Histopathological Diagnosis of Rhinofacial Entomophthoramycosis in a 16-Year-Old Girl: A Case Report

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Abstract
Rhinoentomophthoramycosis is an uncommon and severely disfiguring disease. It mainly involves the mucosa of the nares, nasal passages, nasal sinuses, nasopharynx, mouth and spreads to adjacent tissues causing disfigurement of face. Histopathological examinations and mycological cultures are the gold standard for confirmation of entomophthoramycosis. We report a case of a 16-year-old girl who presented with swelling and ulcer of face. Clinical presentation along with typical histopathologic findings were diagnostic in this case.

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Keywords: Entomophthoramycosis, zygomycosis, fungal infection of face, fungal granuloma, splendore-Hoeppli reaction

Introduction

Rhinoentomophthoramycosis is not so common in Bangladesh as well as other parts of the world. It is a grossly disfiguring disease. The medically important class zygomycetes are in two orders, the Mucorales and the Entomophthorales. Rhinofacialentomophthoralesmainly affects the mucosa of the nares, nasal passages, nasal sinuses, nasopharynx, mouth, and spreads to adjacent tissues causing disfigurement of the face. It occurs predominantly in immunocompetent individuals and live as saprophytes in soil and decaying plant matter.[1] Rhinofacialconidiobolomycosis affects the subcutaneous tissues of the face, especially the paranasal sinuses as well as the deeper organs.[2] We report the case of a teen-aged female who presented to us with facial swelling and ulcer and was diagnosed by histopathology.

Case Report

An immunocompetent16-year-old girl from Chittagong presented to the outpatient department of Sheikh Hasina National Institute of Burn and Plastic Surgery with a one year history of progressive nasal and maxillofacial swelling. Swelling of face started from the nasal bridge and gradually spread into the left side of the face. For the facial swelling she had received multiple treatments, including glucocorticoids and antibiotics. But for the last one month she developed multiple ulcers with purulent discharge over the swelling. The physical examination reveals an ulcer over upper part of left cheek and swelling over bridge of nose. Adjacent area revealed erythema, edema, and tenderness over the nasal dorsum and forehead, extending to the soft tissue around left eyes (Fig. 1). Initially she has undergone biochemical and radiological investigations.

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Laboratory investigations included a haemoglobin of 11.6 gm/dl, total leucocyte count 12.36x10^9/L with a differential count within normal range, and platelet count was 400.1x 10^9/L. Other biochemical tests were within normal limit. Serology for hepatitis B surface antigen and human immunodeficiency virus 1 and 2 were negative. MRI of face revealed diffuse soft tissue thickening involving the paranasal sinuses, skin and subcutaneous tissue in left side of face extending into the left zygomatoco-temporal region. Direct naso-endoscopic examination revels left sided middle meatus. Septum and lateral wall of nose were congested. Middle meatus was adherent to the lateral wall of nose. At right side, crest of nose, middle meatus was distorted, nasal septum was absent/dehiscent on posterior part. There was no growth on nasopharynx. Biopsy specimens were obtained from multiple sites, including the forehead and the nose. The gross specimen consisted of two skin covered piece of tissue; largest one measured 4x3x1.5 cm and smaller one measures 1.5x0.8x0.5 cm. Skin surface showed multiple ulcers. The cut surface was solid and tan gray. Histopathological examination showed a chronic granulomatous inflammation (Fig. 2) with broad nonseptate branching hyphae surrounding amorphous eosinophilic substance, the Splendore-Hoeppli reaction (Fig. 3). Marked lympho-plasmacytic cell infiltrate with tissue eosinophilia and foreign body type of giant cells containing fungal elements were present. Periodic acid Schiff and Gomori-Methenamine-Silverstain highlighted the fungal elements and the surrounding amorphous eosinophilic material (Fig. 4 and 5). She was diagnosed as a case of Rhinofacialentomophthoramycosis. The patient was then on systemic antifungal therapy.

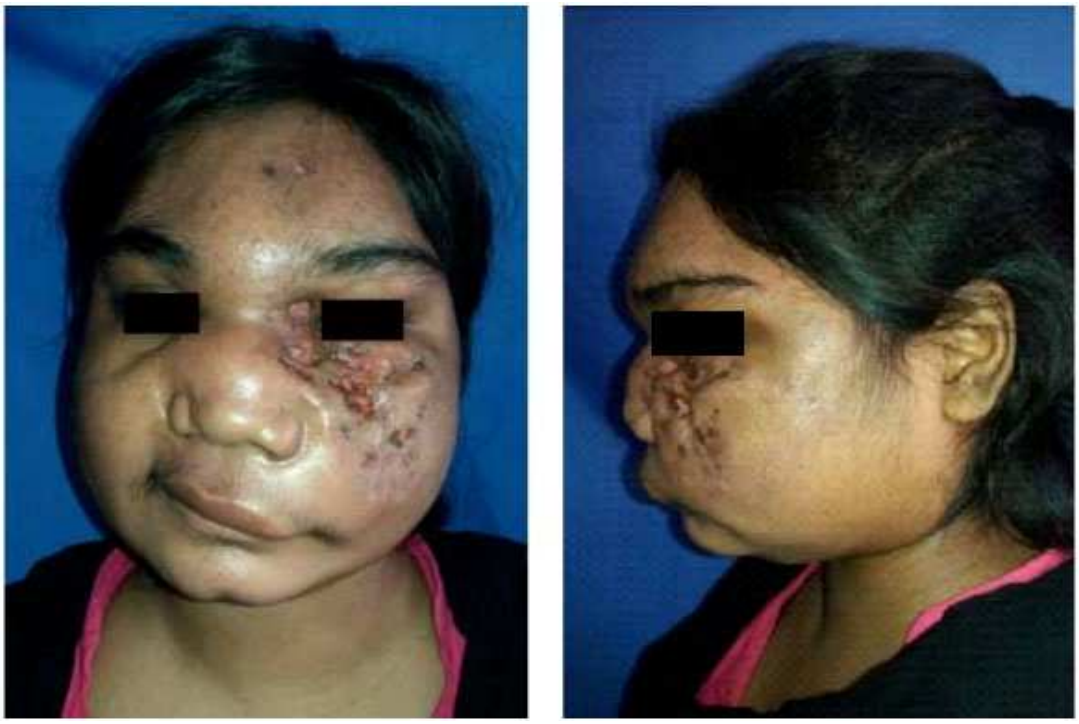

Figure 1. Ulcer in face front and lateral view of patient

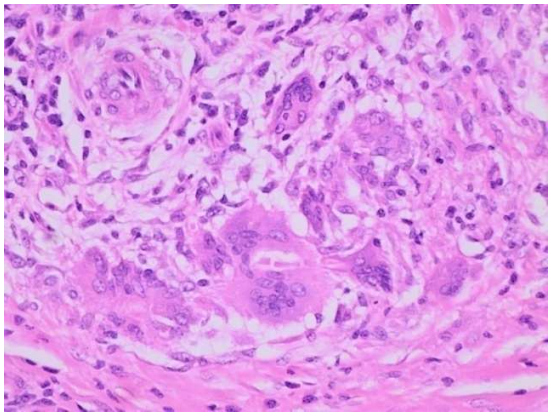

Figure 2. Epithelioid granuloma and giant cells containing fungal elements (H & E, 400X).

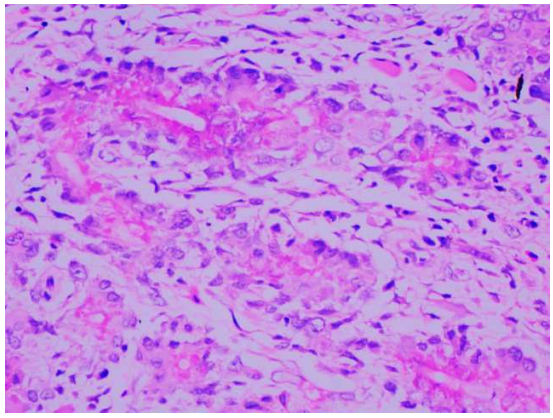

Figure 3. Splendore-Hoeppli phenomenon and dense inflammatory infiltrate (H & E, 400X).

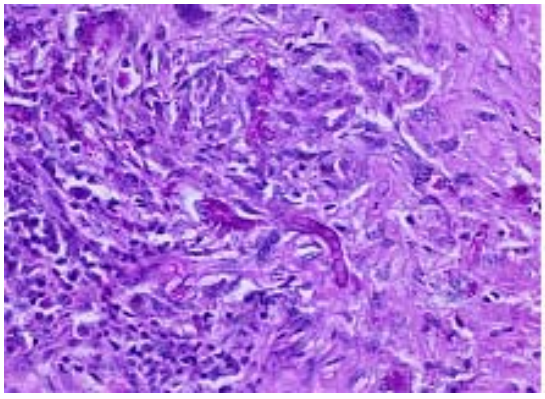

Figure 4. Fungal elements, broad hyphae in (PAS stain, 400X)

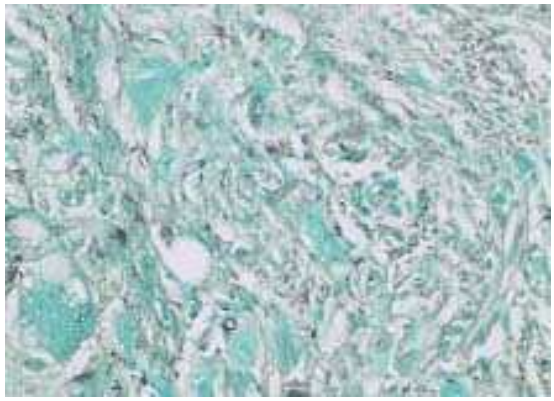

Figure 5. Hyphae in Gomori-Methenamine-Silver stain (GMS), 400X

Discussion

Rhinofacialentomophthoramycosis is an uncommon fungal infection; it mostly occurs in the tropical and subtropical regions of different parts of the world. G. Bras reported the first case of a Jamaican native in 1965. It is predominantly a chronic mucocutaneous and subcutaneous infection. The name *Entomophthorales* was coined from the Greek word "*Entomon*" meaning insect implicating their pathogenic nature in insects. Formerly, the two orders, namely *Mucorales* and *Entomophthorales,* we re classified in the phylum *Zygomycota*. Hibbett *et al*. suggested a comprehensive phylogenetic classification of the kingdom Fungi, and the phylum *Zygomycota* was eliminated as a result of polyphyletic characteristics.[3] Therefore, the taxa belonging to *Zygomycota* were distributed among the phylum *Glomeromycota* and four subphyla of uncertain placement (incertaesedis). *Entomophthorales* and *Mucor ales* as well as two other orders (*Kickxellales* and *Zoopagales*) were raised to the rank of subphyla and renamed as *Entomophthoromycotina*, *Mucoromycotina* , *Kickxellomycotina*,and *Zoopagomycotina*.[4] *E ntomophthoromycotina* encompasses twogenera that cause human infection, *Basidiolus* and *Conidiolus*.

Humans suffering from rhinoentomophthoromycosis get infected by the attachment of conidia of *C. coronatus* to nasal/sinusoidal mucosa. Initially, the disease presents like sinusitis.[5] A nodule at the nostrils indicates expansion into the subcutaneous fat.[6] The infection spreads within the subcutaneous fatty layers of the nasal bridge, eyelids, cheek, and upper lip. Swellings are firm, indolent, and, initially, often reddened and warm, while later they are often itchy.[7] Mucosal swellings rarely affect laryngeal structures or cause dyspnoea. Ulcerations of skin or mucosa may occurs, as we found in our case. Skin-adherent structures, eye motility, and vision usually remain unaffected; and bones, vessels, muscle, and lymph nodes are rarely involved. The course of the disease is usually benign.[8]

The diagnosis is based on a combination of mycologic and histopathological tests, and clinical presentation.Histological examinations and mycological cultures are the gold standard for confirmation of entomophthoromycosis. Biopsy of skin lesions is preferred for diagnosis than pus, as the chances of positive identification with potassium hydroxide preparation and culture are better with tissue specimens.[9] Entomophthoromycosis can be easily differentiated from other fungi by their characteristic hyphal morphology. The hyphae are broad, aseptate, or sparsely septate, with right-angle branching.[10] The histological inflammatory reaction shows infiltration with lymphocytes, plasma cells, epithelioid cells, multinucleate giant cells, and histiocytes with an area of central necrosis that is surrounded by eosinophilic infiltration. This phenomenon is called Splendore–Hoeppli phenomenon.[10] Our patient had all these typical features. PAS stain and GomoriMethenamine-Silver (GMS) stains are useful to demonstrate the fungal hyphae. Examination under fluorescent microscopy using fluorescent dye (Blankophor) wet mount preparation increases the sensitivity of diagnosis.[11] Definitive diagnosis requires culture, polymerase chain reaction testing, and immunohistochemistry.

Treatment for endomophthoromycosis ismedical and surgical. Systemic antifungal therapy and or surgical debridement is the primary choice in most cases. Several antifungal agents are used for the treatment of endomophthoromycosis such as itraconazole and amphotericin B.[12]

Conclusion

The entomophthoromycosis is a severe fungal disease that can affect both immunocompetent and immunocompromised individuals. Despite the clinical features, the disease requires biopsy for diagnosis, as histological examinations and mycological cultures are the gold standard for confirmation of entomophthoramycosis.This disease have a favorable prognosis if early treatments can be ensured.

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