Encephalitis of the Basal Ganglia in an Injection Drug User
(See pages 1479 for the Photo Quiz)

Diagnosis: Isolated cerebral mucormycosis of the basal ganglia.

Brain biopsy tissue was obtained by stereotactic biopsy of the right basal ganglia ring-enhancing lesion (figures 1 and 2). Microscopic examination of samples stained with hematoxylin and eosin (figure 3) and Grocott methenamine silver (figure 4) revealed pauciseptate irregularly branching fungal hyphae, associated with granulomatous inflammation and acute hemorrhage. The hyphae were morphologically consistent with members of the division Zygomycota and order Mucorales. Fungal culture of the specimen grew *Pseudomonas, Penicillium,* and *Alternaria* species, whereas bacterial cultures remained sterile, indicating gross contamination of the fungal culture. Therefore, ribosomal DNA was amplified by PCR from paraffin-embedded tissue using broad host-range fungal-specific primers [1, 2]. The amplified products were cloned and sequenced. When compared using BLAST with sequences available in GenBank, the closest match (>90% sequence match) was to *Rhizopus arrhizus.*

Zygomycetes are ubiquitous saprophytic organisms [3]. Classically, CNS zygomycosis has been reported in patients with diabetic ketoacidosis and other immunocompromised states as a result of direct extension of sinus disease into the orbit, eye, optic nerve, and brain parenchyma, including the frontal and temporal lobes [3–5]. Zygomycosis may also present as cavernous sinus thrombosis (11%) or, more rarely, as isolated ischemic infarction caused by internal carotid or basilar arteritis [4, 6].

Zygomycetes are angioinvasive, producing tissue necrosis in addition to inflammation, and patients may also present with hemorrhagic infarction secondary to formation and rupture of a mycotic aneurysm [3].
Figure 3. Brain biopsy specimen stained with hematoxylin and eosin (original magnification, ×120) showing pauciseptate fungal hyphae (arrows) with surrounding granulomatous inflammation and hemorrhage.

Figure 4. Brain biopsy stained with Grocott methenamine silver (original magnification, ×180) demonstrating irregularly branching fungal hyphae (arrow).

Approximately 30 cases of isolated cerebral zygomycosis in immunocompetent individuals have been reported, and most of these patients have been injection drug users [7–12]. In contrast with the presentation in immunocompromised patients, zygomycetes show a remarkable predilection for the basal ganglia and thalamus in immunocompetent patients [3, 7, 9–16]. These lesions are typically unilateral, although bilateral involvement has been reported [10, 15]. Other CNS sites affected include the corpus callosum, frontal lobes, and brainstem [10, 11, 14]. Exposure is thought to be secondary to inoculation with fungal spores during drug injection [10, 12], because there is no evidence of direct extension from rhinocerebral disease in these case reports. The basis for the predilection of zygomycetes for the lentiform nuclei in injection drug users is unclear, although it has been proposed that microvascular injury from the injected drug may predispose to seeding of zygomycete spores in this heavily vascularized brain tissue, which is characterized by small, penetrating arterioles without the potential for collateral flow [8, 9, 13]. The location of fungal invasion may be determined by the circumference of vessels in the basal ganglia relative to the diameter of the fungal spores.

This case illustrates the importance of considering cerebral zygomycosis in the differential diagnosis of a patient with a history of injection drug use who presents with encephalitis and basal ganglia or thalamic lesions visible on neuroimaging. Other diagnostic considerations should include bacterial or tubercular abscesses, aspergillosis, septic infarction, lymphoma, toxoplasmosis, and an acute inflammatory demyelinating process, all of which can present with centrally necrotizing and peripherally enhancing cerebral lesions [10, 16]. However, it would be very unusual for these other pathogens and disorders to involve the bilateral basal ganglia while sparing other areas of the brain.

In patients with isolated CNS zygomycosis who are not immunocompromised, mortality is reduced from 92% to 41% with immediate, aggressive treatment with intravenous amphotericin B [17]. Our patient was administered intravenous amphotericin B and defervesced within 48 h, began following commands, and was successfully extubated. At transfer to a rehabilitation facility after 15 days of therapy, she was alert and able to follow commands, but she remained mute.

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