Emery–Dreifuss muscular dystrophy with cardiac manifestations

Introduction

The authors discuss the diagnosis of a rare muscular dystrophy associated with classical cardiac manifestations in a 40-year-old man. Genetic diagnosis was delayed owing to a combination of mild phenotypic features plus no prior confirmatory genetic tests. The insertion of a VVIR pacemaker was indicated owing to high risk of bradyarrhythmic death.

Case Report

An asymptomatic 40-year-old man attended clinic for cardiology assessment before cataract surgery. He had been diagnosed 9 years earlier with a 'non specified limb-girdle muscular dystrophy' following investigation for lower limb muscle weakness. Earlier electrocardiograms (ECGs) showed a bradycardic, junctional escape rhythm of 30–40 beats per minute (BPM). He had previously refused pacemaker insertion.

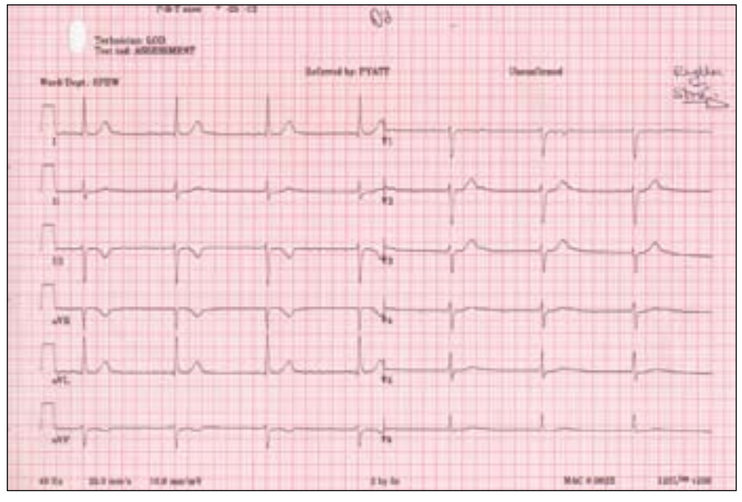
He denied any syncope, shortness of breath or palpitations. He had muscle wasting to his upper arms and calves plus mild elbow contractures. He was normotensive, resting regular heart rate = 42 BPM and cardiorespiratory examination was unremarkable. His ECG showed atrial fibrillation, with a slow junctional escape rhythm of approximately 40 BPM and normal QRS width (*Figure 1*). Blood tests showed no haematological, electrolyte or thyroid dysfunction and no impaired glucose tolerance.

Echocardiography showed good left ventricular function and 24-hour ECG Holter monitoring showed 8 pauses (longest 2.13s), with a heart rate varying between 29 and 79 BPM. He was commenced on clopidogrel to prevent thromboembolic complications and then he agreed for a VVIR system to be implanted to avoid bradyarrhythmic death. No complications ensued and he remains well at present.

The patient also had two brothers, one died suddenly and the cause of death was not clearly determined. His elder brother was 52 years old and was diagnosed with a non-specific muscular dystrophy also associated with a junctional rhythm. He had a VVIR permanent pacemaker inserted in April 2003 following recurrent episodes of dizziness.

An hereditary skeletal myopathy in association with pathognomic cardiac abnormalities suggested a diagnosis of Emery–Dreifuss muscular dystrophy (EDMD). Prognostically and therapeutically a definitive genetic diagnosis was required. Genetic testing confirmed that both siblings had inherited the X-linked form of EDMD involving a single base change of the emerin gene.

Figure 1. Junctional escape rhythm of 30–40 beats per minute.



Discussion

Emery–Dreifuss muscular dystrophy (EDMD) was originally described as a classical triad: muscle contractures (achilles, cervical and elbows), muscle weakness and wasting in the humeroperoneal distribution, and lastly conduction system disease, with or without cardiomyopathy (Emery and Dreifuss, 1966). EDMD has three inheritance patterns:

1. The X-linked form was the first to be genetically identified. It is caused by a mutation in the STA gene localized to chromosome Xq28. The gene encodes for a nuclear membrane protein called emerin. Mutation causes either absence and more rarely a functional defect (Bione et al, 1994; Boriani et al, 2003).
2. The autosomal dominant form of the disease was identified in the 1990s. It is characterized by anomalies in the lamin A/C architecture of the nuclear envelope encoded by the LMNA gene on the long arm of chromosome (Emery and Dreifuss, 1966; Bonne et al, 1999).
3. The autosomal recessive type of EDMD is rarer than the former two and involves the LMNA gene.

Different genetic varieties of EDMD have similar but non-identical cardiac clinicopathological variabilities – notably left ventricular dysfunction or cardiomyopathy is associated with the autosomal dominant form. It is useful for prognostication, screening and cardiology follow up to confirm the inherited form of EDMD.

Persons with emerin and LMNA mutations can display a spectrum of phenotypic skeletal features, from none, to the full set of characteristics in addition to cardiac manifestations – conductive, myopathic or both (Fatkin et al, 1999; Boriani et al, 2003; van Berlo et al, 2004). Even in families with the same mutation, the expression can show great heterogeneity (Boriani et al, 2003).

Dr D Cullington *is Senior House Officer in Cardiology, The Cardiothoracic Centre, Liverpool NHS Trust, Liverpool L14 3PE and* **Dr JR Pyatt** *is Consultant Cardiologist, The Royal Liverpool and Broadgreen University Hospitals NHS Trust, Liverpool*

Correspondence to: Dr D Cullington

Cardiac manifestations

Arrhythmias have developed in nearly all X-linked and autosomal dominant EDMD patients by the second to third decade (Boriani et al, 2003). Cardiac involvement is characterized by sinus node dysfunction or an atrioventricular conduction defect. These manifestations are progressive and ultimately require permanent pacemaker system insertion owing to the risks of intrinsic pacemaker failure and death (Boriani et al, 2003). Classically patients with EDMD have atrial standstill with a slow junctional rhythm; however, more prevalent are atrial fibrillation, atrial flutter or atrial tachycardia possibly with a bundle–branch block.

The autosomal dominant form of EDMD has more diverse cardiac disease manifestations – conduction system disease with no associated cardiomyopathy, conduction system disease with a dilated or non-dilated cardiomyopathy and sudden cardiac death as a result of tachyarrhythmias (Fatkin et al, 1999; van Berlo et al, 2004). Asymptomatic and phenotypically normal relatives of persons with LMNA mutations should be screened. The risks of embolization in EDMD patients who have atrial arrhythmias or standstill warrant anticoagulant or antiplatelet agents for prevention (Boriani et al, 2003).

There are no formal guidelines for follow up. Patients with the disease require at least yearly echocardiography and regular pacemaker checks, depending on their current underlying cardiac function and the occurrence of any new symptoms.

Conclusions

Before current analytical genetic techniques a specific diagnosis is difficult to make in patients not expressing the classical phenotypic features of EDMD. Genetic analysis was invaluable to predict potential cardiac dysfunction in this patient for the future and guided the authors' decision to insert a pacemaker at the earliest opportunity. **BJHM**

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