



Clinical Manifestations and Prognosis of Anti-Signal-Recognition-Particle Myositis

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Dear Editor,

Idiopathic inflammatory myopathy (IIM) is a rare autoimmune disease of significant clinical importance owing to its treatability. Myositis-specific antibodies (MSAs) and myositis-associated antibodies (MAAs) have recently received increased attention in the diagnosis and classification of IIM.¹ The discovery of anti-SRP (signal recognition particle) and anti-HMGCR (3-hydroxy-3-methylglutaryl-coA reductase) antibodies has led to the inclusion of immune-mediated necrotizing myopathy (IMNM) as a distinct subgroup within IIM.² The prognosis and clinical features of IMNM can vary significantly with the specific MSA involved. A recent study explored the clinical characteristics of anti-HMGCR myopathy in the Republic of Korea,³ but information regarding anti-SRP myopathy in Korean patients with IIM is scarce. Therefore, this study aimed to investigate the clinical characteristics of anti-SRP myopathy in Korean patients and provide an overview of their clinical features.

We reviewed the medical records of patients who were diagnosed with IIM and confirmed as carriers of the anti-SRP antibody in serum from three tertiary referral hospitals in the Republic of Korea between January 2019 and June 2023. Demographics and clinical data were collected. Line-blot immunoassays were applied with the following panel of 16 MSAs/MAAs (Euroimmun, Lübeck, Germany): antibodies to Ro52, OJ, EJ, PL-12, PL-7, SRP, Jo-1, PM75, PM100, Ku, SAE1, NXP2, MDA5, TIF1- γ , Mi-2b, and Mi-2a.

Nine patients (including 66.7% females) with SRP-positive myopathy were enrolled in this study. The median age at onset was 56 years (range, 34–88 years). Seven patients (77.8%) presented with moderate-to-severe muscle weakness. Two patients (22.2%) had comorbid interstitial lung disease, and one of them had accompanying cardiac involvement. All patients had markedly elevated creatinine kinase (CK) levels, ranging from 1,100 to 35,675 IU/L (median, 4,581 IU/L). The demographics and clinical data of our study population are summarized in Table 1. Previous studies have found that anti-SRP myopathy commonly occurs in females and middle-aged individuals, and presents as severe muscle weakness with markedly elevated CK levels.^{4–6} We found that the clinical manifestations of our Korean patients with anti-SRP myopathy were similar to those in previous studies.

Concomitant SRP and other MSAs/MAAs were present in 55.6% of our patients, with the most common MSA/MAA being the anti-Ro52 antibody. The potential risk of a false-positive result in a line-blot immunoassay meant that we could not rule out the possibility of the false positive of a second MSA/MAA. However, in our study, 60% of patients who were double positive for anti-SRP antibody and other MSAs/MAAs had high titers ($\geq 2+$) of both antibodies. Previous studies observed the coexistence of multiple MSAs in 3%–15% of patients with IIM, with the proportion varying with the test methods.^{7,8} It is particularly interesting that the anti-Ro52 antibody has also been the most commonly detected myositis autoantibody in Korean patients with anti-HMGCR myopathy.³ Further studies with larger study populations that apply multiple antibody detection methods are necessary to determine the

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Table 1. Demographics, clinical data, and outcomes of the patients with anti-SRP myopathy

Variable	1	2	3	4	5	6	7	8	9
Age at onset (yr)	56	39	67	34	61	68	88	46	47
Sex	M	F	M	F	F	M	F	F	F
Duration* (months)	2	12	4	6	8	2	1	50	120
Motor weakness									
Proximal dominant	+	+	+	+	+	+	+	+	+
Severity†	Severe	Moderate	Mild	Mild	Severe	Moderate	Severe	Moderate	Moderate
Dysphagia	-	+	-	-	-	-	+	-	+
Muscle atrophy	-	-	-	-	-	+	-	-	+
Myalgia	+	+	-	+	+	+	+	-	-
Fatigue	-	-	-	+	+	-	-	+	-
Weight loss	-	-	7 kg/month	-	-	-	-	-	-
Fever	+	-	-	-	-	-	-	-	-
Interstitial lung disease	-	-	-	-	-	-	-	+	+
Cardiac involvement	-	-	-	-	-	-	-	-	+
Skin rash	-	-	-	-	-	-	-	-	-
Raynaud's phenomenon	-	-	-	+	-	-	-	-	-
Arthritis	-	-	-	-	+	-	-	-	-
Rheumatic disease	-	-	-	-	-	-	-	-	-
Cancer	-	-	-	-	-	-	-	-	-
Statin exposure	-	-	-	-	-	-	+	-	-
Anti-SRP antibody titer	3+	3+	3+	3+	3+	3+	1+	2+	1+
Other MSA/MAAs	Ro52 (3+)	OL (1+)	-	Ro52 (3+)	Ro52 (2+)	-	-	Ro52 (1+)	-
ANA	1:320	1:1,280	-	1:320	1:640	1:640	1:40	-	1:40
Muscle biopsy	+	+	+	+	+	+	Not done	+	+
Inflammation	EM, PV	EM	PF	-	-	EM, PV	N/A	EM, PV	EM
Degeneration and regeneration	+	+	-	+	+	+	N/A	N/A	+
Necrotic change	+	-	-	-	-	-	N/A	N/A	-
Perifascicular atrophy	-	-	-	-	-	-	N/A	N/A	-
CK level at first visit (IU/L)	7,746	4,550	4,581	5,394	14,441	3,476	35,675	1,745	11,00
CK level at last visit (IU/L)	193	275	144	182	517	230	120	1,267	1,541
mRS score at first visit	5	3	3	1	5	4	4	2	4
mRS score at last visit	1	2	0	0	2	1	6	4	4
No. of recurrent attacks	2	0	1	1	1	0	0	3	3
Treatment	Steroid, IVIG	Steroid	Steroid	Steroid	Steroid, IVIG	Steroid	Steroid, MTX, MMF	Steroid, AZA, MMF, IVIG	Steroid, IVIG, AZA, MMF, RTX, MTX
Follow-up duration* (months)	88	49	70	30	21	5	1	121	103

*Duration between symptom onset and the first visit to one of our hospitals; †Severity was classified into three categories: mild (Medical Research Council [MRC] grade ≤2), moderate (MRC grade 3), and severe (MRC grade ≥4); *Duration between symptom onset and the last visit to one of our hospitals.

ANA, antinuclear antibody; AZA, azathioprine; CK, creatinine kinase; EM, endomyositis; F, female; IVIG, intravenous immunoglobulin G; M, male; MAA, myositis-associated antibody; MMF, mycophenolate mofetil; mRS, modified Rankin Scale; MSA, myositis-specific antibody; MTX, methotrexate; N/A, not applicable; PF, per fascicular; PV, perivascular; RTX, rituximab; SRP, signal recognition particle.

clinical implications of the anti-Ro52 antibody in patients with seropositivity for IMNM.

Six of our patients (66.7%) had a favorable outcome (modified Rankin Scale [mRS] score=0–2) after treatment at the latest visit. However, three patients (33.3%) had a poor outcome (mRS score ≥ 3) despite receiving aggressive treatment. They included one elderly patient who was in a poor general condition at the initial visit and later died of cytomegalovirus pneumonia. A poor prognosis of anti-SRP myopathy has previously been found in 25%–30% of patients.^{5,6,9} The prognostic factors for anti-SRP myopathy are still unclear. A previous study found that some patients with anti-SRP antibody had at least two immunoglobulin G (IgG) isotypes,¹⁰ most commonly IgG1 (80% of sera), followed by IgG4 (30% of sera).¹⁰ The different IgG isotypes might affect treatment responses and clinical prognoses. Therefore, future studies will need to investigate the prognostic factors and predictors of treatment responses in anti-SRP myopathy.

Our study had some limitations. First, the testing for anti-SRP antibodies was conducted at different time points, which may have influenced the anti-SRP antibody titers in our data. Second, the validation of anti-SRP-positive samples was not checked using other methods such as immunoprecipitation. The line-blot immunoassay has the potential risk of false-positive results, which can therefore not be ruled out completely in our samples. To address this limitation, the enrollment of our study population included comprehensive considerations of clinical, laboratory, and histopathological findings. Third, our assessments of histopathological findings were limited by a reliance on retrospective medical record reviews, and we obtained histopathological data solely from muscle biopsy reports. Further studies with multiple antibody tests and muscle biopsies would be needed to clarify these issues.

In conclusion, this study has demonstrated heterogeneous clinical findings and prognoses in Korean patients with anti-SRP myopathy. Further studies with larger numbers of patients are needed to further elucidate the clinical, laboratory, and histopathological features and prognostic factors in Korean patients with anti-SRP myopathy.

Ethics Statement

This study was approved by the Institutional Review Board (IRB) of Korea University Anam Hospital (IRB No. 2023AN0367). The IRB of Korea University Anam Hospital waived the requirement to obtain written informed consent from participants due to the retrospective study design.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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Conflicts of Interest

Byung-Jo Kim, the Editor-in-Chief of the *Journal of Clinical Neurology*, was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

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