Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Anti-Signal Recognition Particle-Positive Immune-Mediated Necrotizing Myopathy with Acute Inpatient Myocarditis and Pharyngeal Involvement in a Young Adult: A Case Highlighting the Importance of Early Biologic Escalation – A Case Report

Bhvika Zutshi

bhvikazutshi@gmail.com

Maulana Azad Medical College

Sandeep Garg

Maulana Azad Medical College

Praveen Bharti

Maulana Azad Medical College

Sourav Kumar

Maulana Azad Medical College

Amit Kumar

Maulana Azad Medical College

Annesha Chakraborty

Maulana Azad Medical College

Mahima Mehra

Maulana Azad Medical College

Bhavya Bhutani

Maulana Azad Medical College

Arpit Singh Chahal

Maulana Azad Medical College

Vayan Raj

Maulana Azad Medical College

Case Report

Keywords: Immune-mediated necrotizing myopathy, Anti-signal recognition particle antibody, Myocarditis, Cardiac involvement, Rituximab, Inflammatory myopathy, IMNM, Anti-SRP

Posted Date: August 28th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10398087/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Immune-mediated necrotizing myopathy (IMNM) is a rare and clinically severe subtype of idiopathic inflammatory myopathy, characterised by predominant myofibre necrosis with a paucity of lymphocytic infiltration. Anti-signal recognition particle (anti-SRP)-positive IMNM represents a particularly aggressive disease phenotype, frequently resistant to corticosteroid monotherapy and complicated by extramuscular manifestations, of which cardiac involvement remains under-recognised.

Case Presentation:

We report a 26-year-old Indian woman who presented with a two-month history of symmetric, insidious-onset proximal limb weakness, one month of truncal weakness, and ten days of dysphagia. Investigations revealed markedly elevated creatine kinase (peak 7,112 IU/L), anti-SRP antibody positivity on a myositis-specific line-blot panel, concurrent strong positivity for anti-Ro52 and anti-SS-A antibodies without fulfilling criteria for Sjögren's syndrome, a myopathic electromyogram, and muscle biopsy findings of necrotising autoimmune myopathy. Concurrent corticosteroid and methotrexate therapy produced clinical deterioration. On the eighth inpatient day, probable immune-mediated myocarditis supervened, manifest as sinus bradycardia, anterior T-wave inversions, and a positive cardiac troponin T (cTnT) in the absence of wall-motion abnormality on echocardiography. Sequential immunosuppressive escalation encompassing pulse methylprednisolone, intravenous immunoglobulin (IVIg), and rituximab was required, resulting in near-complete normalisation of creatine kinase and recovery to MRC grade 4+/5 power at four months.

Conclusion

This case illustrates the cardinal features of anti-SRP IMNM i.e. early extramuscular involvement, steroid refractoriness, and the necessity of timely biologic escalation, and highlights cardiac involvement as an under-recognised, prognostically significant complication that warrants proactive surveillance.

INTRODUCTION

Idiopathic inflammatory myopathies (IIM) encompass a heterogeneous group of acquired, immune-mediated skeletal muscle diseases affecting approximately 2–25 individuals per 100,000 population.[1] Immune-mediated necrotizing myopathy (IMNM), classified as a distinct IIM subtype by the 224th European Neuromuscular Centre (ENMC) International Workshop in 2016, accounts for approximately 10–19% of all IIM.[2,3] Unlike dermatomyositis or antisynthetase syndrome, IMNM is defined histopathologically by predominantly myofibre necrosis and regeneration, sparse lymphocytic infiltrate,

macrophage-dominated inflammation, and variable sarcolemmal upregulation of MHC class I antigens, in the absence of primary autoimmune inflammation at the endomysium.[2]

Among IMNM subtypes, those positive for anti-signal recognition particle (anti-SRP) autoantibodies represent a phenotypically severe cohort. The signal recognition particle is a ubiquitous cytoplasmic ribonucleoprotein complex involved in co-translational protein targeting to the endoplasmic reticulum; autoimmunity against its 54-kDa subunit (SRP54) drives the myopathic process through complement-mediated myonecrosis.[4] Anti-SRP IMNM is characterised by early-onset severe proximal weakness, high creatine kinase (CK) elevations often exceeding 10 times the upper limit of normal, truncal and pharyngeal muscle involvement, and frequent extramuscular manifestations including interstitial lung disease, arthritis, and increasingly recognised cardiac involvement.[4]

Cardiac involvement in anti-SRP IMNM encompasses a spectrum from subclinical electrocardiographic abnormalities and mild troponin elevations to overt dilated cardiomyopathy and acute myocarditis, with reported frequencies ranging from 2% to over 52% depending on cohort and ascertainment methodology.[5] Notwithstanding these figures, myocarditis presenting as an inpatient complication of anti-SRP IMNM despite treatment, rather than as the initial manifestation remains infrequently reported and adds considerable prognostic weight.

Herein, we report a 26-year-old Indian woman with anti-SRP-positive IMNM who developed probable immune mediated myocarditis during admission, exhibited progressive disease despite conventional immunosuppression, and ultimately responded to rituximab - a case that illustrates the multisystem severity of anti-SRP disease, raises important diagnostic considerations regarding troponin interpretation in myopathy, and underscores the value of early biologic escalation.

CASE PRESENTATION

Patient information: A 26-year-old right-handed Indian woman, a homemaker educated to the higher-secondary level, resident of New Delhi, presented to the Emergency Department with sequentially evolving symptoms: two months of progressive symmetric proximal weakness, of all 4 limbs, one month of truncal weakness, and ten days of dysphagia. She was vegetarian, a non-smoker, and denied alcohol or illicit substance use. She had no prior history of hypertension, diabetes mellitus, thyroid disease, or ischaemic heart disease; no history of statin use or recent vaccination; no significant family history; and was the product of a non-consanguineous union.

Clinical presentation

On presentation, she was conscious and oriented (GCS E4V5M6). Vitals were notable for a blood pressure of 104/70 mmHg, pulse rate 90 beats per minute with regular rhythm, and oxygen saturation 98% on room air. General examination revealed no pallor, icterus, clubbing, peripheral lymphadenopathy, cyanosis, or pitting oedema. Dermatological examination was unremarkable, specifically no Gottron's papules, heliotrope rash, mechanic's hands, shawl sign, V-sign, calcinosis cutis, or periungual

telangiectasias were identified. There was no scapular winging, kyphoscoliosis, or superficial lymphadenopathy.

Neurological examination demonstrated normal higher cognitive functions, intact cranial nerves I through XII, including a present gag reflex, central tongue, and preserved sternocleidomastoid function, with no ptosis, ophthalmoplegia, or facial asymmetry. Motor examination revealed normal tone throughout. Power was graded at MRC 3/5 across the shoulder joint (abduction, flexion, extension) bilaterally and 3/5 across the hip joint (flexion, extension, abduction) bilaterally, with full 5/5 power preserved at the elbow, wrist, knee, and ankle in all planes. Neck flexors and extensors were weak. No muscle atrophy, fasciculations, or pseudohypertrophy was observed. Deep tendon reflexes were normal and symmetric at all tested stations; plantar responses were flexor bilaterally. Sensory examination was intact for all primary and cortical modalities. The gait was waddling with a normal base. Cerebellar examination and signs of meningeal irritation were absent.

Systemic examination revealed bilateral vesicular breath sounds without added sounds, normal heart sounds without murmurs, and a soft, non-tender abdomen without organomegaly.

Diagnostic assessment

Baseline haematological parameters demonstrated haemoglobin 12.2 g/dL, total leucocyte count 6,900/µL (neutrophils 74%, lymphocytes 12%, eosinophils 3%), and platelet count 215,000/µL. Renal and liver function tests were within normal limits (serum creatinine 0.3 mg/dL, AST 28 IU/L, ALT 20 IU/L), with a mildly elevated alkaline phosphatase of 172 IU/L. Serum sodium and potassium were 136 mEq/L and 4 mEq/L respectively. Serum calcium and phosphate were 8.1 mg/dL and 3.6 mg/dL, respectively. (Table 1) The erythrocyte sedimentation rate was notably low at 6 mm/hour, and C-reactive protein was 6 mg/L, reflecting the characteristic hypo-inflammatory laboratory profile of IMNM, which paradoxically contrasts with the severity of muscle necrosis. Lactate dehydrogenase was 118 IU/L. Total CK on admission was markedly elevated at 5,882 IU/L, with CK-MB 290 IU/L (Table 2)

Table 1
Relevant investigations

Investigation	Value	Reference Range
Haemoglobin	12.2	12–15 g/dL
Total leucocyte count	6900	4.5–11 $\times 10^3/\mu L$
Differential leucocyte count	N 74% L 12% M 3%	N 40–75%, L 20–45%, M 2–10%, E 1–6%
Platelets	215	150–450 $\times 10^3/\mu L$
Blood urea	16	19–43 mg/dL
Serum creatinine	0.3	0.52–1.04 mg/dL
Serum sodium	136	135–145 mEq/L
Serum potassium	4	3.5–5.5 mEq/L
Serum calcium (total)	8.1	8.4–10.2 mg/dL
Serum phosphorus	3.6	2.5–4.5 mg/dL
CK-Total	5882	30–135 IU/L
CK-MB	290	0–25 IU/L
Serum magnesium	2.1	1.6–2.3 mg/dL
Serum iPTH	100	13.6–85.8 pg/mL
Serum Vitamin D	< 8	Deficient < 20 ng/mL
Serum angiotensin converting enzyme (ACE)	22	8–25IU/L
Serum total/direct bilirubin	Total: 1.1 Direct: 0.2	Total: 0.2–1.3 mg/dL Direct: 0–0.3 mg/dL
Serum aspartate aminotransferase	28	14–36 U/L
Serum alanine aminotransferase	20	5–35 U/L
Serum alkaline phosphatase	172	50–117 U/L
Serum gamma glutamyl transferase	39	12–43 U/L
Serum total protein	6.8	6.3–8.2 g/dL
Serum albumin	3.7	3.5–5 g/dL
T3	5.7	4.26–8.10 pmol/L

Investigation	Value	Reference Range
T4	18.4	10.0–28.2 pmol/L
TSH	4.0	0.465–4.68 mIU/L

Thyroid function tests were within normal limits (T3 5.7 pmol/L, T4 18.4 pmol/L, TSH 4.0 mIU/L). Eight AM serum cortisol was 231 nmol/L. Vitamin B12 was low at 160 pg/mL. Vitamin D was severely deficient at < 8 ng/mL, with consequent secondary hyperparathyroidism (PTH 100 pg/mL). HIV, hepatitis B surface antigen, and hepatitis C antibody were non-reactive. Rheumatoid factor was negative; serum angiotensin-converting enzyme was 22 U/L (within the normal range, effectively excluding sarcoidosis). Antinuclear antibody (ANA), assessed by line-blot immunoassay and indirect immunofluorescence (IIF) using HEp-2 cells, returned positive at a 1:100 dilution with a dual IIF pattern: nuclear coarse speckled (4+) and cytoplasmic fine speckled (4+). The cytoplasmic fine speckled pattern on IIF is characteristic of anti-SRP antibodies and independently supported the subsequent line-blot result. The full 14-antigen ANA profile demonstrated strong positivity for anti-SS-A/Ro-60 (intensity 76; +++), anti-Ro52/TRIM21 (intensity 81; +++), and anti-SS-B/La (intensity 14; +). All other antigens, including anti-RNP/Sm, anti-Sm, anti-Scl-70, anti-PM-Scl100, anti-Jo-1, anti-centromere B, anti-PCNA, anti-dsDNA, anti-nucleosomes, anti-histones, anti-ribosomal P, and anti-AMA-M2 were negative. Schirmer's test was negative; there were no symptoms or objective findings to support Sjögren's syndrome. The myositis-specific line-blot panel confirmed anti-SRP antibody positivity; anti-HMGCR and all other myositis-specific antibodies were negative. Tumour markers (AFP 1.3 ng/mL, CEA 0.67 ng/mL, CA 19 – 9 30.6 IU/mL, CA-125 24.8 IU/mL) were within normal limits. Ultrasonography of the whole abdomen and pelvis was normal. These investigations collectively excluded a paraneoplastic aetiology.

Nerve conduction studies were normal. Electromyography (EMG) of the proximal limb musculature demonstrated a myopathic pattern characterised by short-duration, low-amplitude polyphasic motor unit potentials without fibrillation potentials or positive sharp waves at rest, consistent with a primary myopathic process without significant ongoing denervation. **(**Fig. 1**)**

Open biopsy of the left vastus lateralis (quadriceps femoris), performed on Day 2 of admission demonstrated the following: maintained fascicular and myofibrillary architecture with variation in fibre size; isolated myofibre necrosis with peripherally sited nuclei and absence of internalisation; infiltrating macrophages positive for CD68 on immunohistochemistry; and focal sarcolemmal overexpression of HLA class I (MHC-I) in necrotic and atrophic fibres. Lymphocytic infiltration was absent; specifically, CD4+, CD8+, CD20+, and HLA class II-positive cells were not identified. No glycogen (PAS-negative) or lipid (Oil Red O-negative) deposits were demonstrated on special stains; Gomori trichrome revealed no ragged red fibres. Enzyme histochemistry (succinate dehydrogenase, NADH) showed a normal checkerboard pattern of type I and type II fibres. A notable ancillary finding was the presence of perifascicular myofibre atrophy. The histopathological impression was necrotising autoimmune myopathy. **(**Fig. 2**)**

MRI of the bilateral thighs (T2-weighted and STIR sequences) demonstrated ill-defined, multifocal hyperintensities within intramuscular and intermuscular fascial planes bilaterally, consistent with active myoedema and perifascicular oedema, typical of the distribution pattern described in anti-SRP IMNM, with preferential involvement of the posterior compartment of the thigh and perithigh fascia. **(**Fig. 3**)**

On Day 8, the patient developed palpitations and precordial unease. A 12-lead ECG demonstrated sinus bradycardia with a ventricular rate of 40 beats per minute and T-wave inversions in leads V1, V2, and V3, representing a new finding from the admission ECG (which was normal). Bedside cardiac troponin T (cTnT) rapid assay was positive. A prompt 2D echocardiogram was performed, demonstrating normal left ventricular size, dimensions, and systolic function, with no regional wall motion abnormality, pericardial effusion, or valvular pathology, that excluded an acute coronary syndrome and overt dilated cardiomyopathy. Pulmonary function testing (spirometry and diffusion capacity) conducted during the admission was within normal limits. HRCT of the chest could not be performed owing to equipment unavailability at the time.

On the basis of the above, the final diagnosis was established as: anti-SRP antibody-positive immune-mediated necrotizing myopathy (IMNM) fulfilling ENMC 2016 criteria, complicated by probable immune-mediated myocarditis and pharyngeal (dysphagia) involvement, with anti-Ro52/SS-A/La seropositivity without classifiable Sjögren's syndrome.

Differential diagnoses systematically excluded included: hypothyroid myopathy, Cushing's myopathy, hyperparathyroid myopathy, statin-associated myopathy, viral myositis, sarcoid myopathy, paraneoplastic myopathy, limb-girdle muscular dystrophy (characteristic pattern on biopsy and positive MSA); and vitamin D deficiency myopathy (CK characteristically normal or mildly elevated but the observed CK of > 5,000 IU/L with a necrotising biopsy is not attributable to vitamin D deficiency alone, though the severe deficiency was concurrently corrected).

Therapeutic Intervention

Nutritional repletion commenced on Day 1 with intramuscular cholecalciferol 600,000 IU (stat), oral calcium carbonate 500 mg twice daily, oral vitamin B12 1,500 µg once daily, and weekly sachet cholecalciferol 60,000 IU, alongside a high-protein diet and active limb physiotherapy. On Day 4, following ANA positivity and pending the myositis panel, oral prednisolone 60 mg once daily (approximately 1 mg/kg/day) and oral methotrexate 10 mg weekly (as a steroid-sparing and disease-modifying agent, with folate supplementation) were initiated. Despite this, the patient deteriorated over the subsequent 48 hours, achieving complete loss of independent ambulation and complete dysphagia by Day 6, meeting criteria for severe disease. This failure of conventional immunosuppression to arrest progression is characteristic of steroid-refractory anti-SRP IMNM. Upon confirmation of anti-SRP positivity on Day 6, intravenous methylprednisolone pulse therapy (1 g once daily for five days) was administered. Probable immune myocarditis on Day 8 prompted initiation of IVIg at a dose of 20 g once daily for five consecutive days (cumulative 100 g, approximating 2g/kg), which resulted in resolution of cardiac symptoms and marked improvement in dysphagia, though proximal limb weakness persisted. On Day 15 intravenous

rituximab 1,000 mg was administered, with a second infusion of 1,000 mg on Day 29. Oral prednisolone and weekly methotrexate were continued throughout the admission and maintained at discharge.

Follow-up and Outcomes: The clinical and biochemical response to rituximab was remarkable. Within 72 hours of the first infusion, the patient demonstrated visible improvement in proximal limb strength and was able to ambulate with minimal support. The CK trend reflected this trajectory precipitously: from a peak of 7,112 IU/L on Day 13, CK fell to 2,169 on Day 15, 432 on Day 20, and 70 IU/L by Day 23 near-complete normalisation within eight days of rituximab initiation. CK-MB correspondingly normalised (Day 13: 136 IU/L → Day 23: 5 IU/L).

At four months of follow-up, the patient had MRC grade 4+/5 power at all joints across all planes of motion bilaterally, was fully ambulant, and had resumed activities of daily living. She remained on a tapering course of oral prednisolone and was receiving monthly maintenance IVIg infusions as part of a planned 6 month maintenance regimen (four doses completed at the time of reporting). No further cardiac symptoms or ECG abnormalities were recorded at follow-up, and repeat anti-SRP titres were planned at 6-month review.

Table 2
Timeline

Day	Clinical Events and Interventions	CK-Total	CK-MB
~ 2 months prior	Onset of bilateral proximal limb weakness	-	-
~ 1 month prior	Addition of truncal weakness	-	-
~ 10 days prior	Onset of dysphagia (equal for solids and liquids)	-	-
Day 1	Admission; baseline investigations; empirical vitamin D, B12 supplementation, physiotherapy	5,882	290
Day 2	Muscle biopsy (vastus lateralis) performed; EMG scheduled	-	-
Day 4	ANA positive (1:100 speckled); anti-Ro52/SS-A/SS-B positive; prednisolone 60 mg once daily + methotrexate 10 mg weekly commenced	5,279	317
Day 6	Clinical deterioration: complete inability to walk unassisted; complete dysphagia; anti-SRP positivity confirmed; IV methylprednisolone pulse 1 g once daily commenced, oral prednisolone withheld	5,694	265
Day 8	Palpitations and uneasiness; ECG: sinus bradycardia (HR 40/min) + T-wave inversions V1–V3; Troponin T positive; 2D echo normal; IVIg 20 g IV once daily commenced	6,182	138
Day 10	IVIg course ongoing; cardiac symptoms and dysphagia improving	6,430	172
Day 13	Peak CK despite combined immunosuppression	7,112	136
Day 15	Rituximab 1000 mg IV (first infusion) per ENMC escalation protocol	2,169	24
Day 17	Significant improvement in proximal power and gait	1,048	22
Day 20	Continued recovery	432	15
Day 23	CK approaching normalisation	70	5
Day 29	Rituximab second infusion (1000 mg IV)	–	–

DISCUSSION

IMNM was delineated as a distinct IIM entity by the ENMC in 2016, on the basis of a clinico-sero-pathological consensus that identified it as biologically and prognostically distinct from dermatomyositis (DM), antisynthetase syndrome, and overlap myositis.[2] The ENMC 2016 criteria require: (i) proximal muscle weakness, (ii) CK markedly elevated (typically > 1,000 IU/L, often > 10× ULN), (iii) myopathic EMG, (iv) histopathological features of predominant necrosis, paucicellular inflammation, and

sarcolemmal MAC/C5b-9 or MHC-I deposition, and (v) exclusion of alternative diagnoses.[2] The 2017 EULAR/ACR classification criteria for IIM have limited utility in IMNM, as they do not incorporate IMNM-specific antibodies or histopathological subclassification; the ENMC framework is therefore the appropriate diagnostic reference.[2,6]

The signal recognition particle is a ubiquitous cytoplasmic ribonucleoprotein complex that escorts newly synthesised transmembrane proteins to the endoplasmic reticulum during co-translational translocation. Autoantibodies targeting SRP54, the GTPase subunit that contacts the ribosome-nascent chain complex, are the MSA defining this subtype.[4] The precise mechanism linking anti-SRP antibodies to myonecrosis involves complement activation, sarcolemmal MAC deposition, and subsequent macrophage-mediated phagocytosis of necrotic fibres, rather than direct T-cell cytotoxicity, a mechanistic distinction that explains the paucity of lymphocytic infiltrate on biopsy, as observed in our patient.

The mean age of onset in the largest published cohort of anti-SRP IMNM - the 100-patient Japanese series by Suzuki et al. was 51 years (range 4–82 years), with a female preponderance (61:39).[7] At 26 years of age, our patient sits well below the typical fifth-decade onset, reflecting the recognition that while juvenile-onset anti-SRP disease has been described, it remains uncommon. More recent multicentre data confirm younger age of onset in anti-SRP versus anti-HMGCR IMNM (median 53 vs 66.5 years), with younger patients showing a more severe extramuscular phenotype.[8] Indian and South Asian epidemiological data on IMNM are sparse, predominantly limited to isolated case reports, making this case additionally instructive in the regional context.

The co-positivity for anti-Ro52/TRIM21 (intensity 81; strong positive) and anti-SS-A/Ro60 (intensity 76; strong positive) alongside anti-SRP merits detailed consideration. Anti-Ro52 is an E3 ubiquitin ligase (TRIM21) with roles in innate immune regulation and is recognised as a myositis-associated antibody (MAA), distinct from the myositis-specific antibody (MSA) group, associated with interstitial lung disease and more severe extramuscular disease in IIM when co-occurring with MSAs.[9]

Critically, strong anti-Ro52/SS-A seropositivity must not be conflated with Sjögren's syndrome. The 2016 ACR/EULAR Classification Criteria for Primary Sjögren's Syndrome employ a weighted scoring system: anti-SSA/Ro positivity contributes 3 points; each of an abnormal Schirmer's test, an ocular surface staining score ≥ 5, and unstimulated salivary flow ≤ 0.1 mL/min contributes 1 point; and a minor salivary gland focus score ≥ 1 per 4 mm^{10} contributes 3 points - classification requiring a minimum score of 4, and carrying a further prerequisite of at least one qualifying symptom of dryness or systemic activity.[10] Our patient scored 3 points (anti-Ro52/SS-A positivity alone), with a negative Schirmer's test, no xerostomia or xerophthalmia, and no sicca symptoms; she therefore does not satisfy the 2016 ACR/EULAR criteria. Minor salivary gland biopsy was deemed unnecessary given the negative Schirmer's test and complete absence of clinical sicca. The seropositivity is best interpreted as a Sjögren's-associated antibody detected as part of a broader autoimmune dysregulatory context, with potential prognostic implications for ILD surveillance, rather than diagnostic Sjögren's overlap. Isolated anti-Ro52

positivity is documented in primary IIM without Sjögren's syndrome and should not independently trigger salivary gland biopsy in the absence of clinical sicca.[11]

Additionally, the dual IIF pattern observed on ANA testing i.e. nuclear coarse speckled (reflecting anti-Ro52/SS-A activity) alongside a cytoplasmic fine speckled pattern (4+) is characteristic of anti-SRP antibodies, which target cytoplasmic particles, and independently corroborates the line-blot MSA result. This composite IIF signal, if present in a patient with proximal myopathy, should prompt reflexive anti-SRP testing even in laboratories without standing myositis panels.[12]

The biopsy confirmed the hallmarks of IMNM - isolated myofibre necrosis, CD68-positive macrophage infiltration, focal sarcolemmal HLA class I overexpression, negative lymphocytic markers (CD4, CD8, CD20) and negative HLA class II, constituting a canonical necrotising autoimmune myopathy pattern per the ENMC 2016 criteria.[2] MAC/C5b-9 deposition and CD31 staining, however, were not performed in this case, though the macrophage-predominant necrotising biopsy pattern, anti-SRP seropositivity, and absence of lymphocytic infiltrate are collectively diagnostic of IMNM per ENMC 2016 criteria.[2]

The co-reported finding of perifascicular myofibre atrophy, however, warrants honest discussion. Perifascicular atrophy is classically and reproducibly the histological hallmark of dermatomyositis, attributed to hypoperfusion of the perifascicular zone secondary to complement-mediated microangiopathy.[13] Its presence in a biopsy otherwise diagnostic of IMNM is atypical. Three interpretations merit consideration: first, sampling artefact - a biopsy positioned near a fascicular periphery may capture atrophic perifascicular fibres not representative of the primary pathological process; second, overlap or transitional pathology - a subset of anti-SRP patients develop histological features bridging IMNM and DM, and rare cases of perifascicular necrosis have been described in antisynthetase syndrome; third, the term "perifascicular atrophy" may, in this context, reflect a descriptive observation of perifascicular variation in fibre size rather than the strictly defined DM criterion.[14] In the presence of confirmed anti-SRP positivity, a macrophage-predominant biopsy, and absence of any DM-specific features, IMNM remains the correct primary classification.

The development of sinus bradycardia (40 bpm), anterior T-wave inversions (leads V1–V3), and a positive cTnT on Day 8 in the absence of wall-motion abnormality on echocardiography and in the clinical context of systemic immune activation is most consistent with immune-mediated myocarditis, representing direct cardiac muscle involvement by the anti-SRP autoimmune process. The T-wave inversions in V1–V3 are characteristic of right ventricular or anteroseptal myocardial inflammation, and the new sinus bradycardia may reflect conduction system involvement.

Cardiac involvement in anti-SRP IMNM has a wide reported prevalence, ranging from 2% in the Suzuki 2015 cohort (based principally on clinically apparent events)[7] to 52.6% in the Liu 2023 systematic analysis when troponin and ECG data were actively sought.[5] This heterogeneity reflects cohort composition, ascertainment methodology, and the proportion of subclinical versus overt cases. The predominant forms of structural cardiac involvement described include dilated cardiomyopathy,[15]

pericarditis, and myocarditis.[5] Most of the published cardiac cases represent either the presenting feature or an early finding identified at diagnosis;[15] the development of myocarditis during the inpatient course, subsequent to the initial cardiac evaluation, as occurred here, adds a temporal dimension that has been less frequently characterised in the literature.

A critical interpretive caveat must be addressed. cTnT is unreliable as an exclusive cardiac biomarker in patients with skeletal muscle disease. Schmid et al. demonstrated that 68.9% of patients with skeletal myopathies had elevated cTnT above threshold, compared with only 4.1% for cardiac troponin I (cTnI), attributed to re-expression of cTnT isoforms in regenerating skeletal muscle and cross-reactivity of contemporary high-sensitivity assays.[16] This finding was corroborated by Rittoo et al.[17] and subsequently by du Fay de Lavallaz et al.[18] In our patient, cTnI was not measured, and cardiac MRI with Lake Louise criteria (the gold standard for non-invasive myocarditis diagnosis)[19] was not performed, representing a limitation of the workup. The cardiac diagnosis in this case therefore rests upon a clinical composite: new dynamic ECG changes (sinus bradycardia with anterior T-wave inversions, distinct from the normal admission ECG), a positive cTnT in a patient with high baseline CK and ongoing skeletal-muscle inflammation, and a normal echocardiogram excluding structural coronary or valvular disease. Notably, the CK-MB fraction declined from Day 6 to Day 8 (265 → 138 IU/L) despite the contemporaneous troponin T positivity, a trend that is more consistent with skeletal muscle-derived enzyme variation than with acute cardiomyocyte injury, where CK-MB typically peaks concomitantly with or after troponin elevation. The subsequent mild rise to 172 IU/L on Day 10 may reflect ongoing muscle inflammation during IVIg therapy. This CK-MB trajectory further supports the troponin T false-positive hypothesis and reinforces the need for high-sensitivity cardiac troponin I and CMR since this composite, while supportive, does not constitute confirmed myocarditis per Lake Louise criteria or endomyocardial biopsy. Future cases should incorporate high-sensitivity cTnI, CMR with T1/T2 mapping, and close cardiology co-management to establish myocarditis with greater precision. We recommend that cardiac MRI be performed on an outpatient basis in this patient to confirm the diagnosis retrospectively and guide long-term cardiac follow-up.

The kinetics of CK response in this patient elegantly illustrate the steroid-refractory nature of anti-SRP IMNM. Despite initiation of prednisolone 60 mg once daily and weekly methotrexate on Day 4, CK rose from 5,279 to 5,694 to 6,182 to a peak of 7,112 IU/L over the ensuing nine days. This rising-CK-despite-immunosuppression pattern is characteristic of anti-SRP disease and well-documented in the literature: Pinal-Fernandez et al. demonstrated that anti-SRP patients have significantly worse functional outcomes and higher rates of treatment failure compared with anti-HMGCR patients, frequently requiring multiple immunosuppressive agents.[8]

The ENMC 224th Workshop recommendations endorse an escalation paradigm for IMNM: first-line high-dose corticosteroids (with intravenous pulsing for severe disease) plus an early steroid-sparing agent, followed by IVIg (particularly in anti-HMGCR disease), and proceeding to rituximab for anti-SRP-positive cases failing these measures.[2] Our management adhered precisely to this framework, though the

simultaneity of IVIg and pulse steroids preceding rituximab creates a confound in attributing the dramatic CK fall and clinical recovery to rituximab alone. The temporal relationship - CK peak on Day 13 (two days before rituximab), with precipitous decline to 70 IU/L by Day 23 is consistent with rituximab-mediated B-cell depletion, though the cumulative immunosuppressive effect of pulse steroids and IVIg undoubtedly contributed, particularly for the early cardiac and pharyngeal improvement. Rituximab-mediated B-cell depletion typically requires two to four weeks to achieve maximum effect;[20] rapid clinical improvement at 72 hours may partially reflect the above confounders, acknowledged as a limitation in attributing response.

Intravenous immunoglobulin played a dual role in this case: providing urgent cardiac stabilisation and improving pharyngeal function during the acute myocarditis episode before rituximab could be initiated. The evidence for IVIg in anti-SRP IMNM is less robust than for anti-HMGCR disease, where Mammen and Tiniakou described IVIg monotherapy responses[21] and Suh et al. demonstrated IVIg-containing regimens achieving significantly higher CK-normalisation rates.[22] Nevertheless, IVIg retains an important role as a bridging or adjunctive agent in severe anti-SRP disease, particularly when rapid pharmacological intervention is required for extramuscular manifestations prior to biologic onset of action.

Rituximab has emerged as the most evidence-supported biologic agent for refractory IMNM. In the systematic review of 34 rituximab-treated IMNM cases by Xiong et al., the anti-SRP-positive subgroup demonstrated a response rate of 77.8% (14/18), compared with 43.8% (7/16) in anti-HMGCR-positive patients.[23] The RIM trial (Rituximab in Myositis), the largest randomised trial of rituximab in inflammatory myopathy, demonstrated overall efficacy in refractory IIM, with autoantibody positivity (particularly anti-synthetase and anti-Mi-2) as predictor of response; anti-SRP was not an independent multivariate predictor in that analysis, although the case series evidence for anti-SRP is robust.[24] Our patient's response is concordant with the 77.8% anti-SRP response rate and supports early rituximab escalation in anti-SRP patients failing conventional therapy, per current ENMC guidance. However, serial CD19 + B lymphocyte counts were not measured to confirm rituximab mediated B cell depletion, limiting attribution to response.

Anti-SRP IMNM carries the most disabling prognosis among IMNM subtypes, with high rates of relapse on steroid taper and frequent requirement for long-term immunosuppression.[8,22] Our patient's recovery to MRC 4+/5 at four months on prednisolone plus monthly IVIg is encouraging, consistent with published outcomes in rituximab responders in the Xiong 2021 cohort.[23] Monthly maintenance IVIg as a steroid-sparing strategy over six months is an evidence-supported approach, primarily derived from anti-HMGCR data but rationally extended to anti-SRP given the shared mechanism of complement-mediated necrosis.[21]

Surveillance priorities for this patient going forward include: outpatient cardiac MRI; periodic reassessment of pulmonary function and consideration of HRCT chest to formally exclude ILD, particularly given anti-Ro52 co-positivity; serial monitoring of muscle strength and CK; and gradual steroid tapering with vigilance for relapse. An endocrine referral for ongoing management of the

profound vitamin D deficiency and secondary hyperparathyroidism is independently warranted, given these may independently impair muscle recovery despite resolution of the inflammatory process.

CONCLUSION

Anti-SRP-positive IMNM is a rare, phenotypically severe, and frequently steroid-refractory autoimmune myopathy that demands early recognition and a low threshold for immunosuppressive escalation. This case illustrates its characteristic multisystem burden - rapid proximal and truncal weakness, pharyngeal involvement, and immune-mediated myocarditis complicating the inpatient course, in an unusually young patient with concurrent anti-Ro52 seropositivity that warranted careful distinction from Sjögren's syndrome. The serial creatine kinase trajectory, rising despite corticosteroids and intravenous immunoglobulin before precipitating with rituximab, serves as a compelling clinical illustration of the ENMC escalation paradigm and the indispensability of early biologic therapy in anti-SRP disease. Clinicians must remain vigilant to the diagnostic limitations of cardiac troponin T in skeletal muscle disease, and cardiac MRI should be sought wherever myocardial involvement is suspected. In rapidly progressive anti-SRP IMNM, delay in biologic initiation carries measurable clinical cost.

PATIENT PERSPECTIVE

"When I was admitted, I could not even swallow water or turn in my bed. I was terrified. After the treatments, little by little I got back my strength. I want other patients like me to know that even when things feel hopeless, the right medicines can help."

The abovesaid has been translated from patient's native language, Hindi.

Declarations

Ethics approval and consent to participate: Reporting conforms to the CARE (CAse REport) guidelines.[25] Institutional ethical approval for publication of de-identified case material was obtained in accordance with local policy.

Consent for publication: Written informed consent was obtained from the patient for publication of this case report and the accompanying images. A copy of the consent is available for review by the Editor on request.

Availability of data and materials: All data generated or analysed during this study are included in this published article.

Competing interests: The authors declare that they have no competing interests.

Funding: This work received no specific grant from any funding agency in the public, commercial or not-for-profit sector.

Authors' Contributions:

B.Z. (corresponding author): Conceptualization; Data curation; Formal analysis (diagnostic criteria mapping, serological interpretation, and literature synthesis); Investigation (primary clinical assessment, history acquisition, diagnostic workup, and therapeutic monitoring); Methodology (CARE guideline adherence and manuscript structure); Visualization (preparation of all figures, histopathological panels, and timeline); Writing - original draft; Writing – review and editing.

S.G.: Conceptualization; Project administration; Resources; Supervision (overall clinical, diagnostic, and academic oversight); Validation (critical appraisal of diagnosis, therapeutic decisions, and manuscript content); Writing - review and editing.

P.B.: Conceptualization; Investigation (senior clinical management, therapeutic escalation decisions including rituximab initiation, and outpatient follow-up); Resources; Supervision; Validation; Writing - review and editing.

S.K.: Investigation (senior inpatient clinical assessment, monitoring of treatment response, and biochemical trend evaluation); Validation (clinical data verification); Writing - review and editing.

A.K.: Investigation (inpatient clinical management and coordination of investigations including electromyography, pulmonary function testing, and serological panels); Resources; Writing - review and editing.

A.C.: Investigation (inpatient clinical care and patient monitoring, including during the acute myocarditis episode); Data curation; Writing - review and editing.

M.M.: Investigation (inpatient clinical care and patient monitoring); Data curation (serial creatine kinase trend documentation and clinical data recording); Writing - review and editing.

B.B.: Data curation (clinical data extraction and case documentation); Methodology (diagnostic workup coordination); Writing - review & editing.

A.S.C.: Investigation (coordination with the Department of Pathology, GIPMER, for histopathological specimen processing; acquisition and organisation of histopathological and immunohistochemical slide images); Visualization (histopathological figure preparation and labelling); Writing - review and editing.

V.R.: Data curation; Formal analysis (supplementary literature search and reference verification); Writing - review and editing.

All authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work in accordance with ICMJE criteria.

Acknowledgement: The authors thank Dr. Ravindra Kumar Saran, Professor, Department of Pathology, Govind Ballabh Pant Institute of Postgraduate Medical Education and Research (GIPMER), New Delhi, for

reporting the histopathological and immunohistochemical analysis of the muscle biopsy specimen. The authors also thank the patient for granting consent for publication of her clinical details.

References

1. Smoyer-Tomic KE, Amato AA, Fernandes AW. Incidence and prevalence of idiopathic inflammatory myopathies among commercially insured, Medicare supplemental insured, and Medicaid enrolled populations: an administrative claims analysis. BMC Musculoskelet Disord [Internet]. 2012;13(1):103. Available from: http://dx.doi.org/10.1186/1471-2474-13-103
2. Allenbach Y, Mammen AL, Benveniste O, Stenzel W. Immune-Mediated Necrotizing Myopathies Working Group. 224th ENMC International Workshop:: Clinico-sero-pathological classification of immune-mediated necrotizing myopathies Zandvoort, The Netherlands, 14–16 October 2016. Neuromuscul Disord [Internet]. 2018;28(1):87–99. Available from: http://dx.doi.org/10.1016/j.nmd.2017.09.016
3. Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, de Visser M et al. 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. Ann Rheum Dis [Internet]. 2017;76(12):1955–64. Available from: http://dx.doi.org/10.1136/annrheumdis-2017-211468
4. Ma X, Bu B-T. Anti-SRP immune-mediated necrotizing myopathy: A critical review of current concepts. Front Immunol [Internet]. 2022;13:1019972. Available from: http://dx.doi.org/10.3389/fimmu.2022.1019972
5. Liu M, Lin Y, Qiao L, Chen J, Shi Q. Characteristics of cardiac involvement in immune-mediated necrotizing myopathy. Front Immunol [Internet]. 2023;14:1094611. Available from: http://dx.doi.org/10.3389/fimmu.2023.1094611
6. Watanabe Y, Uruha A, Suzuki S, Nakahara J, Hamanaka K, Takayama K et al. Clinical features and prognosis in anti-SRP and anti-HMGCR necrotising myopathy. J Neurol Neurosurg Psychiatry [Internet]. 2016;87(10):1038–44. Available from: http://dx.doi.org/10.1136/jnnp-2016-313166
7. Suzuki S, Nishikawa A, Kuwana M, Nishimura H, Watanabe Y, Nakahara J et al. Inflammatory myopathy with anti-signal recognition particle antibodies: case series of 100 patients. Orphanet J Rare Dis [Internet]. 2015;10(1):61. Available from: http://dx.doi.org/10.1186/s13023-015-0277-y
8. Pinal-Fernandez I, Parks C, Werner JL, Albayda J, Paik J, Danoff SK et al. Longitudinal course of disease in a large cohort of myositis patients with autoantibodies recognizing the signal recognition particle: Anti-SRP autoantibodies in myositis patients. Arthritis Care Res (Hoboken) [Internet]. 2017;69(2):263–70. Available from: http://dx.doi.org/10.1002/acr.22920
9. Gong X, He S, Cai P. Roles of TRIM21/Ro52 in connective tissue disease-associated interstitial lung diseases. Front Immunol [Internet]. 2024;15:1435525. Available from: http://dx.doi.org/10.3389/fimmu.2024.1435525
10. Shiboski CH, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM et al. 2016 American College of Rheumatology/European League Against Rheumatism classification criteria for primary

Sjögren's syndrome: A consensus and data-driven methodology involving three international patient cohorts: Acr/Eular classification criteria for primary SS. Arthritis Rheumatol [Internet]. 2017;69(1):35–45. Available from: http://dx.doi.org/10.1002/art.39859

11. McHugh NJ. Ro52, myositis, and interstitial lung disease. J Rheumatol. 2023;50(2):161-3. Available from: http://dx.doi.org/10.3899/jrheum.221067
12. Conrad K, Röber N, Andrade LEC, Mahler M. The clinical relevance of anti-DFS70 autoantibodies. Clin Rev Allergy Immunol [Internet]. 2017;52(2):202–16. Available from: http://dx.doi.org/10.1007/s12016-016-8564-5
13. Pinal-Fernandez I, Casal-Dominguez M, Mammen AL. Immune-mediated necrotizing myopathy. Curr Rheumatol Rep [Internet]. 2018;20(4):21. Available from: http://dx.doi.org/10.1007/s11926-018-0732-6
14. Uruha A, Suzuki S, Suzuki N, Nishino I. Perifascicular necrosis in anti-synthetase syndrome beyond anti-Jo-1. Brain. 2016;139(9):e50. 10.1093/brain/aww125.
15. Thiébaut M, Terrier B, Menacer S, Berezne A, Bussone G, Goulvestre C et al. Antisignal recognition particle antibodies-related cardiomyopathy. Circulation [Internet]. 2013;127(5):e434-6. Available from: http://dx.doi.org/10.1161/CIRCULATIONAHA.112.118877
16. Schmid J, Liesinger L, Birner-Gruenberger R, Stojakovic T, Scharnagl H, Dieplinger B et al. Elevated cardiac troponin T in patients with skeletal myopathies. J Am Coll Cardiol [Internet]. 2018;71(14):1540–9. Available from: http://dx.doi.org/10.1016/j.jacc.2018.01.070
17. Rittoo D, Jones A, Lecky B, Neithercut D. Elevation of cardiac troponin T, but not cardiac troponin I, in patients with neuromuscular diseases: implications for the diagnosis of myocardial infarction. J Am Coll Cardiol [Internet]. 2014;63(22):2411–20. Available from: http://dx.doi.org/10.1016/j.jacc.2014.03.027
18. du Fay J, Prepoudis A, Wendebourg MJ, Kesenheimer E, Kyburz D, Daikeler T et al. Skeletal muscle disorders: A noncardiac source of cardiac troponin T. Circulation [Internet]. 2022;145(24):1764–79. Available from: http://dx.doi.org/10.1161/CIRCULATIONAHA.121.058489
19. Ferreira VM, Schulz-Menger J, Holmvang G, Kramer CM, Carbone I, Sechtem U et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: Expert recommendations. J Am Coll Cardiol [Internet]. 2018;72(24):3158–76. Available from: http://dx.doi.org/10.1016/j.jacc.2018.09.072
20. Valiyil R, Casciola-Rosen L, Hong G, Mammen A, Christopher-Stine L. Rituximab therapy for myopathy associated with anti-signal recognition particle antibodies: a case series. Arthritis Care Res (Hoboken) [Internet]. 2010;62(9):1328–34. Available from: http://dx.doi.org/10.1002/acr.20218
21. Mammen AL, Tiniakou E. Intravenous immune globulin for statin-triggered autoimmune myopathy. N Engl J Med [Internet]. 2015;373(17):1680–2. Available from: http://dx.doi.org/10.1056/NEJMc1506163
22. Suh J, Amato AA. Effectiveness and safety of IVIG for the treatment of HMGCR immune-mediated necrotizing myopathy. Muscle Nerve [Internet]. 2025;71(3):392–7. Available from:

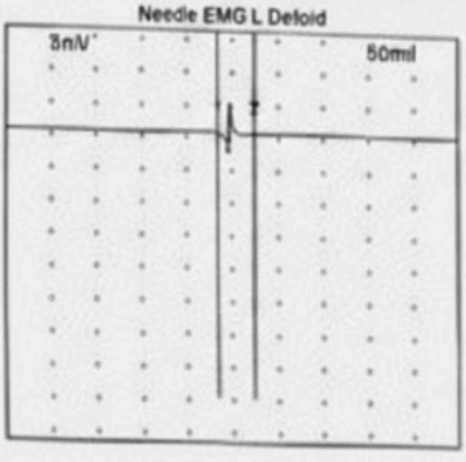
http://dx.doi.org/10.1002/mus.28333

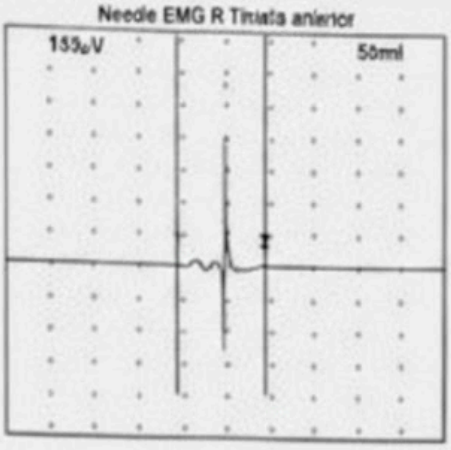
23. Xiong A, Yang G, Song Z, Xiong C, Liu D, Shuai Y et al. Rituximab in the treatment of immune-mediated necrotizing myopathy: a review of case reports and case series. Ther Adv Neurol Disord [Internet]. 2021;14:1756286421998918. Available from: http://dx.doi.org/10.1177/1756286421998918
24. Oddis CV, Reed AM, Aggarwal R, Rider LG, Ascherman DP, Levesque MC et al. Rituximab in the treatment of refractory adult and juvenile dermatomyositis and adult polymyositis: a randomized, placebo-phase trial. Arthritis Rheum [Internet]. 2013;65(2):314–24. Available from: http://dx.doi.org/10.1002/art.37754
25. Riley DS, Barber MS, Kienle GS, Aronson JK, von Schoen-Angerer T, Tugwell P et al. CARE guidelines for case reports: explanation and elaboration document. J Clin Epidemiol [Internet]. 2017;89:218–35. Available from: https://www.limbic-cenc.org/wp-content/uploads/CARE-2017-Guidelines-for-Reporting-Case-Reports-Explanation-and-Elaboration-JClin-Epidemiol.pdf

Figures

EMG Summary Table

Muscle	Nerve	Roots	IA	Fib	PSW	Fasc	Pattern
L. Deltoid	Axillary	C5-C6	Prolonged	None	None	None	N
R. Tibialis anterior	Deep peroneal (Fibular)	L4-L5	Prolonged	None	None	None	N
L. Quadriceps	Femoral	L2-L4	Prolonged	+	None	None	N





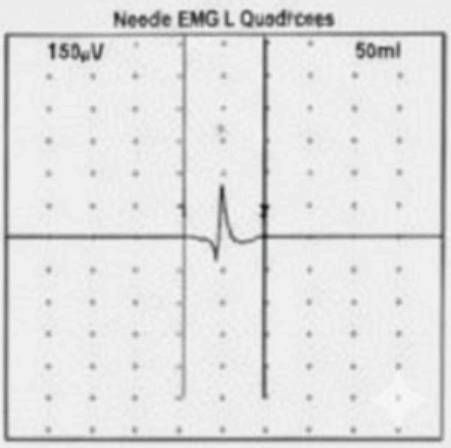


Figure 1

Needle electromyograph demonstrating a myopathic pattern (short-duration, low-amplitude polyphasic motor unit potentials, early recruitment) in respective muscles.

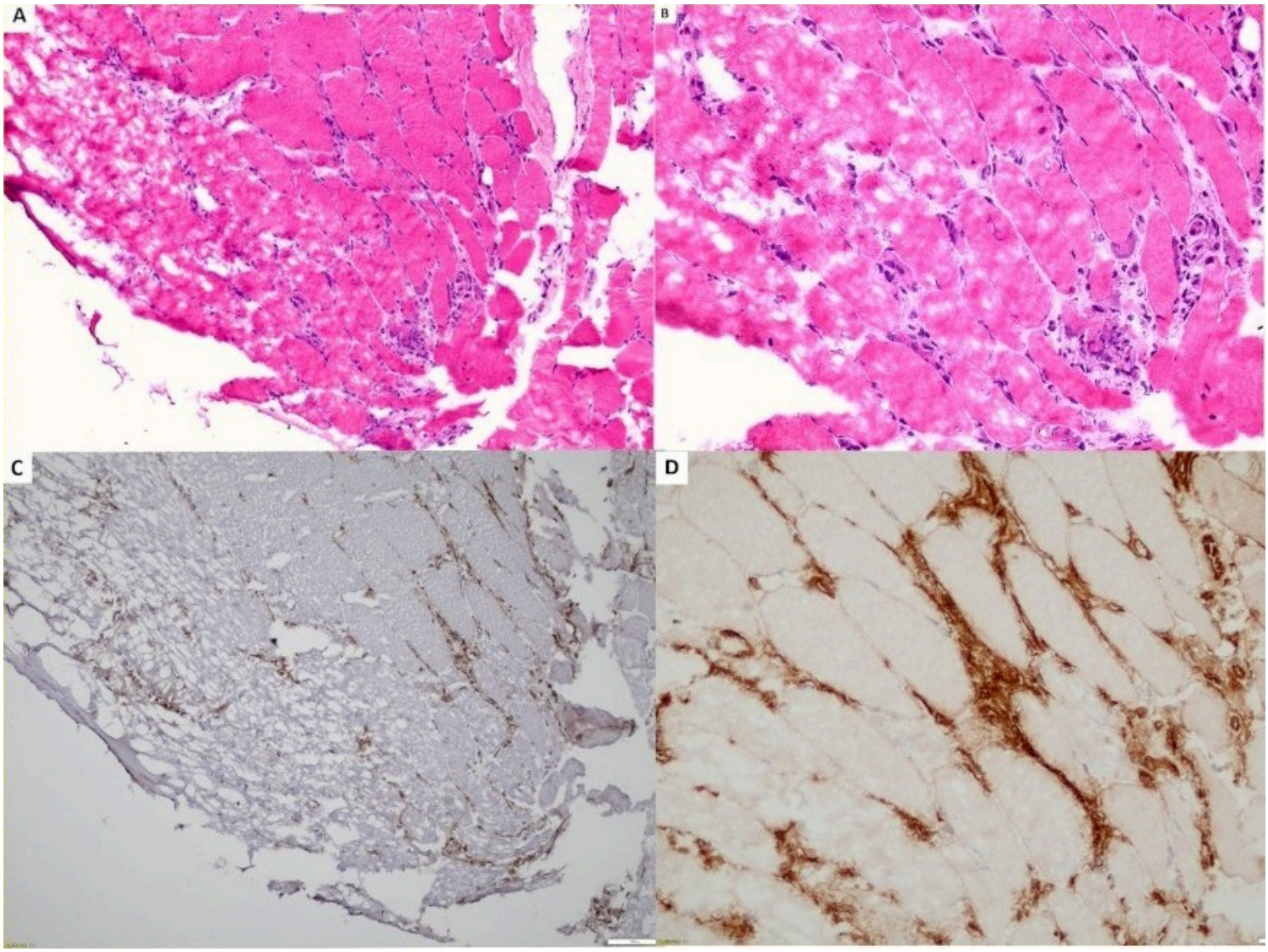


Figure 2

Hematoxylin and eosin staining at 100x **[A]** and 200x **[B]** showing isolated muscle fibre necrosis and perifascicular atrophy **[C]** Immunohistochemical staining for CD68 at 100x showing infiltrating macrophages **[D]** Immunohistochemical staining for HLA1 at 200x showing focal sarcolemmal expression in necrotic muscle fibres

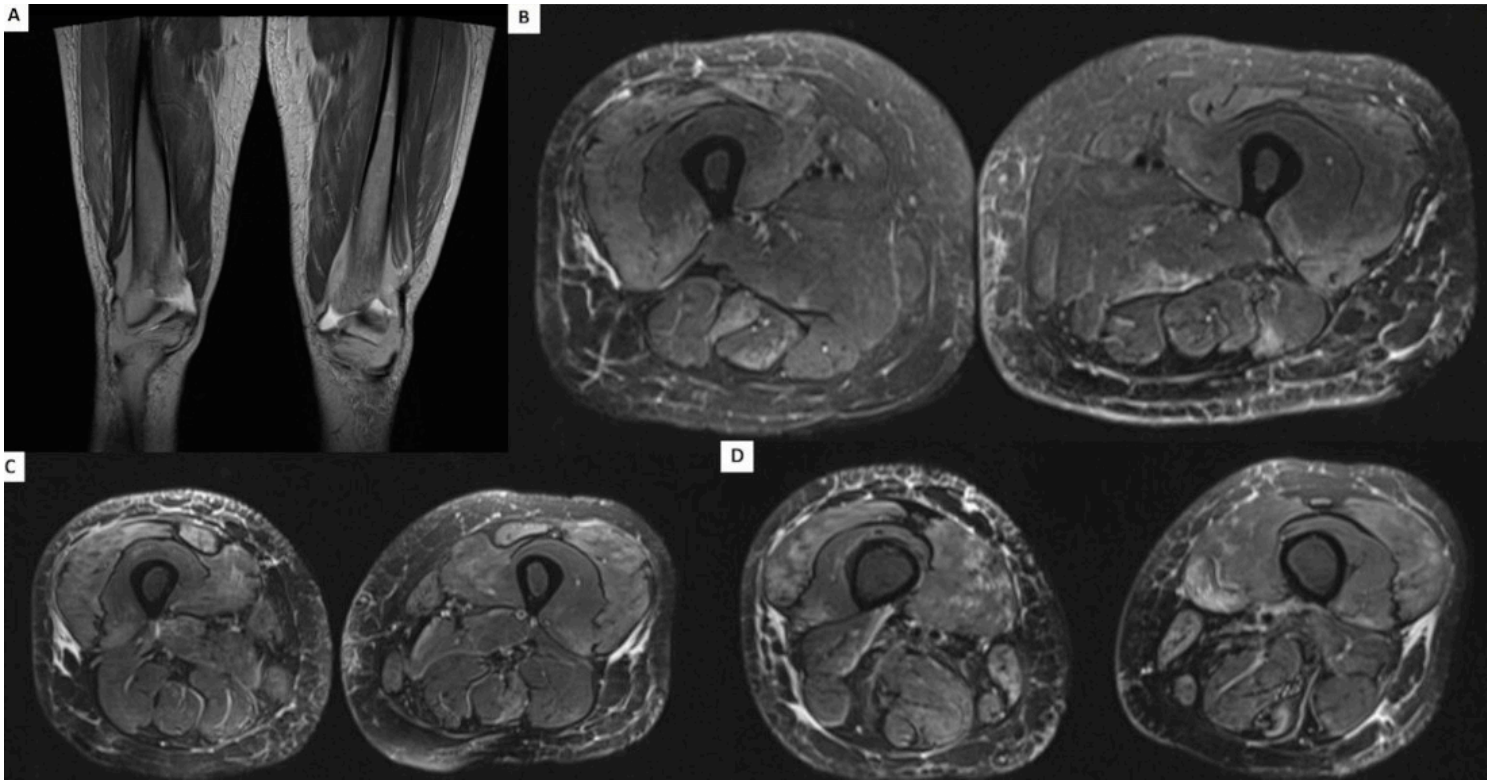


Figure 3

Coronal **[A]** and axial **[B-D]** MRI T2/STIR sequences of bilateral thighs showing ill-defined multifocal hyperintensities in intra and inter muscular planes

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SRPIMNMSoniConsentFormBMCMusculoskeletaldisorders.pdf