



Case report

Glutaric aciduria type 2 presenting with acute respiratory failure in an adult



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A B S T R A C T

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Glutaric aciduria (GTA) type II can be seen as late onset form with myopathic phenotype. We present a case of a 19-year old female with progressive muscle weakness was admitted in intensive care unit (ICU) with respiratory failure and acute renal failure. Patient was unconscious. Pupils were anisocoric and light reflex was absent. She had hepatomegaly. The laboratory results showed a glucose level of 70 mg/dl and the liver enzymes were high. The patient also had hyponatremia (117 mEq/L) and lactate level of 3.9 mmol/L. Tandem MS and organic acid analysis were compatible with GTA type II. Carnitine 1gr, riboflavin 100 mg and co-enzymeQ10 100 mg was arranged. After four months from beginning of treatment tandem MS results are improved.

Respiratory failure, acute renal failure due to profound proximal myopathy can be due to glutaric aciduria type II that responded rapidly to appropriate therapy.

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Introduction

Glutaric aciduria (GTA) type II is an autosomal recessive disease. Different substrates like abnormal amino acids and/or fatty acids metabolites together with high amounts of glutaric acid accumulate due to a block in electron transfer between the acyl-CoA dehydrogenases and the respiratory chain [1,2].

There are mainly three clinical phenotypes which can be seen in GTA type II: First, neonatal form with congenital anomalies. Second, neonatal form without congenital anomalies. And third late onset form with myopathic phenotype and rarely metabolic acidosis [1]. We present a case of late onset GTA type II characterized by respiratory failure and acute renal failure.

Case

A 19-years old female with progressive muscle weakness and dyspnea was admitted in intensive care unit (ICU). In admission the patient was unconscious and intubated. The physical examination showed anisocoric pupils with a right dilated pupil and the light reflex was absent. Examination was normal except hepatomegaly. The patient had hyponatremia, hypoglisemia and hyperlactatemia. The results are shown in Table 1.

Radiologic findings showed cortical changes which were usually seen due to hypoglycemia (Figs. 1 and 2).

Tandem MS and organic acid analysis were compatible with GTA type II (Table 2).

She was treated with carnitine 1gr, riboflavin 100 mg and co-enzymeQ10 100 mg. In addition to the drug therapy hemodialysis was performed to get rid of the accumulated metabolites and glutaric acid. The patient showed progressive recovery and with the help of physiotherapy. Ability to swallow and walk was dramatically improved. After four months from beginning of treatment Tandem MS results are improved (Table 2).

Discussion

We describe a rare cause of acute respiratory failure due to myopathy in a young adult. Differential diagnosis of acute respiratory failure in young adults includes infectious diseases, chronic respiratory diseases, intoxications, neuromuscular diseases and metabolic diseases (causing myopathy) [3]. There are many etiologies of myopathy, including toxicologic, endocrinologic, and metabolic causes.

Late onset GTA type II [4,5] can be the cause of myopathy, especially in cases of childhood onset. The mode of presentation of older patients included a progressive lipid-storage myopathy [6] muscle weakness and myalgia [7], and repeated episodes of hypoglycemia with hypoketosis, accompanied by proximal myopathy

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Table 1
Laboratory findings of patient at admission.

| | Patients results | References |
|----------------------|------------------|------------|
| ALT (U/L) | 412 | <33 |
| AST (U/L) | 1366.7 | <31 |
| GGT (U/L) | 464.9 | <33 |
| ALP (U/L) | 128 | <390 |
| Sodium (mEq/L) | 117.3 | 130–140 |
| Potassium (mEq/L) | 4.8 | 3.5–5.1 |
| Chlor (mEq/L) | 86.4 | 95–110 |
| BUN(mg/dL) | 57.6 | 6–20 |
| Creatin(mg/dL) | 2.5 | 0.5–0.9 |
| Uric acide (mg/dL) | 10.7 | 2.4–5.7 |
| Protein,total (g/dL) | 4.7 | 6.4–8.3 |
| Albumin (g/dL) | 2.8 | 3.4–4.8 |
| LDH (U/L) | 7604 | 240–480 |
| CK (U/L) | 11511 | 26–192 |
| Calcium (mg/dL) | 7.6 | 8.6–9.9 |
| Hemoglobine (g/dL) | 11.3 | 11.7–15.5 |
| Hemotocride % | 33% | 34.5–46.3 |
| WBC (x1000/ μ l) | 14.1 | 4.1–11.2 |
| PLT (x1000/ μ l) | 198 | 159–388 |
| lactate (mmol/L) | 3.9 | 0.8–2 |

and hepatic dysfunction [8]. Although symptoms of hypoglycemia and acidosis may predominate [8,9] as seen in our case muscle weakness is a common finding of patients with late onset glutaric aciduria type II [5]. It predominantly affects proximal muscles and may lead to hypoventilation.



Fig. 1. Brain CT: flattened sulci secondary to the diffuse brain edema.



Fig. 2. Brain MRI: cortical changes which were usually seen due to hypoglycemia.

Table 2
Tandem MS results; before and after treatment.

| | Before treatment | After treatment |
|--------------------------|-------------------|-----------------|
| Free carnitine | 41.24 μ mol/L | 53.11 |
| C5 | 2.88 μ mol/L | (normal) |
| C6 | 0.66 μ mol/L | (normal) |
| C5 OH | 0.80 μ mol/L | normal |
| C8 | 1.47 μ mol/L | 1.58 |
| C10 | 2.67 μ mol/L | 2.65 |
| C10:1 | 0.50 μ mol/L | 0.56 |
| C4DC | 1.62 μ mol/L | 1.68 |
| C5DC | 3.04 μ mol/L | normal |
| C12 | 2.08 μ mol/L | 1.29 |
| C6 | 1.14 μ mol/L | normal |
| Methylglutaryl carnitine | 2.06 μ mol/L | normal |
| C14:2 | 0.54 μ mol/L | normal |
| C14:1 | 1.48 μ mol/L | 0.63 |
| C14 | 0.39 μ mol/L | 0.64 |
| C16:1 | 0.96 μ mol/L | 0.21 |
| C16 | 1.70 μ mol/L | normal |
| C18:2 | 0.87 μ mol/L | 0.70 |
| C18:1 | 2.36 μ mol/L | normal |
| C18 | 0.99 μ mol/L | 0.63 |
| Leucin/isoleucin | 366 μ mol/L | normal |

Acylcarnitine analysis with tandem mass spectrometry is a very useful diagnostic tool for GTA type II. Apart from GTA type II, disorders of riboflavin transport can present with similar clinical and biochemical features. RFT2 (C20orf54) is thought to be primary intestinal riboflavin transporter. RFT2 defects cause Brown-Vialetto-van Laere syndrome, an autosomal recessive disorder that presents with hypotonia and respiratory failure in infancy or, later in life, with deafness and pontobulbar palsy; in the absence of deafness, it is known as Fazio-Londe disease. Fazio-Londe disease, also called progressive bulbar palsy of childhood, is an inherited motor neuron disease found in children and young adults. Blood acylcarnitines and urine organic acids suggest GTA type II, and treatment with riboflavin leads to clinical and biochemical improvement.

As in most inborn errors of metabolism, investigation for electron transfer defects including GTA type II and Fazio-Londe disease starts with a search for abnormal metabolites, particularly acylcarnitines. If the results suggest a specific diagnosis, this is confirmed with by enzyme assays or mutation analysis [10]. In our patient biochemical and clinical findings were typical for GTA type II, however, enzyme or mutation analysis could not be performed.

Urine organic acid analysis may not be helpful in the stable form of GTA type II, because levels are often normal except during a symptomatic period. During acute episodes, the analysis may demonstrate dicarboxylic acid compounds (suberic acid, sebacic acid, and adipic acid), as we demonstrated.

Carnitine supplement may be required, given secondary carnitine deficiency reported in a patient with glutaric aciduria type II [11]. Carnitine supplement alone may not be sufficient. For better outcome riboflavin and co-enzyme Q 10 can be added [7–9,12]. Riboflavin therapy resulted in a dramatic improvement in both clinical and biochemical aspects. In our patient, the defect in co-enzyme binding to electron transfer flavoprotein (ETF) or ETF-dehydrogenase was suspected. However, it was the limitation of our manuscript that, enzyme or mutation analysis could not be performed.

We present a rare cause of respiratory failure, acute renal failure due to profound proximal myopathy that responded rapidly to appropriate therapy. Since late-onset GTA type II is treatable, correct diagnosis is of utmost importance and should be considered in adults.

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