for a period of one year. The patient is asymptomatic without any clinical signs of recurrence, one year after complete resolution of the lesions.

Discussion

Entomophthoramycosis (conidiobolomycosis) is a rare and chronically indolent fungal infection. This localized, subcutaneous zygomycosis is characterized by a painless, woody swelling of the rhinofacial region. It occurs mainly in the tropical rain forests of Africa, South and Central America, and South-East Asia. A few cases have been reported from India. The fungus lives as a saprophyte in soil humus and on decomposing plant matter in moist, warm climates. It can also parasitize certain insects and frogs. Infection is acquired through inhalation of spores, or their introduction into the nasal cavities by soiled hands. Most cases affect men with agricultural or outdoor occupations.

Lesions by *C. coronatus* begin as infiltration of the nasal mucosa and submucosa, extending to the adjacent tissues of the paranasal sinuses, nasal dorsum, upper lip, and face. The lesion shows a nodular appearance with infiltration of the underlying tissues. It is covered by erythematous and fibrotic skin or mucosa, with no clear demarcation from the surrounding tissues. As a rule, the lesions are firmly attached to the underlying tissue, although the bone is spared. The overlying skin and mucosa remain intact. Histopathological examination shows an inflammatory granulomatous reaction, with a predominantly mononuclear infiltrate consisting of lymphocytes, histiocytes, and some multinucleated giant cells, along with plasma cells and eosinophils. The central portion shows broad, thin-walled, irregular branching hyphae, frequently approaching right angles. These hyphae do not usually display septa and are surrounded by a peculiar eosinophilic mass (the Splendore-Hoeppli phenomenon).

The condition is slowly progressive, but seldom life-threatening. The clinical manifestations result from the expansion of the tumour mass. It initially affects the nose first and so the disease is also referred to as rhinoentomophthoramycosis. More advanced cases show involvement of the nasopharynx, oropharynx, palate, cervical region, and even the mediastinum. The first mycologically proven cases in humans were described independently and simultaneously in 1965 in Jamaica and Africa. Adult males are affected more than females. Our case differed in the fact that though the lesions involved the nasopharynx, oropharynx and soft palate, there were no lesions in the nose.

Clinical and histopathological findings may be quite suggestive, but definitive diagnosis is only possible by isolating and identifying the fungus in appropriate culture media. The differential diagnosis should consider scleroma and tumours of the minor salivary gland. In our case, the diagnosis was based on clinical and histopathological examination and confirmed by mycological identification of the fungus.

Treatment of entomophthoramycosis is difficult because the diagnosis is usually established late, but patients often respond to oral itraconazole (200 to 400 mg/day), ketoconazole (200 to 400 mg/day), fluconazole (100-200 mg/day), amphotericin-B, and cotrimoxazole. Itraconazole and fluconazole are both effective and relatively safe. Treatment should be continued for at least 1 month after the lesions have resolved. Combination therapy with oral potassium iodide and oral azoles gives rapid and lasting
results. Surgical resection is seldom helpful and it may hasten the spread of infection. Cryotherapy has been tried with little success. Relapse is common, even after successful treatment.

We used a single drug, i.e., itraconazole, in a dose of 400 mg / day for one year to achieve complete cure. As our patient responded very well to Itraconazole alone, we did not need to give potassium iodide. We continued the drug for 6 months after clinical resolution of the lesions. The patient has been on a regular follow-up for 1 year without any recurrence of the lesions.

**Conclusion**

A high index of suspicion is of utmost importance in diagnosing entomophthoramycosis. The diagnosis has to be confirmed by mycological identification of the fungus. A single drug therapy with itraconazole is effective in achieving cure. The drug therapy needs to be continued even after the lesion has clinically resolved. Also, the patient should be followed up after stopping treatment to detect recurrence of the lesion.

Since this is a rare fungal infection, there is not a lot of data in literature about it to form a treatment protocol. No consensus exists about the drug of choice, the duration of treatment or the follow-up period. This case report would contribute to the existing data, so that a definitive treatment protocol can be set up in the course of time.

**References**