

Fungal infection of the sinus and anterior skull base

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Abstract

Background: Invasive fungal infection is an opportunistic infection caused commonly by mucoraceae and aspergillus. It mostly occurs in patients with underlying disease. Since it has a high mortality and morbidity rate, considering a treatment strategy seems necessary.

Objective: Since there has not been a clear protocol for treating these patients, we decided to establish a protocol for fungal infection of sinus and anterior skull base management.

Methods: This retrospective and descriptive case study series included 30 patients. After confirming the pathogen, the authors came to a proper protocol for treatment which is mentioned later.

Results: The site involvement included nose and orbital cavity (53.3%), anterior skull base and brain in conjunction with sinonasal (36.6%) and simple nasal cavity involvement (10%). 86.6% of the patients had underlying diseases. 56.6% of patients had diabetes as a single underlying disease, while 13.3% had both diabetes and renal failure in combination. Acute lymphocytic leukemia was present in 6.6%, renal failure in 3.3%, lupus in 3.3% and chronic lymphocytic leukemia in 3.3% of patients. Mortality rate was 40%. We categorized the patients into 3 groups: only sinonasal, sinonasal and orbit, and associated anterior skull base and brain involvement.

Conclusion: Early diagnosis is an important factor in improving survival. Anterior skull base and brain involvement has a very poor prognosis.

Keywords: sinusitis, rhinocerebral, nasal, orbital, anterior skull base.

Introduction

Fungi can cause a spectrum of diseases in the sinuses and anterior skull base. They can appear in forms ranging from saprophytes to allergic sinusitis, fungus balls and, in the most severe cases, Invasive Fungal Sinusitis (IFS). IFS is most commonly caused by *Aspergillus* and *Mucoraceae*. However, *Mucoraceae* are more common [1].

Mucormycosis is an opportunistic acute fungal infection that is usually caused by *Mucoraceae* genera. Its subspecies are *Rhizopus*, *Mucor* and *Absidia* [1,2]. *Rhizopus oryzae* are the most common fungi that cause mucormycosis [3,4].

However, they do not usually cause an infection unless an underlying disease condition is present [5-8]. The organism enters the nasal cavity upon inhalation and makes its way to the head and neck area and, in the case of an underlying condition, an invasive infection would

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develop [8].

Factors facilitating patients becoming afflicted by this disease include having a compromised immune system, uncontrolled diabetes mellitus, blood malignancies, severe burns, kidney disease, AIDS, immune deficiency following organ transplant, neutropenia, consumption of corticosteroids, chemotherapy, anemia or malnutrition [8]. Mucormycosis has various clinical forms of which involvement of the Sino-Orbito-Cerebral region and ASB is among the most common clinical syndromes observed by ENT specialists [8].

Diagnosis is based on the signs of sino-orbital involvement and the presence of an underlying disease condition. However, conclusive diagnosis must be made through visualization of mucoraceae.

Proper treatment steps in cases where the sinus, ASB and brain region are involved include performing surgery, correcting underlying problem and administering medications.

The chance of survival for the patient who has no underlying disease or diabetes is estimated at 80 percent. However, the chance of survival for a patient with a serious underlying disease is approximately 50 percent [8].

Considering that there had been no consensus of opinion on the extent of the surgical procedure to be performed in previously published studies, the authors tried to establish a classification system to define the extent of the surgery to be recommended and to accurately assess its outcome following set guidelines.

Methods

30 patients were the subjects of case study review made from 2002 through 2006. Data were collected from patient files and graphs. The patients who were suspected of having IFS and who had contacted this center were immediately subjected to having a biopsy taken from the area of the maxillary sinus and nose.

A positive pathology result (by frozen section) prompted specific treatment steps to be

identified and, in the case where the need for surgery arose, a consult and decision was quickly made. In our study no treatment modality was performed in 3 patients (10%).

A standard dose of Amphotericin B (0.2 mg/kg) was administered to all patients but 3 (10%). In order to prevent allergy reactions, 50 mg promethazine and 8 mg dexamethasone in the form of an intravenous infusion was also administered. Management and stabilization of the underlying problem was also done.

Through a daily check of Na-K-BUN-Cr levels the administered dose of amphotericin B was increased to a maximum of 1.5 mg/kg daily after a week. Patients who had been operated on had daily debridement of the sinuses and nasal cavity while under local anesthesia. They were discharged upon stabilization of their condition and completion of the treatment cycle for a month in average (maximum dose 2.5 to 4gr). Patients then underwent monthly follow up.

Surgery included Caldwell Luc and transantral ethmoidectomy procedures and/or endoscopic sinus surgery and if necessary orbital exenteration.

Results

30 patients were studied. Twenty-one patients (70%) were male and 9 patients (30%) were female. The average age of the patients was 46.4 (SD+15.4) with a range of 4 to 68 years of age.

Twenty-six patients (86.6%) had underlying diseases and only 4 patients (13.3%) had no underlying condition. Seventeen patients (56.6%) had diabetes while 4 patients (13.3%) had renal failure in addition to diabetes. Two patients (6.6%) had ALL, 1 patient (3.3%) suffered from severe acute renal failure requiring dialysis, 1 patient (3.3%) with lupus also had end-stage kidney disease and 1 patient (3.3%) was afflicted with CLL.

Table 1 shows involvement sites and treatment category and Table 2 show survival. 18 patients (60%) survived and 12 patients (40%)

<i>Type of treatment</i>	<i>Number</i>	<i>Percent</i>
Surgery along with prescribing antibiotics	10	33.3%
Surgery along with prescribing antibiotics and exenteration of the orbit	12	40%
Prescribing antibiotics	5	16.6%
No treatment	3	10%
Total	30	100

Table 1. Distribution of absolute and relative number of prescribed treatment.

died.

Discussion

Only one (25%) of the patients who had diabetes and renal failure survived while 10 (58.8%) of the 17 patients with only diabetes and all of the patients without immunodeficiency survived. These statistics are indicative of the fact that the more compromised the immune system is, the higher the possibility is that death will result.

Of the 4 remaining patients whose immune deficiencies were either ALL, CLL or lupus, 3 patients survived (survival chance 75%).

In the 11 patients (36.6%) who had brain and ASB involvement, mortality rate was 100%. This means if a patient with brain and ASB involvement comes in, no apparent benefit comes from performing extensive surgery. This third group of the patients in our protocol did not receive extensive surgical procedures as brain involvement basically equated to the eventual death of the patient. Early diagnosis of disease increased the chance of survival.

The possible routes of brain involvement include: direct involvement of the brain through the cribriform plate, through orbital fissures, through lamina papiracea, orbit and/or the apex of the orbit.

The treatment protocol for fungal infection of sinus & ASB in our department was to classify the patient into 1 of our 3 treatment groups:

The first group included patients whose involvement was limited to the nose and sinuses. For these patients, endoscopic surgical treatment and/or Caldwell Luc operative procedure was adequate.

The second group included those who had

orbital involvement. This group was subdivided into two subgroups. The first subgroup included patients in whom orbital involvement was limited to the preseptal area and only eyelid inflammation was observed or if they had orbital fat involvement without eye movement restriction and/or proptosis. The surgical operation performed on these patients included debridement and complete treatment of sinuses through external ethmoidectomy or Caldwell Luc procedures and debridement of necrotic tissues around the preseptal region.

The second subgroup had clear involvement of orbital muscles and eye movement restriction along with signs of orbital apex involvement, reduced vision or proptosis. The surgical operation for these patients included complete debridement of sinuses in conjunction with exenteration of the orbit.

Third group: This group consisted of those patients having anterior skull base and brain involvement so it was better to perform non-aggressive debridement only.

Bhansali et al calculated the survival rate for their patients at 68%, somewhat higher than the 57% survival rate of our patients. ASB & brain involvement in our patients was shown to be 36.6% while 20% of the patients in Bhansali et al's study had brain involvement. In addition, all of their patients were diabetics [9]; however, diabetic patients formed only 70% of our study

<i>Patient mortality rate (died/patient)</i>	<i>Organ involvement</i>
0% (0/3)	Nose
6.25% (1/16)	Sinonasal and orbit
100% (11/11)	Sinonasal, orbit and ASB brain

Table 2. Occurrence of mortality based on the involvement of various organs.

group. The percentage of survival for our patients was slightly lower than that of patients from other centers around the world. This was attributed to procrastination or delayed center contact on the part of these patients.

As mentioned before, the key to higher survival rate of fungal infection of the sinus and ASB patients is quick and timely diagnosis to start treating the patients at a stage when the least number of organs are involved. This point has been noted in other reports as well including those by Eicken [10], Guevara [11] and Delbrouck [12]. Our emphasis has been on accurate diagnosis and treatment of the underlying condition. Other reports have insisted on these strategies too [9, 11, 12].

Conclusion

Fungal infection of the sinus and anterior skull base can be an aggressive disease with high mortality. The important factor that determines the survival of the patient is the type of underlying condition and the extent of the type of involvement at the time of contacting the physician. Treatment consists of early diagnosis, treating the underlying condition(s), proper debridement and drug therapy. Exenteration of the orbit in all cases where orbital involvement clearly exists is necessary. The prognosis for the patient is poor when there is ASB and brain involvement and we concluded that no treatment steps seem to have any significant impact on enhancing the survival rate for the patient; still this subject is open for future studies.

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References

1. Ferguson BJ, Johnson JT: Infectious causes of rhinosinusitis. In: Cummings CW, Frederickson JM, Harker LA, Richardson MA, Schuller DE, Robbins TK, Reagan TJ, Haughey BH, Flint PW (eds.), *Otolaryngology, Head & Neck Surgery*, 4th Edition (Chapter 50). Philadelphia: Mosby; 2005, pp.1182-1196.
2. Borruat JS, Barruat FX, Duerey N, Uffer F, Pasche P, Maire R: Rhino-cerebral mucormycosis: clinical presentation. *Klin Monatsbl Amgenheikd* 1998; 212 (5): 413-15.
3. Ohara M: Histopathologic diagnosis of fungal disease. *Infection Control* 1986; 7: 78-84.
4. Brown OE, Finn R: Mucormycosis of the mandible. *J Oral Max Surg* 1986; 44: 132-36.
5. Galleta SL, Wule AE, Colddeger HI, Nichols CW, Classer JS: Rhinocerebral mucormycosis: management and survival after carotid occlusion. *Ann Neurol* 1990; 28: 103-07.
6. Ochi JW, Harris JP, Feldman J, Press CA: Rhinocerebral mucormycosis: results of aggressive surgical debridement and amphotericin B. *Laryngoscope* 1998; 98: 1339-42.
7. Butugan O, Sanchez TG, Gancalez F: Rhinocerebral mucormycosis: predisposing factors, diagnosis, therapy, complications and survival. *Rev Laryngol Otol Rhinol Bord* 1996; 117(1): 53-55.
8. Finn DG: Mucormycosis of paranasal sinuses. *Ear Nose Throat J* 1998; 67: 813-22.
9. Bhansali A, Bhadada S, Sharma A, Suresh V, Gupta A, Singh P, Chakarati A, Dash RG: Presentation and outcome of rhinocerebral mucormycosis in patients with diabetes. *Postgrad Med J* 2004; 80(949): 670-74.
10. Eicken J, Preyer S, Wilhelm H: Fatal orbital disorder. *Klin Monatsbl Augenheilkd* 2004; 221(11): 948-52.
11. Guevara N, Roy D, Dutrué Rosset C, Santini J, Hofman P, Castillo I: Mucormycosis: early diagnosis and treatment. *Rev Laryngol Oto Rhinol (Bord)* 2004; 125 (2): 127-31.
12. Delbrouck C, Jacobs F, Fernandez Aguilar S, Devroede B, Chou Fani G, Hassid S: Carotid artery occlusion due to fulminant rhinocerebral mucormycosis. *Acta Otorhinolaryngol* 2004; 58(2): 135-40.