Juvenile dermatomyositis in a Duchenne muscular dystrophy carrier

Sirs,

Juvenile dermatomyositis (JDM) is a systemic autoimmune disease affecting the muscles and skin in childhood. It is characterised by rashes on the face, hand and trunk, as well as symmetrical proximal muscle weakness and elevated serum myoenzyme (1). Duchenne muscular dystrophy (DMD) is a severe X-linked recessive genetic muscle disorder. It also presents progressive weakness and raised creatine kinase (CK) and lactic dehydrogenase (LDH) beginning in childhood. JDM is an important cause of proximal muscle weakness in children, but other diagnoses need to be excluded.

A 6-year-old girl presented with a 2-month history of symmetrical proximal muscle weakness of lower limb and marked fatigue in the absence of any skin rash. She had moderately elevated erythrocyte sedimentation rate (ESR) of 23 mm/h and normal C-reactive protein (CRP) of 5mg/L. Her CK (339 U/L, normal range 20-180 U/L) and LDH (359 U/L, normal range 110-290 U/L) was raised. Myositis specific autoantibodies by blotting hybridisation including Mi-2, NXP2, TIF1γ, SAE, MDA5 were negative. Magnetic resonance imaging (MRI) revealed diffuse myoedema of both thighs (Supplementary Fig. S1). Electromyography (EMG) showed polyphasic motor unit action potentials (MUAPs) of low amplitude and reduced duration in proximal muscle, indicating a myopathic pattern. A muscle biopsy of the quadriceps demonstrated perifascicular atrophy with perivascular lymphocyte infiltration. Major histocompatibility complex I (MHC-I) and myxovirus resistance protein A (MxA) expression was upregulated in the perifascicular areas. When we performed routine immunohistochemistry of dystrophin distribution at muscle biopsy, faint and patchy dystrophin expression was observed unexpectedly (Fig. 1). Further genetic studies revealed a heterozygous nonsense mutation (c.2251C>T) in *DMD* gene (Supplementary Fig. S2). It is a *de novo* mutation, which was classified as pathogenic according to ACMG guideline (2). As she was diagnosed with JDM, oral prednisone (1 mg/kg/d) and methotrexate (7.5 mg/week, 10 mg/m^2) were initiated. Muscle weakness was completely recovered in 8 weeks, as well as CK, LDH and ESR returned to normal. Prednisone was tapered every 4 weeks and stopped in 12 weeks, while methotrexate has been used for maintenance therapy for 2 years. She remains in good condition now, with normal muscle strength.

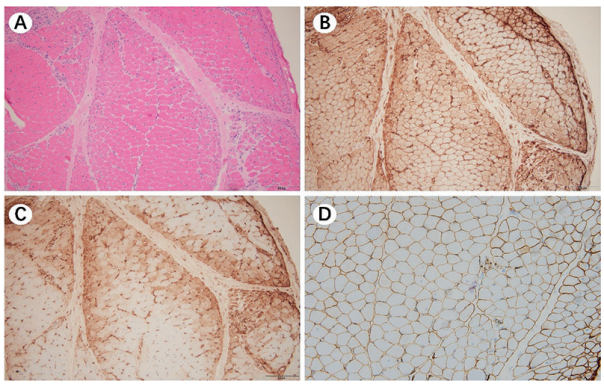

Fig. 1. Pathological findings in quadriceps muscle.
A: Haematoxylin and eosin staining revealed perifascicular atrophy.
B: Diffuse MHC class I overexpression, preferentially in the perifascicular region.
C: Perifascicular sarcoplasmic myxovirus resistance protein A (MxA) positivity.
D: Scattered dystrophin-negative fibres, anti-Dystrophin antibody against the rod domain (**A**-**C** 100× bar=200μm; **D** 200× bar=100μm).

In summary, this paediatric patient had a short history of proximal muscle weakness and moderately raised CK, myoedema on MRI, a myopathic pattern on EMG and muscle biopsy suggestive of dermatomyositis with abnormal dystrophin expression. In conjunction with genetic testing for DMD and good response to treatment, we established the final diagnosed as JDM without evidence of the typical rash and DMD carrier.

Dermatomyositis and DMD are important causes of proximal muscle weakness, and they can present with very similar symptoms. DMD carriers may remain asymptomatic or manifest a spectrum of symptoms from mild to severe muscle cramps or weakness (3), and 10% of cases need medical intervention (4). Unfavourable lyonisation is responsible for mild symptoms in female carriers. Dermatomyositis complicated with DMD is rarely reported, and there was only one case of an adult female patient with dermatomyositis as a DMD carrier (5).

Typical skin phenotype in JDM is important for diagnose. Dermatomyositis sine dermatitis is rare, often leading to a winding diagnostic approach. Differential diagnosis from other muscular disorders including muscular dystrophies is important. Very few DMD carriers develop any symptoms in early years of life. Muscle pathology remained a useful tool for atypical JDM cases and a routine dystrophin staining in biopsy specimens from myositis cases would be beneficial, while genetic studies are necessary for patients with early-onset myositis.

Informed written consent was obtained from the patient's mother.

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