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phenotype is caused by a translation re-initiation downstream for the type, but resulted in a mild Becker muscular dystrophy with generalized hypertrophy. This mutation is predicted to result in a Duchenne phenotype in firming that his large body volume was caused by generalized muscle gene. MRI showed a normal distribution between muscle and fat con-

We present a patient with muscle pain from adolescence. On examination he had generalized muscle hypertrophy, but preserved muscle strength and a 10- to 20-fold elevated CPK. Muscle biopsy was dystrophic, and Western blot showed a 95% reduction of dystrophin levels. Genetic analyses revealed a non-sense mutation in exon 2 of the dystrophin gene. MRI showed a normal distribution between muscle and fat con-

Becker muscular dystrophy leads to progressive proximal weakness. Focal wasting is commonly seen in the calves, less typically in other locations such as the thenar eminence. Generalized muscle hypertrophy has been described with other muscular dystrophies such as LGMD 1A and in a X-linked myopathy with postural muscle atrophy caused by mutation in the FHL gene. Generalized muscle hypertrophy with Becker muscular dystrophy (BMD) has not been reported before. We present a patient with muscle pain from adolescence. On examination he had generalized muscle hypertrophy, but preserved muscle strength and a 10- to 20-fold elevated CPK. Muscle biopsy was dystrophic, and Western blot showed a 95% reduction of dystrophin levels. Genetic analyses revealed a non-sense mutation in exon 2 of the dystrophin gene. MRI showed a normal distribution between muscle and fat con-

Duchenne muscular dystrophy (DMD) is an X-linked disease that is caused by mutations in the dystrophin gene and affects one in 3600–6000 live male births. DMD is characterized by progressive weakness leading to a loss of ambulation, respiratory insufficiency, cardiomyopathy and scoliosis. Boys typically present at 3–5 years of age with evidence of proximal weakness and calf hypertrophy. Here we describe the unusual and complicated clinical phenotype of three patients with hereditary skeletal dysplasias in whom an additional diagnosis of DMD was then established. Two unrelated boys presented each with a diagnosis of osteogenesis imperfecta (types 1 and 4) due to point mutations in COL1A1, and were both subsequently found to have a 1 bp frameshift deletion in the dystrophin gene at age 3 and age 15, respectively. The third patient had an established diagnosis of inherited pseudoachondroplasia and was found to have a deletion of exons 48–50 in dystrophin at age 8 years. We discuss the atypical clinical presentation caused by the concomitant presence of two conditions affecting the musculoskeletal system, emphasizing features that may confound the presentation of a well-characterized disease like DMD. Additional case series of patients with DMD and a secondary genetically confirmed condition are necessary to establish the natural history in this “double trouble” patient population. The recognition and accurate diagnosis of patients with two independent genetic disease processes is essential for management.

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G.P.80

Non-sense mutation in exon two of the dystrophin gene results in mild Becker muscular dystrophy with generalized muscle hypertrophy

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Here we report two half-brothers who called our attention due to their strikingly different phenotypes. The youngest one, currently aged 9, is showing a severe course, enlarged calves and can only walk short distances. His older brother, aged 13 is very mildly affected. Their mother only noticed he was affected when the youngest one was diagnosed. He has some difficulties only for running and climbing stairs but he can walk freely and has discrete calves’ hypertrophy. Serum CK was 3260 U/l in the younger and 3620 U/l in the older brother. DNA analysis revealed that both carry an “out of frame” duplication of exon 2 in the dystrophin gene, which was not present in the mother DNA lymphocytes, indicating a gonadal mosaicism. Surprisingly, muscle biopsies analyzed in blind test revealed a very similar pattern in both, despite the clinical differences. Histopathology showed fiber size variation, internally located nuclei, degenerated and hyla-

line fibers, scattered regenerated fibers and discrete connective tissue replacement in both of them. Dystrophin immunostaining with antibodies against the N-terminal and rod domains showed a weak patchy pattern but was negative with the C-terminal domain antibody. Some clusters of 6–8 positive fibers (revertant fibers) were seen in both of them with all antibod-
ies. Western-blot analysis showed a faint band of about 5% of normal, in both of them but a total deficiency with the C-terminal antibody. Muscle dystrophy deficiency has been associated to a severe course in both humans and golden-retriever muscular dystrophy (GRMD) dogs. How-

ever, a rare DMD patient and an exceptional GRMD dog, Ringo, showing a mild course despite the absence of muscle dystrophin have been previ-

ously reported. Further investigation of these exceptional cases, which is currently underway, may help to identify new genes or “protective” mech-

anisms which might hopefully open new avenues of treatment.

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G.P.81

Duchenne clinically discordant brothers: A “Ringo-like” phenotype in humans?

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Duchenne muscular dystrophy is currently underway, may help to identify new genes or “protective” mechanisms which might hopefully open new avenues of treatment.

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G.P.82

‘Double Trouble’: Diagnostic challenges in DMD in patients with an additional hereditary skeletal dysplasia

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