Case report

# Genetic pattern of 3 cases of Emery–Dreifuss muscular dystrophy in a family

P. Yazdanpanah,[1] A. Javan,[2] B. Nadimi[3] and H.R. Ghaffarian Shirazi[4]

## Introduction

The muscular dystrophies are inherited conditions characterized by progressive myopathy [*1*]. The most common types are Duchenne muscular dystrophy and Becker muscular dystrophy. Emery–Dreifuss muscular dystrophy (EDMD), the type reported here, is less common. Worldwide incidence is estimated to be 1 in 100 000 [*2*], but there is not sufficient evidence on the prevalence of this condition in the Islamic Republic of Iran.

The 3 genetic patterns of EDMD are: X-linked recessive fashion (the commonest form) produced by mutations in the emerin gene, which is located on the X-chromosome (Xq28); autosomal dominant; and autosomal recessive. The 2 latter forms are caused by mutations in the lamin A/C gene on chromosome 1 (1q11–q23) [*3*].

The classic triad of symptoms of EDMD are: early contractures, particularly of the elbows, Achilles tendon, and posterior cervical muscles; cardiac conduction defects; and slowly progressive weakness and atrophy in a humeroperoneal distribution [*2*]. Cardiac involvement can present with heart block, frequently in-late 20- or early 30-year-olds. Early signs are bradycardia and a prolonged PR interval on the electrocardiogram (ECG) [*2*]. Arrhythmias are the primary manifestation of cardiac disease in EDMD [*4*].

ECGs are generally abnormal by age 20–30 years, commonly showing first-degree atrioventricular block. The atria appear to be involved earlier than the ventricles, with atrial fibrillation and atrial flutter or, more classically, permanent atrial standstill and junctional bradycardia, observed. Abnormalities in impulse generation or conduction are present in virtually all individuals by age 35 to 40 years, and permanent ventricular pacing is often required. The severity of cardiac disease is much greater than the myopathy [*4*].

This may explain arrhythmic and cardiomyopathic presentation. The unique localization of emerin in desmosomes and fascia adherens of the intercalated disease that functions in maintaining cell-to-cell adhesion and conduction may be responsible for arrhythmic involvement [*5*].

The early onset of contractures before the onset of any significant weakness is unique to this disease. The elbows are generally held in a semiflexed position, and the child typically begins walking on tiptoe [*2*].

[1]Department of Physical Medicine and Rehabilitation; [2]Department of Internal Medicine; [3]Department of Orthopaedics; [4]Department of Social Medicine, Yasuj University of Medical Sciences, Islamic Republic of Iran (Correspondence to P. Yazdanpanah: parvan1339@yahoo.com).
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There are also contractures of other ligaments, including the metacarpals and other smaller joints [*6*]. In EDMD serum creatine kinase (CK) level is normal or moderately increased.

The course is generally benign, like that of Becker muscular dystrophy, but weakness and contractures can be severe in some cases, and sudden death is a possibility [*7*]. This disorder is considered a slowly progressive myopathy, but the disease spectrum includes patients whose disease is much more severe [*8*]. Some are unable to walk by the time they reach adulthood, but survival is generally into middle age [*9*]. Treatment is primarily focused on the cardiac disease, with a pacemaker being the typical form of treatment. Bracing can also be helpful as the disease progresses. Early, frequent range-of-motion exercise and positioning are also advisable and stretching exercises are indicated to minimize contractures [*2,10*].

This case report will augment information about the course, genetic patterns and complications of this rare disease and may help in better diagnosis and management, including the possibility of partial amelioration of the cardiac and musculoskeletal complications.

## Cases

### Case 1

The patient is a 12-year-old boy, referred with weakness of the muscles of the shoulders and arms. His main difficulty was contracture of the Achilles tendons, which began at 4 years of age with a diagnosis of "bilateral pes equinus deformity". Surgery for release of the Achilles tendons had been done 8 years previously.

Physical examination showed atrophy of the shoulder and arm muscles, positive Gower's sign, moderate contracture of the Achilles tendons and decreased range of motion in the hips. Muscle strength grading of elbow flexors was 3/5, shoulder abductors 3/5 and other muscles 4/5. Sensory examination was normal and deep tendon reflexes were 1/2. The patient showed wide based gait and tiptoe walking.

Electromyography was done, and all nerve conduction readings (velocity, amplitude and latency) were normal. Needle electromyography showed polyphasicity, decreased duration and latency of motor unit, decreased to adequate recruitment. Easy recruitment, specific to myopathy, was seen in the gluteus maximus and deltoid muscles. On the ECG there was atrial flutter with 3:1 atrioventricular block.

### Case 2

The second case was the 3.5-year-old brother of the first patient. He had had difficulty walking (tiptoe walking) for 8 months (Figure 1). On physical examination there was bilateral severe contracture of the Achilles tendons (Figure 1), positive Gower's sign, wide-based gait and normal sensory examination; deep tendon reflexes were 2/2. All the nerve conduction studies were normal. Electromyography showed polyphasicity

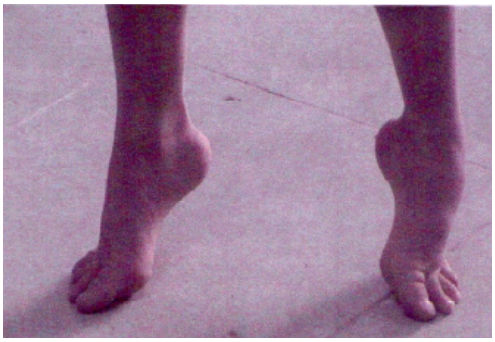

Figure 1 Ankle contracture in the second patient, a boy 3.5 years old

and decreased duration and amplitude of motor units in proximal muscles. Easy recruitment was seen in both gluteus maximus muscles. The ECG of this patient (Figure 2) was similar to that of the first boy.

### Case 3

The third case was a girl 8 years old (the sister of the 2 above cases) who was referred with difficulty in walking and sitting; and had been diagnosed with "bilateral pes equinus deformity" when surgery was done for her 4 years ago. Physical examination showed contracture of the Achilles tendons and hips, and normal sensory examination; deep tendon reflexes were 2/2 and there was weakness of the proximal muscles of the lower limbs. The electrophysiologic studies and ECG of this patient were similar to those of the boys.

Serum CK levels for all 3 patients were within the normal range.

The ECGs of the father and mother of these patients were normal.

## Discussion

EDMD is distinguishable clinically from the Duchenne and Becker forms by absence of pseudohypertrophy of skeletal muscle, early involvement of the arms with elbow contractures, and early onset cardiac conduction abnormalities and atrial dysrhythmia [*11*].

In EDMD, serum CK level is normal or moderately increased, but in Duchenne muscular dystrophy, it can be 300 to 400 times greater than normal. Elevated CK is noted in Becker muscular dystrophy, but it is usually lower than in boys with Duchenne muscular dystrophy [*2*].

The signs and symptoms presented in these 3 patients, primary contracture of the elbows and Achilles tendons, normal level of CK enzyme, cardiac involvement and absence of pseudohypertrophy of calves, are more indicative of EDMD than Duchenne or Becker muscular dystrophies.

Another possible diagnosis is congenital myopathies, which are a group of nonprogressive or slowly progressive myopathies presenting with hypotonia or weakness in the neonatal period. Babies frequently have decreased spontaneous movement and delayed motor milestone achievement. Muscles can feel flabby to palpation. Physical anomalies such as high palate, pectus excavatum, elongated face, and scoliosis can be present as an indication of longstanding weakness. CK level is usually normal [*12*].

Onset of disease occurring at around 4 years, contractures and absence of anomalies, however, support a diagnosis of EDMD rather than congenital myopathy. The presence of contractures, normal amplitude of compound muscle action potentials on nerve conduction studies, myopathic pattern

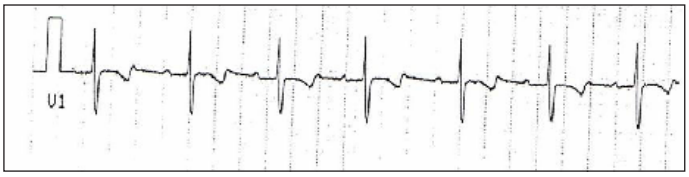


Figure 2 Electrocardiogram of the second patient, a boy 3.5 years old, showing atrial flutter with 3:1 atrioventricular block

of needle electromyography and cardiac involvement also suggest EDMD.

Even though, the conduction system is not primarily affected histologically, sudden death is common in both hemizygous men and heterozygous women; thus, early detection can be life saving [*13*].

Patients with DMD and other myopathies have been reported as having malignant hyperthermia as an adverse reaction to general anaesthesia [*2*] and in EDMD patients the heart may be affected and could complicate an operation. Atrioventricular block can also occur with anaesthesia [*14*]. The anaesthetist must, therefore, be informed of the diagnosis before any surgery is undertaken.

Considering the genetic patterns of EDMD (X-linked recessive, autosomal dominant or autosomal recessive), owing to the equal chance of involvement in male and females, the genetic pattern in this family appears to be autosomal dominant.

Arrhythmia was present in all 3 of these patients. Permanent ventricular pacing is recommended once conduction disease is evident and can be life saving. Cardiac disease, including sudden death, remains responsible for significant mortality in EDMD despite early pacing [*15*].

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