Genetic muscle disorder masquerading as atrial arrhythmias with conduction defects requiring pacemaker implantation

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CLINICAL IMAGE

Genetic muscle disorder masquerading as atrial arrhythmias with conduction defects requiring pacemaker implantation

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SHORT TITLE: Genetics of atrial arrhythmias

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CONFLICT OF INTEREST: none declared
Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, with an increasing prevalence with age and associated cardiovascular comorbidities [1]. We present a case of young 28-year old male who was admitted due to newly diagnosed AF following pre-employment medical screening. He had no history of medications and drugs intake. He complained only about sporadic dizziness and fatigue during vigorous activities. Upon further questioning, a history of weight loss, despite increased food consumption in last 6 months was elicited. Clinical examination revealed elevated blood pressure of 140/90mmHg, bilateral elbow and ankle contractures with asymmetric muscle wasting, especially of the right arm and left lower limb (Figure 1A,B). In hindsight, the patient recalled this abnormality since his late teens, but no further investigations were done that time. Family history was relevant to sudden unexplained death of maternal male family members before their forties. Initial referral ECG demonstrated a regular junctional escape rhythm of 35 bpm, low amplitude baseline deflections suggestive of atrial flutter activity (AFL) (Figure 1C). Holter 12-lead ECG monitoring confirmed episodes of AF/AFL/atrial tachycardia with a slow ventricular response and significant pauses up to 3.86 sec. Doppler echocardiography revealed normal left ventricular ejection fraction (LVEF=63%), marked bi-atrial enlargement and the complete absence of A-waves, indicating loss of right and left atrial mechanical activity. Late gadolinium-enhanced cardiac magnetic resonance showed no signs of myocardial fibrosis or inflammation. Serum creatine kinase concentration was modestly elevated 724U/l (N: 39-308) and hs troponin T concentration was high 90.32ng/l (N<14).

The constellation of family and personal history, the examination and imaging findings suggested a diagnosis of Emery-Dreifuss muscular dystrophy (EDMD). Following genetic counselling, the patient underwent testing of the *EDMD* gene, which encodes the muscle-specific
emerin protein. Sanger sequencing revealed a hemizygous p.Ser52AlafsTer13/c.153delC mutation (Figure 1D), resulting in a premature truncation of the protein [2].

As the atrial electrical silence is frequently observed in EDMD, ablation was not the therapeutic option for our patient. The patient was referred for pacemaker implantation. After right ventricular lead placement electrical cardioversion of AF restored slow sinus rhythm temporarily and the patient was given permanent dual chamber pacemaker. Anticoagulation therapy was administered to prevent thromboembolic events, based on assessment of stroke risk in EDMD patients, the presence of hypertension and the patient’s choice [3,4].

Genetic studies of his mother, mother's sister and a male cousin showed hemizygous mutation suggesting the EDMD diagnosis in the cousin and revealed that both females were heterozygous carriers (Figure 1D). On family assessment patient's male cousin, aged 20, revealed joint contractures, mild limb muscle atrophy and bradyarrhythmias while both female relatives were asymptomatic.

EDMD is a condition characterized by the clinical triad of early-onset contractures, progressive weakness/wasting in humeroperoneal muscles, and cardiac disease with conduction defects, arrhythmia and cardiomyopathy [2]. The disease has X-linked recessive-inheritance and thus typically affects males (cardiac disease may be manifested by some carrier females as well).

Due to the specific clinical manifestation (including muscle atrophy), EDMD could be categorised into group 2 („Arrhythmias in specific clinical settings“) and subgroup O („Other“) of RACDRAs classification (RCDD code:VI-2O) [5].

Our case shows that atrial arrhythmias may be the first clinical manifestation of EDMD. Appropriate clinical assessment with taking into account family history, serum levels of muscle-specific biomarkers and genetic testing may help to establish the primary cause.
REFERENCES:


Figure 1.

A. Bilateral elbow contractures with asymmetric muscle atrophy.

B. Asymmetric muscle atrophy of the left lower limb.

C. 12-lead standard electrocardiogram (speed 50 mm/s). Atrial flutter with junctional escape rhythm of 35 bpm.

D. A p.Ser52AlafsTer13 mutation in the emerin (EMD) gene. The pedigree of family with EMD mutation and the chromatogram shows EMD truncation in hemizygous (proband) and heterozygous (proband’s mother) state.
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