

Not every elevating enzyme tells the same story: unpacking creatine kinase and anti-Jo-1 positivity beyond inflammatory myositis

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ABSTRACT

Gitelman syndrome (GS) is an autosomal recessive familial disorder characterized by hypokalemia and metabolic alkalosis. Rhabdomyolysis due to hypokalemia is extremely rare. The presentation of GS leading to rhabdomyolysis is extremely rare as well. This case report describes a situation in which GS mimicked inflammatory myositis. A 30-year-old woman presented to the rheumatology outpatient clinic with an inability to walk and severe muscle weakness. Her creatine kinase level was elevated at 9900 U/L and her potassium level was low at 2.6 mmol/L. A myositis panel was ordered on suspicion of inflammatory myositis, and the results showed a positive anti-Jo-1. A muscle biopsy, performed with a presumptive diagnosis of inflammatory myositis, yielded pathology results inconsistent with myositis. Despite persistent low potassium levels during follow-up, potassium replacement was administered. The patient's clinical condition improved significantly with potassium replacement, leading to a reduction in muscle weakness.

Keywords: Gitelman's syndrome, creatine kinase, anti Jo-1

INTRODUCTION

Gitelman syndrome (GS) is an autosomal recessive genetic disorder characterized by hypokalemia and metabolic alkalosis [1]. Gitelman syndrome (GS) is typically diagnosed in adulthood. This rare kidney disorder is caused by a mutation in the SLC12A3 (solute carrier family 12 member 3) gene, which encodes the thiazide-sensitive sodium chloride cotransporter in the distal convoluted tubule [2]. Due to the mutation, inactivation of the Na-Cl cotransporter leads to loss of sodium and chloride. This electrolyte imbalance is accompanied by the excretion of potassium and hydrogen, resulting in hypokalemia and metabolic alkalosis. Rhabdomyolysis results from acute necrosis of skeletal muscle fibers and can be a severe condition characterized by abnormally high levels of creatine kinase. Notably, hypokalemia as a cause of rhabdomyolysis is extremely rare [3]. Gitelman syndrome (GS) is usually discovered incidentally, often without symptoms or with mild manifestations. The presentation of GS with rhabdomyolysis is highly un-

usual. In this case report, we describe a case of GS masquerading as inflammatory myositis, characterized by elevated creatine kinase due to hypokalemia and concomitant anti-Jo1 positivity.

CASE PRESENTATION

A 30-year-old woman with a height of 167 cm and a weight of 72 kg presented to the rheumatology outpatient clinic complaining of a loss of ability to walk, comb her hair and brush her teeth. She had no history of similar symptoms, and there was no family history of genetic or neuromuscular diseases. The patient had no chronic systemic diseases or chronic infections, and she denied using herbal medicines, diuretics, laxatives, or glucocorticoids prior to presentation. No concomitant rash was reported. On examination, significant proximal muscle weakness was noted. Muscle strength was 4/5 in the upper proximal extremities and 3/5 in the lower proximal extremities. No Gottron's papules, rash or heliotropic rash were observed on the body.

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Laboratory results showed blood urea nitrogen (BUN) 17 mg/dL (normal range: 10-20 mg/dl), creatinine 0.8 mg/dL (0.5-1.1), sodium 136 mmol/L (135-145), potassium 2.6 mmol/L (3.5-5.5) and magnesium 1.2 mg/dL (1.7-2.3). Other blood tests showed a hemoglobin of 12.4 g/dL (12-15), a white blood cell count of $6.8 \times 10^3/\mu\text{L}$ and a C-reactive protein of 5 mg/dL. The creatine kinase level was markedly elevated at 9900 U/L (normal range: 26-192 U/L). Arterial blood gas analysis showed metabolic alkalosis with a pH of 7.59 (7.35-7.45). In view of the physical examination and laboratory findings, a myositis panel was ordered on suspicion of inflammatory myositis, which was positive for anti-Jo-1. A muscle biopsy was performed with a preliminary diagnosis of inflammatory myositis, but the biopsy results showed no evidence of myositis. Despite persistent low potassium levels during follow-up, potassium replacement was administered, resulting in a significant improvement in the patient's clinical condition and a significant reduction in muscle weakness. The patient was not treated with corticosteroids until the biopsy results were available. As the patient's hypokalemia and creatine kinase elevations persisted despite replacement, rhabdomyolysis due to hypokalemia was considered. Consultation with nephrology revealed renal potassium wasting. DNA analysis identified compound heterozygous likely pathogenic variants in *SLC12A3*, confirming the diagnosis of Gitelman syndrome. The patient's clinical condition remained stable during follow-up with potassium replacement.

DISCUSSION

Gitelman syndrome is a relatively rare condition with an estimated prevalence of approximately 1 in 40,000. It is noteworthy that most cases remain asymptomatic before the age of six, and in many cases the diagnosis is not made until adulthood, mirroring the circumstances of our case [4]. A study of fifty Gitelman patients with confirmed mutations found that Gitelman syndrome is not typically asymptomatic. The study highlighted musculoskeletal symptoms as the most common manifestation, including muscle weakness, inability to walk, muscle pain and cramps. These findings highlight the significant impact of musculoskeletal symptoms in people diagnosed with Gitelman syndrome [5]. Similarly, our case presented significant muscle weakness and an inability to walk, consistent with the typical musculoskeletal symptoms associated with Gitelman's syndrome. In addition, the most common biochemical abnormalities - hypokalemia, metabolic alkalosis and hypomagnesemia - were present in our case, reinforcing the consistency of the clinical and biochemical profile with Gitelman syndrome [6].

The additional abnormality observed in our patient was the presence of rhabdomyolysis with ele-

vated creatine phosphokinase levels. This was attributed to hypokalemic rhabdomyolysis secondary to Gitelman syndrome (GS). Potassium plays a crucial role in vascular relaxation in muscle tissue, and in situations of hypokalemia, increased muscle activity can lead to muscle ischemia and subsequently rhabdomyolysis. This association highlights the variety of clinical manifestations and complications that can occur in individuals with Gitelman syndrome

The detection of anti-Jo1 positivity in our patient led us to consider inflammatory myositis. Jo1, specifically histidyl tRNA synthetase, belongs to the group of anti-aminoacyl tRNA synthetase or anti-synthetase antibodies present in all nucleated cells. These antibodies are found in 25-40% of myositis patients. Numerous studies have linked anti-aminoacyl-tRNA synthetase antibodies to muscle inflammation consistent with myositis. Notably, these antibodies have a high sensitivity and specificity for myositis, with reported values of 80% and 93.3%, respectively. However, the pathological findings of the biopsy did not agree with the initial suspicion of inflammatory myositis, highlighting the complexity of autoimmune responses and the need for careful interpretation of clinical and laboratory data [7,8].

The definitive diagnosis of Gitelman syndrome is made by DNA analysis, which identifies the gene mutation [9]. Similarly, in our case, the diagnosis was confirmed by the detection of mutations through genetic analysis. It is recognized that the incidence of autosomal recessive diseases is higher in consanguineous marriages. Therefore, when Gitelman syndrome is identified, it is advisable to screen family members for GS. Unfortunately, our patient's first-degree relatives did not come for screening.

The prognosis for patients with Gitelman syndrome is generally favorable. However, muscle weakness may interfere with daily activities and the pattern of muscle weakness may mimic myositis. Treatment involves the gradual correction of electrolyte abnormalities. In our case, the patient was treated with an intravenous infusion of potassium chloride, which resulted in a rapid reversal of symptoms [10].

Our case report describes a patient with Gitelman syndrome (GS) in whom the presentation of hypokalemic metabolic alkalosis closely resembled myositis, characterized by elevated creatine kinase levels and anti-Jo-1 positivity. Clinical suspicion based on the identification of typical biochemical features was a crucial step in establishing an accurate diagnosis, which was further confirmed by genetic testing.

CONCLUSION

In conclusion, in cases where patients present with muscle weakness resembling inflammatory myositis, both clinically and on laboratory tests, espe-

cially when accompanied by electrolyte disturbances, especially hypokalemia, a thorough differential diagnosis is essential. Diagnosing cases such as ours

can be challenging for clinicians due to the overlapping clinical features.

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