Successful Treatment of Cerebral Aspergillosis with a High Oral Dose of Itraconazole after Excisional Surgery

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We report a case of cerebral aspergillosis which originated from the sphenoid sinus, and involved a progressive decrease of visual acuity. The neurological signs indicated a cavernous sinus invasion. After extensive intracranial surgery we treated the residual aspergillosis with a high oral dose of itraconazole (800 mg/d for 4 months, followed by 400 mg/d for 5 months). The neurological impairments of the patient gradually subsided with the resolution of the fungal lesion shown on MRI. The successful therapy indicated that itraconazole has a significant role in the treatment of advanced cerebral aspergillosis if it is used in high doses (16 mg/kg/d for adults).

Key words: fungus infection, sphenoid sinus, brain abscess, MRI

Introduction

Cerebral aspergillosis due to a primary infection of the nasal sinuses is common in hot and dry areas such as the Sudan, but it is rare in Japan (1, 2). This form of cerebral aspergillus infection has a very poor prognosis in spite of intracranial surgery and conventional antifungal therapy. Recent reviews suggest that high-dose itraconazole (ITZ) is a suitable treatment for cerebral aspergillosis (3). We report a case of a skull base aspergillus infection which originated from the sphenoid sinus. It was successfully treated with high-dose ITZ.

Case Reports

In September 1996 a 47-year-old man with a history of poorly controlled diabetes mellitus was admitted to the Department of Ophthalmology in our hospital. He presented with a loss of left visual acuity which had developed in 1 month. Following a tentative diagnosis of optic neuritis, he received high doses of intravenous corticosteroids as a treatment. However subsequent cranial computed tomography (CT) showed an enhanced lesion in the left sphenoid sinus and also the left optic canal. An external sphenoidectomy was performed and a thick pasty material was aspirated. When the aspirated material was examined microscopically numerous aspergilli were evident. The treatment was then changed to intravenous fluconazole (FLCZ) at 200 mg/d (equivalent to 2 mg/kg of body weight) for 1 week, and then increased to 600 mg/d (equivalent to 12 mg/kg of body weight) for the next 2 weeks, but no clinical improvement was observed. Cranial magnetic resonance imaging (MRI; GE Signa 1.5 tesla system) of the patient revealed a direct extension of the lesion from the left sphenoid sinus to the left frontal lobe (Fig. 1 and 2A). The patient was transferred to the Department of Neurology in October 1996. On admission he complained of a dull pain in the left frontal area which subsided after nonsteroidal anti-inflammatory drug administration. The patient was afebrile, completely conscious and well-orientated, but blind in the left eye with a Marcus-Gunn pupil. Neither extraocular muscle weakness nor ptosis were observed. The other cranial nerves and the cerebellum were intact and abnormalities in the trunk and limbs were not detected. The results of routine hematological and biochemical investigations were within normal limits. The erythrocyte sedimentation rate was normal, and the result of a test for C-reactive protein was negative. The total protein and cell count in the CSF were 65 mg/dl, and 1 lymphocyte and 2 neutrophils per mm³, respectively. The patient’s diabetes mellitus was controlled by insulin therapy and repeat electroencephalograms indicated the absence of any abnormality. After admission he developed ptosis and weak extraocular muscles due to a left oculomotor palsy, but he did not complain of double vision (due to left blindness).

Treatment with ITZ was started initially at 200 mg/d, po, together with FLCZ (600 mg/d, iv). An incomplete recovery of the left extraocular muscles was obtained by this regimen within 2 weeks. Subsequently the FLCZ was reduced and he...
was kept on ITZ at 200 mg/d for 2 months. Proliferation in the dura adjacent to the left ethmoid and sphenoid sinuses and an intensity-enhanced cyst at the frontal lobe base (Fig. 2A and B) were consistently shown in serial cranial MRIs. Due to a sudden increase in headaches in the left forehead and decreased visual acuity of the right eye, he returned to our department in February 1997. Cranial CT scans revealed a new fungal lesion which had expanded beyond the midline to the right optic canal and involved the right optic nerve. The CT scans did not reveal a granulomatous lesion or fluid retention within the right sphenoid and ethmoid sinuses. On the basis of these findings, we concluded that the sudden loss of right visual acuity was probably caused by constriction of the optic nerve by the granulomatous aspergillus lesion within the right optic canal.

A right frontotemporal craniotomy was immediately performed to decompress the right optic nerve. It was observed that the dura over the medial part of the right pterion, tuberculum sella and planum sphenoidale was covered with a thick, soft and grayish-granulomatous tissue. The lesion around the right optic nerve was removed meticulously and the roof of the right optic canal was also removed so that the optic nerve was sufficiently decompressed. Although cranial MRIs demonstrated an aspergillus brain abscess in the deep medial frontal

Figure 1. Axial postcontrast T1-weighted image by Gd-DTPA show an invasive aspergillosis from the left sphenoid sinus to the skull base involving the orbital apex.

Figure 2. Coronal postcontrast T1-weighted images by Gd-DTPA displayed a cyst and an intensity-enhanced dura at the left frontal lobe base during ITZ therapy of 200 mg/d (A. October 8, 1996; B. November 1, 1996). Repeated MRIs failed to show the enhanced cyst (C. March 3, 1997) and the thickness of the dura (D. July 7, 1997) while the therapy was 400 mg/d of ITZ.
Invasive aspergillosis from the sinuses into the skull base

Invasive aspergillosis is usually either a serious complication of immunosuppressive treatment or diseases which profoundly impair normal immunity. Aspergillus infection has been noted in almost every organ and system of the human body (6). Involvement of the lung, sinus, bone and brain was relatively common in the review of 2,121 published cases with invasive aspergillosis (6). Histologically, 20 of 32 necropsies of invasive aspergillosis showed a wide range beyond the lungs, with the brain being the most common site (7).

Invasive aspergillosis from the sinuses into the skull base often affects the orbits, the cavernous sinuses, and involves the cranial nerves. In an advanced stage it causes carotid arteritis, carotid occlusion, meningitis and brain abscesses. The mortality rate is very high in the advanced condition (2). At present, there is no completely effective treatment for aspergil-

Discussion

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