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Correspondence

Response to Finsterer: CPT-II deficiency needs to be detected in army personnel

Response

Thank you for your insightful and interesting comments to our manuscript [1] on CPT-II deficiency [2].

We read this with interest as we had written this sib-pair up partly because of the novel variant in *CPT2* but also because of the unusual presentation with the younger sibling (sister) being enrolled in the army. She joined the army aged 18 and left aged 30 and had frequent episodes of muscle aches, weakness and dark urine ("like coca cola"). This often occurred when "tabbing": 8 mile marches carrying 50 kg packs or on day-long rugby tournaments. Muscle aches occurred after 6–8 miles. The army general practitioner encouraged her to eat more and to drink more fluids, which may well have helped prevent acute renal failure.

We agree with your conclusion that army personnel should have a thorough history and assessment done in order to ensure early identification of personnel with neuromuscular/metabolic disorders. Also, when an army personnel presents with symptoms similar to our patients after strenuous exercise, fatty acid oxidation disorders (FAOD) should be considered as a possible diagnosis and excluded through biochemical testing [3].

Metabolic myopathies remain a challenging diagnosis especially in non-specialist settings, due to their rarity, intermittent presentation, and frequent lack of clinical signs in between attacks. In addition, it is well recognised that rhabdomyolysis may occur following extreme exercise in individuals without identifiable metabolic myopathy, although this is generally not recurrent.

With regards to the offspring recurrence risk for CPT-II deficiency, it is useful to point out that Carnitine palmitoyltransferase II (CPT II) deficiency is inherited in an autosomal recessive manner. The lethal neonatal form of CPT-II deficiency is usually as a result of homozygous *CPT2* pathogenic null variants leading either to truncation of the protein or to mRNA degradation. The myopathic form of CPT-II deficiency as reported in our family is usually a result of homozygous or compound heterozygous missense pathogenic variants in *CPT2*, most notably the common p.Ser113Leu variant which accounts for over 60% of cases.

All the offspring of a patient with myopathic CPT-II deficiency would be 'unaffected' carriers but should not have the full blown features of the condition unless the patient's partner is also a carrier. As such manifesting carriers are rarely reported with severe features of CPT-II deficiency. However, if there is consanguinity, then there needs to be a low threshold to offer carrier testing for the familial variants as identified in the index case.

Nevertheless, we agree that the main take home message is to consider a FAOD in patients with unexplained muscle weakness and myalgia after excess exercise. Raising awareness of this presentation was a goal of writing the report. There should be a low threshold for a through neurological/metabolic work-up and confirmatory genetic testing to clarify diagnosis and offspring recurrence risk in such circumstances.

References

[1] M. Balasubramanian, T.M. Jenkins, R.J. Kirk, I.M. Nesbitt, S.E. Olpin, M. Hill, G.T. Gillett, Recurrent rhabdomyolysis caused by carnitine palmitoyltransferase II deficiency, common but under-recognised: Lessons to be learnt, Mol. Genet. Metab. Rep. 6 (15) (2018) 69–70.

[2] J. Finsterer, CPT-II deficiency needs to be detected in army Personnel, Mol. Genet. Metab. Rep. 59 (2018).

[3] S.E. Olpin, et al., The investigation and management of metabolic myopathies, J. Clin. Pathol. 0 (2015) 1–8.

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