CASE REPORT

Invasive Fungal Sinusitis Involving the Orbital Apex in a Patient with Chronic Renal Failure

Hyera Kang^{1,4}, Yasuhiro Takahashi¹, Kunihiro Nishimura², Yuka Yamagishi³, Hiroshige Mikamo³, and Hirohiko Kakizaki¹

¹Department of Ophthalmology, ²Department of Otorhinolaryngology, and ³Department of Infection Control and Prevention, Aichi Medical University, Aichi, Japan, and ⁴Department of Ophthalmology, University of Seonam College of Medicine, Presbyterian Medical Center, Jeonju, Korea

ABSTRACT

An 82-year-old man with chronic renal failure presented with invasive fungal sinusitis involving the right orbital apex. Intravenous liposomal amphotericin B was immediately administered with an intravenous sodium supplement. Subsequently, endoscopic sinus surgery was performed. *Aspergillus fumigatus* was detected in nasal discharge culture on day 12. Because the patient's renal function had deteriorated by this time, therapy was changed to nasal inhalation of amphotericin B, which was discontinued after 1 month, and oral administration of voriconazole, which was discontinued after 2 months. During 6-month follow-up, the patient did not show recurrence of sinusitis or further decrease in renal function.

Keywords: Liposomal amphotericin B, chronic renal failure, invasive fungal sinusitis, oral voriconazole, orbital apex

CASE REPORT

An 82-year-old man presented with a 4-month history of right periocular pain and a 2-month history of vision loss in the right eye. A neurosurgeon diagnosed idiopathic orbital inflammation and initiated treatment with prednisolone at 30 mg/day. Despite treatment, however, the periocular pain gradually worsened, ptosis appeared, and the patient began to experience ocular motility disturbance. Since age 50, the patient had suffered from chronic renal failure resulting from congenital renal hypoplasia.

At initial examination, the patient's best-corrected visual acuity was no light perception in the right eye and 1.0 in the left eye. The patient did not notice any visual field defect in the left eye. The right pupil was mildly dilated, without direct or indirect light reflex. Hertel exophthalmometry showed a protrusion of 12 mm in the right eye and 8.5 mm in the left eye. Right extraocular muscle motility was completely restricted in all directions (Figure 1A). The right upper

eyelid was completely ptotic with no eyelid movement (Figure 1B). The patient did not have erythematous swelling or tenderness in the eyelids and did not complain of facial numbness. Computed tomography (CT) showed a mass in the right posterior ethmoid sinus with erosion of the medial orbital wall and invasion of the orbital tissue at the right orbital apex (Figure 1C and D). There was no intracranial involvement, including cerebral infarction, sinus thrombosis, cerebral haemorrhage, or meningitis on imaging studies. Blood test results showed elevated blood urea nitrogen (31.8 mg/dL; normal, 8.0–22.0 mg/dL), creatinine (1.73 mg/dL; normal, 0.4–0.7 mg/dL), and β -D-glucan (26.9 pg/mL; normal, <20 pg/mL).

The patient was currently taking prednisolone at 10 mg/day; the dosage was gradually reduced. We administered 3 mg/kg/day of intravenous liposomal amphotericin B (labelled standard dose, 2.5–5 mg/kg/day), while monitoring renal function, to suppress potential causative microorganisms such as *Aspergillus* and *Zygomycetes*. We also

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Correspondence: Hirohiko Kakizaki, MD, PhD, Department of Ophthalmology, Aichi Medical University, 1-1 Yazakokarimata, Nagakute, Aichi 480-1195, Japan. E-mail: cosme@d1.dion.ne.jp

FIGURE 1 (A) The patient's extraocular muscle motility in the right eye was completely restricted in all directions. (B) Complete ptosis of the patient's right upper eyelid without erythematous eyelid swelling. (C, D) Preoperative computed tomography images. (C) Axial section; (D) coronal section. A mass in the right posterior ethmoid sinus is eroding the medial orbital wall and invading the orbital apex in a superomedial to posterior direction through the orbit. (E) Septate hyphae of *Aspergillus fumigatus* were observed in the biopsy sample (Gomori's methenamine–silver nitrate stain, $\times 400$). (F) Axial computed tomography taken on the 24th day of treatment illustrates reduction in the size of the soft tissue density in the right posterior ethmoid sinus and orbit.

administered intravenous sodium supplement to protect against amphotericin B-associated glomerular nephrotoxicity.¹

On the day after initial examination, endoscopic sinus surgery was performed. A sample of nasal discharge was first obtained for microbiological culture. The mass was located predominantly in the Onodi cells and extended to the optic nerve. The mass

was removed and submitted for histopathological examination. The surrounding nasal mucosa and orbital tissues were debrided. Amphotericin B dissolved in saline solution was used to irrigate the lesion.

For 1 month after surgery, daily transnasal irrigation of the lesion with saline was performed. On the 12th day, *Aspergillus fumigatus* was isolated from

culture of the nasal discharge; blood urea nitrogen (35.4 mg/dL) and creatinine levels (2.02 mg/dL) had increased by this time. We therefore replaced the intravenous liposomal amphotericin B therapy with oral administration of voriconazole (400 mg/day) and nasal inhalation of amphotericin B. Intravenous sodium supplement was discontinued on the 22nd day because there was no further deterioration in renal function. On the 24th day, the presence of fungi and osteolytic changes were confirmed in a biopsy sample, allowing us to make a final diagnosis of IFS (Figure 1E).² CT images taken on the same day showed reduced size of the soft tissue density in the right posterior ethmoid sinus and orbit (Figure 1F). At the 1-month follow-up visit, the dose of oral voriconazole was reduced to 200 mg/day and nasal inhalation of amphotericin B was discontinued. At the 2-month follow-up visit, oral voriconazole was discontinued.

During the 6 months of follow-up, the patient did not show recurrence of sinusitis or further decrease in renal function, although his right eye visual acuity did not recover and ophthalmoplegia did not resolve. The patient chose not to undergo ptosis surgery.

DISCUSSION

Invasive fungal sinusitis (IFS) is a potentially fatal disease.^{3,4} Although IFS primarily involves the paranasal sinus, it can spread to the orbital apex. The prognosis in this situation is usually poor because the orbital apex is situated adjacent to the middle cranial fossa via the optic nerve canal and the superior orbital fissure.^{3,4} Aggressive medical and surgical treatments are therefore necessary to save the patient's life.^{3,4} Amphotericin B is a standard antifungal medicine for IFS because it has a wide spectrum and high effectiveness; however, this medication occasionally impairs renal function.^{1,3,5-7}

We treated a patient with IFS involving the orbital apex who also had chronic renal failure. Liposomal amphotericin B was used for initial therapy until detection of *A. fumigatus* because liposomal amphotericin B is effective for the major pathogenic fungi associated with IFS, including *Aspergillus* and *Zygomycetes*.^{1,4,5} Although liposomal amphotericin B suppressed the patient's sinusitis, renal function had decreased by the time *A. fumigatus* was isolated from the nasal discharge culture. Oral administration of voriconazole and nasal inhalation of amphotericin B then replaced intravenous liposomal amphotericin B. Oral voriconazole strongly suppresses *Aspergillus* species and is mainly metabolised by the liver, whereas amphotericin B is metabolised by the kidneys.⁷ Reducing the dose of amphotericin B and replacing it with oral voriconazole, therefore, can restore renal function.⁵ These treatments resulted in

ongoing suppression of IFS without any further decrease in renal function.

Renal function decreased during the intravenous administration of liposomal amphotericin B despite intravenous sodium supplementation. Liposomal amphotericin B is less nephrotoxic than conventional amphotericin B (incidence, 14–19% versus 34–42%).⁵ However, the reduced number of nephrons in our patient with congenital renal hypoplasia may have increased his vulnerability to amphotericin glomerular nephrotoxicity.⁶ This study confirms the necessity of strict monitoring of renal function in IFS patients with decreased renal function.

Early diagnosis is essential to avoid mortality in IFS patients with involvement of the orbital apex.⁴ Possible differential diagnoses in our patient included neoplasia, bacterial infection, and autoimmune inflammation.⁴ However, the patient's sequential development of cranial neuropathies consistent with orbital apex syndrome was a key to diagnosing IFS.⁴ Additionally, elevation of β -D-glucan and deterioration of the patient's symptoms after steroid administration were helpful in raising suspicion of IFS at the initial examination.

Our patient developed vision loss, ptosis, and ocular motility disturbance, in that order. Coronal CT images showed that the lesion extended from the posterior ethmoid sinus at the superomedial aspect of the orbit to the orbital apex at the posterior aspect (Figure 1D). Therefore, the optic nerve and the superior branch of the oculomotor nerve, which are located superomedially at the orbital apex,⁸ were involved earliest in this patient. In contrast, the lacrimal and frontal nerves are positioned most laterally in the orbital apex⁸; therefore, the patient did not experience facial numbness.

In conclusion, we report the case of a patient with potentially life-threatening IFS involving the orbital apex and concurrent chronic renal failure. Because there have been few previous reports that include imaging studies of IFS patients with sequential development of cranial neuropathies⁹ and who have concurrent renal failure,¹⁰ our report will be informative in diagnosing and treating such patients.

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Note: Figure 1 of this article is available in colour online at <http://informahealthcare.com/oph>.

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