**Case Report**

**Meningitis Caused by *Pseudallescheria boydii***

Teng-Yeow Tan, MD; Chia-Wei Liou, MD; Ling-Chang Kung¹, MD

We present a 43-year-old immunocompetent man who developed meningitis caused by *Pseudallescheria boydii*. The patient had no history of near drowning, trauma, steroid administration, operations or any other underlying systemic disease. He presented with intermittent fever associated with headache, bilateral eye pain, and vomiting. Progressive hydrocephalus was noted during the course of the disease. Cerebrospinal fluid (CSF) from the ventricular system allowed culture of the organism. Although the disease was diagnosed antemortemly, the patient died after antifungal treatment. This case is reported because of the unusual pathogen, unresponsiveness to amphotericin B combined with 5-fluocytocin, and immunocompetence of the patient without any predisposing factors. *(Chang Gung Med J 2004;27:228-32)*

**Key words:** meningitis, *Pseudallescheria boydii*, hydrocephalus, diagnosis, therapies.

*Pseudallescheria boydii* (*P. boydii*) is a dimorphic fungus that has been isolated from soil, decaying vegetation, poultry and cattle manure, polluted streams, and coastal water. *Allescheria boydii* and *Petriellidium boydii* (the sexual form) and *Monosporium ampiospermum* and *Scedosporium ampiospermum* (the asexual form) have been previously used as species names.¹⁰ The fungus produces little immunological reaction, and when infected can proliferate, destroy soft tissue, and produce granulomas, sinus tracts, and osseous rarefaction.¹⁰ It is the most frequent etiologic agent of mycetoma in temperate regions of the world¹⁰ and has been reported to cause various focal organ infections and disseminated infections.¹⁰ The patients are usually immunocompromised, debilitated, or have history of trauma. In addition to causing Madura foot, it is frequently found within pulmonary cavities, but the central nervous system involvement presenting as persistent neutrophilic meningitis is extremely rare.¹⁵ We present a healthy, immunocompetent patient who developed meningitis caused by *P. boydii*.

**CASE REPORT**

A 43-year-old man presented with intermittent fever for 3 months which was associated with headache, bilateral eye pain, and vomiting. Detailed studies including chest X-ray, urine analysis, abdominal ultrasound, bone scan and a Gallium scan all showed negative results. Laboratory examination results, including a complete blood count, renal function, liver function, and electrolytes, were normal. Human immunodeficiency virus test and bacteria/fungus culture results were negative. Meningeal irritation signs and bilateral chronic papilledema were found during neurological examinations. An initial brain computed tomogram (CT) with contrast enhancement showed negative findings. Serial cerebrospinal fluid (CSF) analysis revealed persist neutrophilia, but negative cultural results for bacteria and fungus (Table 1). The patient was treated for bacterial meningitis with empirical antibiotics. Sequential follow-up brain CT scans revealed progressive hydrocephalus and the enhanced brain CT...
showed no abscess formation. A shunt was inserted to relieve hydrocephalus. The CSF obtained from the shunt (day 63 and 67) gave positive fungal culture of *P. boydii*. The patient died a month after proven diagnosis despite the use of amphotericin B and 5-fluocytocin therapy.

**DISCUSSION**

CNS infection caused by *P. boydii* was first reported in 1953. Symptoms and signs are non-specific but neurological deficits correlate well with the location involved in CNS. Although one third of the patients with CNS infection caused by *P. boydii* have clinical or radiological involvement other than CNS, no other site of infection was found in our case. Apparent risk factors of CNS infection included near-drowning in polluted waters, granulocytopenia, T-cell immunosupression, and trauma. Medical immunosupression and near-drowning episodes were the most frequent (60%) risk factor for CNS pseudallescheriasis, about 15% of the cases revealed no identified risk factors. No apparent risk factor was found in our case. Walker et al. suggested that *P. boydii* enters the body as an airborne organism through the pulmonary system and hematogenously to CNS. However, CNS infection via direct inoculation after trauma or surgery, by extension of a focus of infection in the vicinity of the CNS, by association with ventricular CSF drainage devices or after rachianesthesia procedures may also occur. Although direct inoculation after surgery and lumbar puncture were the possible routes of the fungus to the CNS in our patient and medical immunosupression causing secondary infection in the late course of treatment in this case should be considered, the persistent increase of neutrophils in the serial CSF analysis suggested that the *P. boydii* was the primary infectious pathogen in the beginning of the disease.

Persistent neutrophilia in the serial CSF analysis in our case showed the unusual finding of CNS infection caused by *P. boydii*. From the review of Nesky et al., brain abscess comprised approximately 80% of CNS pseudallescheriasis whereas 28% of the cases presented as meningitis. A review by Kershaw et al. showed that only half of the reported cases revealed a predominance of neutrophils in the CSF and CSF obtained from ventricular drainage or shunt yields higher positive culture rates. Physicians should strongly suspect the possibility of actinomycosis, norcardiosis, aspergillosis, zygomycosis or pseudallescheriasis in patients with persistence of neutrophils in the CSF. Under normal circumstances, neutrophil chemotactic factors are derived from the interaction of an organism and its products with a variety of the host defense systems especially complement pathogens and intracellular pathogens. They elicit initial neutrophilic host

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<th>Table 1. Serial CSF Findings</th>
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<tr>
<td>Days after onset of symptoms</td>
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<tr>
<td>WBC (cells/μl)</td>
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<td>lymphocytes (%)</td>
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<tr>
<td>Monocytes (%)</td>
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<td>Neutrophils (%)</td>
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<td>Glu (mg/dl)</td>
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<td>Lactate (mg/dl)</td>
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<td>Culture</td>
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<td>bacteria</td>
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<td>fungus</td>
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<td>T.B</td>
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<td>Cryptococcus Ag</td>
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C: CSF, S: serum; T.B: tubeculous bacilli.
* CSF culture from shunt.
† antibiotics given
1 amphotericin B combined with 5-fluocytocin therapies given.
responses which would be supplanted by a mononuclear response in cases of persistent disease. Conversion to a mononuclear cell response did not occur in our patient with meningitis. The mechanism by which the generation of the neutrophil chemotactic factors continued in this patient is not clear but Chinn and Diamond suggested that the neutrophil response was due to the presence of mycelia and hyphae. (12)

The diagnosis of *P. boydii* infection depends on visualization of the septate hyphae or culture and staining of biopsied tissue with fluorescent antibodies. Prompt antemortem diagnosis is not easy due to the rarity of this infection and the lack of specific and sensitive serological and culture tests. It is also complicated by the cross-reactivity to *P. boydii* antigens in the Cryptococcus capsular antigen latex test. (13) Morphologically, dilated, swollen hyphal segments and the pattern of hyphal branching are helpful in differentiating it from similar fungi. (14) Newly developed fluorescent-antibody reagents using adsorbed reagents to detect and identify *P. boydii* provide a rapid, reliable method for histological diagnosis of pseudallescheriasis. (15) Application of a staining procedure with optical brighteners on smears of enriched CSF cells or brain biopsy specimens can offer a crucial improvement in the identification of mycotic CNS infections during life. (16) In our case, as this fungus was cultured from CSF obtained from the shunt, this implies that the concentration of the fungus was high in the ventricle. The CSF obtained from the ventricular system may increase the positive culture rate of the pathogen and culture of the ventricular or cisternal CSF in cases where lumbar CSF fails to establish a diagnosis. (17)

Although amphotericin B is the standard antifungal agent for the empirical treatment of fungal infections, *P. boydii* is often resistant to amphotericin B. Most isolates of *P. boydii* appear to be sensitive to miconazole, ketoconazole and itraconazole. A combination of miconazole and ketoconazole has showed clinical stabilization and gives survival to patients, suggesting a possible role for dual drug therapy. (18) Miconazole given either intrathecally or via a shunt has been reported to be successful in treatment of infections due to *P. boydii*, (19) and voriconazole, a second-generation azole antifungal agent, has been approved for the treatment of infections due to *P. boydii* in the United States. (20)

CNS infection caused by *P. boydii* is usually fatal but among patients with solitary or contiguous abscesses, the prognosis is better. (21) Prompt diagnosis, appropriate treatment, and surgical intervention may improve the prognosis but the major problem is the difficulty in culturing the organism antemortem which creates a delay in appropriate therapy. Clinicians should maintain a high index of clinical suspicion with regard to the patients with persistent neutrophilic meningitis and clinical deterioration. *P. boydii* must be included as an etiologic agent of chronic meningitis even in immunocompetent hosts.

**REFERENCES**

Pseudallescheria boydii腦膜炎

陳廷耀 劉嘉為 孔令璋

本病例為43歲男性，因持續頭痛、發燒、雙眼疼痛而住院。追溯其過去史無特殊處，理
學檢查除顱部僵硬外無其他異常。多次腦脊髓液追蹤檢查顯示持續有嗜中性白血球偏高，多
次腦脊髓液培養無細菌、結核菌或真菌生長。經抗生素治療，住院兩個月後腦部電腦斷層攝
影檢查顯示腦室積水現象，病人因而接受腦室腹腔引流手術，而自引流管獲得之腦脊髓液
中，培養出Pseudallescheria boydii。後雖經改用Amphoteicin B合併5-fluocytocin 治療，病人仍
於住院三個月後死亡。本病例之特點為Pseudallescheria boydii 所引起之持續嗜中性白血球腦
膜炎且無誘因可循。(長庚醫誌 2004;27:228-32)

關鍵字: 腦膜炎, Pseudallescheria boydii, 腦腫症, 診斷, 治療。