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Case Report

Immune-mediated Necrotizing Myopathy With Increased Creatine Phosphokinase and Positive Signal Recognition Particle: A Case Report

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ABSTRACT

Background: Knowledge about Immune-Mediated Necrotizing Myopathy (IMNM) has received significantly attention in recent years. In this study, we report a rare case of IMNM with increased Creatine Phosphokinase (CPK) and positive Signal Recognition Particle (SRP).

Clinical Presentation and Intervention: The case was a 67-year-old male patient referred to Firozgar hospital affiliated to the Iran University of Medical Science, Tehran, Iran in June 2018 with a chief complaint of pain in the proximal lower extremity. According to Medical Research Council Scale for muscle strength, the motor function of proximal upper extremities was 4/5 and for the proximal of the lower extremities, it was 3/5. Laboratory findings showed an increase in CPK, CK-MB, lactate dehydrogenase, creatinine, alanine aminotransferase, aspartate aminotransferase and aldolase levels. Six days after admission, autoantibody test was requested which showed positive SRP. In muscle biopsy, the myopathic atrophy with multiple necrotic and many degenerative/regenerative fibers was associated with mild endomysial fibrosis, and no inflammation was observed. Two g/kg dose of Intravenous Immunoglobulin (IVIG) was administrated after diagnosis of IMNM. Prednisone 50 mg/day orally, calcium vitamin D daily, pantoprazole 40 mg/day, physiotherapy, and occupational therapy were administrated for after discharge.

Conclusion: Reporting a case of anti-SRP associated IMNM and reviewing its pathophysiology, diagnosis and treatment options can help increase the physicians' knowledge of this rare and debilitating condition.

Keywords: Muscular diseases, Creatine kinase, Signal recognition particle

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Highlights

● There is a rare case of immune-mediated necrotizing myopathy with increased creatine phosphokinase and positive signal recognition particle.

Introduction

Knowledge about Idiopathic Inflammatory Myopathies (IIM) has significantly increased in recent years. The IIM subtypes such as inclusion body myositis, dermatomyositis and polymyositis are now relatively well-characterized. Over the past decade, the entity of Immune-Mediated Necrotizing Myopathy (IMNM) has also been recognized as a distinct form of IIM [1], which is characterized by relatively severe proximal weakness, myofiber necrosis with minimal inflammatory cell infiltrate on muscle biopsy, and infrequent extra-muscular involvement [2]. Clinical features of acute or progressive onset, symmetrical proximal limb weakness, Creatine Kinase (CK) elevation, and myopathic change in electromyography and histopathology may be characterized by muscle fiber necrosis and regeneration, as well as lymphocyte infiltration of individual in histopathologic exam [3].

So far, two different autoantibodies have been described in IMNM patients: those targeting 3hydroxy-3-methylglutaryl-CoA reductase (HMGCR) and those targeting Signal-Recognition Particle (SRP), and their role in IMNM pathogenesis is the subject of ongoing research [1]. In this study. we report a rare case of necrotizing myopathy with increased Creatine Phosphokinase (CPK) and positive SRP.

Case Presentation

The case was a 67-year-old male patient referred to Firozgar hospital affiliated to the Iran University of Medical Science, Tehran, Iran in June 2018 with a main complaint of pain in proximal lower extremities. Eight months before admission, the proximal lower extremity pain without progression had been seen, which developed to distal lower extremity weakness later, and gradually progressed to proximal weakness after six months. Lower extremity weakness was on the left side. In physical examination, according to Medical Research Council Scale for muscle strength, the motor function of proximal upper extremities, the distal of upper extremities, the proximal of lower extremities, and the distal of lower extremities were 4/5, 5/5, 3/5, 4/5, respectively. Deep tendon reflex of extremities was +1 with downward two-sided plantar reflex. Sensory examination result was normal and Gower's sign was positive which is associated with the weakness of proximal muscles of lower extremities. The posture was normal, but gait was waddling.

Lab data

The patient's laboratory findings are presented in Table 1. After admission, serological markers such as anti-SRP autoantibodies were evlauated which was positive.

Muscle biopsy

Open muscle biopsy was performed after freezing of the muscle using isopentane cooled in liquid nitrogen. The myopathic atrophy with multiple necrotic and many degenerative/regenerative fibers was associated with mild endomysial fibrosis, and no inflammation were found. After muscle biopsy, tumor marker tests, paraneoplastic panel, SRP, JO1, MF2, and β-Hydroxy β-methylglutaryl-CoA reductase were measured.

Nerve conduction study and electromyography

According early recruitment with small polyphasic motor unit action potential with spontaneous activity in biceps and deltoid muscles and also in lower limbs muscles, the patient's electrodiagnosis was compatible with proximal>distal polymyopathy with denervating feature (irritative).

Treatment

Two gram per kg Intravenous Immunoglobulin (IVIG) was administrated after diagnosis of IMNM. Prednisone 50 mg/day orally, calcium vitamin D daily, pantoprazole 40 mg/day, physiotherapy, and occupational therapy were administrated after discharge.

Discussion

The IMNM is rare; therefore, clinical trials are very difficult to conduct in patients with IMNM. In this rgeard, case reports are very important to unveil the effects of potential new treatments [4]. The current study used the European NeuroMuscular Centre criteria for diagnosing

Table 1. Laboratory findings of the patient from admission to discharge

Tests	Type of Test	Admission	Day								Normal references
			1	4	5	6	7	8	9	15	
Biochemistry	CPK		1996	6336	3928	4085	3975	2500	2020		38-74 u/L
	CK-MB			260					160		Up to 24 u/L
	Lactate dehydrogenase		2290			2022					225-500 u/mL
	Aspartate aminotransferase	229				209				57	<33 u/L
	Alanine aminotransferase	247				220				90	<41 u/L
	Serum iron		20								65-175 Micro g/dL
	Urea	50		46	39		29	33			17-43 mg/dL
Hematology	Hemoglobin			12							14-18 mg/L
	Mean corpuscular volume	60.7		60.8							fl
	Mean corpuscular hemoglobin	18.9		19.1							Pgm
	Mean corpuscular hemoglobin concentration	31.1		31.5							%
	Red cell distribution width			18.2							
Serological markers	Anti-SRP autoantibodies					+					11.8 to 14.5 % in adult males
Bio & Hormone	Aldolase		89			15					Up to 7.6 u/L
Parasitology	Ova & parasite		not seen								Negative
	Fecal occult blood		-								Negative
Urinalysis	Protein									+1	Qualitative =nil
	Blood/ hemoglobin									+2	Negative

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IMNM [5]. The hallmark feature of patients with IMNM is the presence of proximal muscle weakness. In Malartre et al.'s study, it was shown that IMNM patients have more severe muscle weakness predominantly affecting the lower limbs [6]. This is consistent with the current study. In Yamada et al.'s study, a 40-year-old man with a 3-month history of progressive weakness of four limbs were presented. In examinations, the weakness of hip abductor was marked. During walking, shoulder sway was noted as compensation for hip abductor weakness. Blood tests showed a marked elevation of CK level and the presence of SRP antibodies. They suggested that physicians should consider the possibility of anti-SRP antibody-positive myopathy in patients with hip abductor weakness in a subacute onset [7].

Diagnosis of IMNM is based on the clinical features and muscle biopsy. Other parameters such as CK level are often more than 10 times above the normal level at the time of the onset of muscle weakness. Magnetic resonance imaging may show diffuse or patchy edema within muscles [8]. In our case report, it was not seen. As mentioned in Allenbach et al.'s study, anti-HMGCR and anti-SRP myositis-specific autoantibodies are crucial for defining IMNM when muscle biopsy is absent [9]. Abusharar et al. presented a patient with IMNM secondary to simvastatin use. The patient had proximal myopathy, dysphagia, and elevated CK levels, and was subsequently found to have anti-HMGCR autoantibodies with a necrotizing process on muscle biopsy. The patient was further complicated by sequelae of multiple disease processes, ultimately leading to deterioration of

the patient health [10]. In current study, the patient had no such problems after 2 year of follow-up.

Benveniste et al. showed that the level of anti-SRP antibodies is correlated with disease activity, suggesting a pathogenic role for these autoantibodies [11]. In Shelly et al.'s study, of six patients tested for IMNM antibodies, only one patient had anti-SRP positive [12]. Therefore, we can divide IMNM to three sub-categoreis of anti-SRP-positive, anti-HMGCR-positive, and seronegative IMNM. The discovery of specific autoantibodies, increased understanding of the risk factors and clinical characteristics, treatment options, and development of novel classification criteria are significant advances in understanding IMNM.

Conclusion

Reporting a case of anti-SRP associated IMNM and its related pathophysiology, diagnosis and treatment options can help increase the physicians' knowledge of this rare and debilitating condition.

Ethical Considerations

Compliance with ethical guidelines

All study procedures were in compliance with the ethical guidelines of the Declaration of Helsinki, 2013.

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Authors' contributions

Investigation: Seyed Mohammad Masoud Hojati, Payam Saadat; Writing-original draft: All authors; Writing-review & editing: Payam Saadat, Shayan Alijanpour.

Conflict of interest

The authors declared no conflict of interest.

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