Correspondence

Sporotrichosis in the Central Nervous System Caused by *Sporothrix brasiliensis*

To the Editor—The metropolitan region of Rio de Janeiro is hyperendemic for cat-associated sporotrichosis, and *Sporothrix brasiliensis* has been implicated in the majority of cases in this region. A unique clinical profile has been characterized by disseminated cases in nonimmunosuppressed patients, hypersensitivity reactions, and an increase in the number of patients with human immunodeficiency virus (HIV), with a higher incidence of severe disseminated cases, hospitalizations, and deaths [1, 2].

From January 1999 through March 2013, 3618 adult patients were diagnosed with sporotrichosis at the Instituto Nacional de Infectologia Evandro Chagas/Fundação Oswaldo Cruz, the main referral center for the treatment of this mycosis in Rio de Janeiro State. Among these patients, 48 were coinfected with HIV, and the disseminated or disseminated cutaneous forms were present in the majority of these patients (58.3%), in contrast with the localized forms (lymphocutaneous or fixed cutaneous [41.7%]) [2]. The first patient with sporotrichosis and HIV coinfection had meningitis; since that first diagnosis, all patients with disseminated sporotrichosis have undergone a lumbar puncture to exclude central nervous system (CNS) invasion. Furthermore, the remaining 3 patients had fungus present in the cerebrospinal fluid (CSF). All but 1 patient was male, and the median $CD4^+$ cell count was 104/μL. *Sporothrix brasiliensis* was identified using T3B polymerase chain reaction fingerprinting [3]. Patients had skin lesions and developed subacute meningoencephalitis during the infection. Two patients died due to hydrocephalus complications. One patient presented with *Cryptococcus neoformans* coinfection of the CNS and died of complications that were not related to sporotrichosis. The first diagnosed patient is still alive 16 years after the onset of sporotrichosis. Three of these cases have been previously reported [4, 5].

CNS involvement in sporotrichosis, although rare, has been previously described in immunosuppressed patients, particularly within recent decades due to the HIV pandemic. When we analyzed this cohort of HIV-infected sporotrichosis patients, we found a considerable number of patients with disseminated forms of the disease, in whom *S. brasiliensis* was found in the CSF (14.3%). In a murine model, *S. brasiliensis* was the most virulent member of the *Sporothrix schenckii* complex, with dissemination to different organs including the CNS [6]. *Sporothrix brasiliensis* produces large amounts of urease and melanin, which are virulence factors that can promote penetration into tissues and evasion from the immune system [7]. We propose that *S. brasiliensis*, similar to what has been observed in *C. neoformans* infection, is neurotropic in humans, although the mechanisms implicated in CNS invasion and persistence are not yet completely understood [8, 9].

These findings highlight the potential aggressiveness of *S. brasiliensis* in immunosuppressed patients, particularly patients with HIV and advanced disease. CNS involvement is challenging to treat and is associated with a worse prognosis because its sterilization is difficult. In areas where HIV and sporotrichosis overlap, physicians should be aware of this potentially disastrous association and should perform an early lumbar puncture to aggressively treat CNS disease. Close follow-up of patients is necessary in order to document CSF sterilization, and alternative treatment strategies, such as novel azoles and combination therapy, may be considered.

Notes

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Earlier Treatment and Improved Outcome in Adult Bacterial Meningitis Following Guideline Revision Promoting Prompt Lumbar Puncture

To the Editor—We congratulate Glimaker et al for their study on the timing of lumbar puncture (LP), delay in antibiotic treatment, and outcome in a large nationwide retrospective database of patients with bacterial meningitis, in which they show that early treatment improves outcome [1]. The authors state that in patients with suspected bacterial meningitis, an altered level of consciousness or new-onset seizures should not be a reason to perform a cranial computed tomographic scan before doing the LP, as it delays the time to antibiotic treatment.

Bacterial meningitis is often suspected, but only a minority of patients are eventually diagnosed with the disease [2, 3]. The differential diagnosis may include viral meningitis, tuberculous meningitis, stroke with concomitant infection, subdural empyema, and cerebral abscess [4]. The information considering patients in whom bacterial meningitis was suspected, but who were eventually diagnosed with a different condition, is not presented in the study by the authors, while these patients also have the risk of complications due to the LP. A meta-analysis of cerebral abscess patients showed that clinical deterioration attributed to an LP occurred in 7% of patients with brain abscess in whom LP was performed [5]. Therefore, studies assessing the diagnostic sequence used in bacterial meningitis and outcome should include patients with suspected bacterial meningitis, as this is the at-risk population for LP-related complications.

Another issue with the study is that the authors compared 2 time periods to assess the effect of introduction of the guideline. Between these time periods, other interventions may have been introduced that could have influenced prognosis. The authors previously reported on intracranial pressure monitoring that improved outcome between time periods, which includes the same patient group [6]. Dexamethasone was introduced as standard adjunctive therapy between 2004 and 2006. Timing is important for this drug; given together with the first dose of antibiotics, dexamethasone is beneficial, but administered after clinical deterioration, corticosteroids are ineffective. As timing of steroid therapy is not provided, this may also be a confounding factor [7].

The diagnostic criteria the authors have used to define bacterial meningitis are "clinical criteria with or without cerebrospinal fluid analysis." As the authors rightfully claim, cerebrospinal fluid is a mainstay in the diagnosis of bacterial meningitis, so patients with no LP should have been excluded from this study. Furthermore, the clinical criteria for bacterial meningitis are not specified by the authors. The clinical presentation of bacterial meningitis can be atypical [8], and therefore it is unclear what patient population was included in this study.

Finally, it is unclear at what point the physicians were asked to fill out the questionnaire on timing of treatment. If this is not done shortly after admission, a recall bias may occur, in which physicians may be tempted to respond that they complied with the new guideline and that timing of antibiotics was short.

We encourage every attempt to shorten time to antibiotic treatment in patients with bacterial meningitis, as there is no question this improves outcome. However, the current study leaves too many questions unanswered to provide meaningful data on the best diagnostic strategy in patient suspected to have bacterial meningitis.

Note

Potential conflict of interest. Both authors: No reported conflicts.

Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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