Title:

Response: Brain biopsy in children and adults with neurological diseases of unknown aetiology: two sides of the same coin?

Submission category:

Letter to the Editor

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Word count: 438
Reference count: 4

Disclosure of Conflicts of Interest:

None. All authors had access to the data and a role in writing the manuscript.

Funding:

None

Keywords:

Brain biopsy, infection, immunocompromise, neoplasm

Previous presentations:

Not applicable.

Dear Editor,

We would like to thank Mathon and colleagues for their comments[1] regarding our paper[2], reported in this issue of the *Journal of Neurosurgery (Pediatrics)*, on the utility of brain biopsy in cryptogenic neurological disease in children. We read with interest the article of Mathon *et al.*[3], which is similar in outlook, but deals with a larger adult series from their tertiary referral centre. The similarities between these two studies are striking, and it is only due to their contemporaneous publication that the works were not mutually cited originally.

Firstly, as Mathon *et al*. point out in their letter, there is a broad concordance in the key results of both series: both in diagnostic yield (which was slightly higher in adults than in children), and in the concomitant changes to clinical management in around three-quarters of patients. There was also a low incidence of severe complications in both series, and similar 1-year survival rates (75.8% in adults vs 76.6% in children). Secondly, immunosuppression – which was common in both series (42.7% in adults, 25.5% in children) – emerged as a key predictor of yielding a diagnosis from brain biopsy. In our paediatric series, immunocompromised patients had a significantly increased odds ratio of yielding an infective diagnosis.

The wide variety of eventual diagnoses in patients of all ages (36 separate diagnoses in 178 patients in the adult series, 22 in 47 patients in our paediatric series), each with different management paradigms, we feel precludes a specific algorithmic approach, as has previously been put forward[4]. The actual distribution of diagnoses differed slightly between the paediatric and adult series. In the latter, the most numerous single diagnosis was cerebral vasculitis, which occurred in only one patient in our series.

Patients presenting with cryptogenic neurological disease should be managed in centres with availability of neurology, neuroradiology, neurosurgery and neuropathology expertise to optimise diagnostic and treatment outcomes. Particularly important is the involvement of neurosurgeons early on in the patient's illness, although modifiable surgical factors such as biopsy technique were less important in determining biopsy safety than patient factors such as immunocompromise and thrombocytopaenia.

The composite results of these papers, where biopsy samples are scrutinised under the full spectrum of modern histopathological, microbiological and metagenomic next-generation sequencing techniques has increased the diagnostic yield of the procedure compared to older series, and brings the implementation of brain biopsy for non-neoplastic disease into the 21st century. We agree with Mathon *et al.* that the results of these two studies should be viewed in concert, as they demonstrate the high potential impact, and favourable safety profile, of brain biopsy for cryptogenic neurological disease across the entire age spectrum.

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