Case 50
Carrying Shopping Can Be Difficult, Especially for Men

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History

A nineteen year old man presented with a long history of progressive limb weakness and deformity at the elbows. He was the product of a normal delivery with normal feeding and breathing. At one year, his parents noticed that he was unable to support his head independently. He otherwise reached normal motor and cognitive milestones. At four, he was especially slow at running with frequent trips and falls. He continued to be poor at sports and discontinued sporting activity aged twelve. He became progressively more fatigued when walking and using his arms. He also found increasing restriction of movement at his elbows. His swallowing and breathing were normal and there was no clinical history to suggest nocturnal hypoventilation. There was no history of kyphoscoliosis and in general his symptoms were stable with minimal progression over the past few years.

There was no evidence of cardiomyopathy on ECHO or conduction defects on ECG.

He had two brothers who were unaffected but his mother was mildly affected with upper limb weakness. His maternal grandfather developed a similar clinical course.

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Examination

Examination of the cranial nerves demonstrated mild symmetrical facial weakness. His upper limbs and distal lower limbs below the knees demonstrated reduced muscle bulk. There was weakness in biceps to MRC grade 4/5. There was a reduced carrying angle to 140° at the elbow bilaterally associated with contractures in the biceps. Otherwise upper limb power was normal. In the lower limbs, he had preserved power, and he was able to walk on his toes and heels. He was able to rise from crouching with arms crossed. Reflexes were present throughout and sensory examination was normal. General examination was otherwise normal. Lung function testing demonstrated FEV1 3.58 L and FVC 3.76 L. His creatine kinase level was 792 (<240)

Genetic testing
Deletion c.705_722del18 in exon 6 of the emerin gene

Diagnosis

X-linked Emery Dreifuss Muscular dystrophy (EDMD).

Discussion

Emery Dreifuss Muscular dystrophy was first described in 1966 with neuromuscular presentation in early childhood. The course of the disease is slower and more benign in comparison with Duchenne muscular dystrophy. Early loss of ambulation is rarely seen. The phenotype is characterised by three cardinal manifestations. Firstly, contractures of the Achilles tendons, elbows, and/or posterior cervical muscles usually occur early, and before there is clinically significant weakness. Secondly, slowly progressive muscle wasting and weakness with a humeroperoneal distribution occurs early in the course of the disease. Later weakness extends to the proximal limb-girdle musculature. Thirdly, dilated cardiomyopathy usually manifests as spectrum of cardiac conduction defects such as sinus bradycardia, prolongation of the PR interval, or complete heart block. This may necessitate cardiac pacemaker implantation. Atrial paralysis with absent P waves on electrocardiography should always prompt exclusion of this form of muscular dystrophy. Evidence of cardiac disease is usually present by age 30 years and becomes more evident as muscle weakness progresses. Serious cardiac manifestations can arise in the absence of muscle weakness and is a possible cause of sudden death in apparently healthy young adults.

Emerin-associated EDMD is inherited as an X-linked recessive trait and is caused by mutations in the STA gene at Xq28, which encodes the nuclear membrane

protein emerin. In almost all cases, there is complete absence of emerin on muscle biopsy analysis. Immuno-histochemistry of skin fibroblasts may show a mosaic pattern of expression of emerin in female carriers, thus providing a valuable test for identification of such individuals.

The autosomal dominant form of EDMD can present with a more severe clinical phenotype compared with X-linked, but with marked inter-generational variability. It is caused by mutations of the LMNA gene at 1q21. This gene encodes lamins A and C, which comprise part of the nuclear lamina which is a fibrous layer on the nucleoplasmic side of the inner nuclear membrane. Diagnosis of autosomal dominant Emery-Dreifuss muscular dystrophy can only be verified by mutation analysis, and not by muscle protein studies. There is a rare, more serious autosomal recessive form of EDMD, which is also caused by mutations of the LMNA gene as well as other forms of EDMD caused by mutations in other genes such as FHL1.

The diagnosis of EDMD should be considered in any patient with a neuromsucular phenotype who presents with prominent early contractures. The prominent cardiac manifestations should raise early concerns regarding counselling of family members for genetic testing and cardiac screening.

References

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