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Case Report

Anti-SRP Immune-Mediated Necrotizing Myopathy and Recent Cytomegalovirus Infection: A Case Report

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Abstract

Anti-signal recognition particle immune-mediated necrotizing myopathy (IMNM-SRP) is a rare, severe form of idiopathic inflammatory myopathy (IIM), marked by proximal muscle weakness, elevated creatine kinase levels, and significant muscle necrosis. This case report describes a 73-year-old woman with IMNM-SRP following a recent cytomegalovirus (CMV) infection, who presented with progressive proximal muscle weakness, dyspnea and dysphagia. Despite the initial severity, the patient showed substantial clinical improvement with an intensive immunosuppressive regimen, including corticosteroids, intravenous immunoglobulin, rituximab, and plasmapheresis. This case highlights the possibility of CMV as a triggering factor for IMNM-SRP, a rare association in current literature. The report emphasizes the role of early recognition and aggressive treatment in optimizing outcomes in immune-mediated necrotizing myopathies and underscores the need for further research into viral infections as potential contributors to its pathogenesis.

Keywords: ***anti-SRP; anti-RO52; Immune-Mediated Necrotizing Myopathy; cytomegalovirus; Idiopathic Inflammatory Myopathies.***

Introduction

Idiopathic inflammatory myopathies (IIM) are a group of rare autoimmune diseases, with an estimated incidence of 9 to 14 cases per 100,000 inhabitants in European countries [1]. These conditions present a heterogeneous phenotypic spectrum, characterized by skeletal muscle inflammation and weakness, as well as various systemic extramuscular manifestations, which can result in multiorgan dysfunction, increasing both morbidity and early mortality [2].

The European Neuromuscular Centre (ENMC) currently classifies IIM into five subgroups: anti-synthetase syndrome-associated myositis (ASS), overlap myositis (OM), dermatomyositis (DM), sporadic inclusion body myositis, and immune-mediated necrotizing myopathy (IMNM) [3]. Polymyositis (PM) remains a controversial entity, as it may be categorized into various groups such as ASS, OM, and IMNM [3].

IMNM represents a small proportion of IIM cases and has been described as a distinct form, characterized by myonecrosis with minimal lymphocytic infiltration [1,2,4,5]. It is currently subdivided into three categories: two mediated by autoantibodies (signal recognition particle - SRP, also known as IMNM-SRP, and 3-hydroxy-3-methylglutaryl-CoA reductase - IMNM-HMGCR) and a third category negative for these autoantibodies [1,4].

The factors responsible for this immune response are not yet fully understood; however, there is a strong established association between the use of statins and IMNM-HMGCR [2,4,5]. Certain genetic, paraneoplastic, medications and infections, especially viral, have been linked to the development of some IIM [2]. Cytomegalovirus (CMV) infections have been associated with certain forms of IIM, such as DM; however, these cases are rare, and the available literature on this association remains limited [6].

IMNM-SRP occurs more frequently after the fourth decade and is more common in women than in men [4,5]. It presents itself as a predominantly proximal muscle weakness, with an acute or subacute onset, and very high serum creatine kinase (CK) concentrations, which correlate positively with the extent of muscle weakness and necrosis [1,5]. The clinical presentation may also include myalgias, dyspnea, dysphagia, and muscle atrophy, with occasional involvement of distal, bulbar, and axial muscles [1]. Cardiac involvement is rare but can be severe, and mild interstitial lung disease (ILD) has also been described in some cases [1,4,5]. Diagnosis is based on clinical and analytical findings, including the detection of serum anti-SRP autoantibodies [4]. Muscle biopsy, although not essential for diagnosis, may reveal significant muscle necrosis with minimal inflammatory infiltrates, and electromyography (EMG) can show predominantly proximal myopathic patterns [2,4]. Magnetic resonance imaging typically reveals diffuse or patchy muscle edema, as well as muscle atrophy and increased adipose tissue [1,3].

In general, IMNM-SRP cases present with high clinical severity and a variable response to immunosuppressive therapy [5]. There are no specific guidelines for the treatment of IMNM-SRP, and current recommendations are based on experts opinions [4,5]. According to the 224th ENMC International Workshop, treatment should include induction with prednisolone or methylprednisolone (MPDN), possibly in combination with another agent such as rituximab, methotrexate, or intravenous immunoglobulin (IVIg) [5].

In severe or refractory cases, plasmapheresis, cyclophosphamide, and/or cyclosporine may also be considered [5]. After remission, maintenance therapy includes tapering corticosteroids to the minimum effective dose. Only after long-term disease control, with minimal or no corticosteroids, should the discontinuation of other agents be considered [5].

Case Report

We present the case of a 73-year-old woman with a medical history of obesity (body mass index 36.1 kg/m²), with no other relevant health conditions or chronic medication.

The patient had been healthy until ten weeks prior to her admission to the Emergency Department (ED), when she developed a likely viral condition, characterized by fever (axillary temperature peaking at 38,5ºC) and myalgias lasting for two weeks. After these symptoms resolved, she experienced progressive muscle weakness in both lower and upper limbs, leading to frequent falls, an inability to walk or maintain a seated position, and ultimately, dependence on others for basic daily activities such as hygiene and eating. In the two weeks preceding her ED visit, she developed resting dyspnea, edema in all four limbs, and dysphagia predominantly to solids. Upon admission to the ED, she was hemodynamically stable, eupneic, with a peripheral oxygen saturation of 95% on room air, and no signs of respiratory distress. Neurological examination revealed marked dysphonia but no cognitive deficits. She exhibited cervical flexion weakness with preserved lateral cervical rotation, facial hypomimia without asymmetry, and proximal tetraparesis with a distal motor deficit (2/5), while sensory function and deep tendon reflexes were globally preserved. Generalized symmetric edema was present in both the upper and lower limbs.

Laboratory tests revealed markedly elevated levels of lactate dehydrogenase at 860 U/L (< 280), CK at 2474 U/L (< 70), myoglobin (Mb) at 1322 µg/L (25-58), and high-sensitivity troponin T (hs-TnT) at 1166 ng/L (< 14), without evidence of renal dysfunction or significant fluctuations on serial assessments. N-terminal pro-B-type natriuretic peptide was within the normal range at 580 pg/mL (< 623). Mild cytolysis was also observed, with aspartate aminotransferase (AST) at 222 U/L (8-33) and alanine aminotransferase (ALT) at 138 U/L (4-36). Arterial blood gas analysis showed mild hypercapnia (pCO_2 47 mmHg) and mild hypoxemia (pO_2 68 mmHg), without acidemia and HCO3- 38 mEq/L. The electrocardiogram and transthoracic echocardiogram were unremarkable. Chest radiography and computed tomography (CT) scans of the brain, as well as the cervical, thoracic, and lumbar spine, revealed no significant findings.

Given the suspicion of myositis, the patient was admitted to an Internal Medicine ward for further investigation. EMG confirmed a myopathy, revealing predominant proximal muscle involvement and evidence of muscle fiber necrosis. Extensive virological testing was conducted, including human immunodeficiency virus, hepatitis A, B, and C viruses, severe acute respiratory syndrome coronavirus 2, Epstein-Barr virus (EBV), parvovirus B19, influenza A and B, enterovirus, and CMV. CMV testing was positive for both IgM at 2.4 (positive cut-off >1.0) and IgG at 639 U/L (positive cut-off >1.0), despite a negative viral load. In the autoimmune panel, antinuclear antibody was positive (fine speckled cytoplasmic pattern), and the myositis panel revealed positivity for anti-SRP and anti-Ro52 antibodies, establishing the diagnosis of IMNM-SRP.

On the third day of hospitalization, intravenous MPDN pulses (1 g/day) were initiated, resulting in a slight overall improvement in muscle strength. However, after the third day of corticosteroid therapy, the patient's respiratory status worsened, progressing to global respiratory failure that required orotracheal intubation and invasive mechanical ventilation (IMV), prompting transfer to the intensive care unit (ICU). Chest CT revealed moderate bilateral pleural effusion with atelectasis in adjacent pulmonary segments. The echocardiogram showed preserved biventricular function, no valvular disease, and a calculated pulmonary artery systolic pressure of 72 mmHg. Following endotracheal intubation, there was improvement in the atelectatic areas, which consequently led to a reduction in pleural effusion.

She remained in the ICU for twenty-seven days, during which she underwent three sessions of plasmapheresis, IVIg therapy, and two doses of rituximab administered two weeks apart. A gradual tapering of corticosteroid therapy was initiated. Weaning from IMV was successfully achieved, followed by extubation to supplemental oxygen through a tracheostomy. She was subsequently transferred back to the Internal Medicine ward, where oxygen therapy was discontinued, and the tracheostomy was successfully closed. She initiated physiotherapy, occupational therapy, and speech therapy, showing significant clinical improvement. She was later transferred to the Physical Medicine and Rehabilitation ward for an intensive rehabilitation program, where she remained for an additional two months.

At the time of hospital discharge, while on 30mg of oral prednisolone, she was described as free of dysphonia, dysphagia, or dyspnea, with preserved facial mimicry and recovered cervical muscle strength. She was able to independently transfer between bed and chair, maintain a seated position on her own, and walk with the aid of a walker. She was self-sufficient for eating, although she still required assistance with other daily activities, such as hygiene.

Table 1: illustrates the analytical evolution over time, from admission to the ED (day zero - D0) until hospital discharge on day 106 (D106). A favorable analytical trend was observed during the course of treatment, with a progressive decrease in muscle necrosis markers, which improved significantly by the time of discharge.

	Normal range	D0	D3	D6	D9	D13	D32	D34	D106
CK	**< 70 U/L**	2474	1523	1202	786	322	91	71	56
Mb	**25-58 µg/L**	1322	1482	1545	---	---	---	187	---
hs-TnT	**<14 ng/L**	1166	1163	1715	---	---	439	318	34
AST	**8-33 U/L**	222	193	177	131	115	58	36	33
ALT	**4-36 U/L**	138	127	114	83	71	39	34	32

Table 1 Analytical evolution since hospital admission to discharge. ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine kinase; hs-TnT: high-sensitivity troponin T; Mb: myoglobin

Discussion

IMNM-SRP is recognized as one of the most severe forms of IIM, characterized by profound muscle weakness, extensive necrosis and atrophy, elevated CK levels, and an unpredictable response to immunosuppressive therapy, making its management particularly challenging [5].

A high frequency of recent CMV infections has commonly been associated with other autoimmune diseases, notably systemic lupus erythematosus, systemic sclerosis and rheumatoid arthritis,

and has occasionally been reported in cases of IIM [6,7]. The association between IMNM-SRP and acute EBV infection has already been described. However, the role of CMV in IMNM remains unclear [8].

In our patient, the possibility of a post-infectious immune response to CMV was made, based on the initial clinical presentation suggestive of a viral infection, compatible with CMV. This hypothesis was further supported by the subsequent development of predominantly proximal myopathy and laboratory findings showing elevated CMV-specific IgG titers, low IgM levels, and undetectable viral load. To the authors' knowledge, this is the first case suggesting a potential link between IMNM-SRP and CMV, which may provide new insights into the pathogenesis of IMNM.

Respiratory failure in IMNM arises from two pathophysiological mechanisms, which may operate independently or in combination. The first mechanism involves direct respiratory muscle weakness due to inflammation and fibrotic necrosis of myocytes in both respiratory muscles (diaphragm and intercostal muscles) and accessory respiratory muscles (scalene and sternocleidomastoid muscles) [4]. This results in a progressive decline in the contractile capacity required for effective ventilation, ultimately leading to inadequate alveolar ventilation, hypercapnia, and respiratory acidosis [4]. The second mechanism is related to pulmonary complications caused by ILD, which are less common in cases with anti-SRP autoantibodies and more frequently associated with the presence of anti-Ro52 autoantibodies [9,10]. ILD is characterized by an autoimmune inflammatory process that promotes thickening and fibrosis of the pulmonary interstitial space, leading to hypoxemia, ventilation-perfusion mismatch, and reduced pulmonary diffusion capacity [9]. The combination of these two mechanisms increases the respiratory workload and exacerbates ventilatory failure. In the specific case analyzed, additional factors contributing to global ventilatory dysfunction include prolonged immobilization and the potential presence of Obesity Hypoventilation Syndrome. The coexistence of anti-Ro52 and anti-SRP autoantibodies is associated with a particularly severe clinical phenotype characterized by high morbidity and mortality [10,11]. This presentation includes profound and rapidly progressive muscle weakness with extensive necrosis attributed to anti-SRP autoantibodies, along with a high risk of developing inflammatory or fibrotic ILD mediated by anti-Ro52 autoantibodies [10,11]. The combination of these factors poses a significant risk of progression to respiratory failure and chronic functional disability. Patients generally require aggressive immunosuppressive therapy and continuous pulmonary monitoring, even in the initial absence of ILD [9-11].

Despite the guarded prognosis, clinical evolution varies and depends on several factors [2,4]. These include the degree of muscle involvement, the presence of systemic manifestations such as ILD, early disease identification, prompt initiation of appropriate immunosuppression, the effectiveness of the treatment response, and strict control of complications [2,4].

Despite the initial gravity of this case, characterized by extensive muscular involvement and rapidly progressive respiratory symptoms culminating in global respiratory failure requiring ventilatory support, the patient demonstrated a favorable clinical outcome following treatment. This highlights the potential for recovery in severe cases with timely and effective intervention. Another factor that may have contributed to this positive outcome was the absence of fibrotic ILD. Biochemical improvement in muscle necrosis markers during treatment correlated with clinical progress, reflecting the beneficial impact of the multidisciplinary and immunosuppressive approach, which was crucial for stabilizing her condition and supporting gradual recovery.

Conclusions

This case highlights a potential association between IMNM-SRP and recent CMV infection, suggesting the latter as a possible trigger. Although IMNM is characterized by a particularly severe clinical phenotype, associated with high morbidity and mortality, early diagnosis and the implementation of effective immunosuppressive strategies are crucial for improving patient prognosis and quality of life. The potential link between CMV and the development of IMNM is rarely documented in the literature, opening new avenues for research into the pathogenesis of this rare and complex myopathy. Further investigation is needed to clarify the precise role of CMV and other viral infections in modulating immune responses and influencing the clinical progression of IMNM-SRP.

List of abbreviations

ALT: Alanine aminotransferase
ASS: Anti-synthetase syndrome-associated myositis
AST: Aspartate aminotransferase
CK: Creatine kinase
CMV: Cytomegalovirus
CT: Computed tomography
DM: Dermatomyositis
EBV: Epstein-Barr virus
ED: Emergency Department
EMG: Electromyography
ENMC: European Neuromuscular Centre
hs-TnT: High-sensitivity troponin T
ICU: Intensive care unit
IIM: Idiopathic inflammatory myopathies
ILD: Interstitial lung disease
IMNM-HMGCR: 3-hydroxy-3-methylglutaryl-CoA reductase immune-mediated necrotizing myopathy
IMNM-SRP: Anti-signal recognition particle immune-mediated necrotizing myopathy
IMNM: Immune-mediated necrotizing myopathy
IMV: Invasive mechanical ventilation
IVIg: Intravenous immunoglobulin
Mb: Myoglobin
MPDN: Methylprednisolone
OM: Overlap myositis
PM: Polymyositis

Declarations

Ethics approval and consent to participate

Consent was given by the patient for the writing of this article.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Authors' contributions

BS was actively involved in patient care, collected and analyzed the patient data, and drafted the manuscript. FG, ML, and JT contributed to patient care and played a significant role in critically reviewing and revising the manuscript. MR also participated in patient care. All authors have read and approved the final version of the manuscript.

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