Genetic confirmation of dysferlinopathy is required before attributing obsessive compulsive disorder to Myoshi myopathy

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Keywords
distal myopathy, mutation, muscle biopsy, brain, heart, multisystem

Letter to the Editor

In a recent article, Parmar et al. reported about a 28yo male with obsessive-compulsive disorder (OCD) and Myoshi myopathy (distal myopathy with weakness of calf muscles) being attributed to a dysferlinopathy. Dysferlin staining was reduced on immunoblot of the muscle biopsy but the diagnosis was not confirmed genetically. OCD was regarded as a clinical manifestation of the dysferlinopathy. We have the following comments and concerns.

The main shortcoming of the study is that the diagnoses “dysferlinopathy” was not genetically confirmed. Sequencing of the DYSF gene is easily available and affordable. Genetic confirmation of the diagnosis is crucial as there is the possibility that reduced dysferlin on Western blot or abnormal localisation on immunohistochemistry in the muscle can be secondary, particularly in muscle disease with sarcolemmal injury, such as dystrophinopathy, polymyositis, or late-onset Pompe disease.

A further shortcoming is that the diagnosis “Myoshi myopathy” is uncertain. This is because the patient not only had weakness of the calf muscles but obviously also weakness of the proximal limb muscles. He had developed difficulties getting up from the squatting position. Furthermore, the patient is reported to have developed weakness of the upper limb muscles, which is also atypical for Myoshi myopathy.

The wording that “electromyography” revealed normal motor and sensory nerve conductions and normal F-wave latencies and amplitude, is misleading. This is because electromyography is usually an investigation with needles via which electrical activity is receded from muscle cells in vivo. Thus, it is required that “electromyography” is replaced by nerve conduction studies not to confuse the reader.

Cadiac involvement in dysferlinopathies may not always become symptomatic. Particularly in the early stages of the disease cardiac disease may remain subclinical. This is why treating physicians need to actively look for the presence or absence of subclinical cardiac disease in these patients. Asking the patient for cardiac symptoms is not sufficient to exclude cardiac involvement. Long-term ECG recordings and a transthoracic echocardiography examination are the minimum requirement to confirm or exclude cardiac disease. Cardiac disease in dysferlinopathies includes cardiomyopathy and arrhythmias. Generally, however, cardiac disease in dysferlinopathies is rare and mild.

Cerebral involvement in dysferlinopathy has been repeatedly reported and includes progressive chorea or epilepsy. Thus, we should be informed if EEG recordings were carried out and if seizures were definitively excluded to explain parts of the phenotype. Since SPECT investigations revealed hyperfusion of the cingulate cortex, the basal ganglia, and the thalamus, it would be interesting to know if hyperperfusion was also found on MR perfusion studies. In particular we should be informed if the modalities “time-to-peak”, “mean cerebral blood flow”, or “mean transit time” were abnormal on PWI in the regions of increased perfusion on SPECT.

Overall, this interesting case report could be more meaningful if the diagnosis of “dysferlinopathy” would be genetically confirmed, if the heart would have been prospectively investigated for concomitant cardiac disease, and if the diagnosis of Myoshi myopathy would be revised. Multisystem involvement in dysferlinopathies is quite likely but should be prospectively investigated by investigations for multiorgan disease and by long-term follow-up investigations.

References


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