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Pseudallescheria boydii Infection of the Brain: Imaging with Pathologic Confirmation

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Summary: ***Pseudallescheria boydii* is a rare opportunistic microorganism that usually infects immunosuppressed hosts. In this patient with cerebral infection by *P boydii,* imaging findings included enhancement of the ependyma of a lateral ventricle and of the caudate nucleus.**

Index terms: Brain, infection; Transplants

Pseudallescheria boydii (also known as *Petriellidium boydii, Allescheria boydii, Scedosporium apiospermum,* and *Monosporium apiospermum)* is a ubiquitous fungus of soil and polluted water (1). *P boydii* is a well-known cause of mycetoma, which is a chronic, subcutaneous fungal infection of the lower extremities (2). Infection of the central nervous system (CNS) with *P boydii* is uncommon. We found 25 cases in the literature published since 1953. Most CNS infections occur in patients with predisposing conditions, including immunosuppression, near drowning, or trauma (3–29). *P boydii* has been reported to cause osteomyelitis, pulmonary infection, endocarditis, suppurative arthritis, keratosis, sinusitis, and disseminated disease (30–35).

Case Report

A 27-year-old man with end-stage cystic fibrosis received a double lung transplant. When he was discharged from the hospital 32 days after surgery, he was receiving antibacterial, antiviral, and immunosuppressive therapies. Five days later, he presented with fever, chills, vomiting, and severe bifrontal headache. Results of tests on his cerebrospinal fluid showed no organisms, a white blood cell count of 3.3×10^6/L and glucose of 3.8 mmol/L. His cerebrospinal fluid was nonreactive to the VDRL, and the results of tests for cryptococcal antigen were negative.

Contrast-enhanced computed tomography (CT) showed ependymal enhancement in the frontal horn of the right lateral ventricle (Fig 1A). Magnetic resonance (MR) imaging of the brain showed focal punctate enhancement in the deep white matter of the right frontal lobe and subependymal enhancement in the anterior horn of the right lateral ventricle (Fig 1B–D). The paranasal sinuses were normal.

A brain biopsy was performed. Sections of right frontal white matter and biopsy specimens from the right lateral ventricular wall showed reactive changes and perivascular lymphohistiocytic infiltrate, aggregates of epithelioid histiocytes consistent with granulomas, and acute inflammatory cells (Fig 1E–G). Tissue submitted for culture showed true hyphae. The organism was identified as *P boydii.* Amphotericin B therapy was started. A chest CT scan showed bilateral pulmonary infiltrates and pulmonary nodules of unknown origin. A transbronchial biopsy yielded evidence of diffuse alveolar damage but no organisms. Despite aggressive antifungal therapy, the patient's pulmonary status declined and he died.

At autopsy, the brain weighed 1540 g, an abnormally high weight, which was assumed to be caused by edema of the right frontal lobe. Coronal sections showed a $1.5 \times 1.5 \times 1.0$-cm encapsulated, hemorrhagic mass within the frontal horn of the right lateral ventricle (Fig 1H and I). There were no daughter abscesses. The meninges appeared normal, and the cerebrospinal fluid was not cultured.

Discussion

The course of *P boydii* infection of the CNS is unclear. The organism appears to spread to the CNS by several mechanisms. Direct inoculation after surgery or trauma has been reported (6, 8, 15). The CNS can also be affected by direct extension of the organism from a source near the brain, such as the paranasal sinuses (16), or by hematogenous spread from pulmonary or disseminated disease (3).

The frequency of CNS infection with *P boydii* has increased in the last two decades because of the increasing numbers of immunocompromised patients (3). Of 25 reported cases of CNS infection, 10 patients were immunocompro-

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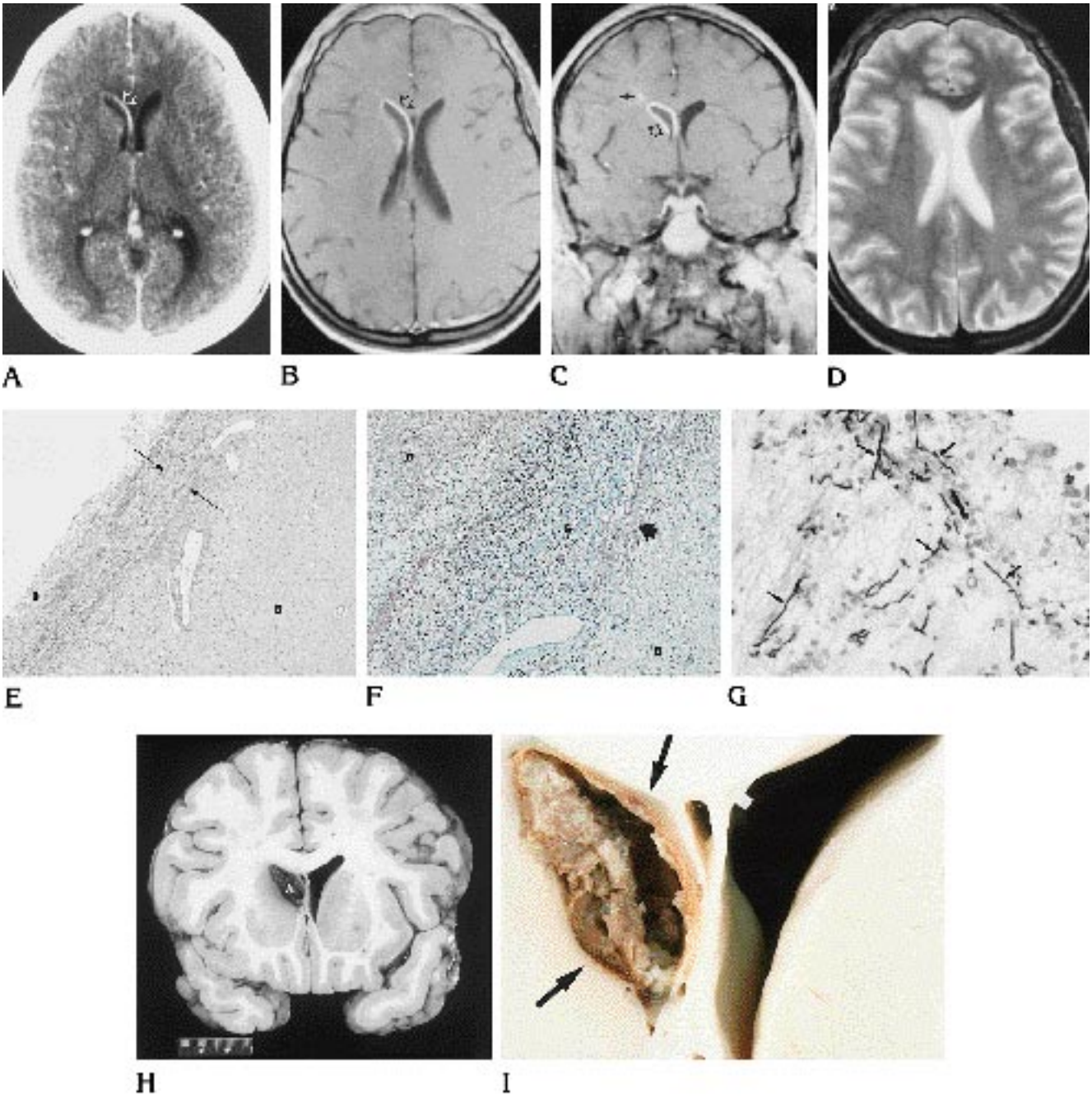

Fig 1. Patient with *Pseudallescheria boydii* infection of the brain.

A–D, Imaging studies. *A,* Contrast-enhanced CT scan shows ependymal enhancement in frontal horn of the right lateral ventricle *(arrow)*. *B,* Axial contrast-enhanced T1-weighted MR image (630/15/1 [repetition time/echo time/excitations]) shows ependymal enhancement in anterior horn of the right lateral ventricle *(arrow)* and faint enhancement of the medial aspect of the head of the right caudate nucleus. *C,* Coronal contrast-enhanced T1-weighted MR image (630/15/1) shows focal punctate enhancement in the white matter of the frontal lobe *(closed arrow)* and ependymal enhancement in the anterior horn of the right lateral ventricle *(open arrow)*. Note slightly increased signal intensity from cerebrospinal fluid in the right lateral ventricle.

D, Axial T2-weighted MR image (2500/90/1) shows abnormally increased signal intensity from the right caudate nucleus head and genu of corpus callosum. Cerebrospinal fluid is slightly decreased within the frontal horn of the right lateral ventricle.

E–G, Photomicrographs. *E,* Microscopic examination of the abscess wall shows a thin blue band of vascularized fibrous tissue (granulation tissue) (between *arrows*) separating brain *(B)* from necrotic debris inside the ventricle *(D)* (Masson trichrome stain, magnification ×200). *F,* High-power (×500) section shows few remaining ependymal cells *(arrow)* adjacent to the granulation tissue *(G)* encapsulating the abscess. *B* indicates brain; *D,* debris inside ventricle. *G,* Gomoris methenamine silver stain shows numerous filamentous, thin-walled, septated hyphae *(arrows)* compatible with *P boydii* present in the necrotic debris within the abscess (magnification ×1000).

H and *I,* Gross pathology. *H,* Coronal gross section of formalin-fixed brain shows the abscess *(A)* filling the frontal horn of the right

mised (3). Three patients, including our patient, were transplant recipients (20, 32). Five patients who had lymphoma or leukemia and who were undergoing treatment had *P boydii* infections (3, 10, 19, 27, 28). Two patients were alcoholics (17, 22). Two patients were diabetic (16, 17). Near drowning was the main predisposing factor in 6 patients (13, 14, 17, 18, 21, 23), and trauma was associated with 3 cases (6, 8, 15). One patient had an infected ventriculoperitoneal shunt (9). One otherwise healthy patient was infected as a complication of epidural anesthesia (4). Three patients had no known underlying disease or predisposing factors (11, 12, 29).

Manifestation of *P boydii* infection of the CNS may present several ways. In the 25 cases found by our literature review, 16 patients had cerebral abscesses, 6 had meningitis, 2 had pachymeningitis, and 1 had cerebritis with an epidural abscess. Two patients had intracranial vascular involvement with the organism. Of the 16 with cerebral abscesses, 3 had concomitant ventriculitis.

P boydii infection of the CNS is uniformly fatal without treatment. Even with treatment, mortality is high. Of the 25 patients whose cases we reviewed, 18 died, 6 survived, and 1 was lost to follow-up (3, 21, 24). Treatment is limited to surgical resection and drug therapy with miconazole, because amphotericin B and ketoconazole are ineffective (24).

P boydii hyphae in tissue sections may vary widely in appearance, but they generally are thin-walled, septated, and branched, and they measure 2.5 to 5 μm. They are often indistinguishable from the hyphae found in *Aspergillus* organisms. Lung and brain abscesses often exhibit fungal hyphae in pus. A neutrophilic inflammatory infiltrate and, less frequently, a chronic granulomatous response can result from invasive infection. Those patients with severe neutropenia may have areas of necrosis with minimal infiltrate. The hyphae of *P boydii,* like those of *Aspergillus* organisms, have a high affinity for blood vessels. The distinguishing characteristics of *P boydii* include terminal or lateral conidia with thin-walled cleistothecia and elliptical ascospores (2).

In our patient, microscopic evaluation of the right ventricular mass revealed an abscess with associated ventriculitis and choroid plexitis (Fig 1H and I). The abscess consisted of necrotic material with areas of hemorrhage and inflammation and was encapsulated by a thin band of fibrous connective tissue. Special stains, including periodic acid-Schiff and Gomori's methenamine silver, revealed numerous filamentous, irregular branching, and thin-walled septated hyphae present throughout the necrotic mass (Fig 1E–G). The majority of the organisms were present within the encapsulated mass. Adjacent to the mass were acute subependymal and white matter inflammatory infiltrates with areas of necrosis, cellular debris, hemorrhage, and fibrosis, but no true daughter abscesses were seen. The leptomeninges showed moderate acute and chronic inflammation.

Findings of CNS infection with *P boydii* may be compatible with brain abscesses, diffuse cerebritis, ventriculitis, infarcts, and hydrocephalus (12, 15, 17–20). Imaging characteristics of CNS *P boydii* infection are similar to those of *Aspergillus* organisms. Findings include focal ring-enhancing large vessel cerebral infarcts and meningitis (25).

Contrast-enhanced CT scans in our patient showed ependymal enhancement of the medial aspect of the anterior horn of the right lateral ventricle consistent with ventriculitis (Fig 1A). MR images of the brain showed similar findings, with areas of focal punctate enhancement in the white matter of the right frontal lobe (Fig 1B–D). T2-weighted MR images showed increased signal intensity in the head of the caudate nucleus and corpus callosum and mildly decreased signal intensity within the frontal horn of the right lateral ventricle. Because no other systemic foci were found, the origin of the infection in our patient is uncertain. Rupture of paraventricular abscesses may result in ventriculitis. However, brain abscesses were not present in our patient. The spread of infection via the choroid plexus can cause ventriculitis. In our patient, choroid

lateral ventricle at the level of the head of the caudate nucleus. The medial aspect of the head of the right caudate nucleus shows some hemorrhage, which corresponds to a region of faint enhancement seen on the MR image in *B*. The left ventricle is slightly dilated. *I,* Magnified gross section shows a subependymal capsule of granulation tissue *(arrows)* surrounding the intraventricular mass of necrotic tissue and hemorrhage. The area of enhancement seen on CT scans and MR images corresponds to the zone of granulation tissue. The abnormality of the head of the right caudate nucleus seen in *H* is not seen in this section.

plexitis was shown by microscopy; therefore, this may have been the route of the extension of the infection into the right lateral ventricle. This infection may have resulted from an undetected and subclinical septicemia from the patient's lung disease.

P boydii is a ubiquitous organism that occasionally causes disease in immunocompromised patients and in persons who have experienced near drowning or trauma. CNS infection with *P boydii* may clinically and radiologically resemble infection with *Aspergillus* organisms. CT and MR findings are nonspecific. Identification of *P boydii* is essential because treatment with amphotericin B is not curative. The most effective treatment is surgery with adjunctive miconazole therapy. Without treatment, *P boydii* CNS infection is lethal (24).

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