JOURNAL OF COMMUNITY HOSPITAL INTERNAL MEDICINE PERSPECTIVES
2020, VOL. 10, NO. 5, 462–465
https://doi.org/10.1080/20009666.2020.1793478

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CASE REPORT

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Utilization of myositis antibody-specific panel for diagnosis, treatment, and evaluation of disease progression

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ABSTRACT

The idiopathic inflammatory myopathies (IIM) are rare sporadic disorders with an overall annual incidence of approximately 1 in 100,000 and with a higher incidence in women. IIM is an autoimmune process leading to muscle inflammation due to a 'dysfunctional adaptive immune response evidenced by cell-mediated myocytoxicity, a high prevalence of autoantibodies and overexpression of Major Histocompatibility (MHC) I and II molecules on the muscle sarcolemma'. These autoimmune processes can be appreciated as inflammatory infiltrates in muscle biopsies. Common clinical findings in patients diagnosed with IIM include proximal muscle weakness, elevated creatinine kinase levels, circulating autoantibodies, radiological findings of muscular inflammation, and sometimes edema; in some patients, systemic symptoms such as dysphagia can also be present. Currently, there is no specific IIM classification scheme that incorporates all IIM subtypes; however, the four major IIM subtypes include dermatomyositis, polymyositis, inclusion body myositis, and immune-mediated necrotizing myopathy (IMNM). Two clinical cases are presented in this case report to illustrate a smoldering IIM, antisynthetase syndrome, and a more progressive IIM, anti-signal recognition particle IMNM; highlight the utility of the myositis-specific autoantibody panel for early diagnosis, targeted therapy, and prognosis; and offer primary care providers clues to IIM diagnosis.

ARTICLE HISTORY
Received 15 May 2020
Accepted 30 June 2020

KEYWORDS
Idiopathic inflammatory myopathies; autoimmune muscle inflammation; myositis-specific autoantibodies; antisynthetase syndrome; anti-SRP immune-mediated necrotizing myopathy; primary care provider

1. Introduction

The idiopathic inflammatory myopathies (IIM) are rare sporadic disorders with an overall annual incidence of approximately 1 in 100,000 and with a higher incidence in women [1]. The pathophysiology of IIM is not fully understood; however, it is known that it involves an autoimmune process leading to muscle inflammation due to a 'dysfunctional adaptive immune response evidenced by cell-mediated myocytoxicity, a high prevalence of autoantibodies and overexpression of Major Histocompatibility (MHC) I and II molecules on the muscle sarcolemma' [2]. Common clinical findings in patients diagnosed with IIM include proximal muscle weakness that may involve both the upper and lower extremities, and systemic symptoms such as shortness of breath, cough, and dysphagia can also be present. Significantly elevated serum creatinine kinase (CK) levels and unique serum circulating autoantibodies are characteristically present in IIM patients.

Currently, there is no specific IIM classification scheme that incorporates all IIM subtypes; however, the four major IIM subtypes include dermatomyositis, polymyositis (PM), inclusion body myositis, and immune-mediated necrotizing myopathy (IMNM) [4].

The degree of muscle involvement and the presence of extramuscular manifestations vary among the IIM spectrum, making an early diagnosis imperative to prevent long-term disability in IIM patients [4]. This case report illustrates a smoldering IIM, antisynthetase syndrome, and a more progressive IIM, anti-signal recognition particle (SRP) IMNM; highlights the utility of the myositis-specific autoantibody (MSA) panel for early diagnosis, targeted therapy, and prognosis; and offers primary care providers clues to IIM diagnosis.

2. Case 1

A 64-year-old female with a history of smoking, hypertension, hyperlipidemia, and 1 year of chronic shortness of breath and tachycardia with negative workup with an echo and chest-ray presented with a 1-month history of progressive shortness of breath, nonproductive cough, and fever. She fell at home and was unable to get back up for 2 h, prompting admission.

Admission vital signs were temperature 38.8°C, BP 125/78 mmHg, heart rate 131 bpm, respiratory rate 18, and O_2 saturation 97% on room air. There were bibasilar rales and 2+ lower extremity edema. There

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Table 1. Case 1 and Case 2 main clinical laboratory findings

Test	Case 1 (64)	Case 2 (57)	Normal
White Blood Cells (WBC)	19.9	Normal	4.00–11.00 10^3/μL
Aspartate Transaminase (AST)	152	193	4–31 IU/L
Alanine Transaminase (ALT)	113	133	4–31 IU/L
Troponin	<0.301	<0.301	≤0.302 ng/mL
C-Reactive Protein (CRP)	8.75	1.3	≤0.50 mg/dL
Erythrocyte Sedimentation Rate (ESR)	86	9	≤30 mm/h
CK	2990	5061	24–170 IU/L
Aldolase	74.3	48.8	≤8.1 U/L
Antinuclear Antibody (ANA) 1:640	Negative	Negative	
Sm/RNP Ab	Negative	Negative	Negative
Thyroid Stimulating Hormone (TSH)	12.88	Normal	0.380–4.700 uIU/mL
Myositis Ab panel*	+ Jo-1, <100	+ SRP-Ab,	<11 SI

was mild weakness in the proximal lower extremities. The remainder of the exam was normal.

Laboratory findings are noted in Table 1. A CT scan showed hazy ground-glass density within the lungs bilaterally (Figure 1). There was no improvement following hydration and antibiotics.

MRI of the left thigh demonstrated edema on T2-weighted images involving the proximal sartorius, mid rectus femoris and mid to distal vastus intermedius, and medialis muscles. Muscle bulk, neurovascular, and subcutaneous tissues were normal (Figure 2). Anti-Jo1 antibody was positive. Quadriceps muscle biopsy showed mild necrotizing myopathy with mild perimysial and perivascular macrophagic inflammation (Figure 3).

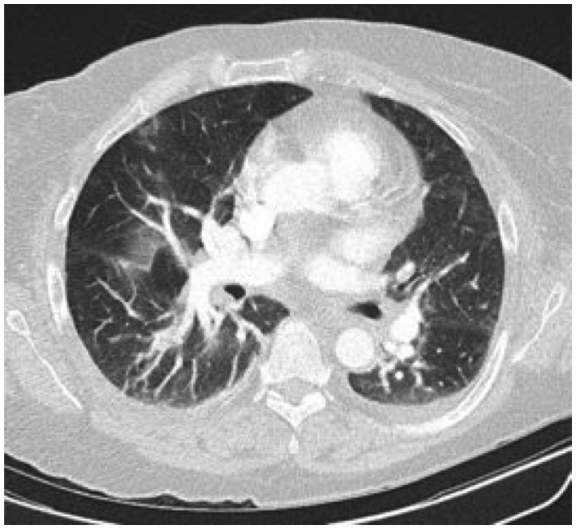

Figure 1. CT scan showing hazy ground glass density within the lungs bilaterally. This can be seen in interstitial lung disease

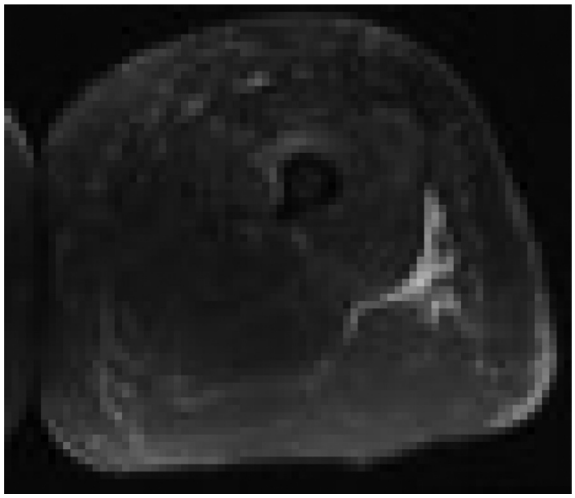

Figure 2. Case 1 MRI of the left thigh demonstrated edema on T2 weighted images involving the proximal sartorius, mid rectus femoris and mid to distal vastus intermedius and medialis muscles. Normal muscle bulk, neurovascular, and subcutaneous tissues.

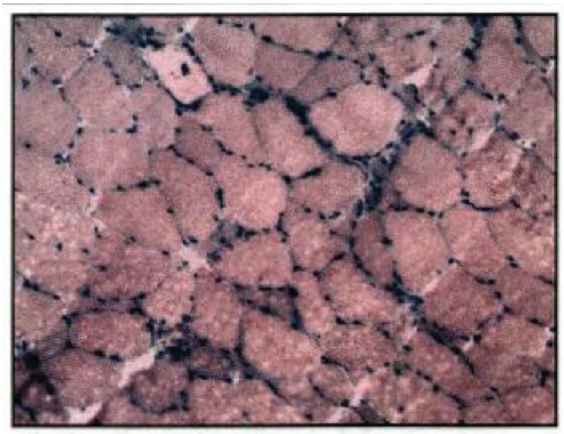

Figure 3. Case 1 quadriceps muscle biopsy showed mild necrotizing myopathy with mild perimysial and perivascular macrophagic inflammation.

2.1. Diagnosis

The diagnosis was IIM subtype PM consistent with anti-synthetase syndrome (anti-Jo-1 Ab+) and interstitial lung disease (ILD).

2.2. Treatment

Oral prednisone 60 mg daily produced immediate response, and the patient was discharged.

2.3. Prognosis

If skeletal muscle involvement is the sole manifestation of antisynthetase syndrome, patients respond well to glucocorticoids and immunosuppressive therapy and do fairly well [5]. Despite advances in therapy, the development of ILD is associated with increased mortality in patients with myositis [6].

3. Case 2

A 57-year-old female with a history of hypertension, hyperlipidemia, and recent workup for right flank pain revealing transaminitis presented to her primary care provider with rapidly progressive muscle weakness involving primarily proximal upper and lower extremities.

On presentation, her vital signs were temperature 37°C, blood pressure 179/83 mmHg, pulse 82 bpm, respiratory rate 18/min, and O_2 saturation 99% on room air. On physical exam, there was 4/5 proximal thigh weakness, shoulder strength was normal, and there was no muscle atrophy.

Laboratory findings are noted in Table 1. CT of the chest was remarkable only for nonspecific scattered nodules ranging from <1 to 4 cm (Figure 4).

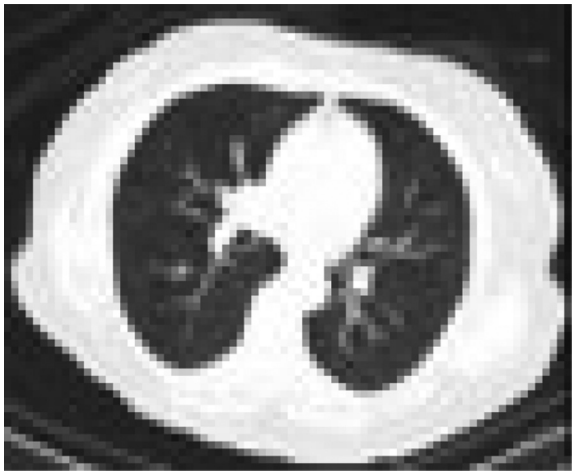

Figure 4. Case 2 Chest CT scan showed nonspecific scattered nodules ranging from <1cm-4cm

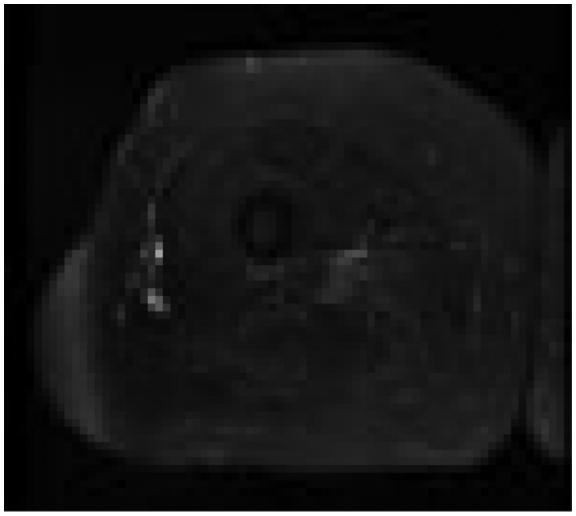

Figure 5. Case 2 MRI of the right thigh showed edema on T2 weighted images involving the pectineus, adductor magnus and obturator externus muscles

MRI of the right thigh showed edema on T2-weighted images involving the pectineus, adductor magnus, and obturator externus muscles (Figure 5).

Anti-SRP autoantibodies were positive. Quadriceps muscle biopsy demonstrated moderately severe necrotizing myopathy, mild atrophy, and extensive, severe round and polygonal atrophy with fiber degeneration and necrosis with myophagocytosis.

3.1. Diagnosis

The diagnosis was IIM, subtype IMNM, with positive anti-SRP antibody.

3.2. Treatment

She was treated with prednisone 60 mg daily and methotrexate, and CK fell modestly from 5000 to 2700, but she did not improve symptomatically.

3.3. Prognosis

IMNM with positive anti-SRP antibody is a severe disease with very elevated creatine kinase levels, dysphagia, and severe proximal muscle weakness. Unfortunately, these manifestations may not respond to immunosuppressive therapy, and patients are refractory to treatment [2].

4. Discussion

These two IIM cases illustrate the critical role of MSA panel in the diagnosis of IIM subtypes which guides treatment and prognosis. In these cases, muscle MRI findings were supportive but nonspecific, and even the muscle biopsy findings did not differentiate among IIM subtypes. The MSA panel was critical in the diagnosis of the IIM subtype. MSAs are highly selective and are associated with a particular clinical phenotype within the myositis spectrum. The classical MSAs, which are often mutually exclusive, include the synthetase (Jo-1, EJ, OJ, PL-7, PL-12) antibodies and Mi-2 and SRP antibodies [1].

In case 1, the shortness of breath likely causing tachycardia triggered the initial contact with the patient's PCP. A year later, progression of symptoms along with proximal muscle weakness led to a hospital admission where positive anti-synthetase anti-Jo-1 Ab was diagnosed. The fever and elevated WBC were part of the inflammatory response and not from an infectious etiology. Unfortunately, at that time, she had ILD radiological findings which are associated with increased mortality [6,7].

In case 2, the initial patient presentation was for right flank pain which was originally thought to be

due to transaminitis. Unfortunately, within a 2-month period, she presented again with increasing fatigue followed by acute proximal muscle weakness prompting a rheumatological workup confirming a rapidly progressing IMNM with positive anti-SRP antibodies.

5. Conclusion

- Two cases of IIMs are presented, a smoldering type, antisynthetase PM, and a more progressive type, anti-SRP IMNM.
- A readily available myositis-specific antibody panel has shown to be extremely important in early diagnosis, targeted therapy, and prognosis of IIM and its subtypes [7].
- Antisynthetase PM is associated with mild–moderate muscle weakness, higher risk of cancer, and ILD, and it responds well to immunotherapy [4].
- Anti-SRP IMNM is associated with severe necrotizing myopathy and muscle weakness, dysphagia, low risk for ILD, and malignancy. Frequent relapses are common and multiple treatment lines are needed [8].
- A comprehensive history, physical exam, and review of systems in female patients presenting with fatigue are extremely valuable in keeping IIM as a differential diagnosis.
- A lower threshold in ordering an MSA panel in female patients presenting with fatigue, muscle weakness, CK levels >1000 IU/L, and an elevated AST to ALT ratio may aid in early diagnosis.
- Further research is needed to understand the timing of the appearance of serum autoantibodies in IIM patients critical for early diagnosis and avoid misdiagnosis.
- There is a need for a unifying classification scheme that incorporates the MSAs and allows room to add those autoantibodies that are yet to be discovered.

Disclosure statement

No potential conflict of interest was reported by the authors.

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