

PENILE AND SCROTUM SWELLING IN JUVENILE DERMATOMYOSITIS

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Abstract

Edema is a well-known feature of juvenile dermatomyositis (JDM). However, to our knowledge localized penile and scrotum swelling was not previously reported. During a 27-year period, 5,506 patients were followed up at the Pediatric Rheumatology Unit of our University Hospital and 157 patients (2.9%) had JDM. One of them (0.6%) had concomitant localized penile and scrotum swelling. He had severe disease activity since he was 7-year-old, manifested by diffuse cutaneous vasculitis, recurrent localized edema (limbs or face) and only one episode of generalized edema. At the age of 10, he presented edema of the genitalia associated with mild skin erythema. Penis, scrotum and testicular ultrasound as well as magnetic resonance imaging showed skin edema without testicular involvement. He was taking prednisone, methotrexate, cyclosporin, hydroxychloroquine and thalidomide. Improvement of skin rash, penile and scrotum swelling was noticed only with rituximab therapy. No adverse event was observed during anti-CD20 infusions and after six months of follow up. Penile and scrotum edema was a rare manifestation of JDM which improved with anti-CD20 monoclonal antibody treatment.

Keywords: Juvenile Dermatomyositis; Rituximab; Penis; Scrotum; Edema.

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Introduction

Juvenile dermatomyositis (JDM) is a systemic disease characterized by nonsuppurative inflammation of the skeletal muscle and skin^{1,2}. The disease is initially marked by the presence of vasculitis and later on by the development of calcinosis³.

Constitutional symptoms, such as fever, alopecia, weight loss, fatigue, headache and irritability, are usually present at the disease onset⁴. Of note, edema is a well-known feature of the disease, mainly in localized areas. The most common regions of this manifestation are eyelids, face and distal extremities⁵. Generalized edema associated with JDM was rarely reported⁵⁻⁹. To our knowledge isolated penile and scrotum swelling in JDM patients were not reported.

During a 27-year period (January 1983 to December 2010), 5,506 patients were followed up at the Pediatric Rheumatology Unit of Instituto da Criança, Faculdade de Medicina da Universidade de São Paulo and 157 patients (2.9%) had JDM. We report a unique case of a pre-pubertal JDM patient (0.6%) who presented concomitant penile and scrotum swelling without testicular involvement.

Case Report

A 7-year-old boy was diagnosed with JDM according to Bohan and Peter criteria due to Gottron's papules, heliotrope rash, muscle weakness, elevated muscle enzymes serum levels, inflammatory infiltrate and perifascicular atrophy at muscle histopathology and characteristic electromyographic changes¹⁰. He had severe disease activity, manifested by diffuse cutaneous vasculitis and recurrent localized edema (limbs or face) and one episode of generalized edema. He developed calcinosis in numerous sites of the body and considerable joint contractures, including elbows, wrists,



Figure 1. Penile and scrotum swellings in one juvenile dermatomyositis patient

hips, knees and ankles, despite having been treated with intravenous methylprednisolone, prednisone, methotrexate, cyclosporine, hydroxychloroquine sulphate, alendronate, diltiazem, thalidomide and intravenous immunoglobulin. At the age of 10, he presented an one-month marked painless swelling of the penis and scrotum, associated with mild skin erythema in the pubic region (Figure 1). He also presented periorbital rash, erythematous maculopapular lesions on the extensor surfaces of the hands, vasculitis, photosensitivity, disseminated calcinosis, symmetric proximal weakness with a grade-3 muscle strength and significant muscle atrophy. The Childhood Myositis Assessment Scale (CMAS)¹¹ and the Disease Activity Score (DAS)¹² were not performed due to fixed contractures of the knees. He was taking prednisone 0.12mg/kg/day, methotrexate 1.0mg/kg/week, cyclosporin 5.0mg/kg/day, hydroxychloroquine 6.2mg/kg/day, alendronate 70mg/week, diltiazem 5.6mg/kg/day and thalidomide 2.3mg/kg/day. Erythrocyte sedimentation rate (ESR) was 62 mm/h (normal range 0-20 mm/h), aspartate aminotransferase (AST) 40 U/l (normal range 10-34 U/l), alanine aminotransferase (ALT) 32 U/l (normal range 10-44 U/l), creatine kinase (CK) 50 U/l (normal range 24-204 U/l), lactic dehydrogenase (LDH) 272 U/l (normal range 211-423 U/l), aldolase 11.8 U/l (normal range 1-7.5 U/l), albumin 4.3 g/dl (normal range 3.8-5.6 g/dl), urea 13 mg/dl (normal range 15-45 mg/dl) and creatinine 0.16 mg/dl (normal range 0.6-0.9 mg/dl). He was on pre-pubertal stage and the hormone profile was normal: follicle-stimulating hormone – FSH 4.39

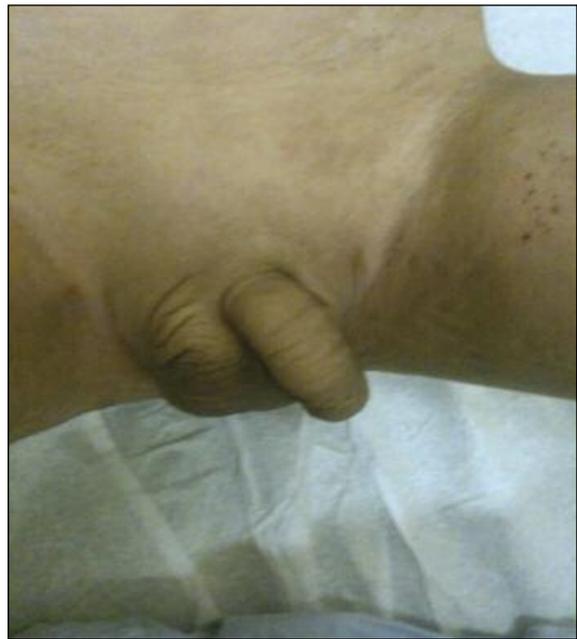


Figure 2. Improvements penile and scrotum swellings after rituximab therapy in one juvenile dermatomyositis patient

IU/l (normal range 1,5-12,4 IU/l), luteinizing hormone – LH 1.09 IU/l (normal range 0,1-7,8 IU/l), and morning total testosterone 0.03 ng/dl (normal range 0,03-0,68 ng/dl). Immunological tests were positive for antinuclear antibodies (ANA) 1:640 (fine speckled pattern) and anti-Ro 52 Kd, and negative for other antibodies: anti-Mi-2, anti-synthetase (anti-Jo-1, anti-PL-7 and anti-PL-12), anti-Ku, anti-PM-Scl, anti-double stranded DNA (anti-dsDNA), anti-Sm, anti-RNP, anti-La and anti-Scl-70. Penis, scrotum and testicular ultrasound showed skin edema without testicular involvement, as it was also observed in the magnetic resonance imaging. He was treated with rituximab 375 mg/m²/infusion for 4 weeks. After the third dose, improvement of cutaneous vasculitis and complete resolution of genital edema was already observed (Figure 2). Six months later, he had grade-4 muscle strength, maintained calcinosis, and CMAS¹¹ and DAS¹² could not still be performed due to the fixed contractures of the knees. Laboratory findings were ESR 26 mm/h, AST 28 U/l, ALT 31 U/l, CK 45 U/l, LDH 201 U/l and aldolase 7,5 U/l. Prednisone was suspended with maintenance of other drugs. No adverse event was observed during anti-CD20 monoclonal antibody infusions and after six months of follow up.

Discussion

To the best of our knowledge, this is the first case of genital edema without orchitis in JDM. Moreover, this manifestation was a rare finding in our Pediatric Unit.

Edema is a clinical feature of JDM, usually confined to the face or limbs. Anasarca has been rarely described at the onset and during the disease course⁵⁻⁹, as reported above. Our recent Brazilian multicenter study, which included 189 JDM patients, reported facial edema in 34% at the onset of the disease and body edema in 15%⁴.

The pathogenesis of edema in JDM is unknown^{1,2}. This manifestation is thought to be mediated by active focal destruction of capillaries. In fact, the activation of the complement cascade induces vessel injury and capillary damage due to membrane attack complex¹³. Up-regulation of adhesion molecule expression also occurs when activated complement C5a binds to endothelial cells¹. The widespread endothelial damage and increased capillary permeability in muscle and subcutaneous tissue may lead to hypoproteinemia and edema¹⁴.

Our patient had an erythematous and homogeneous scrotum and penis edema. Skin infections, renal dysfunction, hypoalbuminemia and cancer were excluded, suggesting that penile edema is one possible feature of JDM. A penis carcinoma with tender swelling of the distal shaft was evidenced in one adult with dermatomyositis¹⁵. In fact, JDM and cancer association was observed in 2/189 (1%) patients in our Brazilian multicenter study, but no penile malignancy was observed⁴.

In addition, other urogenital involvement and gonadal dysfunction associated with JDM were infrequently reported. Dystrophic calcification in ureter area was observed in one of our JDM patients¹⁶. Jalleh *et al* evidenced testicular necrotizing vasculitis in a 7-year-old boy suffering from this disease¹⁷, and scrotum and testicular edema with calcinosis were also recently described in two of our JDM patients¹⁸. Furthermore, Moraes *et al* found minor sperm abnormalities in 5 JDM post-pubertal patients¹⁹.

Our JDM patient had a severe disease and was previously treated with various immunosuppressive drugs concomitantly. Interestingly, genital edema improved only with rituximab therapy. This biological agent targets the CD20 molecule, leading to transient but almost complete depletion of

B cells. In fact, B cells and autoantibodies participate in the etiopathogenesis of this inflammatory myopathy. This drug was beneficial in adult and pediatric patients, without severe side effects, as observed here^{20,21}. Furthermore, the CD19 lymphocyte count was reduced in three JDM patients after the fourth dose of rituximab²⁰.

In conclusion, we report what we believe to be a rare manifestation of JDM, that is, penile and scrotum edema, which improved with anti-CD20 monoclonal antibody infusions.

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