J Inherit Metab Dis
DOI 10.1007/s10545-017-0041-7

IMAGES IN METABOLIC MEDICINE

Carnitine palmitoyltransferase 1A deficiency: abnormal muscle biopsy findings in a child presenting with Reye's syndrome

M. Bellusci[1] · P. Quijada-Fraile[1] · D. Barrio-Carreras[1] · E. Martin-Hernandez[1] · M. Garcia-Silva[1] · B. Merinero[2] · B. Perez[2] · A. Hernandez-Lain[3]

Received: 30 January 2017 / Revised: 21 March 2017 / Accepted: 23 March 2017

A 4-year-old girl was admitted to pediatric intensive care unit due to Reye's syndrome. Her medical history was notable for recurrent episodes of hypoglycemia when ill. Plasma levels of acylcarnitines and free carnitine (C0) were not remarkable, but creatine kinase (CK) level was increased (1674 U/l). A muscle biopsy was performed that showed severe and diffuse accumulation of lipid in muscle fibers (Fig. 1). Acylcarnitine profile was reviewed. Liver isoform of carnitine palmitoyltransferase IA (*CPTIA*) deficiency was suspected because of the increased C0/ [palmitoylcarnitine (C16) + stearoylcarnitine (C18)] ratio: 2190 (normal value 266–1510). With dietary treatment, rapid and dramatic improvement was observed. Two novel variants in the *CPT1A* gene were found: c.627delT (severe mutation) and c.1006G > A (predicted as damaging by several bioinformatic algorithms).

CPTIA deficiency is a rare disorder of fatty acid metabolism secondary to *CPT1A* mutation (Britton et al. 1997). Clinical presentation includes neonatal lethal arrhythmia, recurrent episodes of hypoketotic hypoglycemia, and occasional myopathy triggered by catabolism (Olpin et al. 2001). The increase in muscle CK previously described in *CPTIA* deficiency (Olpin et al. 2001; Haworth et al. 1992; Lee et al. 2015) is difficult to explain, since muscle isoform of *CPTI* is encoded by another gene (*CPT1B*) (Britton et al. 1997). This report shows for the first time the prominent muscle fat accumulation in a patient with *CPTIA* deficiency during acute decompensation. We hypothesized that abnormal circulating levels of *CPTIA*-related metabolites may have contributed to the impairment of muscle fat oxidation. However, an increase in *CPTIA*-related metabolites could not be demonstrated in the samples collected during the acute episode, when the levels of long-chain acylcarnitines, free fatty acids, triglycerides, and organic acids were all normal. We conclude that *CPTIA* deficiency may be misdiagnosed if C0/[C16 + C18] ratio is not considered (Lee et al. 2015; Fingerhut et al. 2001).

Communicated by: Bridget Wilcken

Bellusci M: clinical medical assistance and muscle biopsy evaluation of the patient reported, drafting of the article, elaboration of the figures.
Quijada P: drafting of the article, clinical medical assistance of the patient reported Barrio D: critical revision of the article, clinical medical assistance of the patient reported Martin-Hernandez E: clinical medical assistance of the patient reported, critical revision of the article
Garcia-Silva M: clinical medical assistance of the patient reported, drafting of the article Merinero B: Biochemical evaluation of acylcarnitine profile, critical revision of the article Perez B: genetic testing, critical revision of the article
Hernandez-Lain A: muscle biopsy evaluation of the patient reported, drafting of the article, elaboration of the figs.

✉ M. Bellusci
marcello.bellusci@gmail.com

[1] Inborn Errors of Metabolism and Mitochondrial Disease Unit, "12 de Octubre" University Hospital, Avenida de Cordoba sn, 28034 Madrid, Spain

[2] Centro de Diagnóstico de Enfermedades Moleculares (CEDEM), CIBERER, IdiPAZ, Universidad Autónoma, Madrid, Spain

[3] Neuropathology Unit, "12 de Octubre" University Hospital, Madrid, Spain

Published online: 02 May 2017

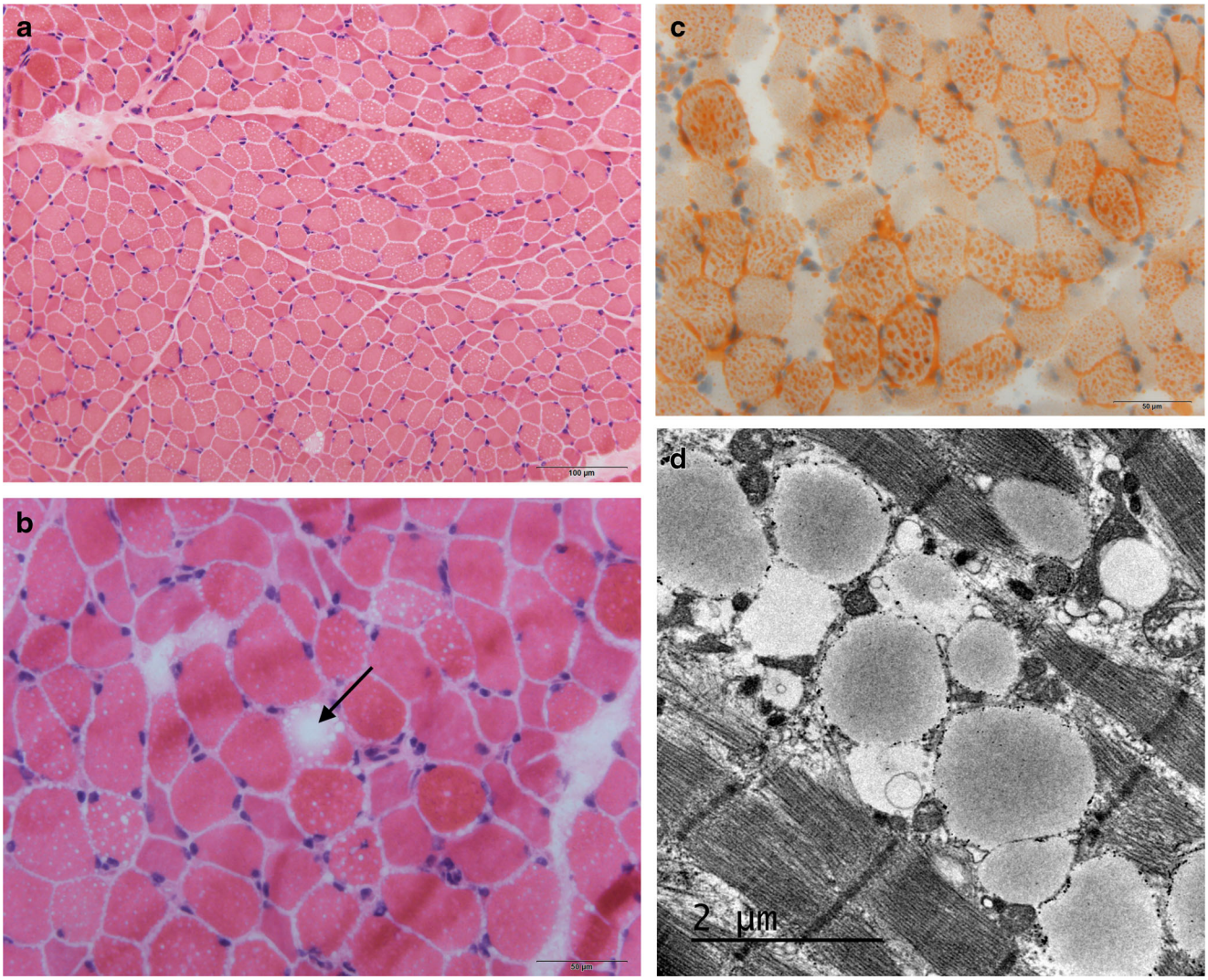

Fig. 1 Muscle biopsy: **a** Abundant vacuoles were identified in most muscle fibers distributed throughout the sarcoplasm (H&E). **b** Vacuoles sometimes occupy most of the fiber (*arrow*) (H&E). **c** Vacuole contents showed positivity using the lipid imaging technique oil red O, showing a striking increase in number and size of the lipid droplets present in types I and II fibers. **d** Electron microscopy shows lipid accumulation between myofibrils and under the sarcolemma with ultrastructurally normal mitochondria

Compliance with ethical standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Declaration of Helsinki, 1975, as revised in 2000. Informed consent was obtained from the mother of the patient.

Conflict of interest None.

Funding No funding was received for this work.

References

Britton CH, Mackey DW, Esser V et al (1997) Fine chromosome mapping of the genes for human liver and muscle carnitine palmitoyltransferase I (CPT1A and CPT1B). Genomics 40: 209–211

Fingerhut R, Röschinger W, Muntau AC et al (2001) Hepatic carnitine palmitoyltransferase I deficiency: acylcarnitine profiles in blood spots are highly specific. Clin Chem 47:1763–1768

Haworth J, Demaugre F, Booth F et al (1992) Atypical features of the hepatic form of carnitine palmitoyl- transferase deficiency in a Hutterite family. J Pediatr 121:553–557

Lee BH, Kim YM, Kim JH et al (2015) Atypical manifestation of carnitine palmitoyltransferase 1A deficiency: hepatosplenomegaly and nephromegaly. J Pediatr Gastroenterol Nutr 60:e19–e22

Olpin SE, Allen J, Bonham JR et al (2001) Features of carnitine palmitoyltransferase type I deficiency. J Inherit Metab Dis 24:35–42