

Case Report

Invasive Fungal Rhinosinusitis in Maharaj Nakorn Chiang Mai Hospital

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Background: Invasive fungal rhinosinusitis, a rare infection, is a life threatening disease. Delay in diagnosis may consequently lead to high morbidity and mortality.

Objective: Encourage early detection and proper management of invasive fungal rhinosinusitis.

Material and Method: Medical records, radiological, and pathological reports of five patients who were diagnosed as invasive fungal rhinosinusitis were reviewed retrospectively.

Results: Four in five cases of invasive fungal rhinosinusitis, confirmed by pathological study, had successful treatment. One patient had intracerebral hemorrhage that may be associated with the disease spreading. Disease extension was evaluated by CT paranasal sinus in all cases, but it usually did not have classic bony erosion.

Conclusion: Curing infection, correcting underlying conditions, and working up fungal infection should be carried out as early as possible, because morbidity and mortality depend on disease extension and host status.

Keywords: Invasive fungal sinusitis, Fungal sinusitis, Fungal rhinosinusitis

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Invasive fungal rhinosinusitis, determined by tissue histology of mucosal invasion⁽¹⁾, is a rare infection of the nose and paranasal sinus, but it is a life threatening disease⁽²⁾. Most infected cases are immunocompromised hosts such as patients with diabetes mellitus^(3,4), hematological malignancy⁽⁵⁾ or those receiving chemotherapy. Recently this infection has had a tendency to occur in immunocompetent hosts too⁽⁶⁾. If diagnosis of this disease is delayed, the patients may consequently have substantial morbidity and mortality. The aims of the present study were to alert medical personnel to detect the infection early and to manage invasive fungal rhinosinusitis properly.

Material and Method

Between January 1, 2001 and December 31, 2006, only five cases of invasive fungal infection of the nose and/or paranasal sinus, which were diagnosed from nasal biopsy and showed mucosal invasion of fungus, had complete medical records and investiga-

tions. Medical record, as well as radiological and pathological reports of these patients were retrospectively reviewed. The details of these cases are presented below.

Case 1

A 75-year-old woman complained of a progressive decrease in visual acuity of both eyes for 1 month until she had left blindness. She also complained of headache and left eye pain for 3 weeks, with ptosis of the left eye 3 days before admission to hospital. She was admitted in the ophthalmologic ward for the treatment of acute ischemic optic neuropathy, but the symptoms did not improve. A computed tomogram of the orbit reviewed bulging of the left cavernous sinus with bilateral maxillary sinusitis. Antral irrigations showed a whitish discharge with a culture result growing light *Pseudomonas aeruginosa*. As a tumor could not be excluded, the patient received a maxillary sinus mucosal biopsy via the Caldwell Luc approach. The pathological report of tissue from the maxillary sinus revealed fungal infection that was morphologically consistent with phycomycosis. She was re-operated

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for endoscopic debridement and was treated with intravenous amphotericin B 2 grams with improvement of nasal symptoms and signs. She also was first diagnosed for diabetes mellitus and hypertension on this admission. Four weeks after operation the patient developed right hemiparesis and she was admitted to Internal medicine ward to rule out middle cerebral artery infarction. A computed tomogram of the brain showed white matter infarction of the left frontal horn and left centrum semiovale. After cerebrovascular disease treatment, she was referred for continued treatment at a community hospital. She had an appointment for follow-up, but she did not show up.

Case 2

A 72-year-old woman developed headache and numbness on the right side of face for 6 months. Her vision had decreased for 4 months. Trigeminal neuralgia was diagnosed, and she was treated with medications and surgical treatment by vascular decompression at cerebellopontine angle. After the operation, her vision still decreased with blindness of the right eye 5 days before admission to hospital. A CT scan showed an infiltrating lesion at the right ethmoid sinus, with extension to the posterior of the orbit (Fig. 1). Nasal endoscopy revealed bulging at the posterior end of the right middle turbinate. Neurological examination showed decreased sensation of the right hemiface, lateral rectus palsy and blindness of the right eye. Biopsy of the right middle turbinate mucosa was done and fungal infection suspect aspergillosis with vascular invasion. She was treated with amphotericin B, itraconazole, and endoscopic debridement. Three months after the operation, due to persistent headache, a CT of the paranasal sinus was performed and showed disease in the right posterior ethmoid and sphenoid sinus. She was re-operated on twice. Two weeks after the last operation, she developed alteration of consciousness ($E_1V_1M_3$) from intraventricular hemorrhage, subarachnoid hemorrhage and obstructive hydrocephalus, which may be sequelae from fungal infection or cerebrovascular disease. A neurologist was consulted, and ventriculostomy was planned, but her relatives refused any further treatment and took her home.

Case 3

A 62-year-old man had had a black ulcer at the left nasal alar (Fig. 2) and oozing of bloody discharge from both nostrils for 3 days. He had had diabetes mellitus for 20 years, hypertension for 4 years and was



Fig. 1 CT paranasal sinus (axial views) showing inhomogeneous soft tissue mass (white arrows) at the right posterior ethmoid sinus extended to posterior aspect of the right orbit



Fig. 2 The pictures showing black necrosis at the left side of the nose and bloody discharge from both nostrils

controlled with medical treatment. On physical examination, he had black necrosis of the left nasal alar, anterior nasal septum and collumella, and granulation tissue at the left anterior nasal septum. Biopsy tissue from the collumella showed non-septate hyaline hyphae, which was compatible with mucormycosis. Pus culture was done which resulted in *Enterobacter aerogenes* and *Enterococcus faecalis*. His CT scan of the paranasal sinus showed infiltrative lesion at the left side of the nose, with no paranasal sinus involvement. While being admitted to hospital, he developed diabetic ketoacidosis that was treated with continued RI intravenous drip for blood sugar control and to correct

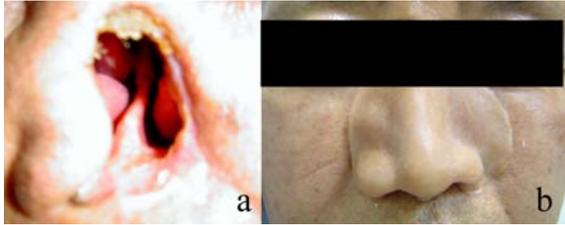


Fig. 3 The picture (a) showing surgical defect of the left nose and nasal prosthesis (b)

electrolyte imbalance. Surgical treatment was done after his condition was stable for general anesthesia. He received endoscopic debridement five times and was treated with intravenous amphotericin B sequentially up to 2 grams. Two months later, he was discharged from the hospital and referred to Mahidol University Faculty of Dentistry for nasal prosthesis (Fig. 3). He had been followed up for 2 years with no recurrent disease.

Case 4

A 36-year-old man had been diagnosed for acute myeloid leukemia and had developed febrile neutropenia after chemotherapy. Although he received empirical antibiotic treatment, he still had a fever. After several investigations for the causes of fever, a CT scan of the paranasal sinus revealed clouding of the right maxillary and anterior ethmoid sinus of both sides. On anterior rhinoscopy, marked swelling of nasal mucosa and necrotic tissue were found at the right inferior meatus, with contact bleeding. Mucosal congestion was found on the left nasal cavity. A tissue biopsy of the right inferior turbinate resulted in fungal infection consisting of zygomycosis with vascular invasion. Pus culture revealed moderate *Enterococcus faecalis*, light coagulase-negative *Staphylococci* and rare *Aspergillus flavus*. The patient was treated by endoscopic debridement 5 times, and intravenous amphotericin B 2 grams (up to 6,035 mg total dose for splenic abscess treatment). Nine weeks after that, the nasal mucosa was normal with 1.5 cm defect of the hard palate, which was closed with a palatal prosthesis. He had an appointment for follow-up after that, but he did not show up

Case 5

A 51-year-old woman with relapse acute myeloid leukemia was referred for chemotherapy. She had neutropenia and fever, swelling, and tenderness of the right cheek and upper lip for 3 days before con-

sultation. On physical examination, congestion of the inferior turbinate, mucoid discharge from the middle meatus, and crust with black necrotic tissue were found at the right nasal vestibule. Because fungal rhinosinusitis could not be excluded, a tissue excisional biopsy was carried out at the lesion, which showed invasive fungal infection, consistent with aspergillosis. A CT paranasal sinus was done, and the patient was treated with intravenous amphotericin B (1mg/kg/day) for 20 days. With marked improvement of nasal lesion, the patient was referred to a local hospital for further amphotericin B treatment up to 2 grams and was lost to follow-up.

All patient data are summarized in Table 1.

Discussion

Invasive fungal sinusitis can be a fatal disease, especially in an immunocompromised host. There have been increasing reports of this disease in recent years. In Thailand, Chetchotisakd et al⁽⁷⁾ reported 11 cases of rhinocerebral mucormycosis. In addition, Sungkanuparph et al⁽⁸⁾ reported invasive fungal sinusitis in four cases that were treated with liposomal amphotericin B after having severe side effects from conventional amphotericin B. From both reports, all patients required aggressive surgical treatment comprising multiple operations in combination with amphotericin B for eradication of the disease. All patients required a pathological study to confirm the diagnosis^(9,10) and a radiological study to evaluate extension of disease. Most of the CT paranasal sinus in this report did not have classic finding of bony erosion, which may be from early course of the disease⁽¹¹⁾. Four of five patients had successful treatment with multiple surgical debridement and amphotericin B, the same as in previous reports, but one patient developed intracerebral hemorrhage, which may be associated with intracranial spreading of the disease. Surgical defects after aggressive surgery in two patients could be corrected with prosthesis. Four of five cases in the present report were immunocompromised hosts, especially patients who received chemotherapy, so there should be close monitoring and early detection of this infection in this group. Most of patients in the present study had a negative result for anti-HIV, except case 1, which was not tested.

In conclusion, invasive fungal rhinosinusitis required pathological, radiological, and microbiological studies. If clinical signs and symptoms suggest invasive fungal rhinosinusitis, a tissue biopsy and radiological study should be performed as soon as

Table 1. Patients' data summary

No.	Age (yrs)	Sex	Predisposing factors	Nasal symptoms and findings	Other symptoms	Management	Follow-up period after treatment	Outcome
1.	75	F	Diabetes mellitus, hypertension (first diagnosis)	None	Pain in the right eye and temporal region for 1 month, bilateral progressive visual loss (left > right) for 1 month and left ptosis for 3 days	Right Caldwell Luc, endoscopic debridement, amphotericin B 2 grams	Loss follow up after treatment	Normal nasal mucosa before discharge
2.	72	F	None	Right nasal obstruction with cold exposure	Headache and right hemifacial numbness for 6 months, progressive visual loss in the right eye for 4 months	Endoscopic debridement 3 times, amphotericin B (plan administration until 2 grams and then oral itraconazole)	None	Intraventricular hemorrhage with communicating hydrocephalus while admission to neurosurgery consultation for ventriculostomy, but her relatives refused further management
3.	62	M	Diabetes mellitus, Hypertension (well-controlled)	Left nasal obstruction for 3 days and bloody discharge with black necrotic tissue of the left nostril	Frontal headache and facial pain for 1 week	Endoscopic debridement 3 times, amphotericin B 2 grams + correct DKA* (consult internal medicine to control blood sugar)	18 months	Disease free (use nasal prosthesis)
4.	36	M	AML#	Bilateral nasal obstruction and pain (right > left) for 4-5 days	None	Endoscopic debridement 5 times, amphotericin B 2 grams	1 month and then he did not show up for appointment	Disease free
5.	51	F	AML#	Right nasal obstruction	Swelling of the right eye lid and cheek	Endoscopic debridement, amphotericin B	Loss follow-up	Normal nasal mucosa before discharge

Acute Myeloid Leukemia, * Diabetic ketoacidosis, CWL = Caldwell Luc approach

possible for definite diagnosis and evaluation of disease extension. Working up for fungal infection, curing infection, and correcting underlying conditions should be carried out as early as possible, because morbidity and mortality depend on disease extension and host status. Because of the present study was retrospectively reviewed, some data were not recorded especially tissue culture, which is important for definite diagnosis. Moreover long term outcome cannot be done in most cases because some patients were lost to follow-up.

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จุกและโพรงไซนัสอักเสบจากเชื้อรา ในโรงพยาบาลมหาราช นครเชียงใหม่

กรรณิการ์ รุ่งโรจน์วัฒนศิริ, สุปราณี พูนันต์, ลักษณะ นาคเสน

ภูมิหลัง: จุกและโพรงไซนัสอักเสบลุกลามจากเชื้อราเป็นการติดเชื้อที่พบบ่อย แต่มีอันตรายถึงชีวิต หากผู้ป่วยได้รับการวินิจฉัยล่าช้า อาจนำไปสู่ความพิการและเสียชีวิตได้ การศึกษานี้มุ่งเน้นให้บุคลากรทางการแพทย์ได้ตระหนักถึงโรคนี้ เพื่อการวินิจฉัยและการรักษาที่รวดเร็วและเหมาะสม

วัตถุประสงค์และวิธีการ: ศึกษาเวชระเบียน ผลการตรวจทางพยาธิวิทยาและภาพถ่ายรังสีย้อนหลังของผู้ป่วย 5 ราย ที่ได้รับการวินิจฉัยเป็นจุกและโพรงไซนัสอักเสบลุกลามจากเชื้อรา

ผลการศึกษา: ผู้ป่วย 4 ใน 5 ราย ที่ได้รับการยืนยันด้วยผลตรวจทางพยาธิวิทยา มีผลการรักษาเป็นที่น่าพอใจ แต่มีผู้ป่วย 1 ราย มีเลือดออกในสมองและเสียชีวิต ซึ่งอาจสัมพันธ์กับการลุกลามของโรค

สรุป: ในกรณีที่สงสัยภาวะโรคจุกและโพรงไซนัสอักเสบลุกลามจากเชื้อรา การรักษาการติดเชื้อ แก่ไขภาวะที่เป็นปัจจัยส่งเสริมให้เกิดโรค และการตรวจยืนยันการติดเชื้อรา ควรทำเร็วที่สุดเท่าที่เป็นไปได้ เนื่องจากความพิการและการตาย ขึ้นอยู่กับการลุกลามของรอยโรคและสภาวะของผู้ป่วย