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CASE REPORT

Emery-Dreifuss muscular dystrophy: Case report☆

Fátima Saraiva[a,*], Dina Rodrigues[b], Helena Andrade[b], Luís Negrão[c], Lino Gonçalves[a], António Marinho[b], Luís A. Providência[a]

[a] *Serviço de Cardiologia, Hospitais da Universidade de Coimbra, Coimbra, Portugal*
[b] *Serviço de Cardiologia, Sector de Cardiologia Pediátrica, Hospitais da Universidade de Coimbra, Coimbra, Portugal*
[c] *Serviço de Neurologia, Hospitais da Universidade de Coimbra, Coimbra, Portugal*

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Abstract Emery-Dreifuss muscular dystrophy type 1 (EDMD1) is a familial disease with X-linked recessive transmission, caused by a mutation in a nuclear envelope protein, emerin. Clinical manifestations usually occur in adolescence and include contractures, muscle atrophy and weakness, and cardiac conduction disturbances. We describe the case of a young male, aged 16, with first-degree atrioventricular (AV) block and limited extension of both forearms. He had elevated CK, and cardiac monitoring showed severe conduction tissue disease, with significant sinus pauses, chronotropic incompetence and periods of AV dissociation during exercise. Immunohistochemical staining using an emerin antibody showed absence of the protein in a fragment of muscle tissue and genetic study identified a mutation associated with EDMD1. Study of his brother, aged 21, also established a diagnosis of EDMD1. Both individuals received a permanent pacemaker but musculoskeletal manifestations at that time did not warrant any other intervention. Screening for certain genetic diseases, including muscular dystrophies, is mandatory following identification of conduction abnormalities in young people.

PALAVRAS-CHAVE
Distrofia muscular;
Emery Dreifus;
Emerina;
Anomalias de condução

Distrofia muscular de *Emery-Dreiffus*: a propósito de um caso clínico

Resumo A distrofia muscular de *Emery Dreifus* tipo 1 (DMED1) é uma doença familiar, com transmissão recessiva ligada ao X, resultante da mutação de uma proteína do invólucro nuclear, a emerina. As manifestações clínicas ocorrem geralmente na adolescência e incluem contracturas, atrofia e fraqueza musculares e perturbações da condução cardíaca. Descreve-se o caso

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* Corresponding author.
E-mail address: saraiva.fatima@gmail.com (F. Saraiva).

clínico de um jovem de sexo masculino, 16 anos, com bloqueio auriculo-ventricular (AV) de primeiro grau e limitação da extensão de ambos os antebraços. Apresentava CK elevada e a monitorização cardíaca demonstrou doença grave do tecido de condução, com pausas sinusais significativas, insuficiência cronotrópica e períodos de dissociação AV durante o esforço. A imunomarcação com anticorpos anti-emerina de um fragmento de tecido muscular confirmou a ausência desta proteína e o estudo genético identificou uma mutação associada à DMED1. O estudo do seu único irmão, de 21 anos, estabeleceu igualmente o diagnóstico de DEMD1. Por apresentarem ambos doença do tecido de condução significativa decidiu-se por implantação de *pacemaker* definitivo nos dois casos. As manifestações músculo-esqueléticas, de momento, não justificavam qualquer intervenção. A identificação de anomalias da condução em idades jovens obriga à exclusão de determinadas doenças genéticas, nomeadamente, distrofias musculares.

Introduction

Emery-Dreifuss muscular dystrophy (EDMD) is a chronic myopathy, first described by Emery and Dreifuss in 1966.[1] They identified a benign X-linked recessive form, now termed EDMD type 1 (EDMD1). Later, in the 1980s, others described EDMD with autosomal transmission[2]; the prevalence of both forms is poorly defined.[3] They result from mutations in genes that code for nuclear envelope proteins. The main clinical manifestations include early development of contractures, progressive muscular atrophy and weakness, and cardiac conduction disturbances. Diagnostic suspicion is based on these clinical and electrocardiographic findings, which can be confirmed by muscle biopsy and genetic study.

Case report

A young male, Caucasian, aged 16, the second child of non-consanguineous parents, was referred for cardiology consultation due to electrocardiographic alterations. The only symptoms he reported were sporadic dizziness and fatigue during sports activities, but no pre-syncope, syncope or palpitations. His personal history included previous diagnoses of allergic asthma and rhinitis. The only relevant family history was the premature death of a maternal aunt, probably due to neuromuscular disease. Physical examination revealed uncharacteristic facial features, normal body mass index, irregular heartbeat on cardiac auscultation but no murmur, normal pulmonary auscultation, palpable and symmetrical radial and femoral pulses, and soft abdomen, with no organomegaly.

Routine laboratory tests revealed no abnormalities, except for creatine kinase (CK) of 887 UI/l, five times the normal upper limit (<171 UI/l). Thyroid hormone levels were normal.

The electrocardiogram (ECG) showed sinus rhythm, first-degree atrioventricular block (AVB), 70° electrical axis, and normal QRS duration and corrected QT interval.

Further cardiac study, including Holter ECG monitoring, showed sinus rhythm, with minimum, mean and maximum heart rates of 32, 54 and 90 bpm, respectively, and periods of first-degree AVB. Frequent supraventricular extrasystoles were also detected, with episodes of supraventricular tachycardia of three complexes, infrequent ventricular extrasystoles and multiple sinus pauses, the longest lasting 11 020 ms, at 00.50 am, asymptomatic. The echocardiogram showed normal-sized chambers, good biventricular function and no valve abnormalities. Exercise testing revealed marked chronotropic incompetence, only 54% of maximum heart rate being attained after 12 min, with periods of atrioventricular dissociation at peak exercise. Electrophysiological study documented sinus node dysfunction, with prolonged recovery time (5280 ms).

Significant conduction defects associated with moderate CK elevation suggested neuromuscular disease with cardiac involvement. When questioned about musculoskeletal symptoms, the patient reported slight limitation of elbow extension only, previously disregarded since it did not significantly limit his functional capacity.

He was subsequently referred to our hospital for a neuromuscular disease consultation. Physical examination revealed moderate contractures of both elbows, with no muscle atrophy or weakness or sensory or motor deficit. Needle electromyography of the deltoid muscles and brachial biceps was normal, as was the study of sensory and motor nerve conduction. Biopsy of the left deltoid muscle revealed increased variation in muscle fiber diameter (Fig. 1), and immunohistochemical analysis using an emerin antibody showed absence of immunostaining in all muscle fiber nuclei (Fig. 2A and B). Genetic study confirmed the diagnosis of