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Case Report

Cardiac transplantation in dermatomyositis: A case report and literature review

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ABSTRACT

Background and objectives: Cardiac involvement has been well recognized in patients with dermatomyositis (DM) and polymyositis (PM) with a variable frequency between 9 and 72%. However, clinically significant heart involvement in DM/PM is relatively infrequent and there have been rare reports of cardiac transplantation in DM. Our aims were to describe a case of severe cardiac involvement in DM requiring heart transplantation and review the literature of cardiac disease in DM and PM.
Methods: A patient with dermatomyositis who was referred to our institution with severe heart failure is described. Pathology of the patient's skeletal and cardiac muscle is reviewed. A MEDLINE database search of reports of cardiac involvement in DM and PM was also conducted.
Results: A 36 year-old man with DM presented with severe heart failure to our institution for evaluation of heart transplantation. After a three month hospitalization he underwent successful cardiac transplantation. Pathological examination of his explant heart revealed a pattern of inflammation and damage similar to DM in skeletal muscle. The patient is currently doing well, 20 months post-transplant, and is maintained on tacrolimus, cellcept, rituximab, and low dose prednisone. To our knowledge, this is the first case report of heart transplantation in dermatomyositis in which the muscle pathology is similar in both heart and skeletal muscle.
Conclusions: Severe cardiac involvement requiring transplantation is rare in dermatomyositis but does occur and appears to be related to a similar inflammatory process as noted in the skeletal muscle.

1. Introduction

Dermatomyositis (DM) and polymyositis (PM) are both idiopathic inflammatory myopathies (IIM) characterized by proximal muscle weakness and inflammatory cell infiltrates within the skeletal muscle [1,2]. Cardiac involvement such as conduction abnormalities, arrhythmias, congestive heart failure, valvular/pericardial/coronary artery disease and left ventricular dysfunction has been reported as a common cause of death [3–5]. Severe cardiac involvement in IIM is rare and only two cases of cardiac transplant in IIM have been reported, one in a patient with PM and the other in which the cardiac muscle pathology showed giant cell myocarditis. In this report, we describe a patient with severe cardiac involvement in DM requiring heart transplant and review the literature of cardiac disease in DM and PM.

2. Case report

A 36 year old African American male previously in good health presented to an outside facility with diffuse muscle pain and proximal muscle weakness. He described difficulty raising his arms above his head and climbing stairs. He had a pruritic, papular rash on his upper back and anterior chest and complained of itching and swelling around his eyes, hoarse voice, and swelling and stiffness of his hands. Labs were significant for a creatine phosphokinase (CPK) of 12,006 and MRI of bilateral femurs showed diffuse muscle edema. He was started on prednisone at 80 mg daily for possible myositis. He subsequently developed dysphagia, and a muscle biopsy of his left thigh showed severe inflammatory myopathy with perivascular inflammation and zones of pan- and perifasicular atrophy consistent with dermatomyositis or variant. Two months after starting prednisone, the patient began methotrexate at 15 mg weekly and the prednisone was tapered. Due to persistent muscle weakness and CPK elevation after 6 weeks on methotrexate, rituximab was added. Within 6 months of presentation, the patient developed severe fatigue and shortness of breath. He was found to have cardiomyopathy with an ejection fraction of 10–15% and normal

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coronary arteries. Over the subsequent 4 months he had multiple hospital admissions at an outside facility with heart failure complicated by atrial fibrillation, ventricular tachycardia, gastrointestinal bleeding with hemoptysis, and a lower extremity deep venous thrombosis. The patient was transferred to our facility for evaluation of orthotopic heart transplantation (OHT).

Past medical history included heart palpitations as a teenager and an isolated episode of endocarditis 12 years prior to presentation. The patient had played college basketball and noted that he could not pursue professional basketball because he was unable to pass the "heart evaluations" required. He noted that his muscle weakness was worse in sites of old basketball injuries including his left quadriceps muscle and right shoulder. Six months prior to presentation with muscle weakness he had onset of Raynaud's phenomenon and numbness in the hands. Electromyogram and nerve conduction study of the upper extremities at that time revealed bilateral median neuropathy at the wrists and "no electrical instability" of the muscles. Social history was remarkable for no tobacco, IV drugs, or alcohol abuse. The patient worked as a personal trainer.

Upon admission to our facility, the patient had residual lower extremity proximal muscle weakness and a mild hyperpigmented rash on his upper chest and back. He was receiving prednisone 10 mg daily, MTX 25 mg SQ weekly and rituxan was dosed 7 months prior to admission. CPK was 126 IU/L. Serologic testing showed the presence of an anti-Ku antibody. The patient had a complicated hospital course including cardiogenic shock requiring placement of an intra-aortic balloon pump followed by bi-ventricular assist devices (VADs). Immunosuppressive medications were not increased due to concern regarding biVAD infections by the Cardiology Transplant service which would preclude OHT. A month following his initial admission, the patient had bleeding and purulent discharge from his VAD sites and the methotrexate was held and prednisone was decreased to 7 mg daily. The patient's lower extremity weakness worsened and hoarseness of his voice returned. His methotrexate was re-initiated at 10 mg weekly, however after several weeks, his CK level rose to 1400 IU/L and moderate dose prednisone at 40 mg daily and IVIG were initiated. Within 2 weeks of this DM flare, the patient underwent a successful orthotopic heart transplant.

On examination of the explanted heart valvular circumferences were within the normal high limits [6]. The tricuspid (13.2 cm in circumference), mitral (11.7 cm in circumference) and aortic cusps (6.8 cm in circumference) appeared mildly thickened. Mitral chorda were attached to both papillary muscles. All three pulmonary cusps were unremarkable and 6.8 cm in circumference. Pathology of the patient's skeletal and cardiac muscle is shown in Figs. 1 and 2 in detail. Tissue samples obtained from explanted heart included left and right ventricular wall and papillary muscle. Histologic examination showed a multifocal chronic and severe fibrosing myocarditis in all areas examined. Active myocardiocyte injury was evaluated using non-specific esterase (NSE), an enzyme reaction with propensity to detect lysosomal activation and active myodegeneration. This consisted of foci of activity and degeneration also multifocal and of variable severity ranging from single fiber necrosis to large areas of perifascicular injury. Perifascicular active myofiber injury and microvascular immunoreactivity with antibodies to membrane-attack-complex (c5b9) were more prominently noted in samples from right ventricular wall. "Active" mononuclear inflammation was present and moderate in density. This consisted mainly of a T-lymphocytes identified in the area immediately adjacent to the fascicles (perimysium) and adjoining connective tissue. Both CD4-helpers and CD8-cytotoxic T cells were present with no apparent predominance. Histiocytes were distributed diffusely and were present in both endomysium and in peripheral connective tissue. Degenerative changes consisted of lipofuscin deposits, myofiber size variation and splitting consistent with ventricular wall hypertrophy, and reactive mitochondrial features seen on light and electron microscopy.

The patient is currently 25 months post-transplant and doing well. His immunosuppressive regimen includes cellcept (500 mg BID), tacrolimus (1 mg qAM/2 mg qPM), rituxan (1000 mg × 2) every 6 months, and prednisone at 5 mg daily. Rituximab was added to the transplantation medications in order to control his DM. The patient currently plays 2 h of basketball three times a week and beats most of his local competition in Los Angeles.

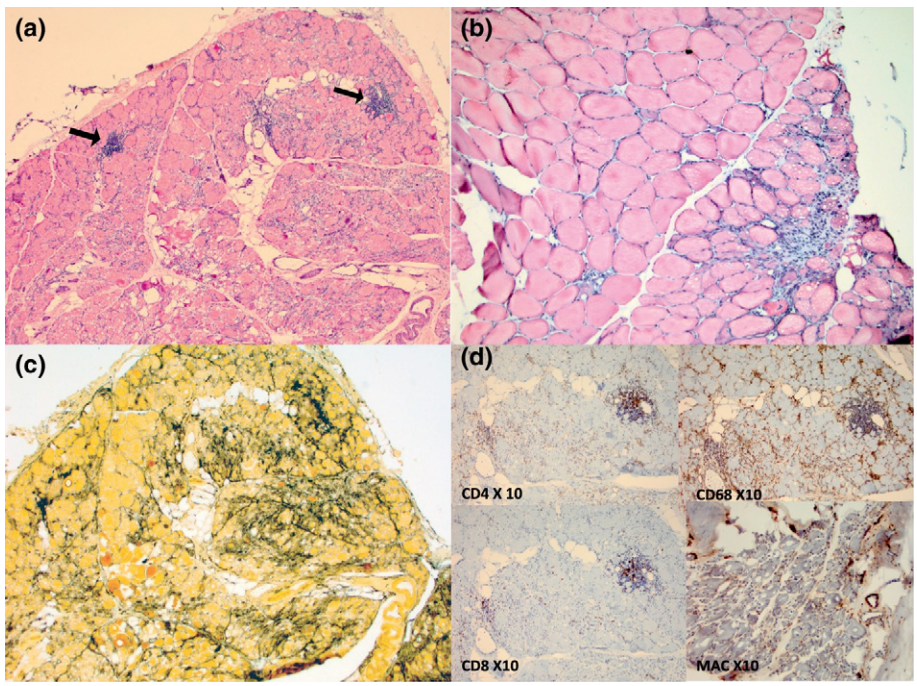

Fig. 1. Skeletal muscle. Skeletal muscle from left thigh showing changes consistent with dermatomyositis (DM) including inflammatory myopathy with perivascular inflammation (arrows), marked fiber damage, and zones of perifascicular atrophy (panels a and b; H&E, original magnification 10×). Additional changes consistent with DM include prominent connective *epi*-/perimysial tissue reaction with alkaline phosphatase (AP) staining (panel c, AP 10×), and increased membrane attack complex (MAC) expression in the muscle microvasculature (panel d). Presence of prominent CD4 lymphocytes and numerous CD68 positive histiocytes was also noted (panel d).