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Neuromuscular Disorders 17 (2007) 266



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Letter to the Editor

Underdiagnosis of X-linked myotubular myopathy and other forms of centronuclear myopathy

I commend your journal and authors Hoffjan, et al., on the fascinating article titled, "Extreme phenotypic variability in a German family with X-linked myotubular myopathy (XLMTM) associated with E404K mutation in MTM1" [1]. The authors describe a 68-year-old male with mild XLMTM. Despite a muscle biopsy at age 65 showing centronuclear myopathy (CNM), he was specifically diagnosed with XLMTM only after his grandson was born with a more severe clinical presentation of XLMTM. The grandson tested positive for a missense mutation of the MTM1 gene. The same mutation was found in this grandfather, while his daughter (the boy's mother) was found to be a carrier.

The extreme phenotypic variability that is so well documented in this article should prompt clinicians worldwide to dramatically alter the threshold for genetic testing in families with known or suspected XLMTM, or other forms of CNM. It seems likely that there are unknown but significant numbers of other patients with clinical manifestations of XLMTM, who remain undiagnosed for decades. Most likely, we as physicians are probably failing to obtain genetic testing often enough, presumably due to failure to realize that XLMTM remains in the differential diagnosis beyond

infancy. We never find what we are not looking for. Only by first making the accurate genetic diagnosis in affected individuals and their families can patients and physicians then reap the benefits of appropriate genetic counseling, properly categorized research groups, and (eventually) gene specific or disease specific treatments.

If the medical community realizes the substantial clinical implications of this article, it will almost certainly lead to more frequent and accurate diagnosis of XLMTM, better understanding of the spectrum of XLMTM, and eventual advancements towards treatments. I applaud the authors for their contribution.

Reference

- [1] Hoffjan S, Thiels C, Vorgerd M, Neuen-Jacob E, Epplen JT, Kress W. Extreme phenotypic variability in a German family with X-linked myotubular myopathy associated with E404K mutation in MTM1. *Neuromuscul Disord* 2006;16(11):749–53.

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