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Elucidation of the genetic background in familial multiple sclerosis requires genetic work-up

Letter to the Editor

With interest we read the article by Katsavos et al. about a retrospective case-control study of 102 patients with definite, familial multiple sclerosis (fMS) compared with 282 patients with definite, sporadic multiple sclerosis (sMS) [1]. Definite MS was diagnosed according to the McDonalds criteria 2010. The authors found younger age at onset and variant distribution of cerebral lesions in fMS compared to sMS patients [1]. We have the following comments and concerns.

Maternal inheritance in 57.4% and paternal inheritance in 39.7% of the fMS cases contradicts with the finding that only 18 fMS patients had a parent with MS, that only 10 fMS patients had a child with MS, and that only 20 fMS patients had a sibling with MS [1]. It should be explained how paternal respectively maternal inheritance was inferred from these data.

A further shortcoming of the study is that the trait of inheritance in the 102 included cases was not provided. Generally, transmission of inherited disease follows an autosomal dominant, autosomal recessive, X-linked, or maternal transmission. Thus, we should be informed in how many of the included families transmission followed an autosomal, X-chromosomal, or maternal trait of inheritance. To draw reliable conclusions concerning familiarity, at least three generations per case should be assessed.

The study also lacks profound discussion of the genetic background of familiarity of MS. Familiarity suggests mutations in genes, nucleotide polymorphisms, or chromosomal defects. Anticipation of age at onset in subsequent generations suggests a nucleotide repeat disorder. Candidate genes possibly mutated in fMS patients include *NLRP3* [2], *MEFV* [3], *GLA* [4], *HFE* [5], *TNFRSF1A* [6], and mtDNA located genes respectively [7].

In summary, the reported study could be more meaningful by clarifying inconsistencies, by providing traits of inheritance, and by discussing more extensively the possible genetic background of fMS.

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