Factors associated with endomysial fibrosis in anti-signal recognition particle antibody immune-mediated necrotising myopathy

J. Yuan[1], M. Yang[1,2], Y. Zheng[1], H. Hao[1], F. Gao[1], W. Zhang[1], Z. Wang[1,3,4], Y. Yuan[1,3,4], Y. Zhao[1]

[1]Department of Neurology, Peking University First Hospital, Beijing;
[2]Department of Neurology, Beijing Jishuitan Hospital, Capital Medical University, Beijing;
[3]Beijing Key Laboratory of Neurovascular Disease Discovery, Beijing;
[4]Rare Disease Medical Center, Peking University First Hospital, Beijing, China.

Abstract

Objective

Anti-signal recognition particle antibody immune-mediated necrotising myopathy (anti-SRP-IMNM) is characterised by prominent muscle weakness and poor neurological outcomes. This study aimed to evaluate the relationship between endomysial fibrosis and the clinical, muscle magnetic resonance imaging (MRI) and myo-pathological features of patients with anti-SRP-IMNM.

Methods

We collected the clinical, imaging, and myo-pathological data of patients diagnosed with anti-SRP-IMNM. Differences between patients with and without increased endomysial fibrosis on muscle biopsy were compared.

Results

Ninety-four patients were included in the study, comprising 12 paediatric and 82 adult patients. The mean age at onset was 41.2±17.3 years. The mean serum creatinine kinase concentration was 6885.8±6300.7 IU/L. MRI revealed muscle oedema in 87.3% of patients and fatty infiltration in 77.5%, which was particularly severe in the muscles of the posterior thigh. Endomysial fibrosis was found in 50% of patients and was significantly associated with early onset (p=0.004), paediatric age (p=0.044), muscle fatty infiltration on MRI of the thigh (p=0.045), and inflammatory cell infiltration on pathology (p<0.05).

Conclusion

In anti-SRP-IMNM, endomysial fibrosis may be the pathological basis of fatty infiltration observed on MRI and may be associated with resistance to immunotherapy.

Key words

anti-signal recognition particle antibodies, immune-mediated necrotising myopathy, endomysial fibrosis, fibrofatty replacement

Jingchu Yuan#, MD
Mengting Yang#, MD
Yiming Zheng, MD
Hongjun Hao, MD
Feng Gao, MD
Wei Zhang, MD
Zhaoxia Wang, MD
Yun Yuan, MD, PhD*
Yawen Zhao, MD*

#contributed equally as co-first authors.
**contributed equally as co-senior authors.*

Please address correspondence to:
Yawen Zhao
Department of Neurology,
Peking University First Hospital,
8 Xishiku Street, Xicheng District,
Beijing 100034, China.
E-mail: 18813187041@163.com

Received on July 6, 2025; accepted in revised form on December 12, 2025.

Funding. This work was supported by the National Natural Science Foundation of China (No.82401636).

Competing interests: none declared.

Introduction

Anti-signal recognition particle (SRP) antibody immune-mediated necrotising myopathy (IMNM) is an autoimmune disorder characterised by the presence of the anti-SRP antibody in serum (1). Compared with other subtypes of myositis, patients with anti-SRP-IMNM tend to present with more severe muscle weakness and a poorer prognosis and require multiple immunosuppressive agents to control the disease (2-5). Our previous study found that quick development of muscle fibrofatty replacement on magnetic resonance imaging (MRI) and greater B cell-activating factor receptor and B lymphocyte infiltration in muscle biopsy samples are closely related to the prognosis of patients with anti-SRP-IMNM and are often an indicator of resistance to immunotherapy (6, 7); however, the pathological mechanism is unclear. Previous studies have revealed that B-lymphocyte and B cell-activating factor are strongly linked to fibrosis in various tissues and conditions (8, 9). Therefore, further study is warranted to determine whether these mechanisms exist in anti-SRP-IMNM. The present study aimed to evaluate the relationship between endomysial fibrosis and the clinical features, muscle MRI findings, and skeletal muscle pathological characteristics in a large cohort of Chinese patients with anti-SRP-IMNM.

Materials and methods

Patients

We retrospectively collected data from patients with anti-SRP-IMNM treated at Peking University First Hospital from January 2010 to February 2023. Based on the 2018 European Neuromuscular Centre criteria, patients meeting the following criteria were diagnosed with anti-SRP-IMNM: presence of anti-SRP autoantibodies, muscle weakness, elevated serum creatine kinase (CK) concentration, and pathological criteria of IMNM (10). Baseline patient demographic characteristics, clinical manifestations, laboratory test results, and medication history were collected from each patient's first visit. Paediatric onset was defined as disease onset before 18 years of age. Disease duration was categorized as subacute when the duration was less than 12 months and chronic when the duration was 12 months or longer (11, 12). Muscle strength was evaluated using the manual muscle strength test 8 based on the modified 0-10-point Kendall grading scale (13). Written informed consent was obtained from all patients. This study was approved by the Clinical Research Ethics Committee of Peking University First Hospital (approval no. 2019-181; date of approval: 21st August 2019).

Detection of myositis autoantibodies

All patients were tested for myositis-specific and myositis-associated autoantibodies using Euroline Myositis Profile immunoblot assays (Euroimmun, Lubeck, Germany) in accordance with the manufacturer's instructions. Serum autoantibodies against SRP were identified and semiquantitatively analysed using densitometry by detecting the 54-kD subunit, as previously described (14). All included patients had an autoantibody concentration of >50 U/L (considered strongly positive).

Muscle MRI

Seventy-one patients underwent MRI of the bilateral thighs during assessment. Among the 71 patients who underwent MRI at our centre, 29 (40.8%) were already receiving immunotherapy, while 42 (59.2%) were treatment-naïve at the time of imaging. Oedema and fibrofatty replacement scores were calculated in the gluteus maximus at the pelvic level and in the thigh muscle groups at the mid-thigh level (anterior group: vastus intermedius, vastus medialis, vastus lateralis, rectus femoris, and sartorius; posterior group: biceps femoris, semitendinosus, and semimembranosus; medial group: adductor magnus, adductor longus, and gracilis). Fibrofatty replacement in each muscle was graded on T1WI sequences in accordance with the scale proposed by Mercuri *et al*. (15). Muscle oedema was graded on T2-STIR sequences on a scale from 0-4 (16).

Muscle pathology

Eighty-seven patients underwent mus-

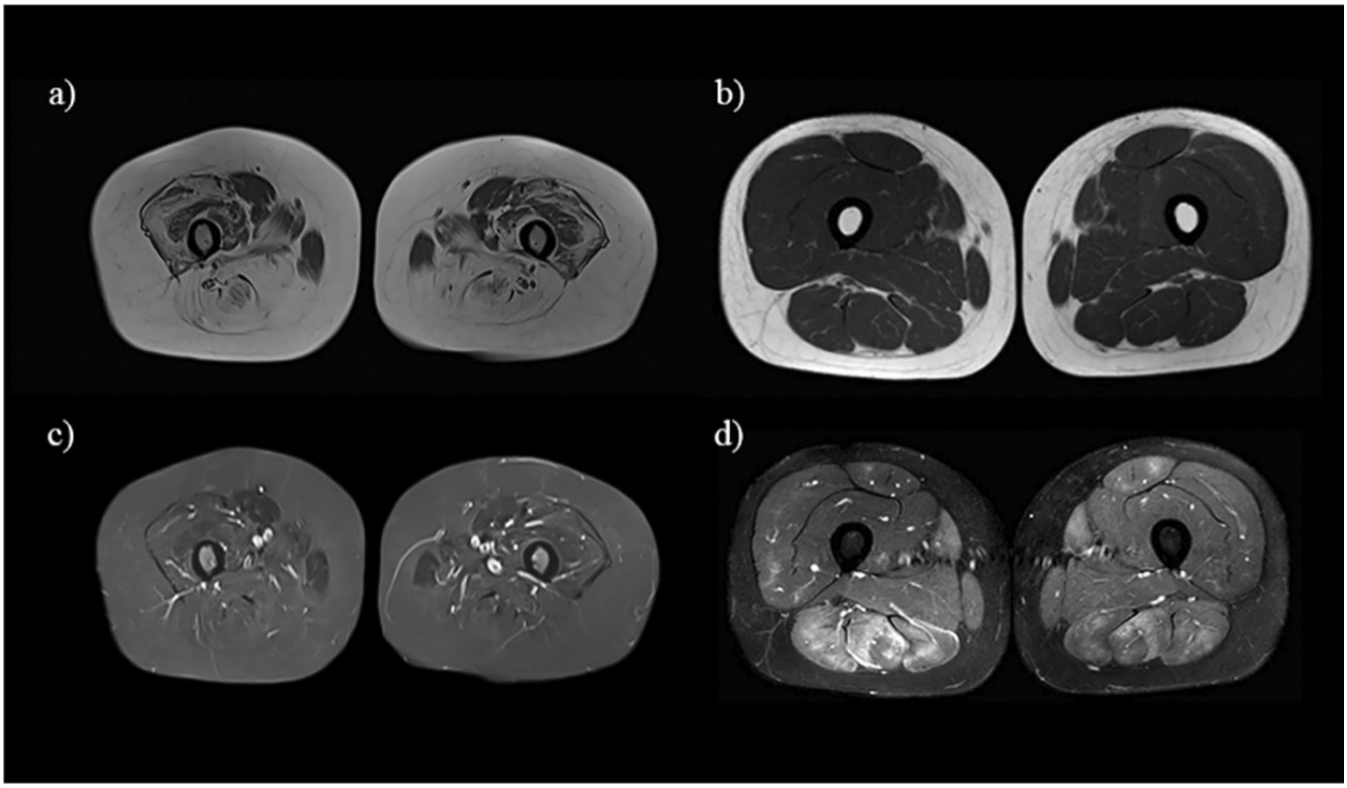

Fig. 1. Muscle MRI in patients with anti-SRP-IMNM. T1-weighted images show muscle atrophy and fatty degeneration (**a, b**), while STIR images demonstrate muscle oedema (**c, d**), particularly in the posterior thigh muscle groups.

cle biopsies for diagnostic purposes. Among the 87 patients who underwent skeletal muscle biopsy at our centre, 34 (39.1%) had initiated treatment elsewhere, while 53 (60.9%) were treatment-naïve at the time of biopsy. Serial frozen sections were stained with haematoxylin and eosin, modified Gomori trichrome, oil red O, periodic acid-Schiff, adenosine triphosphate enzyme (pH 4.5 and 10.8), NADH-tetrazolium reductase, cytochrome C oxidase, and succinate dehydrogenase. The sections were immunohistochemically stained for human major histocompatibility complex class I (MHC-I), membrane attack complex (MAC), CD3, CD4, CD8, CD20, CD68, dystrophin, sarcoglycans, dysferlin, and dystroglycan. Grading of inflammatory cell infiltration and MAC and MHC-I deposition was performed using the criteria proposed by Yang *et al*. (17). Endomysial fibrosis was defined as isolated fibrous tissue deposits located between myofibres and exceeding at least four times that of normal endomysium (18). Based on myo-pathological features, patients were categorised as having anti-SRP-IMNM with or without increased endomysial fibrosis in muscle biopsy specimens. We then compared the clinical, pathological, and imaging features between the two groups.

Statistical analysis

All statistical analyses were performed using SPSS version 26.0 software (SPSS, Chicago, Illinois, USA), with significance set at the 5% level. Q-Q plots were used to assess the normality of data distribution. The clinical, MRI, and pathological features were compared between the two groups using both univariate and binary logistic regression analyses. For variables that were normally distributed, continuous clinical and demographic data were compared using one-way analysis of variance or the Student's t-test for comparisons between subgroups. Categorical variables were analysed using the χ^2 test, Fisher's exact test, Kruskal-Wallis one-way analysis of variance by ranks, or Mann-Whitney U test. For non-normally distributed data, the Kruskal-Wallis test with Dunn's correction was used for multiple comparisons.

Results

Clinical features

The demographic and clinical features of the 94 patients with anti-SRP-IMNM are summarised in Supplementary Table S1. The cohort consisted of 30 males and 64 females. The mean onset age was 41.2±17.3 years (range 3-73 years), and paediatric onset was found in 12 (12.7%) patients. The mean disease duration was 13.0±18.6 months (range 0.5-120 months) (Fig. 1). Subacute onset was observed in 55 patients (58.5%), while chronic onset occurred in 39 patients (41.5%). The initial symptom was limb or trunk weakness in 65 (69.1%) patients, bulbar symptoms such as difficulty swallowing in 7 (7.44%) patients, and myalgia in 14 (14.9%) patients. The muscle weakness was typically proximal-dominant and symmetrical. Seventy-four patients (78.7%) experienced neck weakness, and 41 patients (43.6%) presented with dysphagia. The mean serum CK concentration was 6885.8±6300.7 IU/L (range: 574-28,819 IU/L). Interstitial lung disease (ILD) was observed in 28 of 78 patients (38.4%).

Immunotherapy-related data were available for 72 patients, with a median interval of 9.2 months from disease onset to the initiation of treatment. Treatment strategies were individualised based on patients' clinical conditions and therapeutic responses, and detailed information is provided in Supplementary Table S1. Glucocorticoids (GC) were the most commonly used first-line agent for anti-SRP-positive IMNM, administered to 67 of 72 patients (93.0%). The majority of these patients (36/72, 50.0%) received triple therapy consisting of GC, intravenous immunoglobulin (IVIG), and steroid-sparing immunosuppressants. Notably, 65 patients (90.3%) required maintenance therapy with two or more immunotherapeutic agents, while 4 patients (5.56%) underwent plasma exchange as part of their treatment course.

Muscle MRI findings

The muscle MRI findings in patients with anti-SRP-IMNM are summarized in Supplementary Table S2. Muscle oedema was observed in 62 patients (87.3%), with the adductor magnus being the most severely affected (mean score =1.85), followed by the semimembranosus (mean score =1.73), gluteus maximus (mean score =1.48), and vastus lateralis (mean score =1.41). Fibrofatty replacement was present in 55 patients (77.5%) and was most prominent in the gluteus maximus (mean score =1.44), followed by the semimembranosus (mean score =1.14) and adductor magnus (mean score =1.11). The posterior region of the thigh was the most severely affected by both fibrofatty replacement (mean score =1.07) and oedema (mean score =1.47).

Muscle pathology

The muscle biopsy findings are summarised in Table I. The average interval between symptom onset and muscle biopsy was 13.6 months. Muscle fibre necrosis, regeneration, and atrophy were observed in most patients (84.7%, 96.5% and 98.8%, respectively). Increased endomysial fibrosis was observed in 43 of 86 patients (50.0%). Multifocal MHC-I overexpression occurred in 76 of 79 patients (94.0%), with a median grading of 3 (range, 0-4). There was MAC deposition in necrotic fibres in 51 of 72 patients (70.8%), in the sarcolemma of non-necrotic fibres in 49 of 75 patients (65.3%), and around endomysial capillaries in 23 of 75 patients (30.7%). CD68-positive macrophage infiltration was present in 77 of 79 patients (97.5%), with a median grading of 2 (range 0-3). Infiltration of CD3, CD4, CD8, and CD20-positive lymphocytes was observed in 46 of 67 patients (68.7%), 52 of 69 patients (75.4%), 48 of 78 patients (61.5%), and 12 of 78 patients (15.4%), respectively. The median grading for these lymphocyte infiltrations was 1, 1, 1, and 0, respectively.

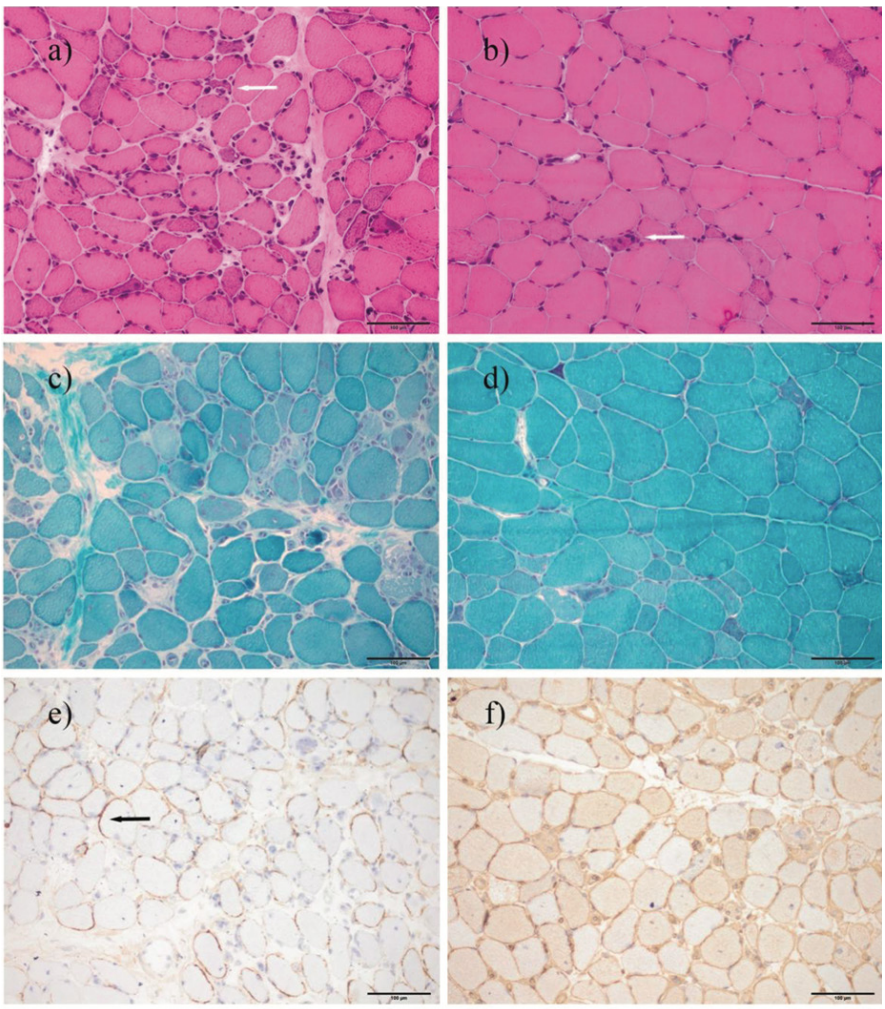

Fig. 2. Muscle pathology of patients with anti-SRP-IMNM (×10). Haematoxylin and eosin staining shows muscle fibre necrosis and regeneration (**a, b**: white arrow). Modified Gomori trichrome staining reveals different grades of endomysial hyperplasia (**c, d**). MAC immunohistochemical staining demonstrates complement deposition in non-necrotic muscle fibres (**e**, black arrow). MHC-I immunohistochemical staining indicates upregulated expression of MHC-I on the membrane and in the cytoplasm of scattered muscle fibres (**f**).

Intergroup comparisons

Table II shows the clinical, muscle MRI, and myo-pathological features of patients with or without increased endomysial fibrosis. Forty-three patients (50.0%) exhibited significantly increased endomysial fibrosis compared with patients without endomysial fibrosis (p=0.044). The mean age at onset was younger in patients with endomysial fibrosis compared with those without (35.7±17.5 years *vs*. 45.9±13.7 years; p=0.004). ILD was less common in patients with increased endomysial fibrosis than in those without endomysial fibrosis (22.9% *vs*. 51.5%; p=0.014). Patients with increased endomysial fibrosis also had higher fibrofatty replacement scores in the rectus

Table I. Pathological findings of skeletal muscle in patients with anti-signal recognition particle antibody immune-mediated necrotizing myopathy.

Pathological features of skeletal muscle	n/N (%)	grading (median, range)
Myofibre necrosis	72/85 (84.7)	-
Myofibre regeneration	82/85 (96.5)	-
Myofibre atrophy	84/85 (98.8)	-
Increased endomysial fibrosis	43/86 (50.0)	-
COX-negative myofibres	14/81 (17.3)	-
Abnormal lipid deposition	63/85 (74.1)	-
Decreased membrane proteins expression	16/76 (21.1)	-
MHC-1 overexpression	76/79 (96.2)	3 (0-4)
Necrotic sarcolemma MAC deposition	51/72 (70.8)	1 (0-4)
Non-necrotic sarcolemma MAC deposition	49/75 (65.3)	1 (0-4)
Endomysial capillary MAC deposition	23/75 (30.7)	0 (0-4)
Inflammatory cell infiltration		
CD68 positive cells infiltration	77/79 (97.5)	2 (0-3)
CD3 positive lymphocytes infiltration	46/67 (68.7)	1 (0-3)
CD4 positive lymphocytes infiltration	52/69 (75.4)	1 (0-3)
CD8 positive lymphocytes infiltration	48/78 (61.5)	1 (0-3)
CD20 positive lymphocytes infiltration	12/78 (15.4)	0 (0-3)

IQR: interquartile range; CK: serum creatinine kinase concentration. *$p<0.05$.

Table II. Comparison of patients with anti-signal recognition particle antibody immune-mediated necrotising myopathy with or without endomysial fibrosis.

	Increased endomysial fibrosis in muscle pathology		
	No (n=43)	Yes (n=43)	*p*
Females, n (%)	25 (58.1)	33 (76.7)	0.03*
Age at disease onset, mean (±SD)	46.0±13.7	35.6±17.5	0.018*
Juvenile onset, n (n%)	2 (4.65)	8 (18.6)	0.044*
Disease duration, median [IQR]	6.000[3.000,12.000]	9.000[5.000,18.000]	0.235
Dysphagia, n (%)	18 (41.9)	24 (55.8)	0.196
Neck weakness, n (%)	32 (74.4)	34 (79.1)	0.610
Interstitial lung disease, n (%)	17 (51.5)	8 (22.9)	0.014*
Peak CK, median [IQR]	5031.0 [3008.0,7377.0]	6632.00 [3954.00,9683.00]	0.112
Score of fibrofatty replacement in gluteus maximus, median [IQR]	1.00 [0.00,2.00]	2.00 [1.00,3.00]	0.069
Score of fibrofatty replacement in rectus femoris; muscle, median [IQR]	0.00 [0.00, 1.00]	0.00 [0.00, 1.00]	0.045*
CD3+ lymphocytes infiltration, median [IQR]	1.00 [0.00,1.00]	2.00 [0.00,2.00]	<0.001*
CD4+ lymphocytes infiltration, median [IQR]	1.00[0.00, 2.00]	2.00[1.00, 3.00]	0.045*
CD8+ lymphocytes infiltration, median [IQR]	1.00 [0.00,1.00]	2.00 [0.00,3.00]	0.126
CD68+ positive cells infiltration, median [IQR]	2.00 [2.00, 3.00]	3.00 [2.00, 4.00]	0.0034*
CD20+ lymphocytes infiltration, median [IQR]	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.045*

COX: cytochrome C oxidase; MHC-1: major histocompatibility complex class I; MAC: membrane attack complex.

femoris muscle compared with those without fibrosis (mean 0.00, IQR 0.00–1.00 *vs*. mean 0.00, IQR 0.00–1.00; $p=0.045$). The grades of $CD3^+$, $CD4^+$, and $CD20^+$ lymphocyte infiltration, and $CD68^+$ macrophage infiltration were significantly higher in patients with increased endomysial fibrosis compared with those without ($p<0.001$, $p=0.045$, $p=0.034$, and $p=0.045$, respectively).

Discussion

Patients who tested positive for anti-SRP antibodies tended to have a poor prognosis. A previous study reported that 77% of patients anti-SRP-IMNM with require additional immunotherapy alongside prednisone, and more than half are refractory to various treatment regimens (12). In our cohort, the proportion of patients with refractory anti-SRP-IMNM was relatively high (83.3%), and most patients required long-term immunotherapy, often involving more than two treatment regimens. Paediatric IMNM is a rare subgroup, accounting for only 2.9% in juvenile idiopathic IIM (19). Several cases of paediatric onset have been reported in anti-SRP-IMNM (20-22), and paediatric onset was observed in 12 (12.7%) patients in our study. The difference in the prevalence of anti-SRP-IMNM between paediatric and adult patients might come from the underdiagnosis of paediatric anti-SRP-IMNM owing to its relatively slow onset and dystrophic pattern of muscle pathology, which makes the diagnosis challenging in paediatric patients (20). It has been suggested that early identification and prompt treatment of anti-SRP-IMNM are necessary for better outcomes (20), and that patients with paediatric onset require more aggressive therapy (21).

On muscle MRI, 77.5% of patients exhibited fibrofatty replacement, which is a much higher prevalence than the 38% reported in an American study (22). Previous studies have suggested that fibrofatty replacement is a compensatory response to muscle damage that typically occurs in the chronic stage of inflammatory myopathies (6, 23-26). Moreover, muscle fibrofatty replacement is closely related to the prognosis of patients with anti-SRP-IMNM and is often considered a marker of poor response to immunotherapy (6, 7). Additionally, previous studies have proposed that endomysial fibrosis in muscle biopsies may serve as the pathological basis for the fibrofatty replacement seen on muscle MRI (6), suggesting that endomysial fibrosis could be linked to the prognosis of anti-SRP-IMNM.

In the present study, muscle biopsies of patients with anti-SRP-IMNM showed that necrotising myopathy was still the predominant form, while deposition around endomysial capillaries occurred in 30.7% of our patients, similar to the 26%-31% reported previously (3, 23). In our cohort, half of the patients had increased endomysial fibrosis on muscle biopsy, a finding that has been less frequently reported in the literature. Intergroup comparisons showed that early disease onset, paediatric onset, fibrofatty replacement on MRI, and inflammatory cell infiltration in muscle pathology were associated with endomysial fibrosis. Of note, these factors overlap with those previously linked to poor outcomes

(7, 12), suggesting that endomysial fibrosis on muscle biopsy may underlie disease refractoriness. In patients with Duchenne muscular dystrophy, factors influencing muscle fibrofatty replacement are critical contributors to clinical variability, and endomysial fibrosis in muscle biopsy is associated with poor clinical outcome (18, 24, 25). Fibrous and adipose tissues in skeletal muscle originate from the FAPs, which can be triggered by muscle inflammation response, genetic modifiers, and some microRNAs under pathological conditions and differentiate into fibrous and adipose tissues (24, 25, 27). In inclusion body myositis, skeletal muscle cell dysfunction may be linked to FAP senescence by a change in the collagen composition of the latter (28). Further study is warranted to determine whether these mechanisms exist in IMNM.

Our study has several limitations. First, although our findings suggest that anti-SRP-IMNM is more prevalent in Chinese paediatric patients compared with other ethnic populations, we did not explore the underlying causes of the disease in children, particularly the genetic factors that may contribute to its onset. Second, while we observed that patients with refractory anti-SRP-IMNM exhibited endomysial fibrosis, the underlying cause of this pathology remains unclear. Further investigation is needed to explore these mechanisms. Third, we did not examine which drug combinations might delay the progression of fibrofatty replacement or endomysial fibrosis, which is a critical area for future research.

Conclusion

Early disease onset, paediatric onset, fibrofatty replacement on MRI, and inflammatory cell infiltration in muscle pathology were associated with endomysial fibrosis in anti-signal recognition particle antibody immune-mediated necrotising myopathy. endomysial fibrosis in anti-SRP-IMNM may be the pathological basis of fibrofatty replacement observed on MRI and may be an indicator of disease refractory.

Acknowledgments

We are thankful to all the patients for participation in this study. We would like to acknowledge Dr. Jing Liu, Dr. Yuewan Zou, and Dr. Qingqing Liu at Laboratory of Neuropathology and Molecular Biology for preparing muscle biopsy. We thank Kelly Zammit, BVSc, from Liwen Bianji (Edanz) (www.liwenbianji.cn/), for editing the English text of a draft of this manuscript.

References

1. BETTERIDGE Z, MCHUGH N: Myositis-specific autoantibodies: an important tool to support diagnosis of myositis. *J Intern Med* 2016; 280(1): 8-23. https://doi.org/10.1111/joim.12451
2. PINAL-FERNANDEZ I, PARKS C, WERNER JL *et al*.: Longitudinal Course of Disease in a Large Cohort of Myositis Patients with Autoantibodies Recognizing the Signal Recognition Particle. *Arthritis Care Res* (Hoboken) 2017; 69(2): 263-70. https://doi.org/10.1002/acr.22920
3. WATANABE Y, URUHA A, SUZUKI S *et al*.: Clinical features and prognosis in anti-SRP and anti-HMGCR necrotising myopathy. *J Neurol Neurosurg Psychiatry* 2016; 87(10): 1038-44. https://doi.org/10.1136/jnnp-2016-313166
4. MA X, XU L, JI S, LI Y, BU B: The Clinicopathological Distinction Between Seropositive and Seronegative Immune-Mediated Necrotizing Myopathy in China. *Front Neurol* 2021; 12: 670784. https://doi.org/10.3389/fneur.2021.670784
5. KAO AH, LACOMIS D, LUCAS M, FERTIG N, ODDIS CV: Anti-signal recognition particle autoantibody in patients with and patients without idiopathic inflammatory myopathy. *Arthritis Rheum* 2004; 50(1): 209-15. https://doi.org/10.1002/art.11484
6. ZHENG Y, LIU L, WANG L *et al*.: Magnetic resonance imaging changes of thigh muscles in myopathy with antibodies to signal recognition particle. *Rheumatology* (Oxford) 2015; 54(6): 1017-24. https://doi.org/10.1093/rheumatology/keu422
7. ZHAO Y, ZHANG W, LIU Y, WANG Z, YUAN Y: Factors associated with refractory autoimmune necrotizing myopathy with anti-signal recognition particle antibodies. *Orphanet J Rare Dis* 2020; 15(1): 181. https://doi.org/10.1186/s13023-020-01431-7
8. DONG P, MEI C, YANG Y *et al*.: Blocking BAFF Alleviates Hepatic Fibrosis in Schistosoma japonicum-Infected Mice. *Pathogens* 2023; 12(6). https://doi.org/10.3390/pathogens12060793
9. MATSUSHITA T, KOBAYASHI T, MIZUMAKI K *et al*.: BAFF inhibition attenuates fibrosis in scleroderma by modulating the regulatory and effector B cell balance. *Sci Adv* 2018; 4(7): eaas9944. https://doi.org/10.1126/sciadv.aas9944
10. ALLENBACH Y, MAMMEN AL, BENVENISTE O *et al*.: Clinico-sero-pathological classification of immune-mediated necrotizing myopathies Zandvoort, The Netherlands, 14-16 October 2016. *Neuromuscul Disord* 2018; 28(1): 87-99. https://doi.org/10.1016/j.nmd.2017.09.016
11. YANG HX, TIAN XL, JIANG W *et al*.: [Clinical and pathological characteristics of immune mediated necrotizing myopathy]. *Beijing Da Xue Xue Bao Yi Xue* Ban 2019; 51(6): 989-95. https://doi.org/10.19723/j.issn.1671-167X.2019.06.002
12. SUZUKI S, NISHIKAWA A, KUWANA M *et al*.: Inflammatory myopathy with anti-signal recognition particle antibodies: case series of 100 patients. *Orphanet J Rare Dis* 2015; 10: 61. https://doi.org/10.1186/s13023-015-0277-y
13. RIDER LG, WERTH VP, HUBER AM *et al*.: Measures of adult and juvenile dermatomyositis, polymyositis, and inclusion body myositis: Physician and Patient/Parent Global Activity, Manual Muscle Testing (MMT), Health Assessment Questionnaire (HAQ)/Childhood Health Assessment Questionnaire (C-HAQ), Childhood Myositis Assessment Scale (CMAS), Myositis Disease Activity Assessment Tool (MDAAT), Disease Activity Score (DAS), Short Form 36 (SF-36), Child Health Questionnaire (CHQ), physician global damage, Myositis Damage Index (MDI), Quantitative Muscle Testing (QMT), Myositis Functional Index-2 (FI-2), Myositis Activities Profile (MAP), Inclusion Body Myositis Functional Rating Scale (IBMFRS), Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), Cutaneous Assessment Tool (CAT), Dermatomyositis Skin Severity Index (DSSI), Skindex, and Dermatology Life Quality Index (DLQI). *Arthritis Care Res* (Hoboken) 2011;63 Suppl 11(0 11): S118-57. https://doi.org/10.1002/acr.20532
14. ZHAO Y, LIU X, ZHANG W, YUAN Y: Childhood autoimmune necrotizing myopathy with anti-signal recognition particle antibodies. *Muscle Nerve* 2017; 56(6): 1181-7. https://doi.org/10.1002/mus.25575
15. MERCURI E, CINI C, PICHIECCHIO A *et al*.: Muscle magnetic resonance imaging in patients with congenital muscular dystrophy and Ullrich phenotype. *Neuromuscul Disord* 2003; 13(7-8): 554-8. https://doi.org/10.1016/s0960-8966(03)00091-9
16. MORROW JM, MATTHEWS E, RAJA RAYAN DL *et al*.: Muscle MRI reveals distinct abnormalities in genetically proven non-dystrophic myotonias. *Neuromuscul Disord* 2013; 23(8): 637-46. https://doi.org/10.1016/j.nmd.2013.05.001
17. YANG M, JI S, XU L *et al*.: The Clinicopathological Distinction between Immune-Mediated Necrotizing Myopathy and Limb-Girdle Muscular Dystrophy R2: Key Points to Prevent Misdiagnosis. *J Clin Med* 2022; 11(21). https://doi.org/10.3390/jcm11216566
18. DESGUERRE I, MAYER M, LETURCQ F, BARBET JP, GHERARDI RK, CHRISTOV C: Endomysial fibrosis in Duchenne muscular dystrophy: a marker of poor outcome associated with macrophage alternative activation. *J Neuropathol Exp Neurol* 2009; 68(7): 762-73. https://doi.org/10.1097/NEN.0b013e3181aa31c2
19. KISHI T, RIDER LG, PAK K *et al*.: Association of Anti-3-Hydroxy-3-Methylglutaryl-Coenzyme A Reductase Autoantibodies with

DRB1*07:01 and Severe Myositis in Juvenile Myositis Patients. *Arthritis Care Res* (Hoboken) 2017;69(7):1088-94. https://doi.org/10.1002/acr.23113
20. WANG CH, LIANG WC: Pediatric immune-mediated necrotizing myopathy. *Front Neurol* 2023; 14: 1123380. https://doi.org/10.3389/fneur.2023.1123380
21. BINNS EL, MORAITIS E, MAILLARD S *et al*.: Effective induction therapy for anti-SRP associated myositis in childhood: A small case series and review of the literature. *Pediatr Rheumatol Online J* 2017; 15(1): 77. https://doi.org/10.1186/s12969-017-0205-x
22. PINAL-FERNANDEZ I, CASAL-DOMINGUEZ M, CARRINO JA *et al*.: Thigh muscle MRI in immune-mediated necrotising myopathy: extensive oedema, early muscle damage and role of anti-SRP autoantibodies as a marker of severity. *Ann Rheum Dis* 2017; 76(4): 681-7. https://doi.org/10.1136/annrheumdis-2016-210198
23. MERLONGHI G, ANTONINI G, GARIBALDI M: Immune-mediated necrotizing myopathy (IMNM): A myopathological challenge. *Autoimmun Rev* 2022; 21(2): 102993. https://doi.org/10.1016/j.autrev.2021.102993
24. UEZUMI A, ITO T, MORIKAWA D *et al*.: Fibrosis and adipogenesis originate from a common mesenchymal progenitor in skeletal muscle. *J Cell Sci* 2011; 124(Pt 21): 3654-64. https://doi.org/10.1242/jcs.086629
25. HOFFMAN EP: Causes of clinical variability in Duchenne and Becker muscular dystrophies and implications for exon skipping therapies. *Acta Myol* 2020; 39(4): 179-86. https://doi.org/10.36185/2532-1900-020
26. FIONDA L, LAULETTA A, LEONARDI L *et al*.: Muscle MRI in immune-mediated necrotizing myopathy (IMNM): implications for clinical management and treatment strategies. *J Neurol* 2023; 270(2): 960-74. https://doi.org/10.1007/s00415-022-11447-7
27. SUGIHARA H, TERAMOTO N, NAKAMURA K *et al*.: Cellular senescence-mediated exacerbation of Duchenne muscular dystrophy. *Sci Rep* 2020; 10(1): 16385. https://doi.org/10.1038/s41598-020-73315-6
28. NELKE C, SCHROETER CB, THEISSEN L *et al*.: Senescent fibro-adipogenic progenitors are potential drivers of pathology in inclusion body myositis. *Acta Neuropathol* 2023; 146(5): 725-45. https://doi.org/10.1007/s00401-023-02637-2