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Rhinophycomycosis

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Abstract
Rhinophycomycosis, a subcutaneous fungal infection, is less uncommon than many other frequently cited granulomatous lesions of the paranasal sinuses. Four illustrative cases are presented with their characteristic clinical, radiological and histopathological features. The initial origin of the swelling was always in the region of the nasal vestibule and ala. The therapeutic response to potassium iodide, ketaconazole and fluconazole was dramatic and sustained.

Key words: Phycomycosis; Nasal Cavity

Introduction

In fungal taxonomy the order Entomophthorales includes two histopathologically similar, but clinically and mycologically distinct genera: basidiobolus and conidiobolus.[1] Both basidiobolomycosis and conidiobolomycosis present as subcutaneous infections in immunocompetent hosts. Basidiobolomycosis however predominantly involves the trunk and limbs, while conidiobolus primarily involves the nose and facial soft tissues.[2] These nasal/facial manifestations of *Conidiobolus coronatus* have been variously termed as rhinophycomycosis, conidiobolomycosis, rhinoentomophthoromycosis, and nasofacial zygomycosis.

The first clinical description of rhinophycomycosis was given by Martinson[3] in 1963, while Bras *et al*.[4] in 1965 identified *Entomophthora coronata* as the causative agent. The majority of cases described subsequently have been from tropical areas.[5–9] Cases have however also been reported from the developed world.[10–12]

The clinical presentation, though characteristic, is nevertheless often unrecognised, primarily because of a lack of awareness of his pathological condition. We report here four cases seen at our department over a two-year period, which are illustrative of the characteristic clinical, histological and radiological features.

Case report

A 55-year-old male from eastern India presented with a slowly progressive painless swelling in the mid-face present for six months. The swelling involved the left cheek, nasal dorsum, upper lip, lower eyelid and buccal sulcus (Figure 1) and also caused medial displacement of the lateral nasal wall. It was firm in consistency and the overlying skin was stretched and shiny and infiltrated. There was no tenderness, ulceration, fixity to bone, rise in temperature, malocclusion or distortion of the upper alveolus or palate. A biopsy of the subcutaneous tissues performed by the sublabial route demonstrated a gritty, whitish soft tissue mass superficial to the facial bones. Histopathological examination of the mass showed, fibrocollagenous tissue with inflammatory infiltrates consisting of lymphocytes,

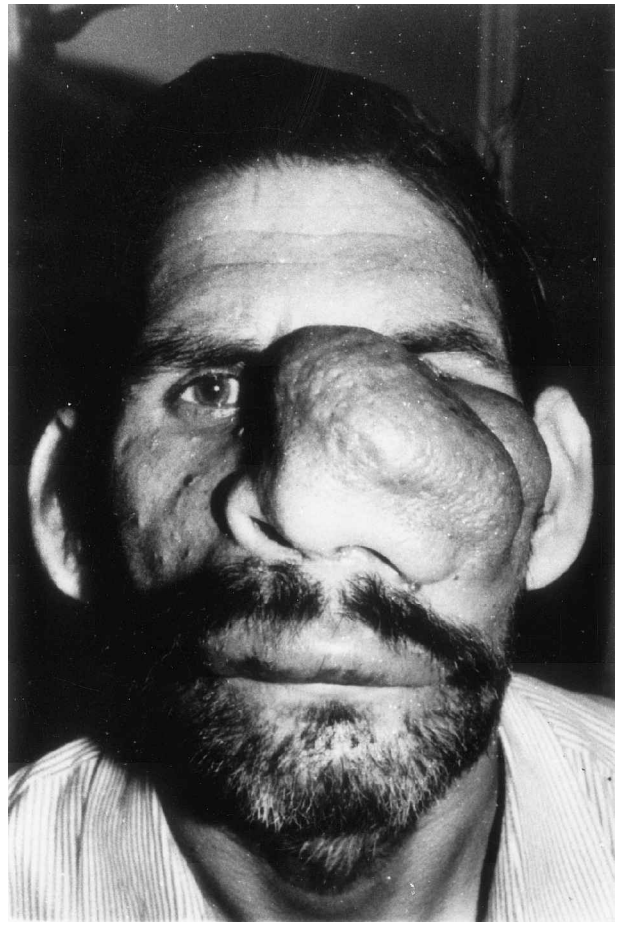

Fig. 1

Case 1 displaying the characteristic clinical appearance of rhinophycomycosis. The swelling is entirely subcutaneous and displays no fixation to the underlying bone.

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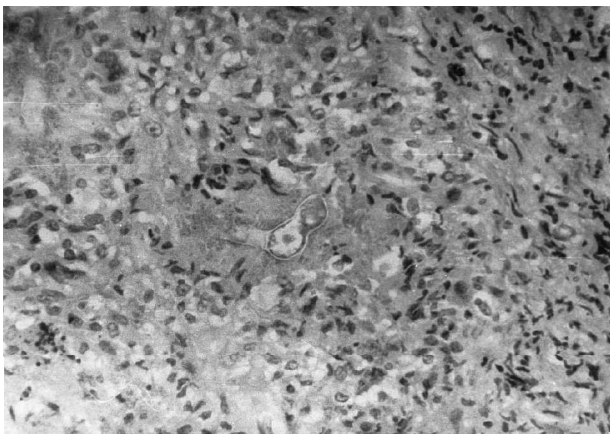
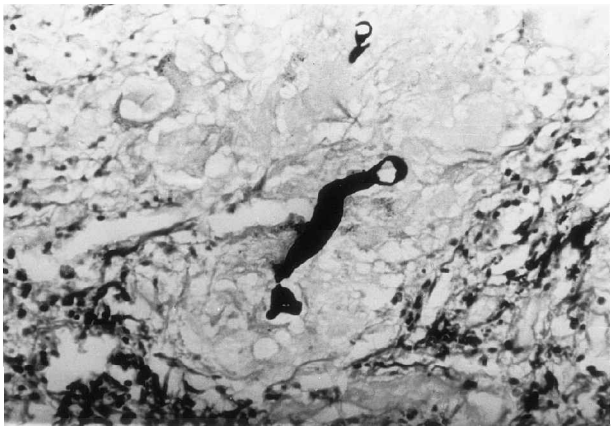


(a)



(b)

FIG. 2a, b.

(a) Photomicrographs demonstrating fungal hyphae surrounded by an eosinophilic acellular homogeneous material (Splendore-Hoeppli phenomenon) amid an inflammatory infiltrate (H&E × 200). (b) Fungal hyphae are stained black with the silver-methenamine stain (× 200).

plasma cells, eosinophils and foreign body giant cell reaction. Some fungal hyphae were seen along with surrounding eosinophilic material (Figure 2). The fungal hyphae stained better with Periodic acid-Schiff (PAS) and silver methenamine stains. No vascular invasion was seen. On the basis of these histological findings a diagnosis of entomophthoromycosis was made.

Treatment was started with oral fluconazole (100 mg o.d.) and saturated solution of potassium iodide (1 g/ml) at an initial dose of 1 ml/day in three divided doses and subsequently increased to 3 ml/day. An initial rapid response was noted within three days with subsequent slow resolution over the ensuing few months (Figure 3). The treatment was continued for a total of nine months and the subcutaneous swelling subsided completely, though some of the initially expanded skin remained in excess. This excess skin has since been surgically excised and the excised specimen did not show any residual fungus.

This case and the three other cases are described in Table I. All four cases were residing in rural areas and had involvement of the mid-facial soft tissues with no fixity to the underlying bone. Involvement of the nasal ala was invariable. Histological confirmation of the diagnosis either by an incisional sublabial biopsy or by an excision biopsy (Case 4) was obtained in all cases. Case 2 demonstrated an additional non-enhancing soft tissue

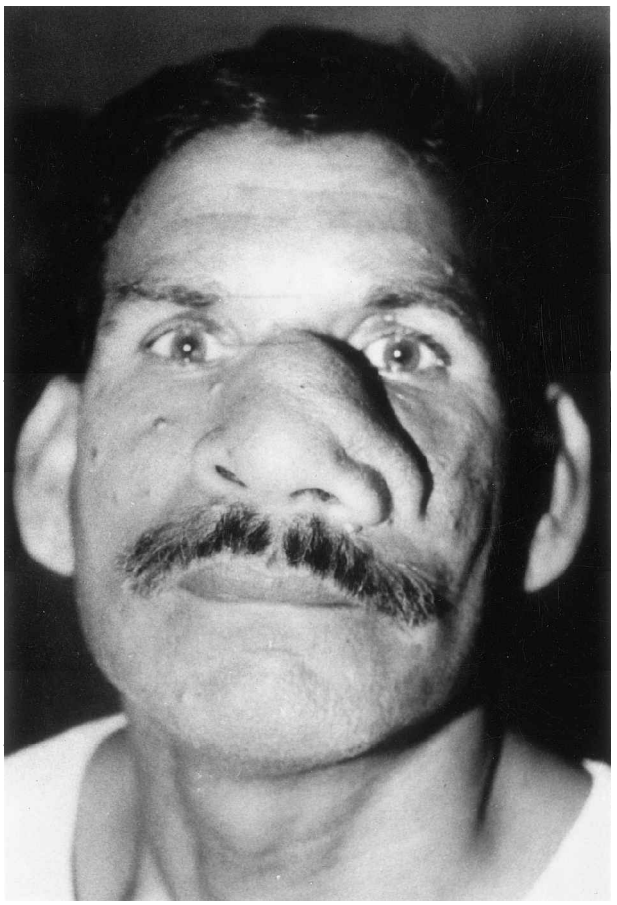


FIG. 3

Same patient as in Fig. 1 at nine months following initiation of treatment. By nine months the subcutaneous mass had completely disappeared, but excess skin remained.

opacification of the ipsilateral maxillary sinus. The attenuation value of the maxillary sinus opacification was however clearly different from the subcutaneous/submucosal mass and was therefore thought to represent mucosal secretions secondary to ostial obstruction. Subsequent surgical exploration of the antrum undertaken concurrently with the sublabial biopsy of the subcutaneous mass confirmed that the antrum was uninvolved and only demonstrated mucosal thickening, which was histologically unremarkable.

Discussion

Rhinophycomycosis, though uncommon, is nevertheless in our department commoner than many of the other more usually cited sinonasal granulomatous lesions such as syphilis, leprosy, yaws and sarcoidosis. Little reference, however, to this condition is found in the otorhinolaryngological literature. It is entirely unmentioned in most standard texts and only very rarely reported in other literature.[6,11,13] This report aims to make the practising otolaryngologist aware of the condition.

The clinical presentation of a mid-facial, painless, slowly progressive subcutaneous mass which usually infiltrates and expands the overlying skin but is freely mobile over the underlying bone (Figure 1) is characteristic and also quite diagnostic of rhinophycomycosis. The differential diagnosis includes neoplasia, paracoccidiomycosis and leishmaniasis. In one of our cases plexiform neurofibromatosis was also considered as an initial clinical diagnosis. Few of these other lesions, however, present with a

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TABLE I
CLINICAL AND TREATMENT PROFILES OF STUDY GROUP

Case no.	Age/ sex	Duration of Symptoms	Extent	Treatment	Post-treatment course
1.	55 M	6 mths	Lt cheek, nasal dorsum, upper lip, gingivo-buccal sulcus, lateral nasal wall	Potassium iodide (1–3 g/day) x 6 mth Fluconazole (100 mg/day) x 9 mth	Complete resolution of mass. Excess residual skin subsequently excised
2.	21 M	2 mths	Rt ala, cheek, nasal dorsum, upper lip, rt. inf. turbinate	Potassium iodide (1–3 g/day) x 4 mth Fluconazole (100 mg/day) x 4 mth	Complete clinical resolution by 3rd month of therapy
3.	28 M	6 mths	Rt ala, nasal dorsum and nasion, upper lip, bilateral lateral nasal wall	Potassium iodide (1–3 g/day) x 6 mth Ketoconazole (200 mg/day) x 6 mth	Complete clinical resolution
4.	42 M	3 mths	Nodule on rt nasal ala- Excised completely	Potassium iodide (1–3 g/day) x 2 mth Fluconazole (100 mg/day) x 4 mth	Residual induration at biopsy site; no progression on cessation of treatment

M = male; Mths = months; Rt = right; Lt = left.

predominant and near-exclusive involvement of the subcutaneous tissues. Also, the dramatic response of rhinophycomycosis to treatment with potassium iodide is again not manifested by these other entities.

Though our cases demonstrated submucosal involvement of the nasal tissues, no bone erosion or necrosis was observed, nor was any fungal involvement of the sinus cavities noted, The radiological opacification of the maxillary sinus as seen in one case was secondary to collected secretions caused by an ostial block, and not due to direct invasion of the fungus. Such absence of bone destruction or bone reaction has also been noted previously.[14]

Conidiobolus species are present naturally in soil, decaying vegetation and insects.[15] Infection in horses and mules has been documented. The exact mode of infection in humans is not known and it is postulated that the organism is introduced into the subcutaneous or submucosal tissues by trauma, inhalation of spores or insect bite.[14] Most reported cases including the cases in this report are from rural or forested areas. The disease typically affects immunocompetent young adult males[16] – presumably a reflection of the somewhat higher exposure risk in this group.

It has been our observation that the swelling has invariably initially originated in the region of the vestibule and nasal ala. Possibly, digital trauma and nose-picking may serve to introduce the organism from the fingernails or the nasal vestibular skin onto the submucosal tissues of the nasal vestibule.

The disease usually runs an indolent and gradually progressive course but there are reports of spontaneous regression.[17] In the immuno-compromised it may however run a fulminant mucormycosis-like course.[12] Systemic involvement with pneumonitis and mediastinal involvement have been reported with entomophthora species other than *Conidiobolus coronatus*.[18,19] Death due to entomophthoromycosis has also been reported.[12,20]

Routine haematological and biochemical parameters are not usually altered. X-rays and CT scans can help in delineating the extent of disease. Potassium hydroxide 10–20 per cent mounts (KOH) scrapings from the nasal mucosa may demonstrate broad non-septate or sparsely septate hyphal elements with granular inclusions.[1] Culture of the fungus is, however, difficult with a reported positivity rate of only 15 per cent.[11] Serodiagnosis by immunodiffusion has been described.[21]

The diagnosis is best established by a skin or nasal biopsy.[5] A specimen from the paranasal sinus may, however, be misleading as such involvement may be the result of obstruction rather than invasion. On biopsy the involved tissue appears whitish and gritty with tiny foci of yellowish exudate.[2] In early lesions the subcutaneous tissue contains collections of neutrophils and eosinophils around large aseptate hyphae which measure 3.5–10 μm in diameter. In older lesions eosinophils become less numerous and histocytes, lymphocytes and epitheloid cells surround the hyphae. A characteristic histopathological feature, the Splendore-Hoeppli phenomenon (Figure 2), refers to the presence of eosinophilic tissue response around the organism, and is thought to reflect the immune response of the host. Vascular invasion as seen in mucormycosis is not a feature of rhinophycomycosis.[2,10,12]

The response of the swelling to potassium iodide is dramatic and may itself be an aid to the diagnosis. Dosages of 2–8 g/day continued fo four weeks to one year are described.[5] The combination of sulfamethoxazole plus trimethoprim with potassium iodide has also been described.[22] Resistance to potassium iodide has been reported and amphotericin B,[4] ketoconazole[23] and itraconazole[24] have been used in these situations.

All our patients were treated with the combination of potassium iodide with fluconazole or ketoconazole and responded well. Recrudescences after initial successful treatment have however been reported,[5,6] and these patients therefore remain on continuing long-term follow-up.

Conclusion

Rhinophycomycosis, though unusual, presents with the characteristic clinical profile of a subacute painless subcutaneous mass. Travel or residence in a tropical rural area should enhance clinical suspicion of this disorder. The response to potassium iodide is rapid and may itself indicate the diagnosis.

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