

# Acute heart failure and rhabdomyolysis: a clue for the diagnosis of polymyositis with cardiac involvement

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## SUMMARY

Polymyositis is an idiopathic inflammatory myopathy, characterized by proximal muscle weakness and sometimes extramuscular manifestations.

We report the case of a 51-year-old male, with history of complete heart block, which required pacemaker implantation, and subsequently heart failure, presenting to the emergency department with worsening of dyspnea and peripheral edema. He was admitted to the Internal Medicine ward with acute heart failure and started on diuretic therapy. During hospitalization, he was discovered to have marked rhabdomyolysis. Examination revealed proximal symmetrical muscle weakness and arthralgia. The immunological study, electromyography and muscle biopsy confirmed polymyositis. The patient was started on prednisolone with clinical improvement and resolution of rhabdomyolysis. The presence of conduction defect, ventricular dysfunction, mitral valve regurgitation, segmental hypokinesia (myocardial scintigraphy without perfusion defects) and pulmonary hypertension, as well as elevated troponin with improvement after specific therapy, points to cardiac involvement. Polymyositis is a rare entity, with an insidious evolution and a myriad of extramuscular features that can mimic other conditions. In particular, cardiac involvement may be the first and only recognized manifestation. The key point for the diagnosis is to contemplate the possibility of polymyositis.

**Key words:** *Inflammatory myopathies; Polymyositis; Rhabdomyolysis; Heart involvement; Acute heart failure.*

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## ■ INTRODUCTION

The inflammatory myopathies are a heterogeneous group of acquired disorders, in which the immune system is thought to play an important pathogenic role. The major subtypes are: dermatomyositis (DM), polymyositis (PM), immune-mediated necrotizing myopathy, and inclusion body myositis (1).

PM is characterized by proximal skeletal muscle weakness and by evidence of muscle inflammation. Extramuscular features are common and include: cutaneous manifestations, interstitial lung disease, and involvement of the heart, articular and vascular systems, emphasizing its systemic nature (2, 3).

It is a rare disease and classified as a sepa-

rate entity among idiopathic inflammatory myopathies, being the least common (1). The estimated prevalence is confounded by frequent misdiagnosis of inclusion body myositis and muscular dystrophies as PM. Traditionally, it has been considered more prevalent (70 per million), but comparative studies with attention to previous diseases have found a prevalence of 35 per million (4).

This article reports a case of PM with cardiac involvement.

## ■ CASE REPORT

A 51-year-old Caucasian male, unemployed, came to the Emergency Department (ED) in February 2015 complaining of dyspnea and peripheral edema.

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His significant past medical history included: alcoholism and smoking habits; chronic liver disease and chronic pancreatitis associated with alcohol; a periampullary carcinoma diagnosed in December 2011, for which a cephalic duodenopancreatectomy had been performed (pT2 N0 R0 - AJCC 7<sup>th</sup> ed.), without evidence of recurrence. In the sSpring of 2013, elevated values for creatine kinase (CK) were found varying from 5900 U/L to 10635 U/L (reference value: <171 U/L); these were thought to be associated with physical traumatic events due to several falls related to alcohol abuse. In July 2013, he developed a 3<sup>rd</sup> degree atrioventricular (AV) block, which had required pacemaker implantation. One year later, he was diagnosed with heart failure with reduced ejection fraction of unknown etiology, presumably alcoholic, usually in functional class II NYHA. Transthoracic echocardiogram showed a moderate systolic left ventricular dysfunction, moderate mitral regurgitation, pulmonary hypertension (estimated pulmonary systolic arterial pressure of 40 mmHg) and lateral, posterior and mid-basal inferior wall motion alterations; the myocardial perfusion scintigraphy excluded ischemia and confirmed these contractility changes. He had therefore been medicated with furosemide and carvedilol, but with low compliance.

Over the three months before admission, the patient had had worsening of dyspnea, orthopnea and peripheral edema. On physical examination, he presented cyanosis, polypnea, jugular venous distension, crackles on pulmonary auscultation and significant peripheral edema.

The blood gas analysis showed mild hypoxemic respiratory failure, C-reactive protein was 11.9 mg/L (reference value: <3 mg/L), brain natriuretic peptide (BNP) was 1400 pg/mL (reference value: <100 pg/mL); complete blood count, erythrocyte sedimentation rate, glucose, serum creatinine/blood urea nitrogen and electrolyte panel were unremarkable. The electrocardiogram (ECG) showed pacemaker rhythm and chest radiograph

revealed moderate pleural effusion bilaterally.

The patient was admitted to the Internal Medicine ward with the diagnosis of acute heart failure. Diuretic therapy with intravenous furosemide was started, with substantial improvement of dyspnea and peripheral edema, nevertheless the pleural effusion persisted. Considering the previous history of gastrointestinal cancer, a thoracentesis was then performed which showed evidence of a transudate. Serum lactate dehydrogenase (LDH) was high (836 U/L, reference value: 135-225 U/L), and a broad laboratory assessment was performed: aspartate transaminase (AST) was 137 U/L (reference value: 10-37 U/L), CK was 7229 U/L, myoglobin was 2378.3 ng/mL (reference value: <146.9 ng/mL), aldolase was 142.4 U/L (reference value: <7.6 U/L); CK-MB mass was 157.00 ng/mL (reference value: <6.4 ng/mL) troponin I - 1170 ng/L (reference value: <40 ng/L); the liver panel (with the exception of AST) and the thyroid function tests were normal.

Review of the clinical history in view of this incidental rhabdomyolysis revealed that the patient already suffered from asthenia, myalgia and loss of muscle strength with difficulty of getting up from a chair, climbing stairs or carrying weights, as well as some peripheral arthralgia of both inflammatory and mechanical nature. He denied any recent trauma. Other causes of rhabdomyolysis were also excluded such as endocrine, electrolyte disturbances, pharmacological/toxic causes, or infections. The investigation was focused on the inflammatory myopathies. The immunological study revealed positive antinuclear antibodies (titer 1:320, speckled pattern) and negative anti-extractable nuclear antigens. Other antisynthetase antibodies (to the OJ, EJ, PL-7, PL-12, KS, Zo, Ha antigens) and antibodies to signal recognition particle (SRP) could not be tested as these were not available at our hospital.

Electromyography showed a myopathic pattern with low-amplitude and short-duration polyphasic motor unit potentials,

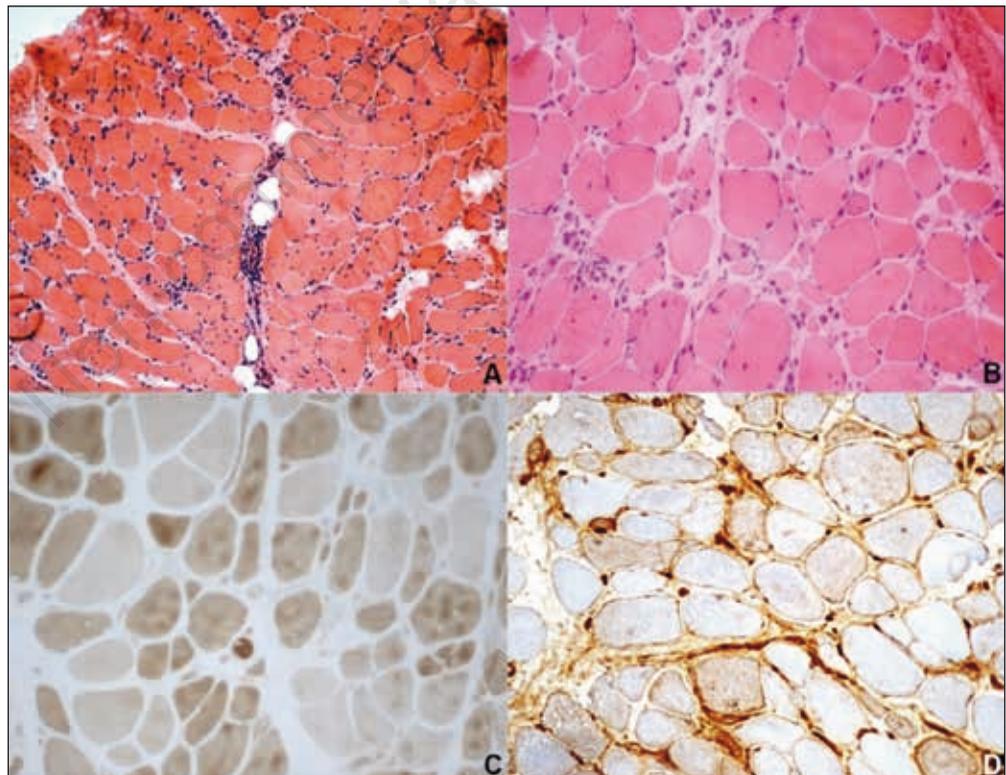
as well as complex repetitive discharges and spontaneous fibrillations which were more obvious in the proximal muscles of the upper-extremities.

A deltoid muscle biopsy was performed. Cryostat sections showed various abnormalities. There were interstitial aggregates of lymphocytes, some in septa and others within fascicles (Figure 1A). There were scattered necrotic fibers. Clear invasion of non-necrotic fibers by lymphocytes was not seen. There were numerous atrophic fibers with rounded contours, possibly indicating incomplete regeneration (Figure 1B). The majority, but not all, were of histochemical type 2 (Figure 1C). Perifascicular atrophy was absent. The sarcolemma of all fibers showed positivity with the antibody to the major histocompatibility (MHC) antigens type 2 (Figure 1D). Electron microscopy showed exten-

sive reduplication of the basal lamina of most muscle fibers. Small rounded granular osmiophilic aggregates were observed surrounded by basal lamina next to some muscle fibers. Such structures are commonly encountered in biopsies of polymyositis, but they can be seen to a minor degree in some dystrophies (5). Nonspecific myofibrillar disorganization with Z disc streaming was seen in some fibers. Endothelial cells did not show tubuloreticular inclusions (Figure 2).

This patient fulfilled the criteria of PM namely: symmetric proximal muscle weakness, elevated serum muscle enzymes (up to 50-fold normal), myopathic changes on electromyography and a muscle biopsy showing an inflammatory myopathy consistent with polymyositis.

Prednisolone was started at a dose of 1 mg/kg per day, with obvious improve-



**Figure 1** - A) The muscle biopsy showed variation in the fiber size and a chronic lymphocytic inflammatory infiltrate, mainly around vessels in the septa, but also within fascicles (HE); B) Presence of numerous atrophic and regenerating fibers; C) The majority, but not all, of these were of histochemical type 2 (ATPase pH 9.4); D) Increased expression of MHC-2 in the sarcolemma (immunohistochemistry - MHC-2).

ment of muscle strength, dyspnea and as-thenia, with resolution of rhabdomyolysis as well as normalization of serum CK-MB mass and troponin levels.

## ■ DISCUSSION

Idiopathic inflammatory myopathies constitute a group of skeletal muscle diseases characterized by weakness and chronic inflammatory infiltrates in the muscle. The pathophysiology of various forms of inflammatory myopathy are poorly understood.

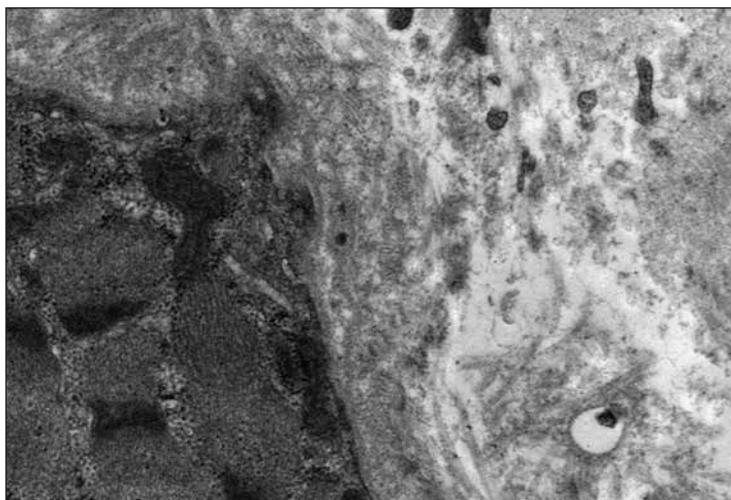
PM is a multisystem disorder with a wide range of clinical manifestations. Muscle weakness is the most common feature (affecting over 90% of patients at presentation), and it usually has an insidious development, with gradual worsening over a period of several months. It is characteristically symmetric and proximal, affecting the deltoids and hip flexors. Distal muscle weakness, when it occurs, tends to be mild and usually does not cause significant functional impairment (3, 6, 7).

A careful clinical history, complete physical examination, laboratory testing with electromyography and muscle biopsy should confirm the diagnosis (8).

Although the skeletal muscle involvement is predominant in PM, the disease has a systemic nature with frequent extra-muscular manifestations (3, 9). Patients may suffer from arthralgia and/or arthritis, a variety of skin disorders (in conjunction with or without DM), and general symptoms or signs such as fatigue, weight loss, fever or Raynaud's phenomenon. The gastrointestinal, pulmonary, and cardiac systems may be involved too, and adversely affect prognosis. These manifestations may precede or follow the development of myositis, and their severity may be independent of the degree of myositis (3, 9, 10).

Overlap with other rheumatic diseases may be present, for example with systemic lupus erythematosus or systemic sclerosis (10).

Several immunological findings are characteristic of PM: autoantibodies (includ-



**Figure 2** - The electron micrograph shows multiple detached segments of basal lamina close to a muscle fiber. A small collection of dense osmiophilic granules lies within a circle of basal lamina. Such structures are commonly encountered in biopsies of polymyositis, although they can occur in other conditions (5). Scale bar = 200 nm.

ing antinuclear antibodies) in up to 80% of patients; myositis-specific autoantibodies in at least 30-40% of patients (antisynthetase antibodies and antibodies to signal recognition particle - SRP); and myositis-associated autoantibodies (anti-Ro, anti-La, anti-Sm, or anti-RNP antibodies) especially in patients with overlap syndromes (11).

### *Cardiac involvement*

Heart involvement is one of the main prognostic factors of PM, representing a major cause of death (3, 12). Subclinical manifestations are often reported and are dominated by conduction abnormalities and arrhythmias detected by ECG (often asymptomatic). Clinical manifestations are less frequent and appear as conduction abnormalities (which may lead to complete heart block), coronary artery disease and congestive heart failure (3, 12, 13). The identification of heart involvement is extremely reliant upon the patient's reporting suggestive cardiac symptoms and subsequent investigations. Nevertheless, due to the high impact of cardiac involvement on prognosis, it is mandatory to perform an accurate study in all patients

**Table I** - Proposed investigations to assess the presence of heart involvement in PM.

<b>First-level examinations</b>	Medical history, family history, signs and symptoms
	12 lead ECG
	Markers of cardiac necrosis: ultrasensitive troponin I, cardiac creatine kinase, myoglobin
	BNP or pro-BNP
<b>Second-level examinations</b>	Cardiac ultrasound
<b>In selected cases</b>	Cardiac stress test
	Cardiac magnetic resonance imaging
	24-hour holter monitoring

Adapted from Miller, 2012 (9).

independently from the presence of overt clinical manifestations (Table I) (13).

As far as this case is concerned, the patient presented several features of cardiac involvement such as: 3<sup>rd</sup> degree AV block (requiring pacemaker implantation 18 months before); an echocardiogram with left ventricular dysfunction, mitral valve regurgitation, segmental hypokinesia (myocardial perfusion scintigraphy without evidence of ischemia) and pulmonary hypertension, all of these reported to be associated with PM; congestive heart failure and elevation of biomarkers of myocardial damage (CK-MB mass and troponin I) which normalized after beginning a specific therapy. A heart MRI was not requested, due to the pacemaker which contraindicated this exam.

### Treatment

Most patients with PM are treated with corticosteroids and generally respond well. Treatment usually begins with prednisolone (or equivalent) at 1mg/kg/day orally until significant improvement occurs (typically 1 to 3 months), followed by gradual taper of 10mg/day per month (9, 14, 15). Second-line agents include azathioprine, methotrexate, mycophenolate mofetil, tacrolimus, and intravenous immunoglobulin. They may be used to spare patients chronic high doses of corticosteroids, or in those whose response to corticosteroids alone is insufficient. As treatment of refractory

disease is difficult, there is growing interest in evaluating novel therapies that target various pathways implicated in the pathogenesis of myositis. Several small series and a limited number of clinical trials tried to evaluate the potential use of biologic therapies in PM, even though efficacy data remains limited. Additional well-designed controlled clinical trials are required to assess the role of biologics in myositis and to develop an evidence-based approach to the treatment of refractory PM (16).

### CONCLUSIONS

The present report describes a case of polymyositis with cardiac involvement, with an unusual clinical presentation. As demonstrated, cardiac involvement seen in PM may be the first and only recognized manifestation. Therefore, better awareness of this disease and its characteristic clinical features is an essential step to make an accurate diagnosis.

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