

Despite being an extremely rare and variable condition, Haberland syndrome has some distinctive clinical and radiological features. Both neurologists and radiologists should therefore evaluate these findings as a whole to diagnose the condition as early as possible.

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Emery-Dreifuss muscular dystrophy type 2: New de novo mutation in the lamin A/C gene[☆]



Distrofia muscular de Emery-Dreifuss tipo 2: nueva mutación de novo en el gen la lamina A/C

Dear Editor,

Emery-Dreifuss muscular dystrophy (EDMD) is characterised by the following clinical triad: joint contractures beginning in childhood and initially affecting elbows, ankles, and neck; muscle weakness initially in a humero-peroneal distribution that subsequently extends to the scapular and pelvic girdle muscles; and cardiac manifestations (palpitations, syncope, heart failure, ventricular or supraventricular arrhythmias, conduction disorders, dilated/hypertrophic cardiomyopathy, and sudden death). Symptoms normally appear in the second decade of life or later.^{1–3} Prevalence is estimated at 0.13 to 0.2 cases per 100 000 population.⁴ To date, 3 genes responsible for the disease have been identified: *EMD* (encoding emerin); *FHL1* (encoding FHL1), both causing X-linked EDMD^{1,5–7}; and *LMNA* (encoding lamin A and C), responsible for autosomal dominant EDMD (AD-EDMD) and autosomal recessive EDMD (AR-EDMD).^{1,2,8} We present the case of a patient with AD-EDMD and a

heterozygous mutation in *LMNA*, c.1588C>T, which has never been described in the literature.

The patient came to our department due to muscular dystrophy which started when he was an infant; he had no relevant family history. During his first year of life he experienced difficulty maintaining the position of his head due to cervical hyperextension; he displayed toe walking, frequent falls, and showed a positive Gowers sign. A muscle enzyme test (CPK) conducted when he was 2 yielded normal results; the EMG study revealed an interference pattern with short, low-amplitude, and occasionally polyphasic potentials. Fibrillations at rest were also recorded. At the age of 4, our patient had lumbar hyperlordosis and irreducible equinovarus feet. By the age of 10, he had difficulty walking and needed a wheelchair due to muscle retractions and weakness at the scapular belt and pelvic girdle; he also experienced loss of strength in the upper limbs (2/5) and lower limbs (3/5). A muscle biopsy performed when he was 13 revealed nonspecific changes, including considerable variation in muscle fibre size. At the age of 19, he developed restrictive chronic respiratory failure secondary to chest deformities. When he was 29, he underwent pacemaker implantation due to complete atrioventricular block. Given a suspected case of EDMD with a lack of relevant family history, we sequenced the lamin A/C gene (*LMNA*). The gene was found to include the heterozygous variant c.1588C>T, leading to a missense mutation with substitution of p.Leu530Phe, resulting in an altered protein; the in silico analysis confirmed the pathogenicity of this mutation. Neither of the parents expressed this mutation; our patient was diagnosed with AD-EDMD. He developed ventricular tachycardias requiring the implantation of an automatic defibrillator. He died in his fourth decade due to pulmonary aspiration.

The variant found in our patient (c.1588C>T) has never been described in the literature. However, a similar variant (c.1589T>C) has been reported; this variant results in a

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missense mutation (p.Leu530Pro) and it is associated with AD-EDMD.⁹ AD and X-linked variants are usually similar in terms of neuromuscular and cardiac manifestations.^{1,2,6,10} However, there is no clear correlation between genotype and phenotype when the mutation affects the *LMNA* gene,^{1,2,11} although some authors suggest that patients with missense mutations typically present early musculoskeletal changes.¹² In patients with EDMD, EMG studies usually reveal a myopathic pattern whereas results from nerve conduction studies are normal, as in our case. However, neuropathic patterns have been described in some cases of autosomal dominant and X-linked forms.¹³ Muscle biopsy results normally reveal nonspecific myopathic/dystrophic changes, including changes in muscle fibre size; however, immunohistochemical studies can guide the diagnosis (this technique was not available when our patient underwent a biopsy).¹ In summary, we describe the case of a patient with the typical clinical triad of EDMD^{1,14} and an autosomal dominant mutation not described to date. We should have a high level of clinical suspicion in cases of muscle dystrophy of unknown origin associated with contractures beginning in childhood despite the absence of cardiomyopathy, which typically appears at later stages of EDMD type 2.^{1,2}

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