Asymptomatic Sporadic Dysferlinopathy Presenting with Elevation of Serum Creatine Kinase. Typical Distribution of Muscle Involvement Shown by MRI but not by CT

Satomi Okahashi¹, Go Ogawa², Mikiya Suzuki¹, Katsuhisa Ogata¹, Ichizo Nishino³ and Mitsuru Kawai¹

Abstract

We report an 18-year-old man with elevation of the creatine kinase (CK) level to 11,068 IU/L. There was no muscle atrophy or fat replacement on CT while muscles in the posterior compartment of lower legs showed high T2 signal intensity on MRI. We performed muscle biopsy from the gastrocnemius muscle. Immunohistochemical analysis demonstrated an absence of dysferlin leading to a diagnosis of preclinical dysferlinopathy. Typical distribution of muscle involvement was demonstrated not by CT but by MRI which may have contributed to facilitating diagnosing the earliest stage of preclinical dysferlinopathy, presenting with asymptomatic elevation of serum creatine kinase.

Key words: dysferlinopathy, asymptomatic hyper-CK-emia, muscle imaging

Introduction

Miyoshi myopathy, limb-girdle muscular dystrophy (LGMD) type 2B (1-3) and distal myopathy with anterior tibial onset (4) are autosomal recessive allelic disorders caused by mutation of skeletal muscle gene DYSF encoding dysferlin which resides at chromosome 2p13 (5). Age of onset tends to be around 20 years with characteristic difficulties in walking on the toes accompanied by relative sparing of periscapular muscles (6). Patients are completely asymptomatic before the onset of weakness. However, calf pain has been reported to precede the muscle weakness in rare cases (7). Extremely high serum creatine kinase (CK) is characteristic and may precede weakness several years before clinical onset (8, 9). Thereby presymptomatic patients with dysferlinopathy may be diagnosed as idiopathic or benign hyper-CK-emia. In hyper-CK-emia, the indications for muscle biopsy remain controversial.

We report a patient presenting with elevation of serum creatine kinase, occasional calf pain and MRI signal change in the posterior compartment of the lower leg muscles, in whom the typical distribution of signal change was a strong indication for muscle biopsy to establish a final diagnosis of dysferlinopathy.

Case Report

An 18-year-old man in good health was employed by a railway company. He was the only son of non-consanguineous parents and there was no history of neuromuscular disorders in his relatives. On routine medical checkup including blood examination, elevation of transaminases was noted. During new employee training, he noticed persistent muscle pain in both calves, and was referred to a hospital. Serum CK was high at 11,068 IU/L. Serum aspartate aminotransferase (AST) was 221 IU/L, and alanine aminotransferase (ALT) was 234 IU/L. He was diagnosed as having rhabdomyolysis and underwent fluid repletion followed by observation. Although serum CK soon declined, it remained high at 5,000-6,000 IU/L. The patient was suspected to have a neuromuscular disorder and was referred...
On neurological examination, the patient was quite normal except for slight persistent calf fatigue. There was no muscle weakness or atrophy and the patient could walk on his toes. We performed needle electromyogram (EMG) examination. EMG did not show any fibrillation potentials or fasciculations in the muscles investigated. Gastrocnemius muscle showed a few polyphasic action potentials. The level of action potentials in the muscle was normal. The interference pattern was well preserved. Computed tomography (CT) findings were normal (Fig. 1A, C). Then magnetic resonance imaging (MRI) using short-time inversion recovery sequence (STIR) was performed on the lower and upper legs. MRI demonstrated a high intensity in the gastrocnemius, soleus, semimembranosus and biceps femoris muscles (Fig. 1B, D). Muscle biopsy was obtained from the medial head of gastrocnemius muscle. Hematoxylin eosin-stained frozen section showed a moderate variation of fiber size with a few necrotic and regenerating fibers (Fig. 2). There was no inflammatory cell infiltration. Dysferlin was absent on immunohistochemical analysis. He was diagnosed as having presymptomatic dysferlinopathy.

A few weeks later, calf fatigue was gradually relieved. He returned to work as a railway company employee with careful avoidance of intense muscle activity. MRI obtained from lower legs 2 months after muscle biopsy showed similar signal changes in gastrocnemius and soleus.

Discussion

In dysferlinopathy, muscle CT and MRI clearly show characteristic muscle involvement of the posterior compartment of the legs (10, 11). The hallmark can be seen in the earliest stage or even in the preclinical stage of disease (11, 12).

Brummer et al showed that MRI change precedes CT change by observing dysferlinopathy family members serially (13). The CT change was replacement of muscle by fat tissues, while the MRI change was considered to be tissue edema, which was the most sensitive feature to detect dystrophic alteration in skeletal muscles (13).

Edema-like changes on MRI can also be seen in calf muscles in physiologic condition or in extreme muscle use (14, 15). MRI performed 2 months later in the absence of muscle pain and fatigue showed the same signal change.

The patient was initially diagnosed as having rhabdomyolysis and underwent inappropriate treatment. The indication for muscle biopsy in oligosymptomatic hyper-CK-emia remains controversial. Clinicians must determine the usefulness of an invasive investigation such as muscle biopsy, which is usually a difficult decision when the patient shows...
normal neurological findings. As in this case, the typical
distribution of abnormal muscle signal intensity strongly in-
dicates muscle biopsy, which may establish an accurate di-
agnosis. We must take into account the certain pattern of
muscle involvement when the diagnosis of dysferlinopathy
is suspected.

This is the first case report of asymptomatic sporadic dys-
ferlinopathy whose accurate diagnosis was suggested by
characteristic changes in muscle MRI but not CT and an ex-
tremely high CK level. MRI is a sensitive method for de-
tecting the earliest changes in dysferlinopathy.

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