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Case report

Scoliosis surgery in a patient with "de novo" myosin storage myopathy

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Abstract

Myosin storage myopathy is a rare neuromuscular disorder, characterized by subsarcolemmal inclusions exclusively in type I skeletal muscle fibers, known as hyaline bodies. Its clinical spectrum is diverse, as are its modes of inheritance. Myosin storage myopathy, also called hyaline body myopathy, is caused by a pathogenic mutation in the *MYH7* gene, encoding for the slow/β-cardiac myosin heavy chain.

We describe a patient with this uncommon myopathy, caused by a new p.K1784delK mutation in the *MYH7* gene. The patient developed a severe thoracolumbar scoliosis and had scoliosis surgery.

Keywords: Myosin storage myopathy; Hyaline body myopathy; Scoliosis surgery; *MYH7* gene

1. Introduction

Myosin storage myopathy (MSM) is a rare chronic congenital myopathy of childhood. Since its first description in 1971 about 30 patients have been reported in literature [1,2].

Modes of inheritance include autosomal dominant, autosomal recessive and sporadic patterns [3–5]. The clinical phenotype ranges from asymptomatic hyperCKemia to scapuloperoneal myopathy, proximal and distal myopathy with muscle hypertrophy, with or without cardiomyopathy and may even show striking variability within the same family [6,7]. Scoliosis has been described in three patients [8].

The characteristic histopathological and immunohistochemical features, with exclusively type I fibers affected, make the final diagnosis. Creatine kinase is usually moderately elevated. Electromyographic studies show nonspecific myopathic features at most and electrocardiogram is generally unremarkable [3,4].

We describe clinical and histopathological findings of a patient with MSM, with a new mutation in the *MYH7* gene, who had scoliosis surgery.

2. Case report

A 14-year-old boy was referred because of symptomatic deterioration of walking, progressive forward deviation of the spine and contractures. He walked at the age of 16 months, had a normal mental development, but had never been as good in gymnastics as his peers since age 2 years, with difficulty running and less muscle strength. He was able to play soccer, although with worsening of symptoms after exertion. There was no family history of

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muscle weakness or scoliosis. His 12 year old brother was reported healthy, as were the parents.

On referral, he had a waddling steppage gait, due to general muscle weakness, foot drop, spine deviation and contractures of hip and knee flexors and foot extensors bilaterally. He was unable to sit up from the supine position without using his arms. He had a striking appearance with a short cachectic stature (1.55 m, 38 kg) and prominent contractures of the spine and limbs. Cervical spine rotation and flexion were markedly limited. There was pronounced scapular winging, wasting of rhomboids and pectoralis major muscles and a pectum carinatum. There were contractures of elbow supinators and pronators. At presentation, he had a mild scoliosis and marked forward deviation of the trunk compensated by extension of the spine. Muscle testing revealed general muscle weakness grade 4, with grade 3 in tibialis anterior muscles. The remainder of the neurological examination showed a prominent bulbar speech, brisk tendon reflexes, flexor plantar responses and absence of any cranial nerve, sensation or coordination abnormalities. Within 1 year, the scoliosis progressed and the patient was unable to walk more than 500 m.

Creatine kinase level was 353 U/L (normal value <200 U/L). Electrophysiologic studies displayed normal conduction velocities and myography. Electrocardiogram was unremarkable, echocardiogram demonstrated mild reduced contractility of the left ventricle. Respiratory function tests showed a vital capacity and FEV1 of 70% and 82% of normal values.

Biopsy, taken from the right quadriceps muscle, showed marked variation in fiber size with 9% of the fibers having internal nuclei. Histochemical studies revealed type I fiber atrophy and demonstrated the presence of mostly subsarcolemmal hyaline areas in type I fibers only (Fig. 1A), that stained green with modified Gomori trichome (Fig. 1B). These areas extended quite far in the cytoplasm, sometimes engulfing the nucleus. They showed slight reactivity with ATPase preincubated at pH 10.3 but not at pH 4.2 (Fig. 1D) and showed intense staining with slow myosin but failed to react with fast or other myosin antibodies. On electron microscopy there were sharply limited pale areas within the muscle fibers, devoid of sarcomeres and organelles and filled with finely granular, and sometimes fibrillar material (Fig. 1C and F). There were no signs of inflammation or necrosis. The biopsy findings confirmed the clinical suspicion of myosin storage myopathy.

Mutation analysis was carried out for the full coding exons of the *MYH7* gene. Genomic DNA was extracted from peripheral blood using the Wizard genomic DNA purification kit (Promega, Leiden, The Netherlands). Protein coding sequences and direct intronic flanking regions were amplified by polymerase chain reaction (AmpliTaq Gold, Applied Biosystems, Foster City, CA, USA) and subsequently sequenced with M13 on an ABI 3730 genetic analyzer using BigDye Terminator chemistry v3.1 (Applied Biosystems). Sequence data were analyzed in comparison with reference sequences using Mutation Surveyor 3.2.

In exon 37 of the *MYH7* gene, a novel mutation c.5352_5354delGAA (p.K1784delK) was found. Mutation analysis in both parents indicated the mutation occurred "de novo". False paternity was excluded. The mutation was absent in more than 550 control and cardiomyopathy patients who were referred to our laboratory for *MYH7* analysis.

Because of his progressive thoracolumbar scoliosis within one year after referral, with a progression of Cobb's

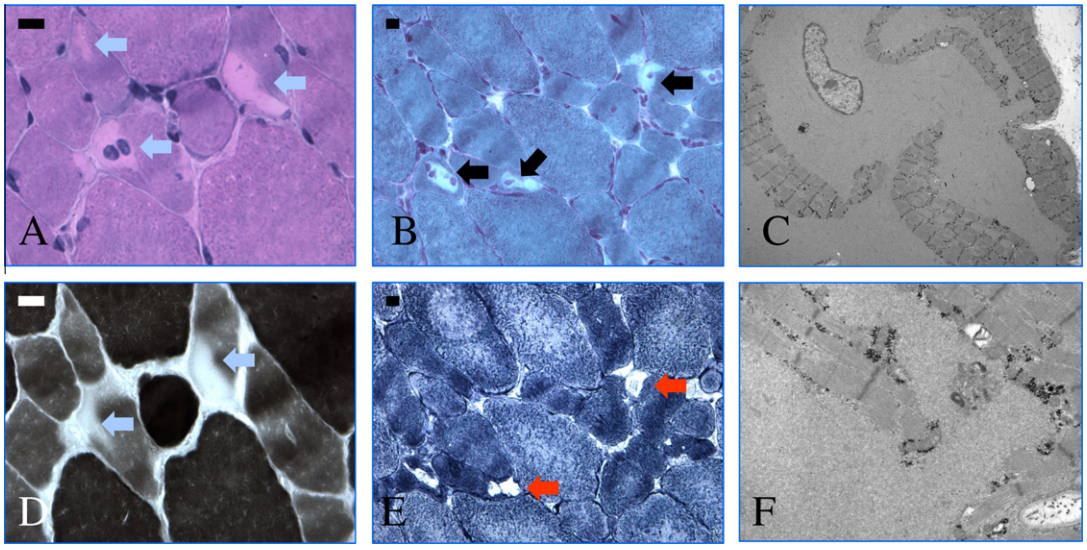

Fig. 1. Quadriceps muscle biopsy with marked variation in fiber size, type I fiber atrophy and mostly subsarcolemmal hyaline areas (arrows) in type I fibers only, that stain green with modified Gomori trichome. On electron microscopy there are sharply limited pale areas within the muscle fibers, devoid of sarcomere and organelles and filled with finely granular, and sometimes fibrillar material. In B and C the hyaline areas are separated from the membrane by some sarcomeres and engulfing the nucleus (A, HE; B, Gomori trichome; D, ATPase pH 10, 3; E, SDH; Bar = 10 μm. C and F, electron microscopy).