Aspergillus Aneurysm of the Middle Cerebral Artery
Causing a Fatal Subarachnoid Hemorrhage
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A rare case of Aspergillus aneurysm of the central nervous system (CNS) leading to subarachnoid hemorrhage (SAH) is reported. An 83-year-old woman developed visual disturbance and headache. Computed tomographic scans showed no evidence of aneurysm or tumor in the intracranium. She suddenly died from SAH. Autopsy revealed massive SAH due to ruptured Aspergillus aneurysm of the middle cerebral artery. Aspergillus was suggested to have extended from the paranasal sinuses. Aspergillosis of CNS should be considered in patients with neurological symptoms such as visual disturbance and trigeminal neuralgia, especially in cases of the aged or immunocompromised.

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Introduction
Rupture of intracranial aneurysm caused by Aspergillus infection follows a drastic clinical course and usually results in sudden death. Aspergillosis of the central nervous system (CNS) is rare and difficult to diagnose. However, recently the incidence has increased with the more widespread use of antibiotics and the growing number of immunocompromised hosts. Therefore this disease should be considered in the differential diagnosis in the case of the immunocompromised patient. We report a case of Aspergillus aneurysm causing fatal subarachnoid hemorrhage (SAH) and review some clinical features of similar cases in the literature.

Case Report
An 83-year-old Japanese woman had been healthy until January 1992 when she suffered from headache, immediately followed by impaired vision in the right eye. The left eye remained normal. She was diagnosed as having right retrobulbar neuritis. Corticosteroid treatment for a few days showed no improvement of symptoms and she was admitted to Kitasato Institute Hospital for further evaluation. The family history was noncontributory and her medical history was unremarkable.

There were no abnormal physical findings except in the ophthalmological examination. Her right best corrected visual acuity was diminished to 0.08, accompanied by central scotoma, and the right pupil was sluggishly reactive to light. The ocular fundi were normal. Other neurological examinations showed no abnormality. Frontal headache was experienced in the region of the first branch of the right trigeminal nerve.

Laboratory examination showed increased erythrocyte sedimentation rate (55 mm/1 h) and a slight increase in C-reactive protein (0.9 mg/dl). Complete blood count and biochemical examination showed almost normal values.

Computed tomographic (CT) scans demonstrated only mucosal thickening within the ethmoid and sphenoid sinuses (Fig. 1). Magnetic resonance images (MRI) showed enlargement of the right optic canal and mucosal thickening of the paranasal sinuses (Fig. 2). No other abnormalities were found. Plain X-ray films showed no abnormalities in the chest or the abdomen. Therefore, the patient’s neurologic and ophthalmologic abnormalities were diagnosed as idiopathic trigeminal neuralgia and right retrobulbar neuritis, respectively.

The headache was reduced through trigeminal nerve block with lidocaine hydrochloride, dexamethasone three times a
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Figure 1. Coronal CT scan reveals mucosal thickening in the left sphenoidal sinus (arrowhead).

Figure 2. T2-weighted sagittal image of MRI demonstrates enlargement of the right optic canal (arrowheads).

Figure 3. CT scan reveals massive hematoma in the right lateral ventricle, third ventricle and Sylvian fissure.

week and carbamazepine. These treatments were continued for two months, throughout the clinical course. However, her right visual acuity gradually decreased accompanied by right visual field loss, and the right ocular fundus became pale. On June 3, she suddenly became comatose during sleep. CT scans showed massive hemorrhage in the right cerebral hemisphere (Fig. 3). She died on June 5, 1992, despite conservative treatment.

The autopsy (KIH 28 ’92) revealed a massive intracranial hemorrhage. The hematoma was present in the area ranging from the subarachnoid space of the right Sylvian sulcus to the right lateral ventricle, destroying the brain tissue of the right temporal lobe and the basal ganglia. A tumorous lesion was present in the skull base, about thumb-tip in size and whitish-yellow in color and somewhat protuberant to the intracranial space. The main part of the tumorous lesion, located in the sphenoid bone just anterior to the hypophyseal fossa, involved the terminal portion of the right internal carotid artery and attached to the right optic nerve. Histologically, the tumorous lesion in the skull base was composed of coalescing granulomas (Fig. 4). Numerous hyphae of fungus, recognized in the necrotic center of the granulomas, were histopathologically identified as Aspergillus (Fig. 5). The sphenoid sinus itself was involved in the granulomatous inflammatory process and its wall was partly destroyed. Suppurative meningitis was present in the cerebral base and the right temporal lobe. A necrotizing suppurative inflammation was noticed in the right optic nerve. A large aneurysm of the right middle cerebral artery had formed and ruptured within the hematoma in the right Sylvian sulcus (Fig. 6), which was disclosed by histologic examination. The aneurysm was located at the main portion of the middle cerebral artery and was saccular in shape measuring about 6 mm at the greatest diameter. Severe neutrophilic infiltration with necrosis was seen in the arterial wall. Hyphae of Aspergillus were
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Discussion

Aspergillosis of the CNS is relatively rare, but the incidence of aspergillosis of the CNS has increased in recent years (1–6). After the first report of Oppe et al in 1897 (7), more than 170 cases have been reported (8). The route of infection for 80% of the cases is hematogenous dissemination originating from a primary pulmonary lesion or intraoperative contamination. In other cases, Aspergillus extends directly from the middle ear cavity, orbit or paranasal sinuses. In the present case, the route of entrance into the cranium was considered to be from a...
primary infection in the paranasal sinuses, as there was no evidence of Aspergillus infection in any other organs. Furthermore, the symptoms of the present case, such as visual disturbance and trigeminal nerve pain, are typical of this route of infection. Tsuoboi et al summarized the clinical features of CNS aspergillosis of this route. While the symptoms of the cases of hematogenous dissemination are variable and nonspecific, the cases of direct extension from paranasal sinuses show characteristic features such as visual symptoms (9).

Sometimes aspergillosis of CNS causes fatal SAH. It is assumed that Aspergillus has a tendency to invade the vessel walls leading to thrombosis or arteritis (3, 5, 6). However, the reason why Aspergillus is likely to invade vessel walls is not elucidated.

Despite recent progress in neuroradiology, aspergillosis of CNS is still difficult to diagnose (10). The radiological findings are often non-specific (9). In the present case, an extensive mass lesion was found in the skull base by postmortem examination; however, CT scans and MRI had revealed only mucosal thickening of the paranasal sinuses and enlargement of the right optic canal. If the possibility of the cerebral aneurysm is considered, MR angiography may be the most useful method for diagnosis (11, 12). The diagnosis of fungal intracranial aneurysm is usually established by histologic examination of surgical and autopsy specimens. CSF analysis is not helpful in most cases because of non-specific findings such as pleocytosis or increased protein content. Furthermore, usually CSF culture is negative for Aspergillus. New techniques for diagnosis are now being developed. New serologic procedures and molecular techniques, such as the polymerase chain reaction, may be applicable to mycosis in the future (10).

Treatment of Aspergillus infection is still unsatisfactory. Only a few cured cases were reported. In all curative cases, early operation was performed (13). Amphotericin B alone or in combination with 5-fluorocytosine is the standard drug of choice. However, its application is often limited due to toxic side effects. Itraconazole which is a new oral triazole antifungal agent is recently being utilized. This therapy has been proven to be effective in preventing invasive aspergillosis in high-risk patients. If early diagnosis can be made, 80% curability may be expected for this therapy (14, 15).

The incidence of aspergillosis of CNS has been increasing in parallel with the wider use of antibiotics, corticosteroids and the growing number of immunocompromised patients. These cases are patients receiving organ transplants (16), or elderly, or those with acquired immunodeficiency syndrome (AIDS) (17, 18). Minamoto et al discussed invasive aspergillosis in patients with AIDS, describing the possible risk factors associated with aspergillosis such as leukopenia, use of corticosteroids, and antineoplastic agents (19). In the present case the use of dexamethasone may have aggravated the condition of Aspergillus infection.

Although the treatment of aspergillosis of CNS is not very promising, a few cases have been reported to be cured by operation. For patients with headache, low grade fever and visual disturbance, it is important to consider the possibility of aspergillosis of CNS in order to make an earlier diagnosis and to prevent fatal rupture of aneurysm.

References