Carotid-Cavernous Sinus Thrombosis Caused by Aspergillus Fumigatus: Magnetic Resonance Imaging with Pathologic Correlation—A Case Report

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Abstract

The authors describe a case of aspergillosis with carotid-cavernous sinus thrombosis diagnosed by use of magnetic resonance imaging (MRI). MRI may aid in early detection of intracranial fungal infection and potentially help decrease morbidity and mortality through the institution of early medical and surgical therapy.

Introduction

Central nervous system (CNS) aspergillosis is a devastating condition that is increasing in prevalence. It occurs most frequently in the setting of immunocompromise. In the case presented here, a fatal carotid-cavernous sinus thrombosis was caused by *Aspergillus fumigatus* infection in a diabetic patient with a depressed immune status secondary to corticosteroid therapy.

Case Report

A seventy-three-year-old man was admitted with a two-week history of right retroorbital pain and severe abdominal pain with nausea and vomiting. He was known to have diabetes mellitus, hypertension, and coronary artery disease. He had received six months of prednisone therapy for presumptive temporal arteritis.

Examination revealed a cushingoid appearing, afebrile male in severe distress with right proptosis and complete ophthalmoplegia. Sensation to light touch and pin-prick was decreased

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in the ophthalmic division of the right trigeminal nerve. Accommodation was absent on the right with minimal pupillary light response. Visual acuity was 20/200 O.D. and 20/40 O.S. Funduscopy revealed pale discs with no evidence of hemorrhages. The remainder of the neurologic examination was unremarkable. Cranial computerized tomography (CT) demonstrated an air fluid level in the right sphenoid sinus. Two days after admission, a right sphenoidotomy produced purulent material that grew *Aspergillus fumigatus*. Treatment was immediately instituted with intravenous amphotericin B. The following day, the patient suddenly developed a left hemiplegia. Magnetic resonance imaging (MRI) demonstrated an increased signal in the sphenoid sinus on T2 weighted images. Abnormal signal was seen in the pons, right occipital lobe, and periventricular white matter. No carotid flow void was identified in the intracavernous right carotid, suggestive of right internal carotid artery thrombosis (Figs. 1, 2). Cerebrospinal fluid (CSF) analysis was remarkable for 1,075 WBCs with 1,053 polymorphonucleocytes, 10 RBCs, a glucose of 108 mg/dL, and a protein of 240 mg/dL with negative bacterial and fungal cultures. Chest x-ray showed a left pleural effusion.

One week after admission, he died suddenly after sustaining cardiac asystole. At autopsy there was bony destruction of the right sphenoid and cavernous sinus. The right cavernous sinus revealed acute and chronic inflammatory changes involving the full thickness of the cavernous portion of the right internal carotid artery, with thrombosis (Fig. 3). Gomori-methanamine silver stain revealed regular, septate fungal hyphae with 45° branching in the cavernous sinus, the wall of the right internal carotid artery, and adjacent sphenoid sinus. Cerebral sections demonstrated multiple focal infarctions and cerebritis with infiltrations by fungal hyphae. The leptomeninges adjacent to the right optic tract was acutely inflamed and infiltrated by fungal hyphae. No evidence of disseminated aspergillosis was found.

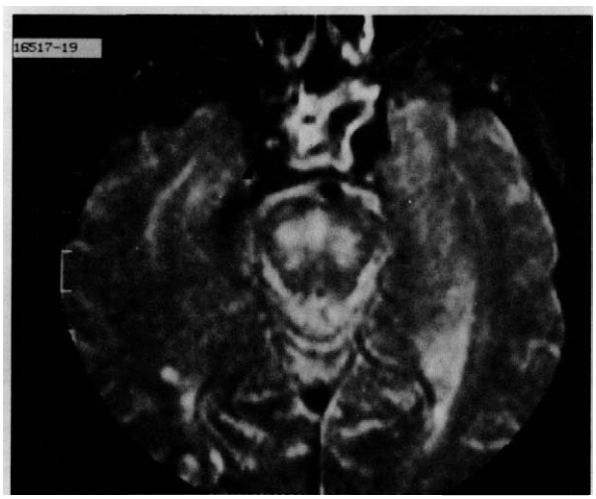

FIG. 1. Axial T2-weighted spin echo (TR2000 msec; TE 100 msec) image at the level of the midsphenoid sinus shows the thrombosis with high signal intensity (arrow) in the right cavernous carotid and the normal flow void phenomenon of the left cavernous carotid. The infected sphenoid sinus and demyelination in the pons are also noted.

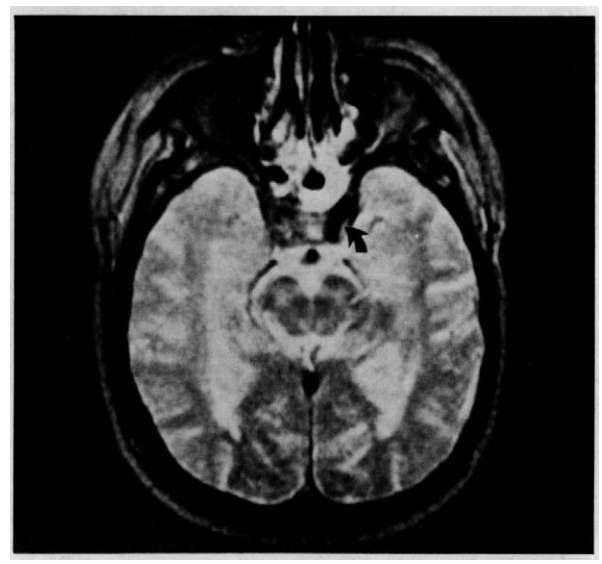

FIG. 2. Axial T2-weighted image at higher level to Fig. 1 shows the normal horizontal position of the left cavernous carotid artery with flow void phenomenon (arrow), which is not demonstrated at the right side. Again the infected sinus shows high signal intensity.

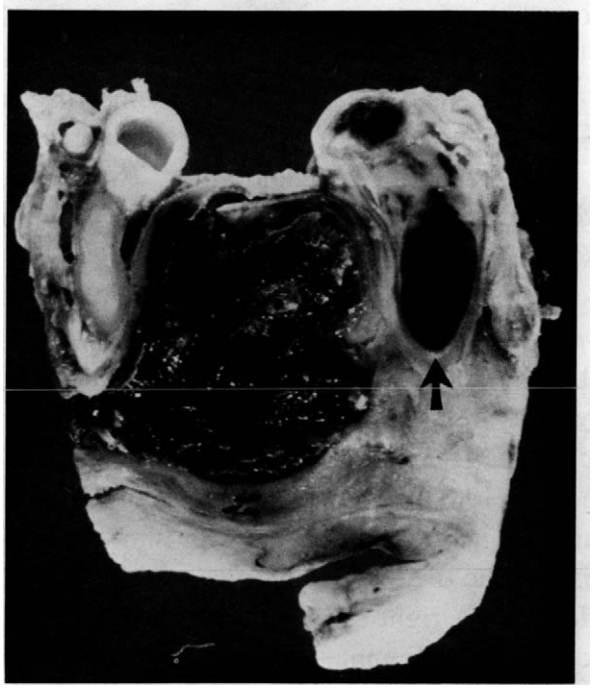

FIG. 3. A coronal section from base of the skull obtained at autopsy shows the thrombosis (arrow) in the right cavernous carotid artery and the infected sphenoid sinus.

Discussion

In 1729, Micheli described Aspergillus ("rough head"), a septate hyphal fungus of the Ascomycete class.[1] More than 350 species of *Aspergillus* exist.[2] Only 7 species are known to infect man, with 90% of human disease caused by *Aspergillus fumigatus*.[3] *Aspergillus* is ubiquitous. It is found in warm, damp climates in decaying debris and soil. It is a contaminant of the external auditory canal and the respiratory tract.[1] Infection can involve the lungs, paranasal sinuses, and orbital bones, appearing as a chronic granulomatous disease or as a disseminated infection characterized by tissue necrosis and hemorrhage. Central nervous system involvement occurs by direct extension from the sinuses and orbits or through hematogenous spread from pulmonary infections.[4]

Isolated paranasal sinusitis due to *Aspergillus* is rare except in the Sudan, where it is endemic, probably secondary to climatologic conditions.[5] Maxillary and ethmoid sinuses are most commonly affected. Oppe[6] reported the first case of isolated *Aspergillus* sphenoid sinusitis in 1879. Although this is the most common fungal infection of the paranasal sinuses, no more than 114 cases had been reported in the world literature as of 1979.[5] By 1983, only 11 cases of isolated sphenoid sinusitis had been described. Of these patients, 5 developed meningitis and only 1 survived after receiving treatment with amphotericin B.[1] Hora[7] classified mycosis of the sinuses into noninvasive and invasive forms. The noninvasive form appears with unilateral nasal obstruction and a foul, purulent drainage. The invasive form often produces palpable distortion of the maxillary and ethmoid sinuses; orbital bony destruction often occurs. The most frequent symptoms include headache, facial pain, and blurred vision. Proptosis and periorbital swelling can occur secondary to spread from the sinus to the orbit

with thrombophlebitis of the communicating veins.[5,8]

Chronic hypertrophic sinusitis, mucocele, and nasal polyps provide an anaerobic environment that induces *Aspergillus* to release an endotoxin with subsequent fibrinoid necrosis of soft tissue and angiitis.[3] The location of the sphenoid sinus allows the spread to the cavernous sinus with potential involvement of the pituitary gland, optic chiasm, internal carotid artery, and cranial nerves III, IV, VI, $V_1$and V_2.[9] Meningitis is the most common complication of sphenoid sinus suppuration.[7]

The first recorded case of disseminated aspergillosis with cerebral involvement was reported in 1943.[6] CNS disease tends to occur in immunocompromised hosts with leukemia, those receiving chronic corticosteroid therapy, and particularly in transplant patients. CNS aspergillosis may manifest in many ways, including meningitis, abscess, granulomas, arterial thrombosis, cerebral hemorrhages, and mycotic aneurysms. Patients appear lethargic or obtunded, and this is often followed by stroke and seizures. Rapid deterioration and death is a not infrequent outcome.[6] Multiple small foci of vasculitis occur with cerebritis, small-vessel angiitis, and granulomatous and suppurative tissue reactions.[10] Arterial invasion may lead to thrombosis and mycotic aneurysms. There have been only 6 recorded cases of internal carotid artery occlusion secondary to *Aspergillus* extending from the sinuses and orbits[6] (see Table I).

Positive cultures and histology of biopsy specimens is diagnostic. Granulomas and giant cells are common. Staining with Periodic Acid Schiff and methenamine silver reveals a septate fungus that forms elongated, branching hyphae in tissues and conidiospores in culture. Characteristically, an intense inflammation can be seen in all arterial layers with occasional thrombosis, rupture, or mycotic aneurysm. Blood cultures are generally negative. CSF analysis demonstrates elevated protein and pleocytosis when meningitis occurs, but cultures are almost never positive.[3]

Aspergillosis is relatively resistant to antibiotics. Intrathecal amphotericin B and/or intravenous flucytosine have some clinical usefulness. Combinations of amphotericin B and rifampin or flucytosine may be synergistic.[3] In sinus infections, antifungals are not effective unless used in conjunction with surgery. The noninvasive form responds to surgical excision

TABLE I
Carotid Artery Occlusion Associated with Aspergillosis

Author/Year	Age	Sex	Lesion	Immuno-suppression	Extracerebral Involvement	Paranasal Sinus Involvement
Nicod/1946[39]	46	M	Ruptured ICA	?	+	+
Schnyder/1948[40]	71	M	ICA and MCA	?	+	+
Wollschlaeger/1970[41]	74	M	Right CCA	–	–	–
Hedges/1976[42]	62	F	Left ICA	–	–	–
Kaufman/1976[43]	31	M	Left ICA + Pca	–	–Mediastinum –Right atrium –SVC	–
Sekhar/1980[2]	37	M	Right ICA	–	+	Sphenoid sinus
Dyken et al/1987	73	M	Right ICA	+	+	Sphenoid sinus

Abbreviations: CCA = Common Carotid Artery
ICA = Internal Carotid Artery
MCA = Middle Cerebral Artery
Pca = Posterior Cerebral Artery
SVC = Superior Vena Cava

with aeration of the involved sinus. The invasive form is resistant to therapy and may recur.[1] Successful surgical treatment of cerebral aspergillosis has been reported in only 3 cases, and no well-documented cure has been reported with use of antibiotics only.[6] By contrast, pulmonary aspergillosis can be successfully treated with amphotericin B. Serologic testing and sputum cultures are often negative, while bronchoscopy and biopsy are generally diagnostic. Aggressive evaluation and treatment before dissemination is of the utmost importance.[6]

Conclusions

Aspergillus infection of the CNS is a serious but relatively rare condition that is increasing in prevalence secondary to the widespread use of immunosuppressant therapies. These patients may be afebrile; therefore, other signs must be closely followed for evidence of sinus and pulmonary infection, which can quickly lead to disseminated disease. The use of MRI can assist in the early detection and treatment of intracranial fungal infections.

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