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### Title

Brain biopsy in atypical dementia and primary angiitis of the central nervous system--reply.

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## Correspondence

### Brain biopsy in atypical dementia and primary angiitis of the central nervous system—reply

Dear Editor,

We thank the authors for their interest in our study on the use of brain biopsy in evaluating neurologic decline of unknown etiology [1].

Regarding the first point raised, brain biopsies in immunodeficient patients are well established, which the authors also state in their article [2]. This may change, specifically in HIV-positive patients in the era of highly active antiretroviral therapy (HAART), and we look forward to the authors' meta-analysis. In a study by Rosenow and Hirschfeld [3], despite a sharp decline in the number of brain biopsies in acquired immunodeficiency syndrome patients performed in the HAART era, the diagnostic yield was high both before (91.3%) and after (96%) the introduction of HAART; the most common diagnoses were lymphoma followed by progressive multifocal leukoencephalopathy, with brain biopsy clearly retaining its utility in select patients. They recommend early brain biopsy after toxoplasmosis, one of the most common intracranial complications in acquired immunodeficiency syndrome, has been ruled out by serology [3].

Second, as we had mentioned, brain biopsies in nontreatable neurodegenerative conditions are generally recommended only to exclude a treatable cause and discouraged when the positive predictive value of a clinical diagnosis, including Alzheimer disease and Creutzfeldt-Jacob disease, is high and sufficient to guide management, and as such, we agree with the authors. In our cohort, only one patient was diagnosed as having Alzheimer disease on biopsy, which was performed because vasculitis was suspected clinically [1]. Cognitive decline was not the sole indication for biopsy but rather seen in approximately 70% of our patients and may not strictly correspond to their "atypical dementia" subgroup. We do suggest the potential of brain biopsies coming to play a more prominent role in neurodegenerative diseases with the emergence of new therapies (eg, immunotherapies) and need to validate new diagnostic modalities such as cerebrospinal fluid biomarkers [4].

Finally, to clarify, the 2 positive biopsies refer to biopsies positive for vasculitis and not to diagnostic biopsies. The

overall diagnostic yield of patients with vasculitis as the primary clinical suspicion or as part of the differential diagnosis was approximately 44% (7/16), which is still lower than the diagnostic yield in their study. However, the discrepancy is not surprising given, again, the differences in patient characteristics. The articles comprising their "suspected primary angiitis of the central nervous system (PACNS)" subgroup included patients specifically suspected of having primary angiitis of the central nervous system or with multifocal neurologic deficits and abnormal imaging studies [2], quite different from our heterogeneous population, which often included a myriad of other possible diagnoses on the differential and hence the need for a brain biopsy. One study that the authors included in the "cryptogenic neurological disease in adults" subgroup reported a diagnostic yield of 14% in patients suspected of central nervous system vasculitis but with mild/atypical angiographic studies, although their overall diagnostic yield (20%) was also lower [5]. However, the numbers of patients are small in both that study and ours, and we concur that large prospective studies would be helpful in guiding the decision to proceed with a brain biopsy.

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