CASE REPORT

Hyperacute muscle weakness in an unusual coexistence of antisignal recognition particle and anti-Mi-2 antibodies

Richard Oluyinka Akintayo,¹ Olanrewaju Festus Agbola,¹
Abiodun Waliyullah Adeyemo,¹ Olufemi Adelowo²

¹Department of Medicine,
University of Ilorin Teaching
Hospital, Ilorin, Nigeria
²Department of Medicine,
Rheumatology Unit, Lagos State
University Teaching Hospital,
Lagos, Nigeria

Correspondence to
Professor Olufemi Adelowo,
femiadelowo2003@yahoo.com

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SUMMARY

Idiopathic inflammatory myopathies are a heterogeneous group of systemic diseases characterised by variable phenotypes of chronic progressive muscle weakness. Myositis-specific antibodies (MSAs) include antibodies to cytoplasmic signal recognition particle (SRP) and various tRNA synthetases as well as the nuclear helicase protein Mi-2. These antibodies are typically found only in a fraction of true myositis cases and they tend to be mutually exclusive. Few cases of coexistence of two MSAs in the same patient have been reported and these cases all involve an antisynthetase antibody coexisting with either anti-SRP or anti-Mi-2 antibody. Peculiar clinical manifestations may be associated with different combinations of MSAs but the rarity of these cases makes their characterisation difficult. We report the first ever case of anti-SRP and anti-Mi-2 copositive polymyositis in a 19-year-old boy who presented with a week history of profound muscle weakness that attained its peak within 24 hours of onset.

BACKGROUND

Idiopathic inflammatory myopathies (IIMs) constitute a heterogeneous spectrum of diseases with diverse phenotypes. Over the years, the identification of antibodies highly specific for these diseases has given rise to the classification of the usually mutually exclusive list of myositis-specific antibodies (MSAs). MSAs are found in a small proportion of patients with polymyositis (PM) and dermatomyositis (DM) and are not found in association with other connective tissue diseases.¹ These antibodies fall into two broad categories: antibodies directed against Mi-2 and Mas antigens and antibodies targeting translational proteins such as various tRNA synthetases, the signal recognition particle (SRP), transcriptional intermediary factor-1 and the melanoma differentiation-associated gene-5.² However, rare cases of coexistence of different MSAs in the same individual have been reported.^{3–5} These findings may form the beginning of a prompt to identify the possible phenotypic attributes of various combinations of MSA. We report a case of rapidly peaked muscle weakness in a Nigerian teenager with PM who had both anti-SRP and anti-Mi2 as well as anti-PM/Scl antibody positivity. To the best of our knowledge, this is the first report of an anti-SRP and anti-Mi-2 copositive PM.

CASE PRESENTATION

A 19-year-old Nigerian man was admitted via the emergency unit on account of inability to lift his arms or rise up from the bed or sitting position of a week-long duration. The muscle weakness was described to have progressed rapidly to maximum within a day of onset. It was associated with prominent dysphagia but there was no respiratory distress or choking on feeding. There was no history of fever, headache, transient ischaemic attacks, dysphonia or myalgia. No drooping of the eyelids, diplopia, facial or neck weakness and there was no sensory disturbance. There was no history of skin rashes, Raynaud's phenomenon or other features of a connective tissue disease. He had no preceding illness or drug use.

On physical examination, he was not pale, anicteric and was well hydrated. Muscle bulk was normal and bilaterally symmetrical. There was marked symmetrical proximal muscle weakness with Kendall's Manual Muscle Testing grade of 2 in all limbs.⁶ He also had poor handgrips on both sides but no distal weakness in the lower limbs. Sensation and reflexes were intact. The cardiovascular, neurological and respiratory examinations were normal. Creatine kinase (CK) was 311 IU/L (reference: 38–174); aldolase 22.2 IU/L (reference: 1.5–8.1); alanine transaminase 89 IU/L (reference: 15–40); aspartate transaminase 53 IU/L (reference: 15–40) and lactate dehydrogenase (LDH) 490 IU/L (reference: 130–300). He had positive anti-SRP, anti-Mi-2 and anti-PM-Scl 75 antibodies. These were detected by immunoprecipitation. Complete blood count, urinalysis, as well as electrolytes, urea and creatinine were normal while the erythrocyte sedimentation rate and serum C-reactive protein were 16 mm/hour Westergren and 16 mg/L, respectively. Biopsies of the deltoids and quadriceps revealed scanty muscle fibre necrosis devoid of inflammatory infiltrates. Chest radiograph, electrocardiography and echocardiography were all normal. Viral screening for HIV, hepatitis B virus and hepatitis C virus was negative.

He was treated with a 3-day course of intravenous pulse methylprednisolone at 500 mg daily and continued on prednisolone tablet at 60 mg daily. He was also started on physiotherapy. Azathioprine was added on as a steroid-sparing drug after 2 weeks but he reacted with a flesh-coloured pruritic papular

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rash over the face and upper trunk which necessitated the drug's withdrawal. The rash disappeared over the following week and did not reoccur afterwards. The azathioprine was later replaced with mycophenolate mophetil. The dysphagia resolved within a week of commencement of treatment and it was followed by progressive improvement in global muscle strength over the following month. At 28 days since onset of treatment, proximal muscle strength had improved to Kendall's grade 7 in all limbs and at 3 months, grade 9. The improvement was sustained at 6-month follow-up and rechecks of CK, aldolase, LDH, aspartate aminotransferase and alanine aminotransferase were all normal. Eight months after the start of treatment, full muscle strength had been attained and the medications he was on were daily 10 mg prednisolone and 1 g mycophenolate mophetil.

DISCUSSION

Systemic autoimmune diseases are complex disorders with a vast range of patterns and severity. PM and DM are subsets of IIMs that are now known to constitute a family of systemic autoimmune disorders characterised by a natural history of chronic and progressive muscle weakness. Acute quadripareisis is a rare presentation of PM as patients typically exhibit insidious symmetric proximal limb and neck flexor muscle weakness over weeks to months.² This weakness tends to spare the distal muscles. A rapid progression of muscle weakness into a complete lack of power within 24 hours is probably associated with the documented aggressive tendency of anti-SRP myositis.⁷ On the other hand, the early presentation compelled by the terrifying experience of the alarming progression of limb weakness and dysphagia is a recognised positive prognostic index.⁸

A number of models have been proposed to explain the reasons for the specific target of certain nuclear and cytoplasmic antigens by autoantibodies in PM and DM. The SRP is a ribonucleoprotein complex (proteins-7SL RNA) with the SRP54 and SRP72 components most frequently targeted by anti-SRP antibodies.⁷ Antibodies to Mi-2, a nuclear helicase protein which is a component of the nucleosome-remodelling deacetylase complex, are strongly associated with DM.⁹ Anti-Mi-2 is rarely found in PM and when it is seen, it is associated with a good prognosis and treatment responsiveness.¹

Going by the Bohan and Peter criteria, our case could be classified as probable PM as electromyography could not be done due to its unavailability in our centre. However, combining the findings with the near 100%-specific MSAs that were detected by immunoprecipitation essentially affirmed the diagnosis.¹⁰ Also, the muscle biopsy findings were sufficient to differentiate PM from inclusion body myositis, a condition that is poorly responsive to immunosuppression and is often negative for autoantibodies.¹¹ Anti-SRP myositis has been described as a distinct phenotype of PM with rapidly progressing skeletal muscle weakness but with a good response to immunosuppressive and immunomodulatory drugs.^{12–14}

There is typically a conspicuous absence of inflammatory cells in the histology of anti-SRP myositis.¹³ Our case conforms largely to the identity of the entity of anti-SRP myositis despite the positivity for anti-Mi-2, another MSA. None of the typical skin lesions of DM like heliotrope rash, Gottron's papule/sign, shawl sign, V-shaped rash or holster sign were found and the biopsy findings did not support DM. It however exhibited an extreme acuteness with complete inability to lift the limbs or rise up from a sitting or recumbent position within 24 hours of onset. The absence of cardiac or interstitial lung involvement is consistent with earlier descriptions of anti-SRP myositis.^{13 15} Previous

cases of coexistence of MSAs described include anti-SRP and different antisynthetase antibodies but not anti-SRP and anti-Mi-2.^{3–5 16} Sugie *et al* had previously reported a case of anti-SRP and anti-Jo1 copositivity characterised by severe and rapid onset of muscle weakness as well as massive pleural effusion with interstitial lung disease.¹⁶ They suggested that this combination of autoreactivity probably portends a more severe disease than the classic PM.

Anti-SRP antibody is found in about 5% of individuals with IIM while anti-Mi-2 is found in 9%.^{7 15} Due to the strong association between anti-Mi-2 antibody and the classic DM, it is to be determined if our patient would later develop typical skin changes of DM. Anti-PM/Scl is associated with PM-scleroderma overlap but as a myositis-associated autoantibody, it may be found in connective tissue diseases other than myositis.¹⁷ Clinical features suggestive of an overlap with systemic sclerosis or any other connective tissue diseases were however absent in our patient.

In conclusion, the unusual variant of PM with coexistence of both anti-SRP and anti-Mi-2 may present as a clinical and histological phenotype indistinguishable from the classic anti-SRP myositis with very rapid progression and good response to immunosuppressive therapy. However, further characterisation of this rarity will be important with future studies capturing several cases.

Learning points

- ▶ Polymyositis may present with coexistence of antisignal recognition particle and anti-Mi-2 antibodies.
- ▶ This dual myositis-specific antibody-positive polymyositis is characterised by a histological findings devoid of inflammatory infiltrates.
- ▶ The progression of muscle weakness may be very rapid and may reach the peak under 24 hours of onset of the disease.
- ▶ The response to immunosuppression is good.

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