Diagnosis of Central Nervous System Mycoses in Solid Organ Transplant Recipients

TO THE EDITOR—We read with interest the informative review by Wright and Fishman about central nervous system (CNS) syndromes in recipients of solid organ transplant (SOT) [1]. However, we believe that at least 2 points of their article deserve comments. First, in their Table 4, the authors report the “approximate incidence and usual post-transplant onset” of aspergillosis, cryptococcosis, and endemic fungi adapted from the Transplant-Associated Infection Surveillance Network (TRANSNET) study [2]. In fact, in the TRANSNET cohort surveillance, the overall incidence of aspergillosis was reported to be 0.7% (instead of 0.2%) and for cryptococcosis 0.2% (instead of 0.1%). More importantly, these incidence rates refer to all the manifestations caused by the invasive mycoses and not solely to those with CNS involvement. Specifically for aspergillosis, 78% of cases were limited to the lungs, but the article does not mention whether the remaining patients had CNS involvement. As far as cryptococcosis is concerned, in the TRANSNET study only 45% of patients had CNS involvement [2], in agreement with previous studies showing that among SOT recipients, as opposed to human immunodeficiency virus–infected patients, CNS cryptococcosis is observed in 34%–52% of cases [3, 4]. Moreover, the TRANSNET study included 48 cases of histoplasmosis, 7 cases of coccidioidomycosis, and 9 cases
of blastomycosis that “most often presented as disseminated infection involving multiple organs” [2]. CNS involvement occurs in approximately 5%-10% of patients with progressive disseminated histoplasmosis [5], 5% of patients with systemic blastomycosis [6], and 3.5% of patients with coccidioidomycosis [7]. Using the TRANSNET numbers, the highest estimates would thus be 5 cases of CNS histoplasmosis and <1 case each of CNS blastomycosis and coccidioidomycosis. For these reasons, we believe that it is both inaccurate and misleading to infer the incidence of fungal CNS involvement among SOT patients using the TRANSNET study data [2].

We would also like to comment on the detection of fungi in cerebrospinal fluid (CSF). The sensitivity of CSF culture in detecting fungi, with the exception of Cryptococcus neoformans, is generally low. In fact, among SOT recipients, Cryptococcus culture was positive in 75% of cases, whereas the antigen was detected in all [8]. By contrast, for Histoplasma capsulatum the sensitivity of CSF culture in nontransplant patients has been reported to be 27%-65% [9], for Aspergillus 31% [10], and for Coccidioides species 20%-38% [11]. Indirect non-culture-based methods may increase the likelihood of diagnosis in cerebral fungal infections. Aspergillus galactomannan antigen (GM) seems to be a useful diagnostic method for CNS aspergillosis in both immunocompetent and immunocompromised hosts, with an overall sensitivity of 87% [10]. Although a threshold value of CSF galactomannan has not yet been established for the diagnosis of CNS aspergillosis, high index values have been repeatedly reported [10]. Interestingly, in a patient with Aspergillus meningitis who underwent 9 serial lumbar punctures, GM was detected in the CSF 45 days before a single culture became positive [12]. Therefore, we suggest that in Table 5 of the article by Wright and Fishman, CSF GM should be added to nonculture methods for use in SOT recipients with CNS syndromes. In patients living in or who have traveled in endemic areas, a Histoplasma antigen assay that can be performed in CSF as well as urine and serum should also be considered for the diagnosis of cerebral histoplasmosis [5, 9]. Finally, it should be noted that both GM and Histoplasma antigen test may cross-react with other fungi, which emphasizes the need to obtain additional laboratory results that must always correlate with a patient’s clinical, radiological, and epidemiological features.

Notes

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