THE METABOLIC TRAP : EPSIODIC WEAKNESS IN A YOUNG MAN WITH MADD

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BACKGROUND & AIMS :

- ✓ Multiple Acyl-CoA Dehydrogenase Deficiency (MADD), also termed glutaric aciduria type II, is an uncommon but potentially treatable disorder of fatty acid and amino acid oxidation. Its adult-onset form may mimic acquired myopathies or mitochondrial cytopathies.
- ✓ Late-onset MADD typically presents with episodic myopathy, fluctuating weakness, and occasionally encephalopathic episodes precipitated by metabolic stress, prolonged fasting, or infection. Because of its nonspecific presentation and spontaneous recovery, the diagnosis is often delayed or missed.
- ✓ **METHODOLOGY** : Here we report a 22 year old male, presenting with episodic proximal limb weakness, ultimately found to have glutaric aciduria

Case Report : A 22-year-old male, born of a third-degree consanguineous marriage and previously healthy, presented with progressive pain and weakness of both thighs and calves over two months, followed by difficulty in climbing stairs and lifting arms for one and a half months. Subsequently, he developed neck weakness for one month, characterized by inability to hold his head upright when bending forward and difficulty rising from supine posture. The onset followed a 24-hour period of intense physical activity and long-distance travel with minimal food intake. Symptoms were aggravated by exertion and partially relieved with rest. There was no diplopia, dysphagia, sensory loss, respiratory difficulty, or bladder involvement. Family history was non-contributory. On admission, his weakness had begun to improve spontaneously. Neurological examination: Tone: Generalized hypotonia. Power: Proximal > distal weakness (MRC grade 4/5 in upper limbs, 2/5 in lower limbs); neck flexors weak. Reflexes: Absent except biceps and ankle jerks (1+). Plantar: Bilateral flexor
Sensory, cerebellar, cranial nerves: Normal. No muscle hypertrophy, wasting, fasciculations, or myotonia were observed. Systemic examination of cardiovascular, respiratory, and abdominal systems was normal

Investigations :

- ✓ Routine blood parameters were within normal limits except for elevated serum transaminases (OT 786 U/L, PT 576 U/L).
- ✓ Creatine kinase was markedly raised at 2876 U/L.
- ✓ Renal function, electrolytes, and coagulation profile were normal. Viral serologies were negative.
- ✓ Cerebrospinal fluid: Normal glucose, protein, lactate, and pyruvate levels.
- ✓ Nerve conduction study: Normal
- ✓ Echocardiogram and abdominal ultrasonography: No abnormalities.
- ✓ MRI Brain (T2/FLAIR): Revealed discrete juxtacortical hyperintensities in bilateral frontotemporoparietal lobes, confluent periventricular hyperintensities, and nodular signal in the right corona radiata — suggestive of metabolic leukoencephalopathy.
- ✓ Whole-exome sequencing: Identified mutations consistent with Multiple Acyl-CoA Dehydrogenase Deficiency.During hospitalization, the patient's strength gradually returned to normal without recurrence of symptoms or new deficits.

RESULT : This patient illustrates the late-onset, riboflavin-responsive form of MADD, characterized by episodic myalgia and weakness triggered by exertion and fasting. The key diagnostic clues were
(1) fluctuating proximal weakness with spontaneous recovery,
(2) Elevated CK and transaminases in the absence of inflammatory markers,
(3) normal electrophysiology excluding neuropathy, and
(4) MRI evidence of reversible white-matter changes.

DISCUSSION AND CONCLUSION : MADD results from defects in ETFA, ETFB, or ETFDH, impairing electron transfer from acyl-CoA dehydrogenases to the respiratory chain. The energy deficit and accumulation of toxic intermediates during metabolic stress lead to transient myopathic and encephalopathic episodes. Differential diagnoses include mitochondrial myopathy, periodic paralysis, glycogen storage disorders, and inflammatory myopathies, all of which were excluded based on laboratory and imaging results.Treatment involves riboflavin supplementation (100–400 mg/day), coenzyme Q10, and L-carnitine, along with a high-carbohydrate, low-fat diet and avoidance of fasting or strenuous exercise. Recognition is vital because early therapy can achieve complete recovery and prevent recurrent or fatal episodes.