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Severe juvenile dermatomyositis: two patients complicated with extra musculocutaneous involvement

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Abstract Here we report two patients with severe juvenile dermatomyositis (JDM) complicated with extra musculocutaneous involvement. The first case (a 10-year-old boy) had unusual initial presentation of JDM complicated with interstitial lung disease documented with high-resolution computed tomography. He had a rapidly progressive course and died in 7 weeks after the onset of the disease despite steroid and immunosuppressive treatment. The second case (a 14-year-old boy) was presented with myositis complicated with hepatitis. He also had a chronic course of JDM with unfavorable outcome. It appears that the prognosis of patients with severe JDM is related with the degree of autoimmune vasculitis on extra musculocutaneous involvement.

Keywords Interstitial lung disease · Hepatitis · Juvenile dermatomyositis · Prognosis

Abbreviation JDM: Juvenile dermatomyositis · HRCT: High-resolution computed tomography

Introduction

Juvenile dermatomyositis (JDM) is an autoimmune systemic vasculopathy, affecting primarily the skin and

muscle, causing characteristic skin rash and proximal myopathy [1–5]. It differs from adult form of dermatomyositis by the presence of vasculitis of the small blood vessels, which can involve the pulmonary and gastrointestinal tract as well as myocardium, in addition to skin and muscle.

The prognosis of JDM is significantly improved with the contribution of the steroid treatment [3, 4]. A favorable outcome has been reported in 80% of children with JDM in the case of therapy started within 4 months of the onset of symptoms [5]. Death can occur in the acute phase due to myocarditis, progressive unresponsive myositis or occasionally due to lung involvement [2]. Here, we report two boys with severe JDM complicated with extra musculocutaneous manifestations.

Cases

Case 1

A 10-year-old boy was admitted to a local hospital with fever, arthralgia, myalgia and weakness. He was misdiagnosed as having acute rheumatic fever and treated with penicillin and acetyl salicylic acid. Acute respiratory distress syndrome (ARDS) was noticed in the second week of therapy and referred to our intensive care unit in the fifth week of the disease. Then he presented with blistering eruptions over his face and a photosensitive red rash over knuckles, elbows, shoulders and face (initially misdiagnosed as antibiotic rash). There were fine crackles on pulmonary auscultation. Interstitial lung disease (ILD) was diagnosed based on chest X-ray and high-resolution computed tomography (HRCT) studies (Fig. 1). Serologic tests for mycoplasma, brucella, Epstein–Barr virus, cytomegalovirus, hepatitis A, B and C, measles, mumps, rubella and blood culture analysis were negative. Lupus anticoagulant, antinuclear antibodies, rheumatoid factor, antineutrophil cytoplasm antibodies were also negative.

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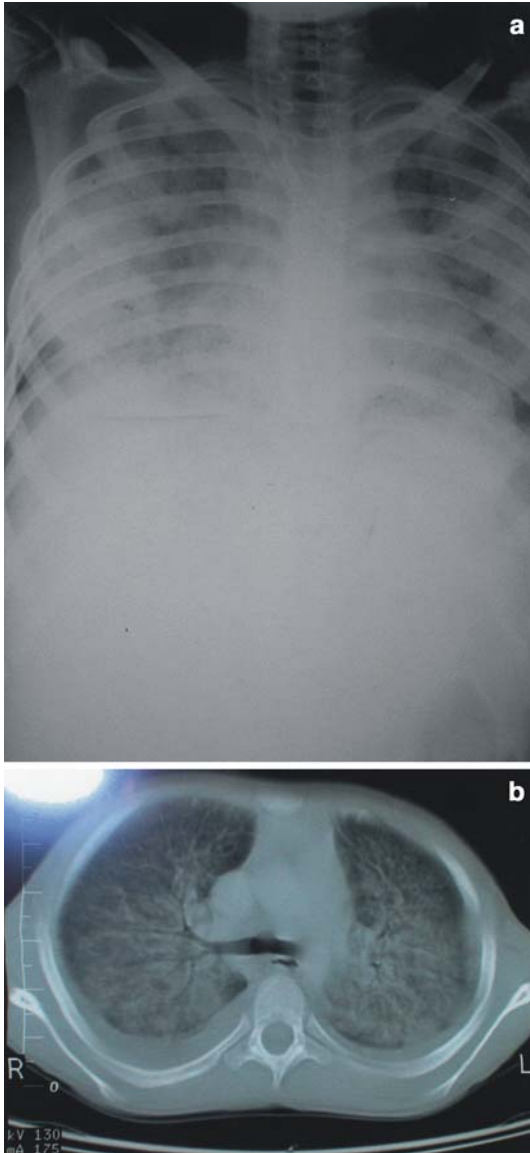


Fig. 1 Case 1: **a** chest X-ray: bilateral pulmonary infiltrates; **b** high-resolution computed tomography (HRCT): pleural effusion of both lungs, significant at the right side. Diffuse alveolar opacities forming air bronchogram in both lungs

Muscle enzymes were creatinine kinase 437 (normally up to 170 U/l), alanine transaminase 318 U/l (N: 3–30 U/l), aspartate transaminase 240 U/l (N: 15–40 U/l), lactate dehydrogenase 3,545 U/l (N: 360–730 U/l) on presentation. Needle electromyography revealed polyphasic and small motor units in the proximal muscles. He was diagnosed with JDM on the basis of clinical, electrographic features and elevated creatinine kinase levels. Muscle biopsy confirmed the diagnosis of JDM with perifascicular atrophy typical for the disease (Fig. 2).

Despite steroid treatment (prednisolone 60 mg daily), he continued to deteriorate with severe ILD. ‘Mechanic’s Hands’ were noted during the sixth week of diagnosis (Fig. 3). Pulse methylprednisolone and

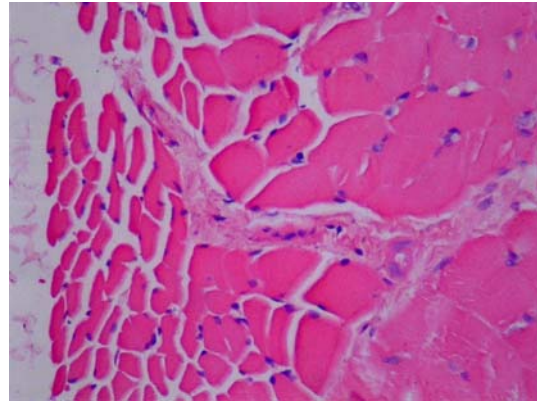


Fig. 2 Case 1: muscle biopsy: perifascicular atrophy in dermatomyositis. HE $\times 200$

cyclophosphamide treatment were initiated for the interstitial lung involvement. With this immunomodulatory and supportive treatment, he showed fulminant progressive course and died 7 weeks after the onset of the disease.

Case 2

A 14-year-old boy was admitted to a local hospital with myalgia and weakness. He was initially diagnosed with hepatitis with elevated alanine transaminase and aspartate transaminase levels. Liver biopsy revealed nonspecific reactive chronic hepatitis. Then he showed progressive deterioration with the loss of weight and muscle weakness within 7 months after the onset of the disease.

On admission to our service, he was cachectic and jaundiced. He had multiple areas of skin ulceration on the extensor side of the arm and heliotrophic rash over his face and generalized muscle atrophy. He had 3 cm hepatomegaly. He was diagnosed with JDM associated with hepatitis. Liver enzymes were high as follows: alanine transaminase 477 U/l (N: 3–30 U/l), aspartate transaminase 350 U/l (15–45 U/l), alkaline phosphatase 317 U/l (N: 100–350 U/l), gamma glutamyl transpepti-



Fig. 3 Case 1: ‘Mechanic’s Hands’

dase 200 U/l (N: 0–23 U/l). However, creatinine kinase was in normal limits 74 U/l (N: 170 U/l). Screening tests for hepatitis A, B and C, Epstein–Barr viruses and cytomegalovirus were negative. Antinuclear antibody, rheumatoid factor, antineutrophil cytoplasmic antibody, lupus anticoagulant, anti-Sm, anti-Jo-1, Scl 70 and liver kidney microsomal antibody were negative. He was treated with ursodeoxycholic acid with the diagnosis of hepatitis with nonspecific etiology. Needle electromyography showed small and polyphasic motor units and deinnervation potentials consistent with primary muscle involvement. Muscle biopsy revealed perifascicular atrophy typical for JDM.

Pulse methylprednisolone (for 5 days) and then oral prednisolone therapy (60 mg/day) were prescribed for 4 months followed by tapering of dosage (1 mg/kg/day) in the following 6 months. Clinical deterioration and progressive ILD developed during the 14th month of therapy. Clinical deterioration with extensive consolidation at chest X-ray and HRCT occurred. He was treated with intravenous immune globulin plus oral 60 mg prednisolone daily. Despite these medications, the patient progressively deteriorated and died with cardiopulmonary arrest 18 months after the initial diagnosis.

Discussion

The diagnosis of JDM can be difficult in patients with absent characteristic rash and symmetric proximal muscle weakness [1–5]. Occasionally the clinical diagnosis of the disease might be complicated with extra musculocutaneous involvement. The overall prognosis for survival is improved after the use of corticosteroids [3–6]. However, delayed diagnosis and presence of extra musculocutaneous involvement such as myocarditis, gastrointestinal tract infarction, ILD might have caused an unfavorable outcome [2, 5, 6]. Both the presented patients with JDM had unfavorable outcome with extra musculocutaneous involvement. The first case had a fulminant course with ILD with acute presentation with fever, dyspnea and lung infiltrates. The second case had chronic continuous course after initial atypical presentation complicated with hepatitis. Both cases died despite immunosuppressive treatment.

The mortality rate in JDM has fallen to less than 5% with contemporary treatment [5]. In recent years, ILD has been reported as the major cause of mortality and morbidity in patients with polymyositis–dermatomyositis with a rate of 5–30%, depending on the method used to assess lung involvement [7–13]. Four main types of ILD have been reported in patients with polymyositis–dermatomyositis: type (I): acute presentation where fever, dyspnea, pulmonary infiltrates appear in less than 2 weeks; type (II): insidious disease with dyspnea, cough and pulmonary infiltrate; type (III): asymptomatic pulmonary infiltrates without respiratory symptoms; type (IV): normal HRCT and chest X-ray findings with

abnormal respiratory function tests [10]. For the first case, acute ILD (type I) with symptoms of dyspnea, fever and respiratory failure appeared after 2–3 weeks of the disease. However, the second patient had no lung involvement at the beginning and he had normal chest CT. The insidious ILD (type II) occurred 14 months after the onset of JDM. Pulmonary involvement was documented with HRCT.

Marie et al. [7] reported that ILD can be diagnosed early in anti-Jo-1 positive dermatomyositis patients by means of periodic pulmonary function testing. However, they also reported that 69% of patients with dermatomyositis and ILD do not have anti-Jo-1 antibodies [8]. Kashiwabara et al. [9] reported a group of dermatomyositis patients who had slight muscular symptoms, slightly elevated serum creatine kinase levels, negative anti-Jo-1 but rapidly progressive ILD. Our patients had negative anti-Jo-1 antibodies. Shibuya et al. [14] reported ‘Mechanic’s Hands’ in three patients complicated with ILD and mild muscular involvement without myositis. They proposed that ‘Mechanic’s Hands’ can occur in association with foot lesions and interstitial pneumonia even if it is not accompanied by myositis. ‘Mechanic’s Hands’ developed in our first case who had fulminant course complicated with ILD.

Gastrointestinal tract involvement including decreased esophageal motility and vasculitis has been reported in patients with JDM [2]. However, hepatic involvement had not been reported in patients with JDM, other than mild elevation of hepatic enzymes. Matsumoto et al. [15] reported different types of liver involvement in 18 adult patients with dermatomyositis–polymyositis: fatty liver (66.7%), hepatic congestion (50%), nonspecific reactive hepatitis (11%) and primary biliary chirosis (5–6%). They concluded that fatty change seen in more than 50% of patients with collagen tissue disease may be due to steroid treatments. Hepatic biopsy of the second patient revealed nonspecific reactive hepatitis and fatty liver changes prior to steroid treatment. We thought that the co-existence of hepatic and pulmonary involvement might have caused the unfavorable outcome in the second case.

Corticosteroid therapy is considered to be the first line of therapy for polymyositis–dermatomyositis patients with ILD. Therefore early diagnosis and management of ILD is very important [7–9, 11]. Administration of cyclophosphamide and corticosteroids together is reported as the most effective treatment in patients with steroid-resistant ILD [7]. Cyclophosphamide was administered to the first patient; intravenous immunoglobulin was administered to the second patient in addition to steroid treatment without clinical response.

In conclusion, the presence of ILD might indicate an unfavorable outcome in patients with JDM. Serial chest X-ray, HRCT, respiratory function test and serum anti-Jo-1 antibodies should be performed for the early diagnosis of ILD in patients with JDM.

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