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Isolated Nasal Septum Necrosis Caused by *Aspergillus flavus* in an Immunocompromised Child

FOUZIA NAEEM, MD¹, JEFFREY E. RUBNITZ, MD, PHD², and HANA HAKIM, MD, MSC¹

¹Department of Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN

²Department of Oncology, St. Jude Children's Research Hospital, Memphis, TN

Abstract

Non-traumatic isolated nasal septal aspergillosis in the absence of sinusitis is a rare but serious infection in immunocompromised patients. Adequate management requires early diagnosis, prompt empiric antifungal therapy, and surgical debridement to prevent progression to life-threatening complications. With the increasing population of immunocompromised children, it is essential for timely management that clinicians have a high index of suspicion for this unusual presentation of aspergillosis.

Keywords

nasal septum; immunocompromised; aspergillus; children

Introduction

Fungal rhino-sino-cerebral infection is a well described complication of myelosuppressive therapy in patients with malignancy or recipients of stem cell or bone marrow transplant. Reported cases with localized fungal infection involving only the nasal septum are rare and usually described as a complication of recent trauma, dental extraction, or surgical intervention in immunocompromised patients. Nasal septal infection can also result from progression of the fungal infection from the adjacent sinuses. Extensive search of the English language literature involving pediatric patients has identified only one case of a 15-year-old boy, an autologous bone marrow transplant recipient for acute myelogenous leukemia, who developed nasal septal necrosis caused by *Aspergillus flavus* without any antecedent trauma or surgery (1). We report the second pediatric case of nasal septum necrosis due to *Aspergillus* infection in a child with acute lymphoblastic leukemia (ALL) with no previous history of trauma or surgical procedures.

Patient

A 5-year-old boy was diagnosed with pre-B cell ALL in November 2009. On day 11 of remission induction chemotherapy, he was hospitalized for fever and neutropenia without any focal signs or symptoms of infection. Because of his ill appearance, empiric broad spectrum antimicrobial therapy was initiated with vancomycin and cefepime. Twelve hours later, the blood cultures collected from the central venous catheter at the time of presentation grew Gram-positive cocci and Gram-negative bacilli, which were identified as viridans

Corresponding author: Hana Hakim, MD, MSc, Department of Infectious Diseases, Mail Stop 600, St. Jude Children's Research Hospital, 262 Danny Thomas Place, Memphis, TN 38105-3678, Hana.Hakim@stjude.org, Phone: 901-595-3300, Fax: 901-595-5068.

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group *Streptococcus* and *Escherichia coli*, respectively. On day 4 of hospitalization and after fever resolution for 2 days, he was discharged to complete a 14 day course of cefepime. One day after discharge, he was re-hospitalized for recurrent fever and left nasal and oral pain. The physical examination was normal. Empiric therapy with vancomycin, meropenem, and micafungin was initiated. Radiographs of the sinuses and panoramic radiograph of dentition were normal. Blood cultures remained negative. Fever resolved within 24 hours of hospitalization and the left nasal and oral pain was managed with oral morphine and gabapentin. On day 5 of hospitalization, he was discharged with the plan to continue cefepime and micafungin for an additional 7 days.

Three days after completion of the antimicrobial therapy, he developed fever, nasal obstruction, and swelling at the left anterior portion of the nasal septum with no history of trauma. He denied headache or nasal drainage. Physical examination revealed a spherical greenish mass, 1 cm in diameter, attached to the anterior inferior part of the left nasal septum. The inferior turbinate was mildly enlarged. He had no facial swelling, erythema, or warmth on palpation. CT scan without contrast of the nose and sinuses showed mucosal thickening with a focal area of soft tissue prominence in the anterior aspect of the left nasal cavity near the left naris and focal demineralization at the anterior aspect of the nasal septum without evidence of sinusitis (See Figure, Supplemental Digital Content 1A). CT scan of the chest and abdomen showed no evidence of fungal disease. He had been neutropenic for 4 weeks with an absolute neutrophil count (ANC) 100 cells/mm^3 ; however, on the day of evaluation, his ANC began to recover to 800 cells/mm^3 . He was hospitalized and empiric therapy with vancomycin, cefepime, voriconazole and micafungin was initiated. The patient underwent fiberoptic endoscopic evaluation and surgical debridement of the necrotic tissue on the left anterior nasal septum. Pathologic examination and fungal staining of the debris revealed necrotic mucosa with invasive branching septate hyphae (see Figure, Supplemental Digital Content 1B). Fungal culture of tissue grew *Aspergillus flavus* (see Figure, Supplemental Digital Content 1C). Blood cultures collected before the initiation of antimicrobial agents did not show growth. *Aspergillus* antigen detection in the serum was negative. On the fifth day of hospitalization, he was discharged after fever resolution for 3 consecutive days. He completed 16 weeks of therapy initially with oral voriconazole and intravenous micafungin followed by oral voriconazole monotherapy, 100 mg twice daily. The patient did not receive granulocyte colony stimulating factors or granulocyte transfusions during the course of therapy. Chemotherapy was resumed after a two-week delay without any worsening of the infection. Twelve weeks after completion of antifungal therapy there was complete resolution of the nasal lesion.

Discussion

This case report illustrates that isolated nasal septal aspergillosis in immunocompromised patients can present without any history of nasal trauma or progression of infection from adjacent paranasal sinuses. Nasal septal fungal abscesses complicating nasal trauma, surgical procedures, sinus and dental infections have been previously reported (2, 3). To our knowledge, there has been only one report of isolated nasal septal aspergillosis in an immunocompromised child without any antecedent traumatic event (1). This was a 15-year-old boy with necrosis of the nasal septum due to *Aspergillus* infection after bone marrow transplantation for acute myelogenous leukemia (1). The patient had no evidence for sinus involvement and no history of trauma. He responded to therapy with amphotericin B and granulocyte colony-stimulating factor (1). This presentation of aspergillosis is likewise rare in adults. Walker and colleagues(4) reported a 64-year-old man with Crohn disease and pulmonary fibrosis treated with immunosuppressive medications who developed nasal septal abscess due to *Aspergillus flavus* without sinusitis or history of traumatic event. A summary of the adult and pediatric cases of isolated nasal septum aspergillosis identified by literature

review is presented in Table 1. Predisposing risk factors for isolated nasal septum aspergillosis include prolonged neutropenia, severe immunosuppression, trauma or surgical procedures, and broad spectrum antibiotics therapy (1–4).

Patients with nasal septal fungal infection present clinically with nasal obstruction and pain, and possibly with rhinorrhea, fever and bleeding. Direct clinical inspection reveals swelling with some necrotic tissue at the site of infection as was observed in our patient. Early diagnosis and treatment are essential to prevent the associated complications that range from cosmetic disfiguration such as saddle deformity of nasal bridge to life-threatening invasive fungal infections such as brain abscess, fungal sinusitis, and cavernous sinus thrombosis (5).

Comprehensive direct inspection of the nasal cavity is important. Focal signs of abscess or mass can usually be appreciated. Definitive diagnosis of nasal septal aspergillosis often requires histopathologic examination and fungal staining with culture of the debrided nasal tissue or mass that may show invasive septate hyphae.

The past decade has witnessed significant advances in the diagnosis of invasive aspergillosis using non-invasive assays that detect a polysaccharide cell wall component, galactomannan, in the serum (6–8). However, the existing knowledge about the diagnostic role of galactomannan assay has been derived from studies evaluating patients with invasive pulmonary or disseminated aspergillosis. Little is known about the role of galactomannan detection assay in the diagnosis of localized nasal septal aspergillosis. A false-negative result of galactomannan detection assay due to micafungin that our patient was receiving is a plausible explanation (9). Once nasal septal fungal infection is suspected, treatment that includes surgical debridement and antifungal agents must be promptly initiated because of the potentially life-threatening consequences of delayed therapy (1). Voriconazole is the primary drug for the treatment of invasive aspergillosis (10). The optimal duration of therapy is unknown; extrapolating from the Infectious Diseases Society of America treatment guidelines for pulmonary aspergillus infection, a duration of at least 6–12 weeks of therapy is reasonable (10). Therapy can be extended beyond this period depending on the clinical response and immune status of the patient. Our patient received almost 16 weeks of therapy to avoid recurrence of infection while receiving intense chemotherapy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Clinical Course of Patients With Isolated Nasal Septum Aspergillosis

Age, Gender	Underlying Disease	Risk Factors	Clinical Presentation	Radioimaging Evaluation	Pathology and Microbiologic Tests	Treatment and Duration	Outcome
15 yr, male ¹	AML, autologous BMT	Neutropenia, broad-spectrum antibiotics	Fever, facial swelling and tenderness	X-ray and CT scan of sinuses: normal	Pathologic examination of tissue: necrosis and septate hyphae; fungal culture of tissue: <i>Aspergillus flavus</i>	Amphotericin B, G-CSF (duration not reported)	Recovery at 1-yr follow-up
17 yr, male ²	ALL	Nasal trauma	Nasal erythema, edema, tenderness, and saddle deformity	CT scan with contrast of sinuses: nasal septal abscess	Fungal culture of drained abscess: <i>Aspergillus flavus</i>	Surgical drainage of nasal septal abscess, voriconazole (duration not reported)	Recovery at 6-wk follow-up
64 yr, male ⁴	Crohn disease	Immunosuppressive therapy	Nasal obstruction and tenderness	CT scan of sinuses: nasal septal abscess	Pathologic examination of tissue and abscess drainage: fungal elements, fungal culture of drained abscess: <i>Aspergillus flavus</i>	Surgical drainage of abscess, intravenous antifungal therapy (not specified) for 6 wk	Recovery at 18-mo follow-up
5 yr, male, present report	ALL	Neutropenia, broad-spectrum antibiotics	Fever, nasal mass, obstruction and swelling	CT scan of sinuses: soft tissue edema of the nasal septum, focal demineralization	Pathologic examination of tissue: necrosis and invasive branching septate hyphae, fungal culture of tissue: <i>Aspergillus flavus</i>	Surgical debridement, voriconazole plus micafungin followed by voriconazole monotherapy for total of 16 wk	Recovery at 12-wk follow-up visit after completion of therapy

AML indicates acute myeloblastic leukemia; BMT, bone marrow transplant; CT, computed tomography; G-CSF, granulocyte-colony stimulating factor; ALL, acute lymphoblastic leukemia.