Invasive paranasal mucormycosis with peripheral eosinophilia in an immunocompetent patient

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A 53-year-old healthy patient was admitted with unilateral nasal obstruction of one month duration which was suspected to be a malignancy because of mass-like finding on radiology and peripheral eosinophilia. The biopsy of the involved sinus showed tissue invasion by aseptate hyphae suggestive of a zygomycete and tissue infiltration of eosinophilia. He was diagnosed as invasive paranasal mucormycosis and treated with complete endoscopic sinus surgery and amphotericin B deoxycholate. Paranasal symptoms with peripheral eosinophilia might be a presentation of invasive fungal sinusitis.

Keywords Mucormycosis, paranasal, sinus eosinophilia

Introduction
Mucormycosis is known to be a fatal, rapidly destructive, and opportunistic infection. It is caused by fungi, of the order Mucorales, family Mucoraceae, which includes the genera Absidia, Mucor, Rhizopus, Rhizomucor, and Cunninghamella. These fungi are ubiquitous in nature and healthy hosts usually have a strong resistance to infections caused by them. However, the organisms may become pathogenic in association with diabetic ketoacidosis or other immunosuppressive disorders [1]. Mucormycosis has been rarely reported in an immunocompetent host. Invasive mucormycosis may be misdiagnosed clinico-radiologically as malignancy, which leads to overtreatment or late diagnosis with resultant fatal clinical course [2]. We describe a case of invasive mucormycosis in a middle aged healthy man with peripheral and tissue eosinophilia and provide additional information to the limited literature on this disease.

Case report
A previously healthy 53-year-old male patient presented with a one-month history of unilateral nasal obstruction. His local practitioner suspected acute rhinosinusitis and prescribed oral 2nd generation cephalosporin. The patient suffered from nasal stuffiness and left orbital pain, which became more intense regardless of his use of antibiotics. He underwent computed tomography (CT) scan (Fig. 1), which showed enhancing mass-like lesion in the left anterior ethmoidal sinus, middle and inferior turbinates. The patient was referred to the tertiary hospital for further evaluation. On admission, swollen septal and turbinal mucosae were seen via endoscopic nasal examination. The physical examination revealed a temperature of 36.8°C with otherwise normal vital signs. The ophthalmologic examination revealed normal findings. Hematological examination disclosed hemoglobin 14.5 g/dl, hematocrit 42%, white blood cell count 8,450/μl, platelet count 245,000/μl, eosinophil count 2197/μl (26%), and atypical lymphocyte 16%. Glucose test was 87 mg/dl and serum serologic tests for human immunodeficiency virus, Hepatitis B and C virus were negative. Skin prick and stool parasite tests were performed to elucidate the cause of peripheral eosinophilia. Helminthiasis such as cysticercosis, paragonimiasis, sparganosis or clonorchiasis were checked by specific IgG ELISA. Skin prick tests demonstrated multiple allergens, i.e., wheat, rice, birch, oak, and a variety of weeds. Other tests were also negative. Serologic studies such as fluorescent antinuclear antibody and antineutrophil cytoplasmic antibody were all negative.

Endoscopic biopsy was performed under the general anesthesia with clinico-radiological suspicion of malig-
nancy. Histopathology revealed necrotizing granulomas consisting of lymphocytes, plasma cells and multinucleated giant cells. Tissue eosinophilia was also shown on hematoxylin-eosin stain material (Fig. 2). Periodic acid Schiff stain (PAS) and Gomori’s methenamine silver stain (GMS) highlighted several right-angle branching fungal hyphae (Fig. 3A and 3B), but the organism failed to grow in culture. The patient underwent radical debridement of all anterior ethmoidal sinuses and necrotic inferior and middle turbinates were completely removed. Pre- and postoperative antibiotics (2nd generation cephalosporin) were used to prevent postoperative secondary bacterial infection. After endoscopic debridement, peripheral eosinophil count decreased to the normal range. Systemic antifungal treatment was started with intravenous standard amphotericin B until a dose of 3.0 g had been provided.

The patient was followed up by endoscopic examination monthly. Post-treatment examination showed clean nasal cavity and no recurrence. He has been free of disease for more than 6 months after the operation.

Discussion

Mucormycosis in the paranasal sinuses presents initially with signs and symptoms of acute sinusitis, often progressing very rapidly into fulminant infections, with most patients immunologically or metabolically compromised. Acidic media rich in glucose have been found to promote invasion of Mucorin experimental animals [3]. However, mucormycosis might also occur in healthy individuals. Well-documented cases of invasive paranasal mucormycosis have been reported in the literature in which the patients had no underlying disorders but were associated with local predisposing factors, such as chronic sinusitis (Table 1).
Table 1 The characteristics of immunocompetent patients with nasal mucormycosis.

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Chief complaint</th>
<th>Duration</th>
<th>Invasion site</th>
<th>Treatment (total dose)</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>M</td>
<td>Facial pain</td>
<td>2 months</td>
<td>Bilateral paranasal sinus</td>
<td>Surgery, amphotericin-B (525 mg)</td>
<td>Cured</td>
<td>5</td>
</tr>
<tr>
<td>65</td>
<td>M</td>
<td>Headache</td>
<td>12 days</td>
<td>Lt. maxilla, premolar region</td>
<td>Surgery, amphotericin-B (2.5 g)</td>
<td>Cured</td>
<td>11</td>
</tr>
<tr>
<td>63</td>
<td>F</td>
<td>Headache</td>
<td>3 months</td>
<td>Rt. sphenoid sinus</td>
<td>Endoscopic sinus surgery</td>
<td>Cured</td>
<td>4</td>
</tr>
<tr>
<td>62</td>
<td>F</td>
<td>Facial pain</td>
<td>2 weeks</td>
<td>Rt. maxillary sinus</td>
<td>Surgery, liposomal amphotericin-B (2 mg/kg/d, 8 weeks)</td>
<td>Cured</td>
<td>12</td>
</tr>
<tr>
<td>40</td>
<td>M</td>
<td>Sinusitis</td>
<td>1 week</td>
<td>Rt. Fronto-ethomoidal sinus. Frontal lobe and basal ganglia</td>
<td>Surgery</td>
<td>Died</td>
<td>13</td>
</tr>
<tr>
<td>53</td>
<td>M</td>
<td>Nasal obstruction</td>
<td>1 month</td>
<td>Left anterior ethmoidal sinus, middle and inferior turbinates</td>
<td>Endoscopic sinus surgery, amphotericin-B (3 g)</td>
<td>Cured</td>
<td>Case</td>
</tr>
</tbody>
</table>

Most cases presented with severe headache and facial pain, with two cases having histories of chronic sinusitis. Duration of symptoms varied from 1 week to 3 months. Most patients’ age was over 60 years old. Treatment in these individuals consisted of surgical debridement and systemic antifungal therapy. However, one study reported healthy patients with limited mucormycosis may be treated with endoscopic debridement alone [4]. The other study documented that the patient could be cured with endoscopic sinus surgery and a small dose of amphotericin B (525 mg) in localized mucormycosis case and the authors suggested that total dose of amphotericin B can be determined by the extent of disease and the postoperative endoscopic finding [5]. In our case, the clinical picture was similar to other earlier cases and the patient was treated with endoscopic sinus surgery and amphotericin B, 1.0–1.5 mg/kg/day, the total dose of 3 g was given over the course of 56 days because the disease was extensive from turbinate to ethmoidal cells.

The presenting symptoms and physical examinations in paranasal invasive mucormycosis of healthy hosts are often nonspecific and subtle. In the immunocompetent patient, invasive mucormycosis was suspected clinico-radiologically as malignant. In this case, nasal obstruction for one month was the only major symptom. At first, malignancy was considered because of radiologic mass-like presentation and peripheral eosinophilia., the latter being one of the manifestations of paraneoplastic. Tefferi et al. reviewed the association of eosinophilic disorder with malignant hematopoietic processes including acute myeloid leukemia, acute lymphoblastic leukemia, chronic myelogenous leukemia, and myelodysplastic syndromes [6]. However, biopsy revealed invasive mucormycosis in our case and peripheral eosinophilia returned to normal levels after the operation. It could explain a possible relationship between eosinophilia and mucormycosis. Hypereosinophilia associated with fungal infection has been described in cases involving disseminated cryptococcosis and phaeohyphomycosis [7,8]. In addition, allergic fungal sinusitis may be a good example that fungal infection can cause eosinophilic infiltration. This theory is supported by the presence of specific IgE to the cultured fungus [9]. However, Ponikau et al. suggested the theory that the response of the eosinophils to the fungi led to the eosinophilic chronic rhinosinusitis primarily by non-IgE-mediated responses, based on their review of allergic fungal sinusitis patients [10]. Although mucor-specific IgE was not available in this study and we couldn’t elucidate the mechanism of eosinophilia, invasion of mucormycosis might lead to peripheral eosinophilia, based on postoperative changes of eosinophil counts. Therefore, we might suggest that differential diagnosis in paranasal sinusitis patients with hypereosinophilia should not only include allergic fungal sinusitis or hematologic malignancy but also invasive fungal infection. Mucormycosis should be considered in the differential diagnosis of severe headache, facial pain and orbital symptoms intractable to conventional therapy, regardless of immunologic status.

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References


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