Cryptococcus and Coccidioides in Sarcoidosis

To the Editor—We read with great interest Kuberski and Yourison's hypothesis that *Coccidioides* spp. and other dimorphic fungi may be the precipitants of sarcoidosis in a proportion of cases [1]. We would like to suggest additional ways to test this hypothesis, as well as suggesting that *Cryptococcus* spp. be included in the list of fungi considered possible precipitants.

A single-center study of severe infections in 585 patients with sarcoidosis from France found that fungi were the most common cause of severe infections after mycobacteria [2]. Ten of the 16 severe infections were fungal, and *Cryptococcus neoformans* and *Pneumocytis jirovecii* were the most common causes. While the *P. jirovecii* infections are likely the result of the immunosuppressants used to treat sarcoidosis, this is not as clearly the case for *Cryptococcus*. A study of all cases of cryptococcosis in the French national mycosis registry, for example, found 18 cases where the individual had preexisiting or contemporaneous sarcoidosis [3]. In 6 cases, the diagnosis of cryptococcosis was made before immunosupressants were commenced. This association may be due to the low CD4 T-cell count associated with sarcoidosis [4], but it may also reflect individuals whose dysregulated immune response to *Cryptococcus* resulted in sarcoid. As Kuberski et al. note, negative fungal polymerase chain reactions of formalin-fixed sarcoid tissue biopsies would not rule out these fungi as precipitants in the sarcoid.

If a dysregulated immune response to various fungi (and other antigens) were responsible for sarcoid, then assessing the antibody and cell-mediated immune responses to a panel of fungi in patients with a new diagnosis of sarcoid would be instructive. Finding enhanced responses to specific fungi in sarcoid cases vs controls would constitute evidence supportive of the fungi-sarcoid hypothesis.

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