Subarachnoid Hemorrhage Caused by *Aspergillus* Aneurysm as a Complication of Transcranial Biopsy of an Orbital Apex Lesion

—Case Report—

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Abstract

A 62-year-old male complaining of unilateral visual disturbance and pain in the involved eye had a small mass at the right orbital apex which was identified as an *Aspergillus* granuloma by transcranial biopsy. One month later, the patient became comatose because of fatal subarachnoid hemorrhage due to a newly developed aneurysm. Autopsy showed a ruptured aneurysm on the right internal carotid-posterior communicating artery. Histological examination demonstrated prominent *Aspergillus* invasion of the arterial wall. *Aspergillus* infection must be taken into consideration in patients with orbital apex syndrome, which may lead to serious cerebrovascular consequences. If sino-orbital lesions are detected by neuroimaging techniques, biopsy using an extradural approach should be performed to obtain a definitive diagnosis.

Key words: *Aspergillus*, *de novo* aneurysm, subarachnoid hemorrhage, visual disturbance, steroid

Introduction

The increasing use of corticosteroids and immunosuppressive agents has led to an increase in fungal infections.^{17,34,35)} *Aspergillus* is one of the most common causes of fungal infection in the central nervous system. Cerebral *Aspergillus* infection is characterized by patches of hemorrhagic necrosis in the acute or subacute phase and granulomatous inflammation in the chronic phase.^{21,26,27,37)} The five major forms of manifestation of aspergillosis in the central nervous system are: meningitis, meningoencephalitis, abscess, single solid granuloma without abscess formation, and vascular disease.^{27,37)}

Cerebrovascular lesions due to fungal infection mainly occur due to direct invasion of the arterial wall by fungi from an intraluminal embolus that extends its hyphae outward, or from fungal meningitis that penetrates the adventitia.^{21,22,27,37)} The resultant

fungal arteritis may cause thrombosis of the inflamed vessel associated with hemorrhagic cerebral infarction or ill-defined abscesses, immediate vessel rupture associated with massive hemorrhage, or focal necrosis of the elastica associated with diffuse expansion of the vessel or a saccular intracranial fungal aneurysm.^{26,27,32)} Subarachnoid hemorrhage (SAH) secondary to rupture of fungal aneurysms is rare, but has been fatal in all reported cases. We treated a patient with a transcranial biopsy of a small lesion at the right orbital apex, which was complicated by rupture of a *de novo* *Aspergillus* aneurysm resulting in fatal SAH.

Case Report

A 62-year-old male with a 2-month history of visual disturbance and pain in the right retro-orbital and frontotemporal regions was admitted to our hospital. He had been healthy for the past 20 years except for mild diabetes mellitus.

On admission, his visual acuity was 0.4 in the right

Fig. 1 Magnetic resonance images demonstrating a small mass at the tip of the right anterior clinoid process (arrow) (left), enhanced by gadolinium (right).

Fig. 3 Intraoperative photographs, showing a small bulging hypervascular mass at the anterior clinoid process (arrows) (upper), but no other lesion at the optic nerve, the internal carotid artery, or the posterior communicating artery (arrows) (lower).

Fig. 2 Cerebral angiograms, performed on November 10, 1991 revealing no vascular lesions (upper), and on April 7, 1992 showing an aneurysm on the right internal carotid-posterior communicating artery (arrow) (lower).

eye and 1.5 in the left eye. Computed tomography (CT) of the head showed no mass near the right optic nerve. However, magnetic resonance (MR) imaging showed a small lesion at the right orbital apex (Fig. 1). Cerebral angiography showed no vascular lesions such as an aneurysm (Fig. 2 upper). Results of examination of cerebrospinal fluid were normal.

The patient was treated with steroids (8 mg/day of betamethasone and 10 mg/day of prednisolone) from November 12, 1991 to February 4, 1992. This steroid regimen relieved his pain, but did not improve his visual acuity, which deteriorated rapidly to 0.05 by day 5, and he became blind on January 30, 1992. He developed right oculomotor nerve palsy on February 24, 1992. Since the symptoms developed very rapidly and seemed to be closely related with the lesion at the right orbital apex, a transcranial biopsy was performed on March 16, 1992.

Fig. 4 Photograph of the main cerebral vessels confirming subarachnoid hemorrhage due to ruptured aneurysm (arrow) (left). Photomicrographs of the ruptured site showing numerous inflammatory infiltrating cells with *Aspergillus* invasion (HE stain, center: $\times 25$, right: $\times 100$).

The dura mater of the right anterior clinoid process was thick and hypervascular (Fig. 3 upper), but no lesion was observed at the optic nerve and the internal carotid artery (Fig. 3 lower). After the dura was excised, a yellowish-white granulomatous lesion was observed between the optic nerve and the anterior cavernous sinus. Small specimens of the granulomatous lesion showed the presence of *Aspergillus*. The excised dura was repaired using the temporal muscle and fascia.

Postoperatively, antibiotic therapy (fluconazole 100 mg/day) was performed for 10 days. His course was uneventful with no infectious signs and symptoms, but blindness and oculomotor nerve palsy in the right eye persisted. On April 7, 1992, the patient suddenly became comatose. CT showed serious SAH (Hunt and Hess grade V). Right carotid angiography revealed a newly developed aneurysm (approximately 5 mm in diameter) on the internal carotid-posterior communicating artery, which was believed to be the source of the SAH (Fig. 2 lower). His consciousness did not improve despite a variety of conservative treatments and he died on April 12, 1992.

Autopsy found diffuse swelling with thick SAH at the base of the brain. Dissection of the cerebral ves-

sels revealed a ruptured aneurysm, 5 mm in diameter, on the right internal carotid-posterior communicating artery (Fig. 4 left). The optic nerves were surrounded by yellowish pus, which extended to the biopsied area of the anterior clinoid process. However, there was no pus in the sphenoid sinus. Histological examination found extensive destruction of the arterial wall with dense inflammatory cell infiltration through the wall of the aneurysm and its neighborhood (Fig. 4 center). The aneurysm was characterized by the destruction of the elastica interna and media, and numerous infiltrating inflammatory cells in the aneurysm wall. A number of branching septate hyphae, morphologically identifiable as *Aspergillus*, were observed in these regions (Fig. 4 right). Aspergillosis was also seen in the mass of the right anterior clinoid process, but not in the sphenoid sinus and other organs.

Discussion

Our present patient died of SAH due to a *de novo* aneurysm resulting from cerebral *Aspergillus* infection as a complication of transcranial biopsy of the lesion at the orbital apex.

SAH due to ruptured fungal aneurysm is

Table 1 Cases of cerebral aneurysm of fungal origin

Case No.	Author (Year)	Age, Sex	Site of aneurysm(s)	Organism	Route of infection*	Associated disease(s)
1	Morriss and Spock (1970) ²³⁾	11, M	ICA	Penicillium	2	sinusitis
2	Davidson and Robertson (1971) ⁵⁾	75, M	BA	Aspergillus	2	sinusitis
3	Visudhiphan et al. (1973) ³⁵⁾	13, M	BA	Aspergillus	3	craniopharyngioma
4		5, M	MCA	Aspergillus	1	pneumonia
5	Sakaki et al. (1975) ²⁸⁾	26, M	ICA	Aspergillus	3	AVM
6	Horten et al. (1976) ¹³⁾	17, F	MCA, ACA	Aspergillus	1	aortic stenosis
7	Glass et al. (1978) ⁷⁾	4, F	ACA	Phycomycetes	1	pneumonia
8	Ahuja et al. (1978) ¹⁾	18, M	ICA	Aspergillus	2	sinusitis
9	Ho (1979) ¹²⁾	48, F	AcomA	Phycomycetes	2	DM, sinusitis
10	Scully et al. (1979) ²⁹⁾	66, M	SCA	Candida	1	stomach cancer
11	Goldman et al. (1979) ⁸⁾	16, F	BA	Candida	2	SLE, sinusitis
12	Mielke et al. (1981) ²²⁾	58, F	BA, ICA	Aspergillus	3	pituitary tumor
13	Partridge and Chin (1981) ²⁴⁾	18, M	VA	Aspergillus	3	periorbital tumor
14	Bullock et al. (1981) ⁴⁾	54, M	ACA	Candida	1	endocarditis
15	Shimosaka and Waga (1983) ³²⁾	23, M	MCA	Chromoblastomycosis	3	orbitofrontal tumor
16	Ichikawa et al. (1984) ¹⁴⁾	72, M	ICA	Aspergillus	1	pneumonia
17	Walsh et al. (1985) ³⁷⁾	64, F	PCA	Aspergillus	1	Cushing's syndrome
18	Kikuchi et al. (1985) ¹⁶⁾	61, M	ACA	Phycomycetes	3	cerebral aneurysm
19	Vu et al. (1986) ³⁸⁾	62, M	ACA	Aspergillus	1	hemodialysis
20	Hadley et al. (1987) ¹⁰⁾	20, F	ICA, BA	Candida	1	pneumonia
21	Asari et al. (1988) ²⁾	48, M	ACA	Aspergillus	3	cerebral aneurysm
22	Scully et al. (1988) ³⁰⁾	27, M	BA	Aspergillus	1	leukemia
23	Piotrowski et al. (1990) ²⁵⁾	40, F	ICA, VA	Aspergillus	3	cerebral aneurysm
24	Barrow and Prats (1990) ³⁾	4, M	BA, VA	Aspergillus	3	brain tumor
25	Iihara et al. (1990) ¹⁵⁾	78, F	BA	Aspergillus	2	sphenoid tumor
26	Komatsu et al. (1991) ¹⁸⁾	61, F	ICA	Aspergillus	3	Rathke's cleft cyst
27	Masago et al. (1992) ²⁰⁾	75, F	MCA	Aspergillus	1	bronchopneumonia
28	Takeshita et al. (1992) ³³⁾	39, M	SCA	Aspergillus	3	facial spasm
29	Kurino et al. (1994) ¹⁹⁾	63, M	VA	Aspergillus	2	temporal base granuloma
30	Present case	62, M	ICA	Aspergillus	3	anterior clinoid lesion

*1: Hematogenous dissemination from a remote extracranial site,³⁷⁾ 2: extension from a contiguous cranial foci such as the nasal cavity and the paranasal sinuses,¹¹⁾ 3: direct introduction in patients who developed fungal infection after neurosurgical procedures.⁶⁾ ACA: anterior cerebral artery, AcomA: anterior communicating artery, AVM: arteriovenous malformation, BA: basilar artery, DM: diabetes mellitus, ICA: internal carotid artery, MCA: middle cerebral artery, PCA: posterior cerebral artery, SCA: superior cerebral artery, SLE: systemic lupus erythematosus, VA: vertebral artery.

rare and has been fatal in all previous 29 cases of ruptured fungal aneurysm (Table 1).^{1-5,7,8,10,12-16,18-20,22-25,28-30,32,33,35-37)} Fungal aneurysms commonly arise from the major cerebral arteries and are large (5 to 10 mm in diameter).²⁷⁾ Fifteen of the 30 aneurysms were located on the internal carotid and/or basilar artery. *Aspergillus* was the common causative organism (21 cases) followed by *Candida* (4 cases). The causative organism may reach the central nervous system by three different routes: Hematogenous dissemination from a remote extracranial site,³⁷⁾ extension from a contiguous cranial foci such as the nasal cavity and the paranasal sinuses,¹¹⁾ and direct introduction in patients who developed fungal infection after neurosurgical procedures.⁶⁾ The first route infection was suspected in 11 cases, the second route in seven, and the third route in 12. Patients suffered ruptured

aneurysms approximately 2 months (4 days–15 months) after the direct neurosurgical procedures. Four of the 12 cases had operations for mass lesions located around orbital apex region, which had fungal infection.

Fungal infections generally occur in debilitated patients with predisposing factors such as routine administration of steroids and immunosuppressive agents, but rarely occurs in the orbit and/or cavernous sinus region of healthy individuals following a contiguous infection in the paranasal sinuses.^{17,27,34,37)} In the latter, high-resolution neuroimaging techniques such as CT and MR imaging may be useful for visualizing lesions.⁹⁾ However, some inflammatory lesions cannot be distinguished by neuroimaging techniques. Consequently, histological examination is required to confirm *Aspergillus* infection. The patient and previous cases of ruptured fun-

gal aneurysm infected via neurosurgical procedures indicate that direct intracranial introduction of fungus may cause fatal vascular lesions. Therefore, extradural approaches such as transsphenoidal, transnasal, and transorbital biopsy should be used to establish the histological diagnosis for a mass lesion in the cavernous sinus, orbital apex, and/or paranasal sinus. A patient with *Aspergillus* granuloma involving paranasal sinuses and cavernous sinus to occlude the internal carotid artery underwent transsphenoidal biopsy and successfully treated.³¹⁾ Ruptured fungal aneurysms are associated with extremely high mortality, so aggressive attempts to obtain an early diagnosis of sino-orbital lesions by neuroimaging techniques and extradural biopsy essential to prevent fungal invasion into the intracranial vessels. If an intracranial fungal infection is suspected during the surgical preparations, appropriate medical therapy using antifungal agents should be maintained for at least 2 months and follow-up studies of cerebral vessels performed by non-invasive methods such as MR angiography.

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