Inflammatory Myopathy with Cardiac Involvement Associated with Anti-Mitochondrial Antibodies

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Authors’ contributions

This work was carried out in collaboration among all authors. Authors BW and BHI managed the literature searches and wrote the first draft of the manuscript. Authors BFF revised the article. Authors AJ, MA, KM, RA, AN and SB took part in the survey and patient care. Author LKC validated the manuscript. All authors read and approved the final manuscript.

ABSTRACT

Aim: Anti-mitochondrial antibodies (AMA) positive myositis is an atypical and rare form with various characteristics. We aim to highlight these specificities through this case report.

Presentation of the Case: We present the case of a young woman diagnosed with frequent polymorphic ventricular extrasystoles and left ventricular dysfunction. Two years after, she developed asthenia and muscle weakness. Clinical and biological tests confirmed the diagnosis of myositis complicated by focal myocarditis. The immunological screening revealed negative antinuclear antibodies and positive AMA type anti-AMA-M2 and anti-M2-3E. A good clinical evolution was noted under corticosteroids and methotrexate.

Discussion: Cases of primary biliary cholangitis (PBC) or positive AMA associated with other autoimmune diseases such as systemic scleroderma, Sjögren syndrome, rheumatoid arthritis and...
myositis have been reported. AMA’s pathogenic role on the musculoskeletal and cardiac systems remains to be clarified.

**Conclusion:** Inflammatory myopathy associated with AMA is a rare and serious entity, characterized by a delayed diagnosis and frequent cardiac involvement, often indicating a heavy treatment.

**Keywords:** Myositis; arrhythmias; myocarditis; antibodies.

1. **INTRODUCTION**

Idiopathic inflammatory myopathies are a large group of diseases characterized by immunological muscle injury. Four subgroups are well distinct: dermatomyositis, inclusion body myositis, immune-mediated necrotizing myopathy, and antisynthetase syndrome [1]. Extra muscular manifestations are common, including cardiac involvement [2]. Antimitochondrial antibodies (AMA) positive myositis is an atypical and rare form with various characteristics [3].

We present a new case of a young woman with arrhythmia preceding the diagnosis of AMA positive inflammatory myopathy.

2. **PRESENTATION OF THE CASE**

A 40-year-old woman with a history of congenital divergent strabismus complained, in 2017, of dyspnea and palpitations. Physical examination was normal. Her electrocardiogram showed frequent polymorphic ventricular extrasystoles. Serum electrolytes and thyroid checkup were normal. Transthoracic echocardiogram showed a moderate systolic left ventricular dysfunction (left ventricular ejection fraction (LVEF) =45-48%). Coronary angiography showed intact coronary arteries. Cardiac magnetic resonance imaging (MRI) was also normal. She had therefore been medicated with bisoprolol, antiarrhythmic drug class Ic (flecainide) and the combination of spironolactone and potassium sparer with stabilization of the cardiac rhythm. Two years after, she presented with asthenia and muscular weakness persistent for several months. She was admitted to the internal medicine department. No other systemic symptoms were found in the clinical review except ocular sicca syndrome. Loss of proximal muscle strength was confirmed by physical examination. The cardiac reevaluation (electrocardiogram and transthoracic echocardiogram) didn’t show new patterns. Chest radiograph was normal. Abnormal blood test results are shown in Table 1.

Complete blood count, erythrocyte sedimentation rate, C-reactive protein, glucose, serum creatinine/blood urea nitrogen, electrolyte panel, blood gas and thyroid function were unremarkable. Myocardial MRI showed a nodular enhancement focus at the infero-lateral basal level compatible with focal myocarditis (Fig. 1).

Flecainide was stopped. Recent trauma, electrolyte, endocrine disturbances, pharmacological/toxic causes, or infections were excluded. Electromyography showed a myopathic pattern with low amplitude and polyphasic motor unit potentials. Inflammatory myopathy was strongly suspected. Muscle biopsy revealed a discreet lymphocytic myositis (Fig. 2).

The immunological screening revealed negative antinuclear antibodies and positive AMA type anti-AMA-M2 and anti-M2-3E. Myositis immunoblot showed positive anti-Mi-2 and anti-Ro-52 antibodies. Liver blood tests normalized.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Value</th>
<th>Reference value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatine kinase</td>
<td>2360 UI/l - 3200UI/l</td>
<td>&lt;195 UI/l</td>
</tr>
<tr>
<td>Lactate dehydrogenase</td>
<td>412 UI/l</td>
<td>140-271 UI/l</td>
</tr>
<tr>
<td>Aspartate transaminase</td>
<td>64 UI/l</td>
<td>&lt;50 UI/l</td>
</tr>
<tr>
<td>Alanine transaminase</td>
<td>57 UI/l</td>
<td>&lt;40 UI/l</td>
</tr>
<tr>
<td>Gamma glutamyl transferase</td>
<td>79 UI/l</td>
<td>&lt;50 UI/l</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>119 UI/l</td>
<td>32-91 UI/l</td>
</tr>
<tr>
<td>Pro-brain natriuretic peptide</td>
<td>303.3 pg/ml</td>
<td>&lt;125 pg/ml</td>
</tr>
<tr>
<td>Troponin</td>
<td>142 ng/l</td>
<td>&lt; 40 ng/l</td>
</tr>
</tbody>
</table>
spontaneously and no morphological abnormalities were detected by the CT scan and the liver elastography.

The patient was treated as an inflammatory myopathy with cardiac involvement associated with AMA with a high dose of corticosteroids (1mg/Kg/d) and methotrexate (15mg/week). After two months, muscles strength was stable and biological patterns (muscle and cardiac enzymes) decreased gradually. No elevation of liver patterns was noted.

3. DISCUSSION

Inflammatory myopathies are a heterogeneous group of autoimmune diseases. Their pathogenesis and clinical characteristics depend on immunological parameters. Various auto-antibodies have been discovered since 1976 [4].

These antibodies have been divided into myositis-specific and myositis-associated autoantibodies [5] leading to more accurate classification of the different types of myopathies.

A high prevalence of positive AMA among connective tissue patients has been highlighted [6]. AMA might be part of myositis-associated antibodies. They are known to be directed against nine mitochondrial antigens. They are detected by indirect immunofluorescence on Hep-2 cells or on rat kidney, liver and stomach substrates, with the specific aspect of multiple nuclear dots, and by immunoblot.

Anti-AMA-M2 antibodies are specific of primary biliary cholangitis (PBC). They are detected in 90% to 95% of the cases [7]. Cases of PBC or positive AMA associated with other autoimmune diseases such as systemic scleroderma, Sjögren syndrome and rheumatoid arthritis have been reported [6].

PBC has been reported to be associated to inflammatory myopathies in 23 case reports since 1974. The first study evaluating the association of positive AMA to inflammatory myopathies was conducted in Japan in 2012 [8]. Since then, many teams [3,9-12], tried to better clarify this subject by leading larger scale
Cardiac manifestations in inflammatory myopathies are variable. They are factors of gravity and poor prognosis leading to mortality in patients with myositis [2,15]. Their frequency in polymyositis/dermatomyositis range between 6% and 75%. They include myocarditis, congestive heart failure, arrhythmias, cardiomyopathy, coronary artery disease. Pericarditis, pericardial effusion, and tamponade are found less commonly. Subclinical cardiac manifestations were found in 13% to 72% of the cases while apparent manifestations occur in less than 10% of the cases [15]. Myocarditis was observed in 3.6% of antisynthetase syndrome [16]. In PBC, 4.1% of the patients may develop cardiac manifestations [17]. Myocarditis and dilated cardiomyopathy are mostly found. On the other hand, 20% to 30% of AMA-positive myositis develop cardiac involvement including decreased LVEF and arrhythmias [18]. Our patient presented arrhythmia with a decreased LVEF preceding muscle involvement by two years.

In fact, anti-AMA-M2 antibodies were found to be an independent risk factor for arrhythmia [13].
Cardiac injury is suggested to be consequent to mitochondrial dysfunction and vegetative nervous system dysfunction leading to arrhythmia [19]. Anti-RO antibodies were also found to be markers of cardiac involvement [20]. AMA titer isn’t correlated with the disease evolution. It shouldn’t be a criterion for aggressive treatment. Furthermore, no correlation has been proven between antibodies titer and PBC activity or progression [12]. The Japanese study suggested AMAs were a severity factor in the addition to cardiac involvement [8]. Therefore, corticosteroids combined with immunosuppressive treatments should be considered. 10 to 90% of patients received immunosuppressive therapies added to corticosteroids [12]. Clinical and biological improvement has been reported in the majority of the cases. Our patient received Prednisone at the dose of 1 mg/Kg per day and Methotrexate 15 mg per week with clinical and biological improvement.

4. CONCLUSION

Inflammatory myopathy associated to AMA is a rare and a serious entity, characterized by a delayed diagnosis and frequent cardiac involvement, often indicating a heavy treatment. Our report relates the challenges of diagnosis and treatment of such myositis.

This entity can’t be classified as a distinct subgroup of overlapping myositis yet. Further prospective and large scale studies may better characterize it.

CONSENT

As per international standard or university standard, patient’s written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


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