

Rather mild phenotype in a patient with homozygous null mutations in the α -sarcoglycan gene

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The dystrophin-glycoprotein complex connects the cytoskeleton of a muscle fiber to its extracellular matrix. Most forms of muscular dystrophy are caused by mutations in the dystrophin gene. Mutations in the α -sarcoglycan gene, a further member of the dystrophin-glycoprotein complex, also induce muscular dystrophy. We report the history of a woman with homozygous null mutations in the α -sarcoglycan gene and an unusual disease course.

The patient started to have difficulty running and climbing stairs unassisted at 6 years of age. At age 12 she was unable to walk and was wheelchair

bound. At the age of 28 she required nocturnal ventilatory assistance. At the age of 38 she gave birth to a healthy girl by caesarean section. She is currently 43-year-old and presents marked generalised muscle wasting. Serum CK is 498 IU/l (normal: 200 IU/l or less). ECG and echocardiography never revealed an abnormal cardiac rhythm or a pathological myocardial function. The first muscle biopsy, taken from the quadriceps at the age of 16, revealed dystrophic features with a wide variation in fibre size, including fibre hypertrophy and increased endomysial connective tissue. A second biopsy at the age of 38 showed mostly connective

Figure 1

Immunohistochemistry with antibodies to α -sarcoglycan shows a complete absence of the protein.

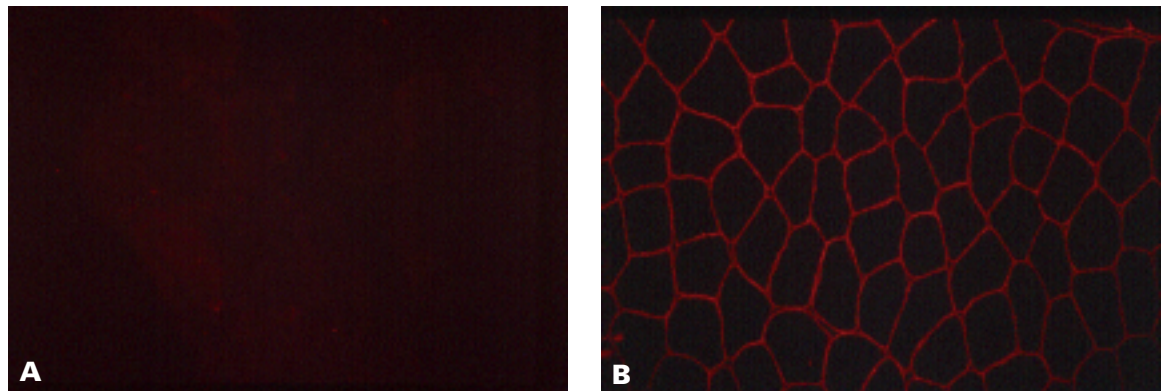
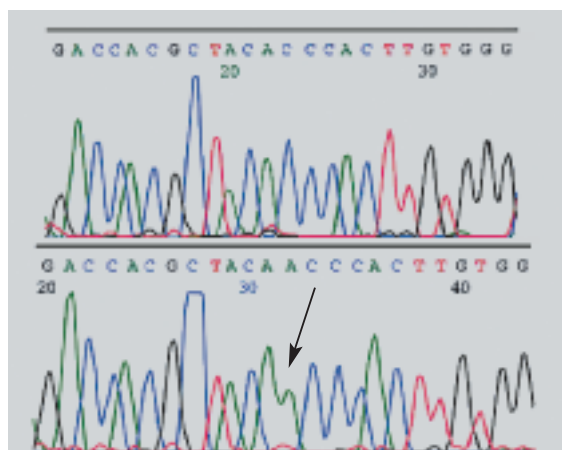


Figure 2

Electropherograms showing part of exon 2 of the α -sarcoglycan gene. Upper panel: wild-type sequence. Lower panel: patient's sequence containing the novel homozygous mutation c.86dupA (arrow).



wild type

patient

tissue and fatty cells with only rare muscle cells. Immunohistochemical analysis demonstrated the presence of dystrophin by staining with three antibodies (Dys 1-3, Novocastra) but absence of α -sarcoglycan (figure 1) and abnormally decreased staining of β - and γ -sarcoglycan. Molecular biology studies revealed a previously unreported homozygous mutation in the α -sarcoglycan gene: c.86dupA in exon 2 (figure 2). Patients homozygous for null mutations in the α -sarcoglycan gene tend to present during infancy with a very severe disease [1–3]. The rather benign disease course

noted in our patient confirms that caution is needed before drawing conclusions regarding genotype–phenotype correlations.

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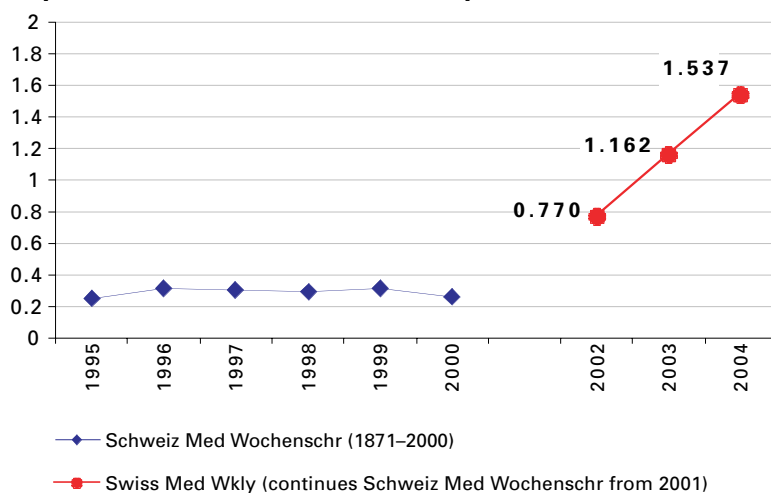
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