ATYPICAL FEATURES IN MULTIPLE ACYL-COA DEHYDROGENASE DEFICIENCY: REPORT OF TWO CASES

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Background

Multiple Acyl CoA Dehydrogenase Deficiency (MADD) is a rare metabolic lipid disorder characterized by exercise intolerance and muscle weakness. MADD is an autosomal recessive disorder caused by defects of Electron Transfer Flavoprotein A, B (ETF-A or ETF-B) or ETF dehydrogenase (ETF-DH). MADD age-onset is variable ranging from neonatal (often lethal) to late-onset forms. [1] The latter are often characterized by rhabdomyolysis, myoglobinuria and muscle weakness. These patients usually respond very well to riboflavin administration (RR-MADD). Recently, severe sensory neuropathy has been reported in six patients with adult-onset MADD[2].

Case reports

Case 1-Clinical history

Male 50-years-old, no family history for neuromuscular diseases. Six months before coming to the hospital, he suffered from an episode of vomiting and fever, followed by difficult chewing, weakness at upper limbs and disesthesias at hands and feet.

Neurological examination

Ataxic gait, positive Romberg maneuver, dropped head, mild proximal muscles weakness at four limbs, absent deep tendon reflexes.

Lab tests

Mildly elevated CK serum levels (CK=400U/L) and LDH=775U/L.

Serum acyl-carnitine profile: medium and long chains acyl-carnitines elevation

Electrophysiological studies

Conventional EMG: neurogenic pattern with reinnervation at tibial and medial gastrocnemius muscles. ENG: reduced VCS on sural nerves on both sides.

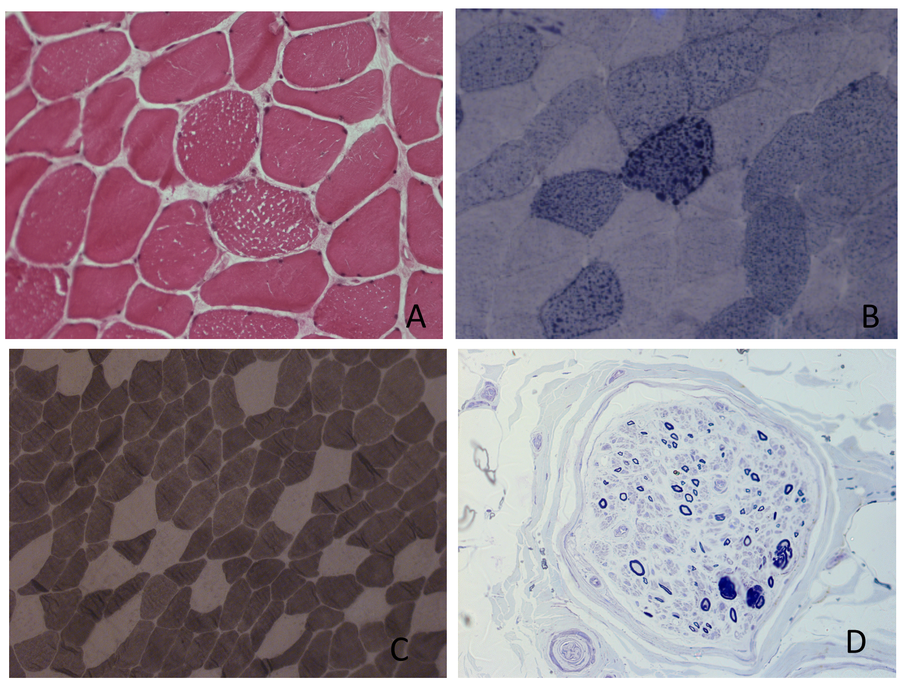

Fig.1 Muscle biopsy. (A) H&E Small vacuoles in some fibers; (B) lipid droplets at Sudan Black; (C) ATPase (Ph 9,4) Type grouping of type 2 fibers; (D) severely reduced density of myelinated fibers and axonal degeneration at sural nerve biopsy

Case 2-Clinical history

Female 61-years-old, no family history for neuromuscular diseases. Hypercholesterolemia treated with statins for 5 years, recently stopped because of hyperCKemia.
She came to our department complaining unsteady gait, distal numbness and paresthesias at four limbs.

Neurological examination

Positive Romberg maneuver, ataxic gait, proximal muscles weakness, absent deep tendon reflexes.

Lab tests

Elevated CK serum levels 2000 U/L and LDH 600U/L.

Serum acyl-carnitin profile: elevation of medium and long chains acyl-carnitines.

Electrophysiological studies

Conventional EMG showed myogenic pattern. ENG: reduced SAPs at upper limbs and absent sural nerves SAPs.

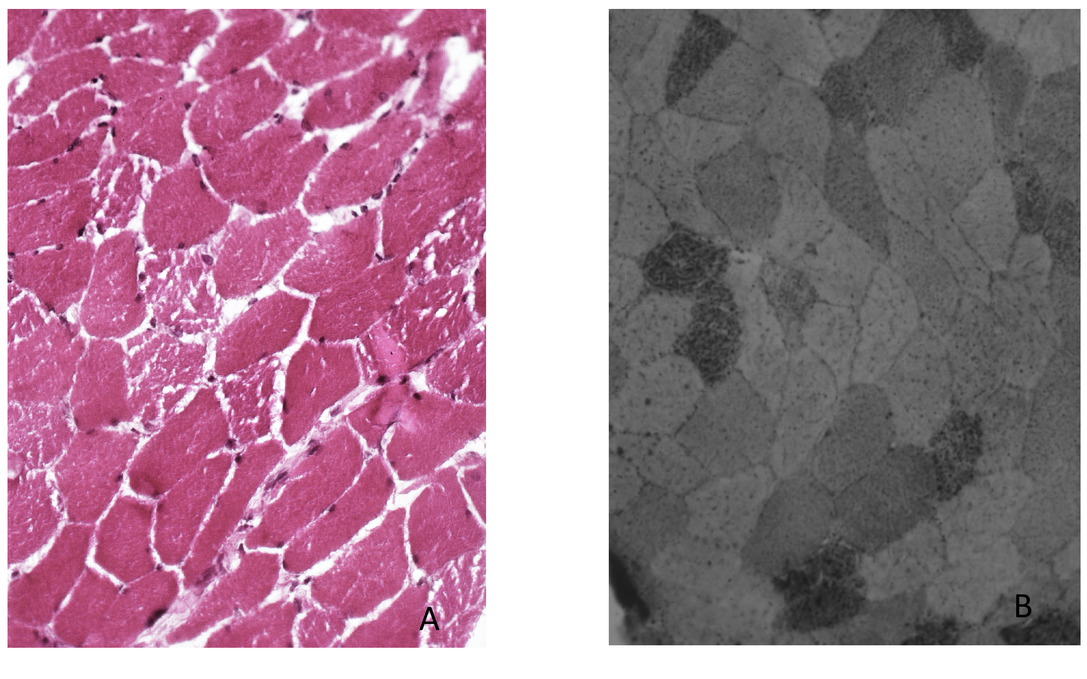

Fig.2 Muscle biopsy. (A) H&E: fiber size variability; (B) some vacuolated fibers cointaning lipids at Sudan Black stain.

Both patients were treated with riboflavin at 400mg/die. They showed an excellent response with a normalization on motor activities and laboratory results.

Conclusions

MADD may present with variable clinical patterns; peripheral neuropathy is indeed an uncommon feature. In these two cases, nerve involvement was predominant, suggesting that, in case of a subacute sensory neuropathy with proximal muscle weakness, hyperCKemia, and even more increased LDH values, MADD should be suspected. In these two cases, muscle weakness was fully reversed by riboflavin treatment whereas sensory neuropathy remained unchanged as previously reported in literature.

References

[1] Zhu M, Zhu X, Qi X, Weijiang D, Yu Y, Wan H, Hong D. Riboflavin-responsive multiple Acyl-CoA dehydrogenation deficiency in 13 cases, and a literature review in mainland Chinese patients. J Hum Genet. 2014 May;59(5):256-61.
[2] Wang Z, Hong D, Zhang W, Li W, Shi X, Zhao D, Yang X, Lv H, Yuan Y. Severe sensory neuropathy in patients with adult-onset multiple acyl-CoA dehydrogenase deficiency.