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Extra-muscular manifestations of TK2 deficiency

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Letter to the editor

Mitochondrial DNA maintenance defects are typically multisystem diseases that most often affect brain, muscle, liver, and gastrointestinal tract. Depending on organs predominantly affected, these disorders can be classified into encephalohepatopathy, encephalomyopathy, encephaloneuropathy, neurogastrointestinal encephalopathy, myopathy, ophthalmoplegia, optic atrophy, or neuropathy [1, 2]. TK2-related mitochondrial DNA maintenance defect affects mainly skeletal muscle and therefore is classified as a myopathic disease. We have recently published the clinical spectrum of 82 previously reported and new individuals with TK2 deficiency highlighting the myopathic features of this disease [3]. Subsequently, Finsterera et al. corresponded mentioning that although skeletal muscles are predominantly affected, other organs can be involved [4]. Indeed, extra-muscular manifestations are occasionally seen in TK2 deficiency.

The predominant features of TK2 deficiency are the muscular manifestations including muscle weakness, atrophy, and hypotonia, elevated CPK, respiratory and feeding difficulties, and myopathic changes in EMG and muscle biopsy [3]. However, occasionally other systems are involved including neurological, cardiac, and hepatic. Neurological manifestations have been occasionally observed with seizures, cognitive impairment, nystagmus, and sensorineural hearing loss being reported in 11, 5, 2, and 2 individuals, respectively. One individual showed neuropathic changes in EMG. Neuroimaging sometimes demonstrates abnormalities. Cerebral atrophy was reported in 9 individuals. White matter and basal ganglia abnormalities were observed less frequently [3]. Cardiac involvement is rare with hypertrophic cardiomyopathy being reported in 3 individuals [3]. Finally, liver is sometimes affects. However, hepatic involvement is relatively mild as severe liver dysfunction or liver failure has not been observed. Elevated liver transaminases (AST and ALT) were described in 18 individuals [3]. Although elevated AST can also be seen with muscle diseases, elevated ALT is specific to hepatic damage and indicates a true liver involvement [5].

In conclusion, although TK2 deficiency is a myopathic disease, extra-muscular manifestations including neurological, hepatic, and cardiac can occasionally be observed.

References

[1] A.W. El-Hattab, W.J. Craigen, F. Scaglia, Mitochondrial DNA maintenance defects, Biochim. Biophys. Acta 1863 (6) (Jun, 2017) 1539–1555.
[2] El-Hattab AW, Craigen WJ, Wong L-JC, Scaglia F. Mitochondrial DNA Maintenance Defects Overview. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJ, Stephens K, et al., eds. Seattle (WA): University of Washington, Seattle; 2018 [cited 2018 Jun 11]. GeneReviews® [Internet], Available from: http://www.ncbi.nlm.nih.gov/books/NBK487393/
[3] J. Wang, E. Kim, H. Dai, V. Stefans, H. Vogel, F. Al Jasmi, et al., Clinical and molecular spectrum of thymidine kinase 2-related mtDNA maintenance defect, Mol. Genet. Metab. 124 (2) (Jun, 2018) 124–130.
[4] J. Finsterer, F.A. Scorza, A.C. Fiorini, A.-C.G. de Almeida, C.A. Scorza, TK2-related mitochondrial disorder is not restricted to the skeletal muscle, Mol. Genet. Metab. Rep. 16 (2018 Sep) 13–14.
[5] E.G. Giannini, R. Testa, V. Savarino, Liver enzyme alteration: a guide for clinicians, CMAJ Can. Med. Assoc. J. J. Assoc. Med. Can. 172 (3) (Feb 1, 2005) 367–379.

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