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A case of limb-girdle muscular dystrophy with serum anti-nuclear antibody which led to a mistaken diagnosis of polymyositis

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ABSTRACT

A 45-year-old woman had first been diagnosed with polymyositis because of the presence of focal necrosis, regeneration and inflammatory infiltration in the muscle fibers, and elevated creatinine phosphokinase levels. However, a pathological re-evaluation and family history led to the definite diagnosis of limb-girdle muscular dystrophy (MD). This case suggests that MD should be taken into consideration in the differential diagnosis of the inflammatory myopathies and genetic surveys including dystrophin molecule may be necessary if the condition manifests during or after adolescence, or when the family history is uninformative. In this case, the serum anti-nuclear antibody was positive, and it may represent the first time that ANA positivity has been found in limb-girdle MD.

Introduction

Muscular dystrophy (MD) is a group of inherited myopathies and includes pseudohypertrophic MD of young males (Duchenne) and older males (Beeker), limb-girdle MD, etc. Limb-girdle MD is characterized by muscle weakness in the shoulder or pelvic girdle, usually begins in the second or third decades and shows an autosomal recessive or rarely dominant pattern.

Here a patient with limb-girdle MD is described, who had presented with the presence of anti-nuclear antibody (ANA). A diagnosis of polymyositis was made based on muscle biopsy and the initial response to corticosteroids.

Case report

A 45-year-old woman was referred to our hospital because of muscle weakness. She had been healthy until 8 months prior when she began to feel muscle weakness in the extremities. At first she ascribed her symptoms to overwork, but it gradually worsened and she could hardly climb stairs 7 months later. An elevation of serum creatinine phosphokinase (CK) was detected elsewhere and she was referred to our hospital. Her family history was uninformative, but she reported later that her mother had died 11 years before. Her mother and brother had pseudohypertrophy in the legs and her brother's serum CK levels were always higher than 500 U/ml (N: 30 - 105).

On physical examination, muscle weakness was present in the shoulder girdle (II), biceps and triceps (II), forearm (IV), femoral (III) and tibial (IV) muscles (II: moves if no gravity, III: against gravity, IV: against light external force). The quadriceps were slightly atrophic and there was a mild pseudohypertrophy in the lower legs. In the laboratory findings, ESR was 50 mm/h, CRP 25 mg/l, CK 11,700 U/l, aldolase 140 U/ml (1.7 to 5.7), AST 335 U/l (7 to 40), ALT 125 U/l (0 to 35), IgG 1,842 mg/dl, IgA 409 mg/dl, IgM 200 mg/dl, and the electrolyte and thyroid hormone levels were normal. The serum electrophoresis showed polyclonal hypergammaglobulinemia, and ANA was positive (diffuse and nucleolar), while anti-Jo-1 antibody was negative. An EMG performed in the biceps and quadriceps muscles showed a myopathic pattern (irritability of myofibrils at rest, polyphasic potentials with short duration and low amplitude on contraction), and a biopsy of the quadriceps revealed focal necrosis, regeneration, size variation of muscle fibers, and non-necrotic muscle fibers invaded by inflammatory cells (Fig. 1a).

A clinical diagnosis of polymyositis was made and 40 mg of prednisolone (PSL) commenced. Four weeks later, muscle weakness improved, ESR and CRP normalized, the CK level gradually decreased, and the dose of PSL was tapered to 30 mg. Since the CK level did not decrease to less than 856 U/1 during the following 2 months, 100 mg of cyclophosphamide (CP) was added without any changes being seen in the CK level for 2 months. A re-evaluation of the muscle biopsy (Fig. 1b) was performed at this stage and it was recognized that infiltration of the inflammatory cells was relatively mild as compared to the extent of necrosis and regeneration and there was a pathological adiposity and large dystrophic fibers. These features, as well as resistance to PSL and CP, were considered to be diagnostic of MD rather than polymyositis.

Immunohistochemical examination using anti-dystrophin antibody showed a homogeneously stained muscle sheath

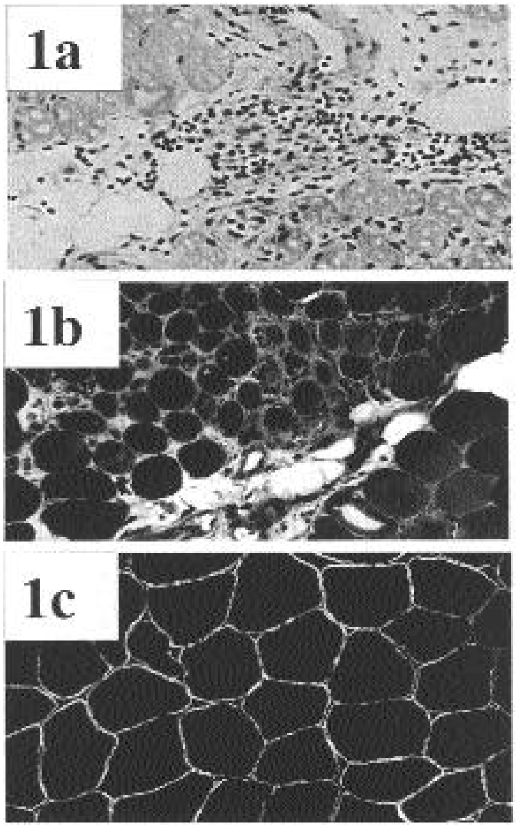

Fig. 1. Muscle biopsy findings (quadriceps) showing focal degeneration, necrosis and regeneration: (**a**) hematoxylin & eosin x250; (**b**) Gomori-trichrome x250. There are size variations in the muscle fibers and infiltration of lymphocytes and macrophages. The muscle sheath is homogeneously stained with anti-dystrophin monoclonal antibody (**c**, x500).

which was thought to be compatible with limb-girdle MD (Fig. 1c). Four weeks later, PSL was tapered off and CP was discontinued. The CK level changed from 800 to 1600 U/l during the following 11 months regardless of the therapy, while it increased transiently after muscular fatigue.

Discussion

It has been reported that there may be reactive inflammation around muscle fibers, especially in the early stages of MD (1-3), although the major findings in MD are degeneration and regeneration of the skeletal muscles. Furthermore, it is known that the mutation of several peptides such as dysferlin or laminin $\alpha 2$ are associated with inflammation (4, 5). Since these pathological findings including inflammatory changes are typical for polymyositis, it may be difficult to distinguish between MD and polymyositis, if the former occurs during or after adolescence, or when the family history is uninformative.

In this case, the presence of ANA and non-necrotic muscle fibers seemed compatible with polymyositis, and the early response to PSL supported this diagnosis. Since the initial reduction in inflammatory parameters and the CK level was not attained by hospitalization alone, PSL was thought to have played a major role. However, the clinical course and re-evaluation of the muscle biopsy, which revealed a low extent of inflammatory cell infiltration, caused us to change the diagnosis to a certain form of MD.

Although an incomplete response to the therapy might represent a refractory case of polymyositis, the family history suggesting autosomal inheritance and the presence of pseudohypertrophy, which is characteristic of Duchenne MD and sometimes of limb-girdle MD, supported MD rather than polymyositis. It is known that, by immunohistochemical examination using anti-dystrophin antibody, the muscle sheath is homogeneously stained in limb-girdle MD, as was seen in the current case, while it is not stained in Duchenne MD or faint and patchy pattern is seen in Becker MD (6). Therefore, this case was thought to be limb-girdle MD.

Recently, the presence of non-organ-specific autoantibodies against myocellular antigens have been reported in myotonic dystrophy (7,8), and ANA was detected in 26% of the patients with progressive MD (9). Therefore, this case might be the first one in which ANA was detected in association with limb-girdle MD. Since the CK level was partially reduced after the administration of PSL, as were the inflammatory parameters, inflammation around the muscle fibers might be not only secondary to muscular degeneration or necrosis, but may also directly affect myocellular damage.

This case suggests that there is a possibility of the presence of the ANA in limb-girdle MD and that clinical and pathological findings of MD resemble those of polymyositis, especially if it manifests during or after adolescence, or when the family history is uninformative. Therefore, MD should be taken into consideration for differential diagnosis of inflammatory myopathies and genetic surveys including dystrophin molecule may be necessary.

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