

# Case Studies

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Several cases can mimic invasive fungal rhinosinusitis, either clinically or radiologically or both. This causes confusion and controversy among clinicians with misdirection of treatment. A few such cases are discussed here.

## Case 1

A 26-year-old immunocompetent lady came with complaints of recurrent rhinitis, headaches, and right diplopia since 4 days. On nasal endoscopy, there was grossly deviated septum to the right with multiple polyps (arrow) in the left nasal cavity (Fig. 1). CT scan of paranasal sinuses was obtained (Figs. 2 and 3).

The patient underwent endoscopic nasal clearance of the sinuses. Intraoperatively, there was inspissated pus and debris (arrow) (Fig. 4) in both the sphenoid sinuses, but the lining mucosa of the sinuses appeared normal.

Histopathology showed typical features of allergic fungal sinusitis (Fig. 4).

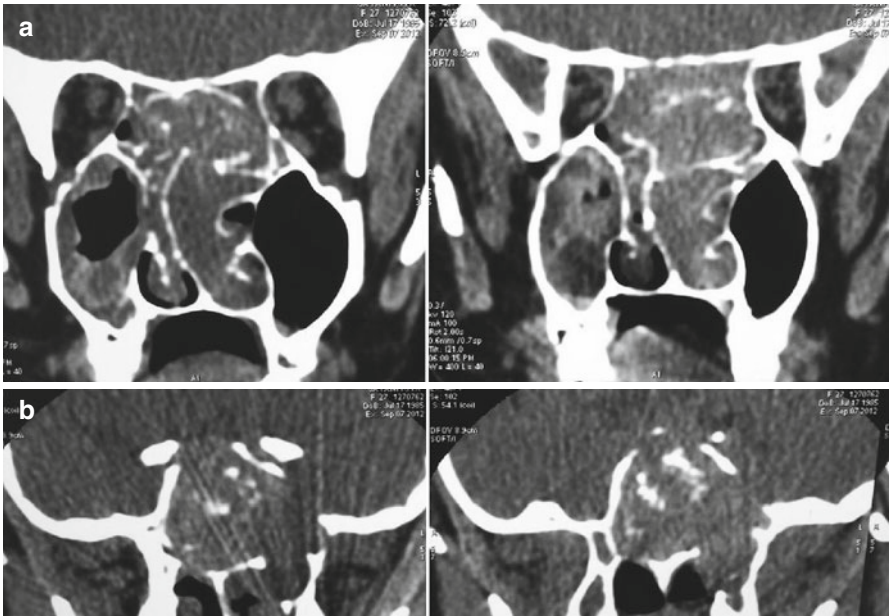
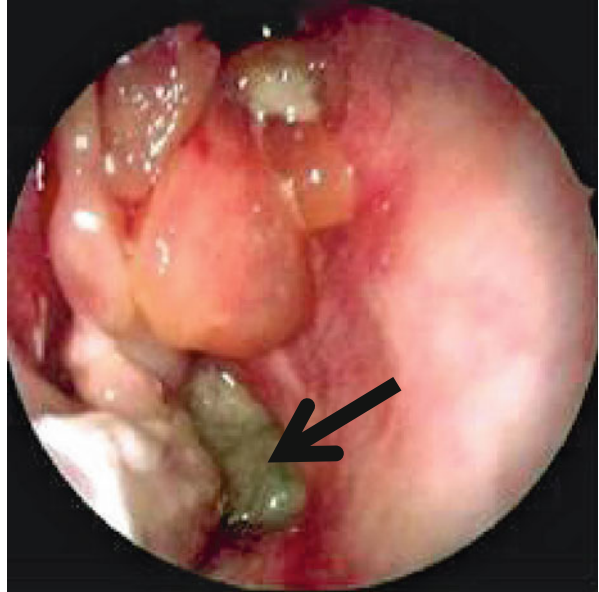
The patient was started on oral and topical nasal steroids with nasal douching following surgery. Three months postoperatively, the patient's diplopia recovered and the appearance of the sphenoid sinus is shown in Fig. 5.

*Discussion:* Allergic fungal sinusitis (AFS) is a noninvasive form of fungal rhinosinusitis. It contributes to approximately 6–9 % of all rhinosinusitis requiring surgery [1]. Patients of AFS usually present with chronic rhinosinusitis with nasal polyps, atopy, and elevated total serum IgE, and their sinuses are filled with characteristic “peanut butter”-like eosinophil-rich “allergic mucin” containing sparse fungal hyphae. CT scan of the sinuses (Figs. 2 and 3) is always abnormal, usually showing bilateral and multiple sinus involvement with near total opacification and

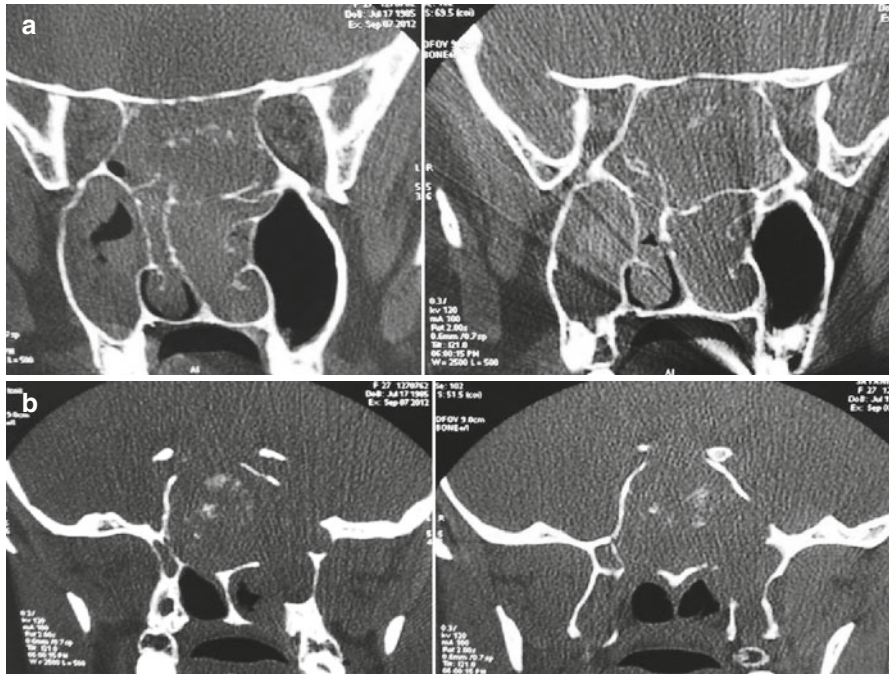
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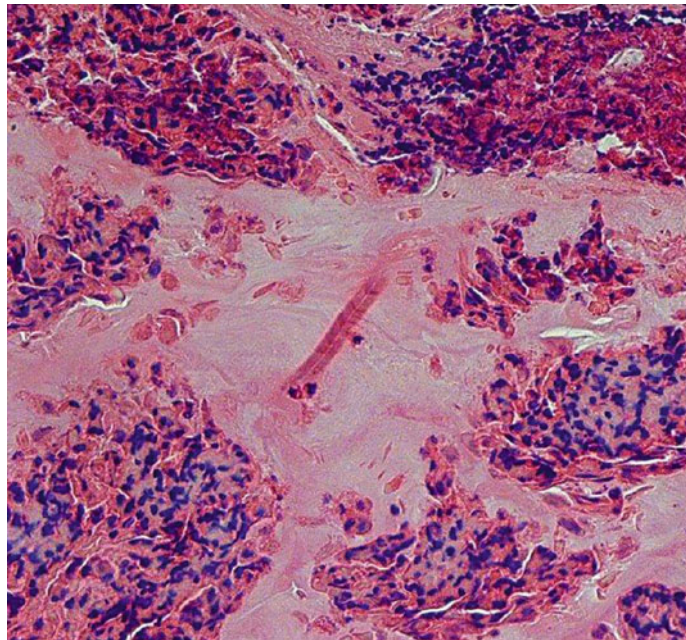
**Fig. 1** Nasal endoscopy showing left nasal polyposis with allergic “peanut butter” mucin (arrow)



**Fig. 2 (a, b)** Case 1: Coronal plain CT scan (soft tissue settings) showing extensive polypoid soft tissue in both ethmoid, sphenoid, and right maxillary sinuses. Note irregular hyperdense areas within them, which may be due to inspissation or superadded fungal infection



**Fig. 3** (a, b) Case 1: Coronal plain CT scan (bone window settings) showing marked attenuation of the bony ethmoid wall, with erosions in the sphenoid sinus wall. Note extension of soft tissue inferiorly towards the left pterygoid and left lateral parasphenoid regions



**Fig. 4** H&E stain showing allergic fungal mucin with Charcot-Leyden crystals

**Fig. 5** Case 1: 6 weeks post-op endoscopic appearance of the right sphenoid sinus



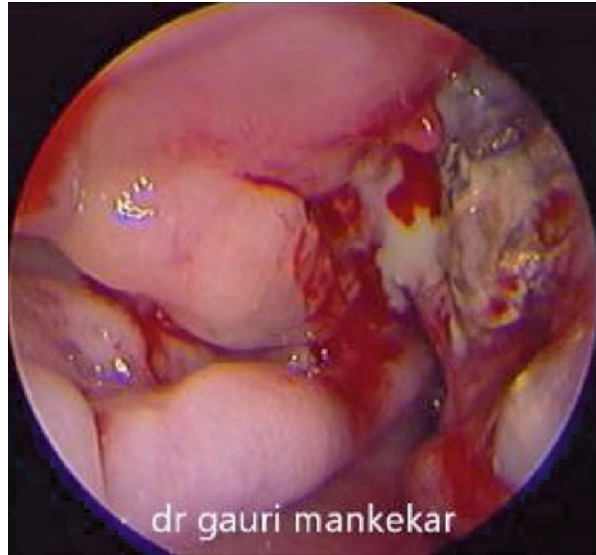
expansion of the sinuses. Expansion, remodeling, or thinning/erosion of the adjacent bony sinus wall is frequently seen, due to the expansile nature of the accumulating mucin. Bony erosions and extension into adjacent vital cavities may be seen in about 20 % cases [1]. AFS allergic mucin, on culture, is typically positive for either dematiaceous fungi like *Bipolaris spicifera* or *Curvularia lunata* or *Aspergillus* species like *A. fumigatus*, *A. flavus*, or *A. niger* [2]. Cases of allergic fungal sinusitis with loss of bony architecture on imaging studies may be misinterpreted as evidence of bony invasion [3] and labeled as invasive fungal sinusitis. But histopathology showing absence of tissue invasion should enable the clinician to diagnose AFS and differentiate it from other forms of both noninvasive and invasive fungal sinusitis. The patient of AFS can be managed with surgical debridement, systemic and local steroids, and nasal douching without systemic antifungals.

Patients with allergic fungal sinusitis showing tissue invasion on histopathology are being encountered and are being termed as “mixed” infection. Such a progression may be due to change in host defenses [4]. These cases may require systemic antifungals, in addition to surgical debridement, nasal douching, and regular follow-up with nasal endoscopy and radiological imaging. Reports suggest oral itraconazole therapy, especially in recalcitrant cases, may avoid or delay revision surgery [5, 6] and even enable patients to reduce or even stop oral steroid therapy [6].

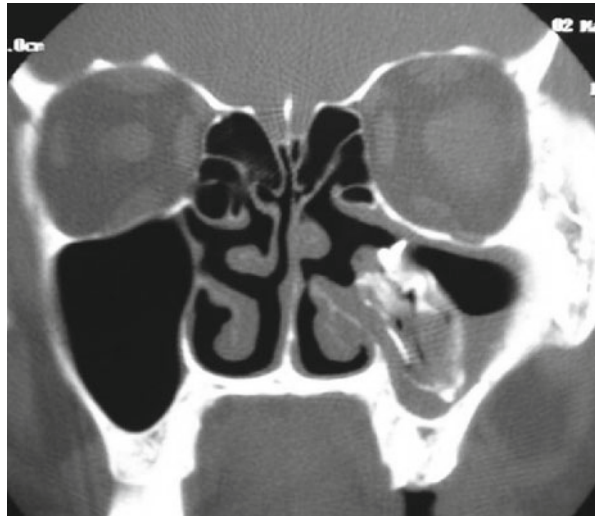
## Case 2

A 55-year-old male patient came with history of foul smelling breath with left purulent rhinorrhea. On examination, his left nasal cavity showed purulent discharge from the left middle meatus region (Fig. 6). A CT scan of the paranasal sinuses was done (Fig. 7).

**Fig. 6** Endoscopic picture of foul smelling purulent discharge from the left middle meatus



**Fig. 7** Case 2: CT coronal image shows a lobulated hyperattenuating fungal ball in the left maxillary sinus



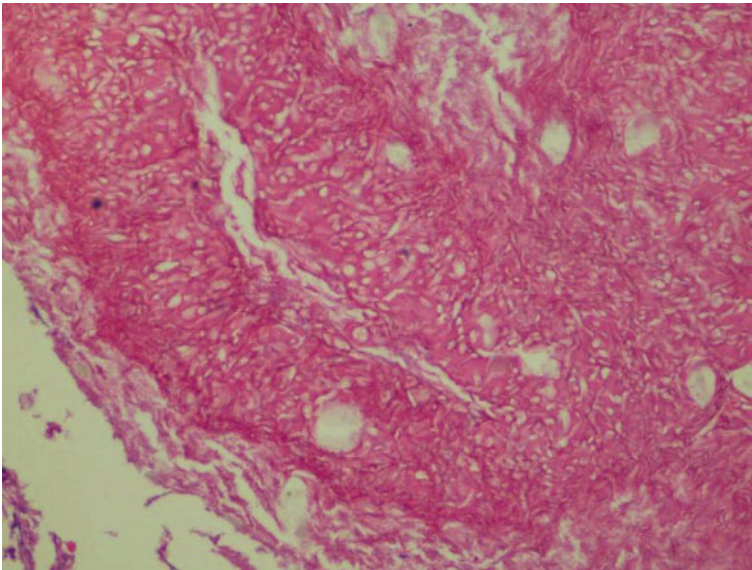
The patient underwent endoscopic debridement of the left maxillary sinus. Intra-op endoscopic appearance of the fungal ball is shown in Fig. 8.

Histopathological appearance is shown in Fig. 9.

Subsequently he was started on saline nasal douches and completely recovered.

*Discussion:* A fungal ball or mycetoma or aspergilloma or chronic noninvasive granuloma is described as the presence of noninvasive accumulation of dense conglomeration of fungal hyphae in one sinus cavity. It usually affects a single sinus,

**Fig. 8** Intra-op endoscopic appearance of the fungal ball (arrow)



**Fig. 9** Histopathology: H&E stain (original magnification 400×) showing fungal ball with compactly packed septate branching fungal hyphae, morphologically resembling *Aspergillus* spp

commonly the maxillary sinus and rarely the sphenoid sinus [7]. It is more common in middle-aged and elderly females, in contrast to invasive sinusitis and aspergillosis which are common in males [8]. The disease is identified due to its characteristic radiologic appearance (Fig. 7) – single sinus opacification with or without radiographic heterogeneity; mucopurulent, cheesy, or clay-like material within the sinus, a dense conglomeration of hyphae separate from the sinus mucosa; nonspecific

**Fig. 10** Case 3: Coronal plain CT scan (soft tissue settings) shows polypoidal soft tissue in the right maxillary sinus, with linear hyperdensity within it



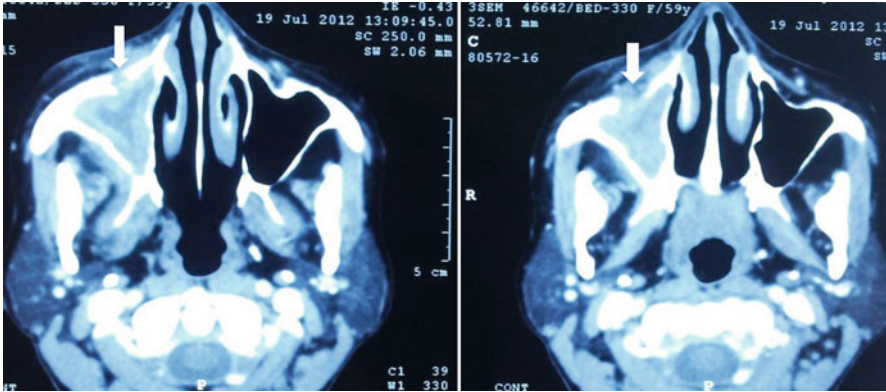
chronic inflammation of the mucosa; lack of predominance of eosinophils or granuloma or allergic mucin; and lack of evidence of mucosal invasion on histopathology [9]. The fungal ball appears like a hyperattenuating mass on non-contrast CT scan due to dense matted hyphae. Occasionally there may be punctate calcifications. The bony walls of the sinus may be sclerotic and thickened or expanded and thinned with focal areas of erosion due to pressure necrosis. On MRI, the fungal ball appears hypointense on T1- and T2-weighted images due to the absence of free water. Signal void is also generated on T2-weighted images due to calcifications and paramagnetic metals such as iron, magnesium, and manganese within the mycetoma.

Such cases could be clinically and radiologically mistaken as invasive fungal sinusitis. But histopathology is diagnostic (Fig. 9) as it does not show tissue invasion. The fungi remain noninvasive in the context of the fungal ball, but could rarely become invasive after substantial immunosuppression, such as in renal transplantation [10]. Identification of *Aspergillus* species as the causative agent may be aided by the use of galactomannan detection in the sinus material [11].

Surgical debridement, as in this patient, is the only treatment required.

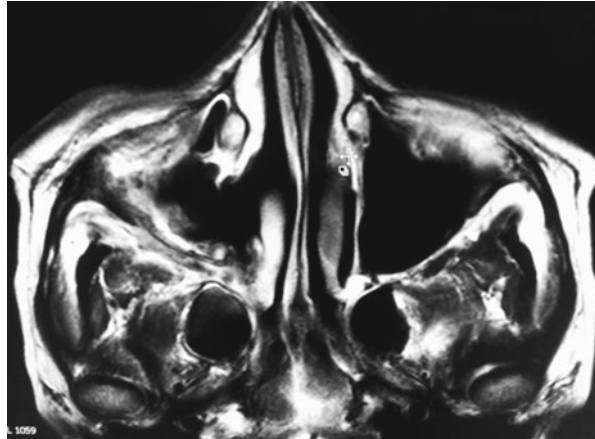
### Case 3

A 59-year-old lady came with complaints of severe pain along the right cheek with diplopia and photophobia. She had history of recurrent rhinitis and had undergone a CT scan of the paranasal sinuses elsewhere. It had shown (Figs. 10 and 11) right maxillary sinusitis with hyperdense foci with sclerosis and erosion of the maxillary sinus and inferior orbital wall with suspicion of fungal sinusitis and local invasion. Based on the scan, she had undergone nasal endoscopy elsewhere, and the tissue from the right maxillary sinus had shown *Aspergillus* species on KOH mount. So she had been started on oral voriconazole. A few weeks after voriconazole, due to



**Fig. 11** Case 3: Axial CT contrast-enhanced scan shows the same lesion in the right maxillary sinus as in Fig. 10. Erosion is seen along the anterior wall of the right maxillary sinus (*arrows*)

**Fig. 12** Axial MRI scan showing decreased mucosal thickening and enhancement within the right maxillary with persistent ill-defined soft tissue and enhancement within the retro-maxillary fat

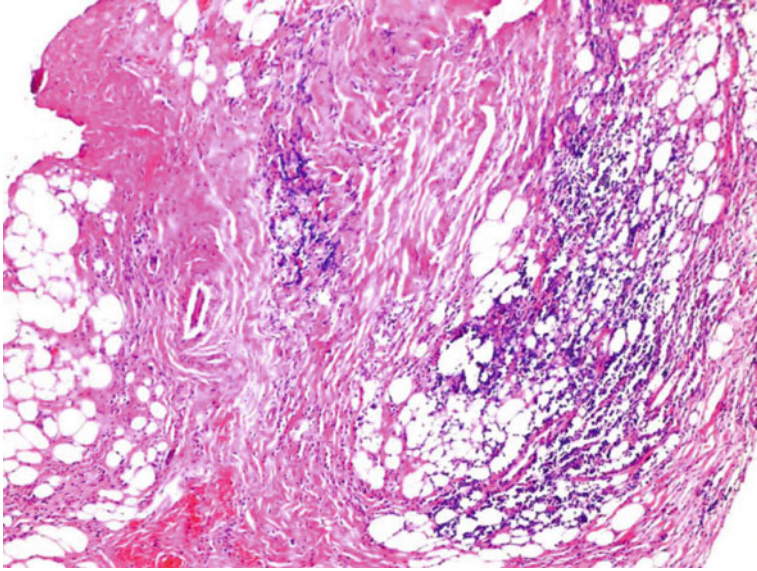


increasing severity of pain, she reported to us for a second opinion. On examination, nasal endoscopy showed only scarring from previous surgery.

Since no histopathological confirmation of the diagnosis of invasive fungal sinusitis was available from the first surgery, it was decided to obtain tissue for histopathology. MRI scan of the orbit and paranasal sinuses done at this time showed (Fig. 12) decrease in the mucosal thickening and enhancement within the right maxillary sinus and along the floor of the right orbit as compared to the previous CT scan. The ill-defined soft tissue and enhancement within the retro-maxillary fat extending into the infratemporal and pterygopalatine fossa were unchanged.

An endoscopic biopsy from the right medial maxillary wall as well as a subconjunctival biopsy from the infraorbital region was performed. On histopathology, the lesion showed moderately dense fibrosclerotic tissue with nodular and diffuse lymphoplasmacytic infiltrate. The lesion was seen eroding the bone, entrapping the vessels, nerves, and mucous glands. The entrapped glands were atrophic. There were no granulomas, no fungal infection, and no lymphoproliferative disorder. The lesion





**Fig. 13** Case 3: H&E  $\times 40$  original magnification: dense sclerotic inflammatory tissue infiltrating into fat

was diagnosed as inflammatory pseudotumor (Fig. 13) on histopathology. The patient was started on oral steroids and voriconazole was discontinued. Microbiology of the tissue was negative for fungus and bacteria. Voriconazole was discontinued, and patient was started on 40 mg oral steroids in divided doses. The patient was relieved of pain within a week of starting steroids. She has been symptom free for the past 5 months.

*Discussion:* Inflammatory pseudotumor (IPT) is a chronic, inflammatory, non-malignant lesion of unknown origin [12]. It is a space-occupying lesion produced by chronic inflammation and tissue fibrosis and is steroid responsive [13]. IPT in the head and neck region can be locally aggressive, with bony erosion and severe neuralgia like infraorbital neuralgia in this patient. Diagnosis is difficult as clinically and radiologically IPT is indistinguishable from invasive neoplasms [14–16] and invasive fungal lesions [17]. In this patient, it is debatable whether the initial treatment with oral voriconazole made it difficult to isolate *Aspergillus* spp. during the subsequent tissue sampling or whether the patient was a case of pseudotumor primarily who had been misdiagnosed as invasive *Aspergillus* sinusitis.

## Case 4

A 45-year-old diabetic male came with an ulcer along the right nasolabial crease (Fig. 14) and a palatal ulcer (Fig. 15) since 3 months. It had been progressively increasing in size. Biopsy elsewhere had been inconclusive. Clinically it could be mistaken for invasive fungal sinusitis.



**Fig. 14** Right nasolabial fold ulcer (*arrow*)



**Fig. 15** Palatal perforation (*arrow*)

The biopsy was repeated, taking tissue from the palate. Histopathology revealed NK/T-cell lymphoma, and the patient was referred for chemotherapy – radiation.

*Discussion:* Clinically, the lesion could be mistaken for invasive fungal sinusitis, but histopathology is diagnostic and immunohistochemistry enables further



**Fig. 16** Subcutaneous swelling (*arrow*) of the right nasal dorsum

classification of the tumor. In most cases EBV genomes are detectable in the tumor cells, and immunophenotyping may show CD56 positivity. NK/T-cell lymphoma is a rare, aggressive subtype of lymphoma associated with extensive necrosis and angioinvasion. It presents in extra-nodal regions, especially, the nasal or paranasal sinus region. Historically, this tumor was considered part of lethal midline granuloma. It may be associated with hemophagocytic syndrome and has a highly aggressive course with poor prognosis. In view of the poor response of the tumor to standard chemotherapy and radiation, some oncologists recommend bone marrow or peripheral stem cell transplantation.

### Case 5

Mr M aged 55 complained of broadening of nose, nasal block, and occasional epistaxis since 5–6 months. On examination, the nose appeared broad (Fig. 16) (arrow) with thickening of the skin over the nasal dorsum. Anterior rhinoscopy showed hypertrophied turbinates, severe nasal mucosal congestion with no visible airway. Subcutaneous biopsy was obtained from the external nasal swelling. The biopsied tissue was sent for potassium hydroxide preparation and fungal culture. Broad

thin-walled nonseptate mycelia were found in the KOH preparation. In the Sabouraud's dextrose agar medium are rapidly growing flat cream-colored colonies with conidia indicative of subcutaneous dermatomycoses or *Conidiobolus coronatus*. Patient was started on oral potassium iodide drops in tapering doses along with tab. fluconazole 200 mg daily. During treatment, the patient's thyroid function tests, SGPT, and serum potassium were monitored. The treatment was continued over 6 months, and the patient responded well with reduction in external nasal swelling. The nasal block disappeared, and the patient was able to breathe comfortably.

*Discussion:* Patients with rhinofacial swelling and unilateral nasal obstruction presenting to the ENT surgeon can present a diagnostic dilemma. Rhinoentomophthoromycosis (conidiobolomycosis) is a rare, chronic, localized, subcutaneous zygomycosis characterized by painless, woody swelling of the rhinofacial region [18]. Usually the lesion is firmly attached to the skin without involvement of the underlying bone. Therefore, tissue for testing has to be obtained from the affected subcutaneous tissue. It is a slowly progressive, but rarely life-threatening condition. It is caused by *Conidiobolus coronatus* (*Entomophthora coronata*), a fungus belonging to the order

Entomophthorales. KOH preparation of the biopsy tissue from the lesion reveals broad, nonseptate, thin-walled mycelial filaments. In Sabouraud's dextrose agar (SDA) medium, colonies of *Conidiobolus coronatus* grow rapidly. Histopathology shows fibroblastic proliferation, chronic granulomatous inflammatory reaction, and broad thin-walled hyphae [19].

Treatment of rhinoentomophthoromycosis is difficult because the diagnosis is delayed. Patients often respond to oral itraconazole (200–400 mg/day), ketoconazole (200–400 mg/day), fluconazole (100–200 mg/day), amphotericin B, and cotrimoxazole [20]. Prolonged treatment and follow-up is required.

Saturated potassium iodide solution (1 g/ml) is useful for patients because of its ease of administration and low cost.

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## Case 5

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