Cerebral aspergillosis following intracranial surgery

Case report

ERCOLE GALASSI, M.D., EUGENIO POZZATI, M.D., MASSIMO POPPI, M.D., AND ATILIO VINCI, M.D.

Second Division of Neurosurgery, Ospedale Maggiore C. A. Pizzardi, Sezione Bellaria, Bologna, Italy

The authors report a case of cerebral aspergillosis. This is only the fifth case following intracranial surgery noted in the literature. Pathogenesis, angiographic findings, and results of cerebrospinal fluid culture are discussed.

KEY WORDS □9 Aspergillus □9 abscess □9 granuloma

Cerebral aspergillosis is an unusual disease. About 80 cases have been reported in the literature; however, all authors agree that there has been an increase in the incidence of this infection in recent years. In fact, between 1897, when Oppe reported the first case, and 1950 only 12 cases were reported; all the others have been noted subsequently. We are describing a case of cerebral aspergillosis that we encountered in a patient who had undergone intracranial surgery.

Case Report

This 59-year-old woman who had suffered from diabetes mellitus for many years was operated on for a meningioma of the left olfactory groove. The operation was successful and no neurological deficit was apparent postoperatively. Antibiotic therapy was prolonged for 2 months to control an intercurrent urinary infection.

About 1 year after surgery, the patient's condition deteriorated rapidly. She developed intermittent fever and partial right-sided seizures, followed by right hemiparesis and aphasia. An electroencephalogram showed focal delta abnormalities in the left frontal region, while a technetium-99 brain scan revealed an increased uptake in the left frontotemporal region. The patient was transferred to our hospital in poor general condition. She was stuporous, with right hemiparesis and aphasia; there was no papilledema.

Examination. The most significant laboratory data were hyperglycemia with 218 mg/100 ml, glycosuria, and hypochromic anemia with 7.6 gm of hemoglobin. A chest x-ray film showed no abnormality; a skull film was normal except for postoperative alterations. A left internal carotid angiogram showed a left frontotemporal mass; there was a large area of pathological hypertascularity within the expanding lesion (Fig. 1).

Operation. A second operation was performed through the previous craniotomy. When the very thick dura was opened, four nodular formations were found extending from the internal surface of the dura into the
Sylvian fissure. The largest of these nodules, about 21/2 cm in diameter, was made up of two abscess cavities containing ivory-colored purulent material. All pathological tissue was removed, including the dura, which was replaced by lyophilized dura. No residual traces of the meningioma were found.

Pathological Findings. Microscopic examination of the surgical specimen showed multiple granulomas composed of foreign-body giant cells mixed with neutrophilic granulocytes and numerous lymphocytic elements. Large masses of foamy macrophages were also present; among the giant cells large and septate mycotic hyphae and some hyaline spores were observed (Fig. 2). The nodules demonstrated a marked tendency to necrosis and in the necrotic areas the hyphae were more numerous. The pathological process involved the meninges with only a narrow band of cerebral inflammatory changes. Culture of the cerebrospinal fluid (CSF) taken from the surgical site revealed colonies of *Aspergillus fumigatus*.

Postoperative Course. The operation was tolerated well; the patient promptly recovered consciousness and became generally alert. The right hemiparesis and aphasia remained unchanged. Parenteral therapy with amphotericin B was started. About 3 months after the operation the patient's condition deteriorated rapidly; she became comatose and died after a few days. Autopsy revealed diffuse purulent meningoencephalitis with wide areas where fungal infestation was evident. It was impossible to localize other foci of aspergillosis in the cranium or elsewhere.

Discussion

*Aspergillus fumigatus* is the most frequent cause of aspergillosis of the central nervous system. The following conditions tend to favor the development of the disease: 1) environmental or professional factors that expose the organism to prolonged contact with the infective agent; 2) depressed immune response acquired iatrogenically from therapy with corticosteroids, antibiotics, cytotoxic, and immunosuppressive agents; or 3) a state of general debilitation (pulmonary tuberculosis, hepatitis, alcoholism and other drug addictions, diabetes, leukemia and other neoplastic diseases).

*Aspergillus* may reach the central nervous system by three different routes. The first route is by hematogenous dissemination from a remote extracranial site, usually the lungs. This route is also responsible in cases of mycotic endocarditis and generalized systemic aspergillosis. The second possible pathway is by extension from a contiguous cranial focus. This focus is most often the nasal cavity and the paranasal sinuses from which the fungus may reach the cranial cavity by direct propagation as well as through local venous channels. In 33 cases reviewed by Mukoyama, *et al.*, a definite...
nasosinus involvement was certain in nine cases. Invasion from an orbital focus with subsequent diffusion through the optic canal or the sphenoid fissure is also frequent. The third possibility is by direct introduction in patients who developed intracranial aspergillosis after neurosurgical procedures. The latter pathway of infection may have been responsible in our case and in four others reported in the literature. Our patient lacked radiological or postmortem evidence of extracerebral involvement, so it seems correct to attribute a pathogenetic role to the first operation, when direct contamination may have occurred. However, like other authors, we feel we cannot exclude a subsequent invasion by the organism. In our case the meningioma was removed from the olfactory groove, so the infection could have spread through the ethmoid.

One may speculate on the roles played in the development of the infection by the diabetes mellitus and the prolonged antibiotic therapy. In our opinion, these two predisposing conditions at least accelerated the progress of disease.

Aspergillosis of the central nervous system may present as meningitis, encephalitis, single or multiple brain abscess, single or multiple solid granuloma, and mycotic arteritis. Abscess and granuloma will act in the same way as other space-occupying processes, while mycotic arteritis may be responsible for acute ictal manifestations. In two cases, the clinical picture was that of a retro-orbital neoplasia. In one case trigeminal neuralgia was secondary to involvement of the Gasserian ganglion. The posterior fossa and upper cervical canal have rarely been involved.

Cerebrospinal fluid examination almost always shows an elevation of protein and quite frequently pleocytosis, especially with increase of neutrophils; glucose is usually normal and culture is not usually positive. In our patient, however, CSF culture was positive but, as in the case of David, et al., the CSF was obtained from the surgical site during the operation.

Plain radiographs of the skull may show signs of increased intracranial pressure; in retro-ocular locations dilation of the optic foramen and destruction of the lesser wing of the sphenoid bone have been reported. The finding of intracranial calcification in a 10-month-old baby reported by Iyer, et al., is unique: in that case an erroneous diagnosis of toxoplasmosis was made.

Radionuclide brain scans reveal areas of increased uptake, almost always in the abscess and granuloma, and not unusually in the area of encephalitis. Negative brain scans,
Cerebral aspergillosis

however, have been described in cases of encephalitis and aspergillosis abscess.\textsuperscript{16,20} The most common angiographic finding with abscesses, granulomas, and encephalitic foci is the existence of an avascular mass; mycotic arteritis may be evidenced by thrombosis or aneurysmal dilatations. In our case a pathological hypervascularity was found in the area of the expanding lesion.

Antifungal therapy with amphotericin B and surgery in cases of abscess or granuloma are the most advisable treatments of cerebral aspergillosis. In spite of these, the disease has a poor prognosis and a cure is reported only rarely. In the cases of David, et al.,\textsuperscript{4} and Benaim and Parisi\textsuperscript{1} survival was documented up to 3 and 6 months after surgery, respectively.

An effective cure after removal of an aspergillotic brain abscess is reported by Hendrick and Conen;\textsuperscript{10} a recent case of survival after \textit{Aspergillus} meningitis is reported by Feely and Steinberg.\textsuperscript{7}

References


Address reprint requests to: Ercole Galassi, M.D., Second Division of Neurosurgery, Ospedale Maggiore C. A. Pizzardi, Sezione Bellaria, Bologna, Italy.