Aspergillus infection complicating transsphenoidal yttrium-90 pituitary implant

Report of two cases

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Diagnosis proved difficult in two cases of Aspergillus infection complicating yttrium-90 ablation of the pituitary. This serious complication occurs rarely. Whatever the initial organism obtained from cases with meningitis of late onset, Aspergillus infection should be considered and cerebrospinal fluid should be cultured for fungi.

KEY WORDS • pituitary gland irradiation • yttrium isotope • aspergillosis • meningitis

A transnasal, transsphenoidal method of implanting yttrium-90 ($^{90}$Y) to destroy the pituitary by interstitial irradiation has been extensively used. Two $^{90}$Y pellets mounted on stainless steel screws are stereotaxically placed in the sella with the screws protruding into the sphenoid sinus. Meningitis is a serious complication of this procedure. Two cases are described in which sphenoidal and intracranial Aspergillus infection developed. A review of the literature revealed no previous reports of this complication.

Case Reports

Case 1

This 57-year-old woman had a transsphenoidal $^{90}$Y implant on February 13, 1970, for acromegaly. She was well when discharged 6 days later on maintenance endocrine therapy. She was readmitted in April, 1970, with meningitis. Cerebrospinal fluid (CSF) analysis showed protein 800 mg/100 ml, and white blood cells (WBC) 1700/cu mm (differential count: 50% polymorphonuclear leukocytes (PMN), 50% lymphocytes). Cultures grew Diplococcus pneumoniae. The patient was treated with ampicillin and recovered.

She was admitted again on December 24, 1974, with a 2-week history of rhinorrhea and a 24-hour history of headache and vomiting. Cerebrospinal fluid analysis showed protein 320 mg/100 ml, and WBC 6100/cu mm (differential count: 78% PMN, 20% lymphocytes, 2% monocytes). She was treated empirically with chloramphenicol and gentamicin. The CSF cultures grew D. pneumoniae. Recovery was slow. On January 6,
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1975, CSF analysis was normal, and the patient was alert and afebrile. On January 18, 1975, the patient suffered an infarct of the terminal ileum and a resection was performed. Eight days later signs of meningitis recurred. Cerebrospinal fluid analysis showed protein 85 mg/100 ml, and WBC 138/cu mm (differential count: 96% PMN, 4% lymphocytes). The next day a left hemiparesis developed. Cerebral angiograms showed occlusion of branches of the right middle cerebral artery. The patient died the next day.

A postmortem examination showed a purulent basal leptomeningitis. Histological section revealed fungi in the subarachnoid space, invading through the walls of blood vessels and a severe vasculitis (Fig. 1). Some vessels were completely occluded and there were multiple cerebral infarctions. Culture showed that the fungus was Aspergillus.

Case 2

This 37-year-old man had been treated 9 years before the present admission for diabetic retinopathy with 90Y implants in the pituitary. In June, 1974, he developed clear rhinorrhea associated with eating or drinking, several episodes of fever, headache, and stiff neck clearing spontaneously in 3 to 4 days, and blurred vision in the right eye. Physical examination was normal except for diabetic retinal changes. Analysis of the CSF showed protein 134 mg/100 ml, and WBC 85/cu mm (differential count: 29% PMN, 64% lymphocytes, 7% monocytes). Despite extensive investigation a CSF fistula could not be confirmed.

He was readmitted on September 14, 1974, with headaches and sudden loss of vision in the left eye. An intrasellar or parasellar mass was suspected but a left carotid angiogram and pneumoencephalogram were normal. The CSF analysis showed protein 331 mg/100 ml, and WBC 8800 (differential count: 90% PMN, lymphocytes 3%, monocytes 7%). Cultures were sterile. He was treated empirically with gentamicin and chloramphenicol and recovered. The screws showed branching hyphal organisms compatible with Aspergillus, and a culture of the tissue grew Aspergillus. The patient recovered after prolonged treatment with amphotericin B.

Fig. 1. Case 1. Photomicrograph shows large septate hyphae compatible with Aspergillus invading an arterial wall. Gridley stain, × 196.

Discussion

From 1963 through 1971, 380 90Y implants were performed at the Cleveland Clinic. These are the only two cases known to have had Aspergillus infection. Many cases of meningitis complicating 90Y implants have been reported, but no cases of fungal infection. Primary aspergillosis of the paranasal air sinuses is a rare disease. In a review of the literature, Hora could find only 24 cases between 1891 and 1965. In only two cases was the sphenoid sinus involved. In 1969, Milošev, et al. reported 17 cases of paranasal sinus aspergillosis from the Sudan. In none of these cases was there evidence of intracranial spread. Zinneman suggests that radical drainage is the best form of therapy for sinus aspergillosis and that antibiotics have no part to play. Aspergillus infection had been reported as an occupational disease in pigeon feeders, wig

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makers, and stockyard workers, but this was not a factor in either of our two cases. In these cases, apparently the presence of foreign material in the sphenoid sinus favored Aspergillus infection, and the screws provided an access route to the subarachnoid space in the sella.

Young, et al., studied 98 cases of aspergillosis. None of these patients had diabetes mellitus. In three cases the disease was primary in the paranasal sinuses. In 13 cases the infection involved the central nervous system, and in 12 it was secondary to a pulmonary lesion. In 11 of these the CSF was analyzed and in seven it was normal. Fungal hyphae were not seen in any specimens.

In 1969, Mukoyama, et al., reviewed all 32 published cases of central nervous system aspergillosis. They found five different pathological types: 1) meningitis (10 cases); 2) meningoencephalitis without granuloma (three cases); 3) multiple brain abscesses (11 cases); 4) solid granuloma without abscess formation (three cases); and 5) single brain abscess (five cases). Wybel reported a case of an Aspergillus granuloma of the cervical spine occurring 3 years after a pneumococcal infection; our Case 1 also had pneumococcal meningitis 3 years before the Aspergillus infection developed.

We can make no definite statement about treatment, but in suspected cases, as in our Case 2, removal of the screws may provide the diagnosis as well as remove an important underlying causative factor. Cerebrospinal fluid should be cultured for fungi.

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References

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