

ASPERGILLOSIS OF THE NOSE AND PARANASAL SINUSES.*†§

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ABSTRACT.

Aspergillosis is becoming an increasingly recognized pathogen in the sinonasal tract. The courses of two patients, one seemingly healthy and one with a terminal malignancy, are reviewed. These patients illustrate the clinical course, difficulties in diagnosis, and management of patients with aspergillosis of the sinonasal tract.

Aspergillus is a common endogenous contaminant of the upper respiratory tract; however, bacterial sinusitis may trigger its growth and proliferation. *Aspergillus fumigatus* is the most common species implicated in paranasal sinus disease in the United States. The maxillary antrum is the most commonly involved site in the paranasal sinuses. Originally, aspergillosis was described in healthy patients, but it has become increasingly recognized in the immunocompromised and the chronically debilitated. Paranasal sinus *Aspergillus* infections are classified as non-invasive, invasive and fulminant. The treatment is primarily surgical. Antifungal chemotherapeutic agents are used in the treatment of central nervous system involvement and in the fulminant form of the disease.

Fungal diseases of the nose and paranasal sinuses are not common. Fungal infections of the paranasal sinuses most often include histoplasmosis, coccidiomycosis, candidiasis, phycomycosis and aspergillosis. *Aspergillus* is the most common fungal pathogen in sinus disease¹ and is the most common primary fungal agent infecting the maxillary antrum.² The number of reported cases of aspergillosis in the nose and paranasal sinuses has been increasing. Since 1968, the number of reported cases has increased threefold. In 1972, only 37 cases had been reported with 17 by a single author.³ This may indicate that aspergillosis in this anatomical area is commonly unrecognized. Paranasal sinus aspergillosis was originally described in seemingly healthy patients, but it has been recognized in immunocompromised patients and those with chronic debilitating diseases such as diabetes mellitus.

This paper reports two cases of aspergillosis of the nose and paranasal sinuses: one in an apparently healthy woman with involvement of the right maxillary, ethmoid and frontal sinuses; and the other in an immunosuppressed patient with only septal involvement.

CASE PRESENTATIONS.

Case 1. In April 1980, a 50-year-old white female who had previously been in good health presented to the Ophthalmology Clinic at Wilford Hall USAF Medical Center with a two-month history of mild right-sided facial swelling. A sinus series showed opacification of the right frontal, ethmoid and maxillary sinuses. She was started on ampicillin and referred for ear, nose and throat evaluation. Three days later she presented to the ENT

Clinic. She denied any past history of significant illnesses. She did not smoke, drink or take any medications, and she denied any allergies. Her only complaint was of right-sided nasal obstruction.

Physical examination revealed mild right-sided facial swelling, edema of the nasal mucosa on the right and swelling of the middle turbinate. Aspiration of the right maxillary antrum was attempted, but no material was obtained. A biopsy of the middle turbinate showed only hyperplastic mucosa. The patient was admitted to the hospital. Admission laboratory and x-ray evaluations revealed a normal chest x-ray, EKG, liver function tests, electrolytes, hematogram and clotting studies. Urine glucose was 4+ and serum glucose was 385. The Endocrinology Service was consulted, and they recommended control of blood sugar with diet alone.

The right maxillary antrum was explored via a Caldwell-Luc approach. A mass of brownish-green material filled the antrum. The anterior wall of the maxilla was eroded. The mass was removed and a large nasoastral window created. Culture of the sinus contents grew *Aspergillus fumigatus*. The patient was discharged on the third postoperative day and instructed to irrigate her maxillary sinus.

One month later she returned with persistent facial swelling. Radiologic examination showed persistent opacification of the right ethmoid and frontal sinuses. Tomograms of the orbit showed thinning of the medial orbital wall. At surgery, the patient was found to have erosion of the lamina papyracea and obliteration of the right anterior ethmoid artery. The right frontal and ethmoid sinuses were filled with greenish-brown material similar to that originally found in the maxillary sinus. The periosteum of the orbit was intact. A frontoethmoidectomy was then performed. The patient's postoperative course was uncomplicated and she was discharged on the seventh postoperative day.

She did well until September 1980 when she presented with right-sided facial swelling and nasal obstruction. The right nasal cavity was filled with white hyperplastic mucosa. Radiographically the right maxillary, frontal and ethmoid sinuses were opacified.

On CT scan, there was a soft tissue mass in the frontal and ethmoid cavities, a single air cell anterior to the sphenoid on the right, and a small amount of air in the maxillary antrum. The patient's blood sugar had remained in good control since her previous procedure.

The patient was again hospitalized and the right frontal, ethmoid and maxillary sinuses were re-explored. There was a small focus of *Aspergillus* found in the intact ethmoid air cell anterior

*Presented at the Meeting of the Southern Section of the American Laryngological, Rhinological and Otological Society, Inc., Atlanta, GA, January 16, 1982.

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§The opinions expressed herein are those of the authors and not those of the United States Air Force.

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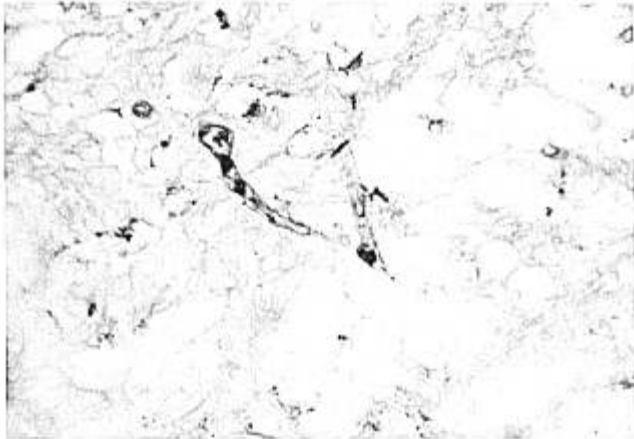


Fig. 1. High-powered view of specimen from Case 1. Note the dichotomous branching, septate hyphae, and 45° angle of branching.

to the sphenoid and the rest of the cavity was filled with hyperplastic mucosa. The mucosa and *Aspergillus* were removed and drains were placed in the frontal and ethmoid cavities. Postoperatively the patient's sinuses were irrigated with saline and the irrigant became clear after several days. On postoperative day seven, the drains were removed. Follow-up 15 months later showed resolution of the facial swelling, patency of the nasal airway, and no reaccumulation of hyperplastic tissue.

Case 2. A 21-year-old white male undergoing chemotherapy for acute lymphocytic leukemia presented at the ENT Clinic with nasal obstruction and a clear nasal discharge. On anterior rhinoscopy, he was found to have black crusted lesions on the nasal septum, bilaterally. These lesions were gently removed. There was minimal bleeding and the mucosa beneath them was insensitive. Histologic examination showed *Aspergillus*. The nasal cavity was debrided daily and irrigated with normal saline. Within 72 hours the crusting had ceased and the patient became asymptomatic.

DISCUSSION.

Seven species of *Aspergillus* have been associated with human diseases.⁴ This fungus is a common saprophyte found in dust, soil and decaying organic material. *Aspergillus* colonies grow in a wide temperature range and can grow in temperatures up to 50°C. This organism tends to thrive in damp decaying vegetation heated by bacterial fermentation. In compost piles, the bacterial components will be inhibited as the temperature rises, and *Aspergillus* may exist as a pure culture.

Aspergillus is pathogenic in birds, animals and man. The most common species implicated in paranasal sinus disease is *Aspergillus fumigatus*. *Aspergillus flavus* is the most common species in the Sudan. *A. niger*, *A. oryzae* and *A. nidulans* have been reported as sinus pathogens.⁵

This fungus grows best anaerobically. Paradoxically the most serious infections involve the respiratory tract and central nervous system. It is frequently seen as a pathogen in the external auditory canal. *Aspergillus* is not contagious and sources of infections are endogenous.

Grossly, *Aspergillus* appears as a greenish-black,

rubbery, greasy material that fills the sinus cavity. Histologically, the organism can be identified by septate hyphae and dichotomous branching. Other phycomycetes are excluded from the diagnosis by the smaller size of the septated hyphae, the dichotomous branching and the 45° angle of branching (Fig. 1).

Two histological patterns have been identified: proliferative and exudative. The proliferative variety accounts for 66% of the cases. The proliferative pattern appears as a pseudotubercle in a fibrous stroma. The arterial walls may become thickened because of proliferation in the intima and swelling of the media. The exudative type has large areas of edematous necrosis and occurs in 10% of cases. The remaining cases have a mixed appearance. Identification is best made with silver stains (Gridley, PAS, methenamine silver). A direct culture should be made on Sabouraud's agar with an antibiotic to inhibit bacterial growth. An immunodiffusion test has been developed for use in the diagnosis of suspected cases of *Aspergillus*.⁶

Aspergillus is oftentimes a contaminant in the paranasal sinuses which becomes pathologic when ventilation of the sinus osteum is impaired. This fungus grows best as an anaerobe so bacterial infection with subsequent occlusion of the sinus osteum leads to conditions that favor fungal proliferation.

There have been three clinical types of aspergillosis in the paranasal sinuses reported: non-invasive, invasive⁷ and fulminant.⁸ The non-invasive type resembles bacterial sinusitis. Patients present with nasal obstruction, pressure and drainage. Radiographs may show only clouding or opacification of the sinus. The maxillary sinus is most commonly involved. Intranasal examination may show polyps, pale and edematous turbinates, or both. Antral lavage will not clear the condition and may not be diagnostic.

The invasive type of aspergillosis may present with extension into the cheek or orbit. It is manifested radiologically as a paranasal sinus mass with orbital displacement and bony erosion. The presenting signs are suggestive of neoplasia, chronic sinusitis with osteomyelitis, or mucormycosis. This type may also extend intracranially.

There is no clear-cut distinction between invasive and non-invasive aspergillosis. The underlying health of the patient may determine the type and severity of the infection, but both invasive and non-invasive types have been reported in seemingly healthy people.

The fulminant form of paranasal sinus aspergillosis occurs in immunodeficient patients. The most susceptible are children with acute leukemia undergoing radiation therapy and chemotherapy.⁸ These patients sometimes present with necrotizing bron-

chopneumonia and hemorrhagic pulmonary infarction.

In the fulminant form, the earliest nasal lesion is crusting of the anterior end of the inferior turbinate or septum. The tissue beneath the crust is insensitive. Within two or three days the lesion progresses to involve the lateral nasal wall. Facial swelling rapidly occurs. Proptosis, chemosis and ophthalmoplegia signify orbital involvement. Disseminated aspergillosis is frequently associated with paranasal sinus disease. Frequently there is involvement of the lungs, spleen and liver. The rapid progression of the fulminant type distinguishes it from other forms.⁸

The treatment of non-invasive and invasive aspergillosis of the paranasal sinuses is primarily surgical. Most cases are cured by surgical excision of the disease and aeration of the involved sinus. However, once the fungus is beyond the confines of the paranasal sinuses, its spread is unrestricted. The *Aspergillus* hyphae invade dura, blood vessels and bones. If the fungus spreads into the orbit or intracranially, a life-threatening situation occurs. Amphotericin B should be administered. A recent report describes the successful use of flucytosine and rifampin in a patient with signs and symptoms of invasive orbital *Aspergillus* that had been unsuccessfully treated with transseptal sphenoidotomy and amphotericin B.⁹

For fulminant aspergillosis, amphotericin B and removal of all gross disease is the treatment of choice. After surgery, repeated irrigation of the nasal cavity and sinuses should be instituted to prevent postoperative crusting. Antifungal susceptibility testing as described by Yu⁷ may be useful in selecting the proper antifungal agent. The life-threatening implications of fulminant paranasal sinus aspergillosis can be seen in McGill's article describing this entity because only 2 of 4 patients survived the disease.⁸

The maxillary antrum is the most common paranasal site of *Aspergillus* infection. Jahrsdoerfer,⁵ in his review, notes maxillary involvement in 46 of 103 cases; 3 had solitary involvement of the ethmoid, 2 of the frontal, and 8 in the sphenoid. Multiple sinuses were involved in the other 44 cases.

SUMMARY.

These two cases demonstrate some typical as-

pects of nasal and paranasal sinus aspergillosis. The first patient waited approximately 3 months after the onset of symptoms before seeking medical attention. Often this process has minimal symptoms. Once she presented, she was felt to have a bacterial pansinusitis. Antral irrigation and biopsy of the middle turbinate were not diagnostic. During the patient's preoperative evaluation, she was found to have adult onset of diabetes mellitus. The correct diagnosis was made only after a Caldwell-Luc exploration. Her symptoms recurred and she underwent two subsequent procedures before remaining asymptomatic.

The finding of hyperplastic tissue may have been a manifestation of hypersensitivity to the remaining focus of *Aspergillus*. The long course of these infections had been previously noted by Hora⁷ who presented a patient with multiple recurrences over 6 years. This emphasizes the need for long-term follow-up in these patients.

In the second case, prompt removal of the crusted lesions resulted in resolution of the patient's problem. Once the focus of aspergillosis in the nasal cavity was removed and irrigations instituted, the problem quickly resolved.

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