Infection

Cerebral Phaeohyphomycosis Masquerading as a Parafalcian Mass: Case Report

Hooshang Saberi, M.D., M.P.H.,* Arash Kashfi, M.D.,* Saeed Hamidi, M.D.,*
Seyed Ali Fakhr Tabatabai, M.D.,* and Parvin Mansouri, M.D.†
*Department of Neurosurgery and †Department of Dermatology, Imam Khomeini Hospital,
Tehran University of Medical Sciences, Tehran, Iran


BACKGROUND
Cerebral phaeohyphomycosis caused by Fonsecaea pedrosoi is a rarity. However, about four cases have been reported in the literature. The disease remains mostly fatal despite employment of new treatment modalities.

CASE
An 18-year-old boy presented seizures of recent onset. Two years back, he developed cutaneous phaeohyphomycosis after a splinter scratch on his chest wall. Imaging revealed a contrast enhancing parafalcian solid mass. Right frontal parasagittal craniotomy was performed and the lesion resected as much as possible, followed by IV amphotericin B and oral itraconazole treatment. The patient has been doing well during a 15-month follow-up period.

DISCUSSION
Cerebral phaeohyphomycosis is an extremely rare lesion, which could masquerade as a parafalcian mass. Radical surgical removal together with antimicrobials remains the cornerstone treatment of cerebral phaeohyphomycosis. © 2003 Elsevier Inc. All rights reserved.

KEY WORDS
Cerebral, Fonsecaea pedrosoi, phaeohyphomycosis, intracranial mass.

Phaeohyphomycosis (PHM), is a term first presented in 1974 by Ajello et al to describe cutaneous, subcutaneous (SC), and systemic infections caused by hyphomycetous fungi, which develop as dematiaceous septated hyphae in the host tissue [1]. PHM is a widespread disease and cerebral PHM also has a worldwide geographic distribution [9,10]. Fonsecaea pedrosoi was isolated in 1913 as an etiologic agent of chromoblastomycosis by Pedroso, later to be dubbed as Hormodendrum pedrosoi by Brumpt (1922). McGinnis and Schell (1980) redescribed the genus Fonsecaea, which had been established by Negroni (1936) for H. pedrosoi [10]. F. pedrosoi is one of the chromoblastomycosis agents and encountered in cases that can be characterized as PHM [15].

Diseases caused by dematiaceous fungi include sinusitis, cerebral abscess, onychomycosis, tinea nigra, keratitis, mycetoma, chronic meningitis, and rarely pneumonia [11]. Cerebral PHM caused by F. pedrosoi is a rarity, and this patient may be the fifth case cited in the medical literature [3,14]. Reported here, we describe the insidious course of a cerebral PHM in an immunocompetent host, presenting as a solid enhancing lesion in an unusual location.

Case Presentation
An 18-year-old boy settled in a seaside village was referred to this center in September 2000 because of seizure episodes of recent onset. He had been doing well until 2 years previously when he developed cutaneous lesions after a splinter scratch on his chest wall during a routine walk in the woods. Since then, he had been receiving antifungal agents intermittently for the diagnosis of cutaneous PHM. The skin lesions progressed and were complicated by nasopharyngeal as well as ethmoidal sinus involvement in addition to posterior cervical lymphadenopathies. The skin lesions appeared to be ulcerative with firm, rough consistency and pinkish-gray color, the scraping of which showed dematiaceous branching hyphae. A blood profile for biochemistry and hematology was within normal limits except for an unexplained eosinophilia (20%). Immunologic surveys gave normal re-
sults for CD4, CD8, and leukocyte chemotaxis. A survey for AIDS as well as HBs Ag and HCV Ab was negative.

The cutaneous lesions had been treated with local antifungal agents with no significant response. However, the nasopharyngeal lesions as well as cervical nodes were amenable to oral itraconazole 200 mg q12h.

The seizures were primarily generalized and started 1 month back without any symptoms of raised intracranial pressure. There was no prior history of pulmonary symptoms and tinea capitis or onychomycosis. He was well nourished and maintained a good general condition. Physical as well as neurologic examinations were normal except for multiple firm skin lesions located over the chest and both cheeks. A direct funduscopy showed no abnormality.

Computed tomography (CT) scan revealed an interhemispheric frontal hypodense lesion uniformly enhancing after contrast injection, well circumscribed and extra-axially situated. Magnetic resonance imaging (MRI) showed a hypointense lesion on T1-, and hyperintense on T2-weighted images, enhancing after Gad-DTPA injection homogeneously (Figure 1).

He was scheduled for elective surgery to resect the lesion and to make a definitive diagnosis. A parasagittal corridor was employed through a right precoronal craniotomy. There was no significant finding in the skull and parasagittal region except for leptomeningeal thickening deep within the interhemispheric sulcus. The black firm lesion could not be seen until opening the thick arachnoid adhesions. Surprisingly, there was no abscess formation, and the firm nigrescent lesion was found to be intermingled with the anterior cerebral vasculature. Despite endeavors, the lesion could not be fully dissected from anterior cerebral arteries and it was removed in a piecemeal fashion as much as possible, saving the vulnerable vessels. The operative site was irrigated with amphotericin B solution in 37°C normal saline.

The postoperative course was uneventful and amphotericin B was administered IV. The direct smear revealed fungal mycelia (Figure 2A) and histopathological preparation showed chronic granulomatous reaction overwhelmed by hyphae without muriform bodies. Culture results on cornmeal agar (CMA) revealed velvety black colonies (Figure 2B). By employing cotton blue staining, cylindrical conidiogenous cells were seen microscopically, with a swollen apex forming a complex branched head along erect conidiophores consistent with *F. pedrosoi* (Figure 2C). Early postoperative CT scan showed fungal remnants adherent to patent anterior cerebral arteries (Figure 3A), and an MRI scan performed 15 months later revealed lesion control with minimal fungal residues (Figure 3B).

Amphotericin B was continued postoperatively and the patient discharged after 3 weeks, when the medication was changed to itraconazole 200 mg q12h for 1 year in addition to oral phenytoin. He is doing well and attends the outpatient department on monthly visits.

**Discussion**

*F. pedrosoi* is an organism that could demonstrate itself as a member of chromoblastomycosis or PHM depending on the presence or absence of muriform bodies [15]; these particles were absent in the obtained biopsy specimen consistent with the diagnosis of cerebral PHM (Figure 2A).

Cutaneous infection follows traumatic implanta-
(A) Direct smear of the biopsy specimen reveals the fungal hyphae within the lesion (×1000). (B) Colony forming in the culture media (cornmeal agar) with its characteristic velvety black appearance. (C) Characteristic form of *F. pedrosol* *Rhinocladiella* (Acrotheca) type in cotton blue preparation. Note distinctive *Rhinocladiella* synanamorph (×1000).
tion of the agent beneath the epidermis via abrasions or other minor wounds or penetration by foreign bodies such as splinters [15]. Cutaneous lesions of the presented patient were due to penetration of a foreign body (branch of tree) to his chest skin and autoinoculation into the cheek skin.

3 (A) Early postoperative axial CT reveals remnants of the lesion adherent to the anterior cerebral arteries. (B) MRI scan performed 15 months later revealed lesion control with minimal fungal residues.
In cerebral PHM, the usual entry site of organism into the body is thought to be respiratory tract and subsequent hematogenous spread into the cranial cavity; however, direct inoculation into the skull is also a possibility [2,7,13]. Pattern of the brain involvement in this patient increases the likelihood of hematogenous spread from the upper respiratory tract. The interaction between cerebral PHM and host defense mechanisms has not been completely understood. Actually, in the era of organ transplantation with compromised immunity in the recipients, cerebral PHM as an ominous event could complicate the disease course [2,11,13]. These observations, as well as Dixon’s experiment on cortisone-treated mice, underscores the immunity status of the host [6]; thus compromised immunity has been considered to increase the risk of cerebral involvement by PHM agents. On the other hand, there are sufficient cerebral PHM reports in immunocompetent hosts [3,12,14,17] to postulate the possibility of cerebral involvement in normal hosts. Because of normal immunologic assays, he can be considered as a case of cerebral PHM with immunologic competence. His cerebral involvement is unique because of presentation as a black firm mass rather than an abscess formation. It may reflect the reaction of the competent immune system in our patient in the shadow of long-standing antifungal therapy. Cerebrospinal fluid eosinophilia has been addressed in a case of cerebral PHM resulting from Wangiella dermatitides [5]; our patient’s blood profile revealed a 20% eosinophilia, which might reflect a role for type I hypersensitivity. On the other hand, if the host defense is poor, the interaction of the fungus and the brain tissue will mostly result in acute abscess formation and brain necrosis [13].

Sinusitis is one of the described entities with dematiaceous fungi, with the ethmoid as the most frequently involved sinus [9], as it was the case in our patient. Although isolated cerebral involvement because of F. pedrosoi without any other apparent lesion has been reported [3,14], in the presented patient it seems that skin or paranasal sinus may be the primary site for hematogenous cerebral involvement.

While CNS involvement of dematiaceous fungi commonly occurs in the form of brain abscess formation, characteristically a multicystic intracerebral lesion with ring enhancement [3,4,14], surprisingly, the imagings were suggestive of a solid parafalcian enhancing mass. Also an intraoperative finding of a black, firm, solid mass confirmed the lesion not to be an abscess.

It has been explained that “double ring sign” may be found on Gad-enhanced MRI [4]. This phenomenon as observed in our case may be because of the mode of local spread of the agent or represent specific host response to the lesion. The inhomogeneous high-signal component in the center of the lesion on T2-weighted images has been suggested to result from liquefactive necrosis, macromolecules, and a high protein component [4]. This finding was not present in our imagings. The characteristic imaging pattern reported in the literature is that of a conglomerate aggregate of adjacent abscesses [4,14], while our patient had a single, well-defined lesion. This may be attributable to the more insidious course in our patient.

Surgery offers not only the best diagnostic option but also the best chance for management. Total resection, if possible, is preferred to partial [9]. In this patient, total resection could not be achieved because of the perivascular invasion of the fungus. Interestingly, although the patient carries the fungal remnants, his general condition is good without any neurologic deficit.

Dematiaceous fungi are usually treated with surgical removal, local thermotherapy, and the administration of antifungal agents or a combination of the above [8]. Although Iijima et al treated a large cutaneous F. pedrosoi lesion only with oral high-dose amphotericin B [8], with cerebral involvement aggressive surgery has to be considered, and partial resection is discouraged [9]. We have employed IV amphotericin B and long-term oral itraconazole to suppress the fungal regrowth.

Prognosis of cerebral PHM has reportedly been poor. al-Hedaithy et al reported three cerebral PHM because of F. pedrosoi with grave outcome [3]. Different fungal species have been the causative agents of cerebral PHM with poor prognosis [5,7,11,12,17]. Conversely, reports of successful management of PHM species could be found [13,16]. Santosh et al reported successful recovery of a 15-year-old patient suffering from F. pedrosoi cerebral abscess with surgery and amphotericin B plus 5-flucytosine [14]; however, drug resistance could be a matter of concern. Our patient has remained well despite fungal remnants within the cerebrum after a 15-month follow-up period. However, definitive results require longer follow-up.

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REFERENCES
COMMENTARY

The advent of optimal diagnostic techniques, as well as the emergence of rare infectious diseases whose current therapeutic approach yields only partial results in which the infectious agent is not eradicated but only contained, produces a novel clinical scenario where several oddities emerge out of diseases whose well-known natural courses have been altered as a result of partly successful therapeutic approaches. We observe this phenomenon in several infectious diseases of bacterial and viral etiology, where drug resistance is frequent, with the emergence of resistant clones and protracted clinical course. In the field of mycology this panorama is likely also mainly due to two circumstances: the notorious scarcity of drugs effective for several mycosis and the growing presence of individuals with immune depression either secondary to chronic diseases (cancer, AIDS, diabetes, etc.) or to chronic immunosuppressive treatment.

The report by Saberi et al shows a strange form of a very rare micotic disease of the brain. Presumably, this presentation, tumor-like rather than an abscess, could be attributable to the fact that the cutaneous mycosis had been adequately diagnosed and treated, albeit with little success during two years prior to the neurological manifestations, which seemed to be a neoplasm by imaging studies and at surgical intervention. Neurosurgeons should be aware of these novel expressions of infectious diseases.

Julio Sotelo, M.D.
National Institute of Neurology and Neurosurgery of Mexico
Mexico City, Mexico

To succeed in politics, it is often necessary to rise above your principles.

—ANON.