Anti-SRP Myopathy with Sensorimotor Polyneuropathy: A Case Report

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Abstract

Purpose: Anti-signal recognition particle (SRP) myopathy is a subtype of immune-mediated necrotizing myopathy. It rarely presents with extramuscular features, involving the skin, lung, and heart. This paper presents a case of anti-SRP myopathy associated with sensorimotor polyneuropathy.

Case Report: A 33-year-old woman with no history of systemic disease presented to our hospital with weakness and numbness of the lower limbs for 1 year. Electromyography and nerve conduction study (NCS) revealed combined myopathy and axonal sensorimotor polyneuropathy. Blood examination revealed increased levels of serum muscle enzymes and anti-SRP antibodies. T1-weighted magnetic resonance imaging revealed diffuse muscular hyperintensities in the thighs, indicative of fatty replacement. She was administered methylprednisolone pulse therapy, followed by oral prednisolone and azathioprine. Muscle power increased, and serum muscle enzyme levels decreased significantly. Subsequent NCS performed 2 years later revealed persistent axonal degeneration in the lower limbs.

Conclusion: Anti-SRP myopathy can present with sensorimotor polyneuropathy. Thus, the possibility that the same pathological process affected the skeletal muscles and peripheral nerves should be considered.

Keywords: **anti-SRP myopathy; immune-mediated necrotizing myopathy; sensorimotor polyneuropathy**

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INTRODUCTION

Idiopathic inflammatory myopathies, also known as myositis, are a heterogeneous group of diseases, including polymyositis, dermatomyositis, inclusion-body myositis, and immune-mediated necrotizing myopathy (IMNM) [1, 2]. These conditions, except inclusion-body myositis, are characterized by proximal muscle weakness, elevated serum muscle enzyme levels, and abnormal muscle biopsy findings. Myositis-specific autoantibodies have played an increasingly important role in classifying idiopathic inflammatory myositis in recent years because of a paradigm shift from histological to serological criteria [3]. IMNM has three serological subtypes, namely, anti-signal recognition particle (SRP) myopathy, anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR)

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myopathy, and seronegative myopathy [4, 5].

The clinical features of patients with IMNM include symmetric proximal muscle weakness and high creatine kinase (CK) levels. Generalized muscle edema (hyperintensity in short-tau inversion recovery sequence), muscle atrophy, and fatty replacement of muscle (hyperintensity on T1-weighted imaging) with minimal fascial edema are generally observed on muscle magnetic resonance imaging (MRI) [6]. Muscle biopsy can reveal different stages of myonecrosis, myophagocytosis, regeneration and a relative paucity of lymphocytic infiltration. Extramuscular features, involving the skin, lung, and heart, have also been reported [4, 5, 7-12]. Among the three IMNM subtypes, anti-SRP myopathy presents with more severe clinical features, and its prognosis is worse than that of anti-HMGCR myopathy, which can be induced by statins. Moreover, extramuscular involvement is more common in anti-SRP myopathy than in other subtypes [8, 13, 14]. Immunological mechanisms are believed to be the underlying pathogenesis, and intense immunotherapy is frequently required.

Herein, we present a case of a 33-year-old woman who presented with weakness in the proximal lower limbs. Anti-SRP antibodies were detected, and electromyography (EMG) and nerve conduction study (NCS) revealed myopathy and axonal sensorimotor polyneuropathy. This case report highlights the uncommon clinical findings of anti-SRP myopathy.

CASE REPORT

A 33-year-old woman with no history of systemic disease presented to our hospital with a 1-year history of progressive weakness in the lower limbs, especially in the thighs. She initially experienced difficulty in climbing the stairs, followed by unsteady walking. She also experienced numbness in her lower limbs, especially in her feet. Myalgia, dysphagia, or joint pain was not observed. The patient denied any smoking or alcohol habits. She also denied taking any medications. She had no known family history of myopathic or neuropathic diseases. Lumbosacral radiculopathy was suspected initially at a regional hospital, but the lumbar MRI did not reveal remarkable findings.

On admission, neurological examination revealed normal cognitive function, fluent speech, and intact cranial nerves. The muscle strength test indicated symmetrical weakness in the hip flexor and extensor muscles (Medical Research Council grade 3 to 4). The deep tendon reflexes were normal in the upper limbs but absent in the lower limbs (both knee and ankle jerk). The sensation examination did not reveal significant abnormalities. The patient had a waddling gait. Blood biochemistry analysis revealed elevated levels of serum alanine aminotransferase (78 U/L), aspartate aminotransferase (68 U/L), low-density lipoprotein cholesterol (110 mg/dL), lactate dehydrogenase (410 U/L), CK (2612 U/L), and myoglobin (473 ng/mL). Blood assays for autoimmune disorders demonstrated remarkable results for high titers of antinuclear antibodies (1:320, cytoplasmic pattern), and myositis-specific antibodies test was positive for anti-SRP antibody (54; normal range, 0–10; immunoblotting method). Other examinations for tumor markers, viral hepatitis markers, and echocardiography were unremarkable, except for abdominal ultrasonography, which demonstrated coarse echogenicity of the liver parenchyma without evidence of a focal lesion. The EMG study revealed decreased amplitude and short duration of polyphasic motor unit action potentials at the quadriceps, indicative of myopathy, and the NCS revealed axonal sensorimotor polyneuropathy, predominantly in the lower limbs (Table 1). Results of further extensive investigations of other causes of polyneuropathy, including infections, toxins, drugs, cancers, nutritional deficiencies, diabetes, and autoimmune disorders, were negative. MRI of the lower limbs demonstrated symmetrically diffuse muscular hyperintensity in the thighs (predominantly central muscle) with bilateral involvement of the quadriceps and adductor muscles on the T1-weighted image, indicative of fatty replacement, and edematous changes on the T2-weighted iterative decomposition of water and fat with echo asymmetry and least-squares estimation image (Figure 1). During muscle biopsy of the right quadriceps, adequate muscle tissue was not obtained for pathological analysis, and only predominantly fibroadipose tissue with mixed inflammatory cell infiltrations was found.

The patient was diagnosed with anti-SRP myopathy based on the serological and clinical criteria. 1 g/day of methylprednisolone pulse therapy was administered for 3 days, followed by 50 mg/day of oral prednisolone. Following steroid therapy, her muscle power increased

Table 1. Nerve conduction study results before (Pre) and after (Post) immunosuppressant therapy

Nerve		Distal latency (ms)		Amplitude (μV)		Velocity (m/s)	
Motor			Normal range		Normal range		Normal range
Right median	Pre	4.8	<3.8	7816	>15000	49	>50
	Post	3.8		24950		57	
Right ulnar	Pre	2.7	<3.8	12380	>15000	53	>50
	Post	2.7		15210		53	
Right peroneal	Pre	4.3	<4.5	5130	>7000	45	>40
	Post	4.9		2568		44	
Right tibial	Pre	4.0	<4.5	9297	>15000	45	>40
	Post	4.2		8616		44	
Sensory							
Right radial	Pre	1.3	<3.0	54	>40	78	>50
	Post	1.6		58		63	
Right median	Pre	3.1	<3.0	49	>60	45	>50
	Post	2.8		58		50	
Right ulnar	Pre	2.7	<3.0	38	>40	51	>50
	Post	2.8		52		50	
Right sural	Pre	2.8	<3.8	5	>10	49	>40
	Post	2.8		7		50	

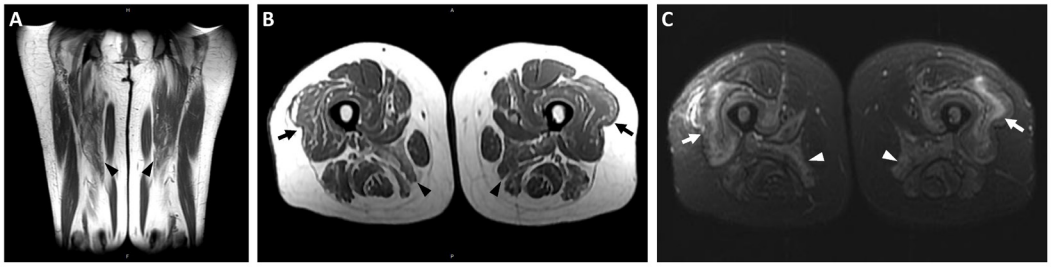

Fig. 1. Magnetic resonance imaging of the thighs. The thighs demonstrate symmetrically diffuse muscular hyperintensity on T1WI, indicative of fatty replacement with bilateral involvement of the quadriceps (arrow) and adductor muscles (arrowhead) (A, coronal view; B, axial view) and edematous change on T2-weighted IDEAL image (C, axial view). T1WI, T1-weighted imaging; IDEAL, iterative decomposition of water and fat with echo asymmetry and least-squares estimation.

gradually from grade 4 to 5. CK levels also decreased significantly from 2612 U/L to 762 U/L. Liver function was normalized. Adverse effects of corticosteroids, including lower-limb edema, were reported after 1 month of follow-up. Therefore, the steroid dose was tapered to 40 mg/day, and azathioprine was added. Muscle strength in the lower limbs was not affected. Two years after her first visit, she had full muscle strength in the lower limbs, although a mild waddling gait was still noted. The CK level was 381 U/L. The NCS revealed improvement of the median nerve compound motor action potential (CMAP), sensory nerve action potential (SNAP), nerve conduction velocity, and ulnar nerve CMAP and SNAP, but persistent axonal degeneration of the lower limbs (Table 1). She took 10 mg of prednisolone and 75 mg of azathioprine daily for maintenance.

Table 2: Summary of the cases of anti-SRP myopathy with polyneuropathy

	Sex/age	Clinical features/NE findings	CK	NCS/EMG findings	Treatment	Outcome
Hanisch et al. 2012[18]	M/56	Complete external ophthalmoplegia, severe bulbar dysarthrophonia and dysphagia, bilateral facial palsy, loss of patellar and ankle jerk reflexes, and symmetrical tetraparesis of both proximal and distal muscles	20-fold increase	NCS: axonal impairment of motor nerves (medial and tibial nerves) with loss or reduced persistence of F-waves and some A-waves EMG: pathological spontaneous activity and premature recruitment	No steroid or immunosuppressant treatment was initiated	Relapsing aspiration pneumonia requiring antibiotics and later tracheostomy; died 14 weeks after the onset of symptoms
Imene et al. 2015[19]	M/35	Rapid onset of proximal and distal muscle weakness with subsequent inability to stand or walk Reflexes were diminished in the upper extremities and absent in the lower extremities; normal sensory examination	7003 U/L	NCS: decreasing velocities EMG: small amplitude and short duration with low potential fibrillation	Methylprednisolone pulse therapy and IVIG	Swallowing difficulties; died of respiratory failure
Below et al. 2021[20]	F/52	Unresolving shortness of breath, heart failure, progressive muscle weakness, and dysphagia	25295 U/L	EMG: diffuse, proximal predominant, irritable myopathy NCS: distal axonal polyneuropathy	Prednisone, IVIG, and mycophenolate mofetil	Tracheostomy and dysphagia requiring nasogastric tube for nutrition, continued needs for assistance with activities of daily living
Present case	F/33	Weakness and numbness of the lower limbs Reflexes were normal in the upper limbs but absent in the lower limbs (both knee and ankle jerk)	2612 U/L	EMG: decreased amplitude and short duration of polyphasic motor unit action potentials NCS: axonal sensorimotor polyneuropathy	Methylprednisolone pulse therapy, oral prednisolone, and azathioprine	Independently

Abbreviation: CK, creatine kinase; EMG, electromyography; F, female; IVIG, intravenous immunoglobulin; M, male; NCS, nerve conduction study; NE, neurological examination

DISCUSSION

Herein, we described a rare case of a 33-year-old woman with anti-SRP myopathy associated with axonal sensorimotor polyneuropathy. Muscle strength increased in the lower limbs, and muscle enzymes decreased significantly after treatment with corticosteroids and azathioprine, but axonal degeneration of the lower limbs

persisted.

The patient presented with proximal weakness in the lower limbs with a waddling gait, which was clinically indicative of myopathy. However, lower-limb paresthesia and areflexia indicated a possible neuropathy, which was confirmed by NCS. Peripheral nervous system involvement is observed in some autoimmune diseases, such as systemic lupus erythematosus, systemic scleroderma, and Sjogren's syndrome [15]. Furthermore, combined myopathy and polyneuropathy have been reported in dermatomyositis and polymyositis [15-17]. Vasculitis, paraneoplastic origin, and viral disease have been included in the pathogenic hypothesis of neuromyositis [5, 17]. A literature review revealed that only a few cases of anti-SRP myopathy complicated by polyneuropathy have been reported (Table 2) [18-20]. One patient was thought to have an overlap of Miller Fisher syndrome, axonal Guillain–Barre syndrome, and Bickerstaff's brainstem encephalitis [18]. Another patient had dysphagia, respiratory failure, and cardiac failure in addition to muscle weakness [20]. The prognosis was poor in both cases.

Our patient's overall response to immunosuppressants was fair, as her muscle power increased, and clinical data, including muscle enzymes and liver function, improved substantially. While most patients with anti-SRP myopathy experienced rapid progression of symptoms [8, 13, 14, 18], our patient had good recovery with a fair response to immunosuppressive therapy. The phenomenon was also observed in some cases [21, 22]. However, elevated CK levels demonstrated that most patients with anti-SRP myopathy indicated continued disease activity after immunosuppressive therapy, despite improvement in strength [8].

In our patient, muscle biopsy failed to obtain adequate muscle tissue for pathological analysis and revealed only a predominance of fibroadipose tissue with mixed inflammatory cell infiltrations. A previous study reported that performing a muscle biopsy in edematous regions increases the likelihood of obtaining a diagnostic biopsy, whereas nondiagnostic biopsies may be more likely when a non-edematous or fat-replaced muscle is selected [4]. The patient was diagnosed with anti-SRP myositis based on serological (anti-SRP antibody) and clinical criteria (high CK and proximal weakness). In the European Neuromuscular Centre criteria, muscle biopsy is not strictly required for diagnosing anti-HMGCR or anti-SRP myopathy. However, muscle biopsy is required for diagnosing an antibody-negative IMNM [4].

CONCLUSION

This case demonstrated that anti-SRP myopathy can present with axonal sensorimotor polyneuropathy. Therefore, the possibility that the same pathological process affected the skeletal muscles and peripheral nerves in our patient should be considered.

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