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CASE REPORT

Syncope and hyperCKemia as minimal manifestations of short CTG repeat expansions in myotonic dystrophy type 1

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Ventricular arrhythmias

Abstract
Introduction: Syncope and palpitations as the only initial manifestations of myotonic dystrophy type 1 (MD1) due to a CTG expansion of 50–100 repeats have not been reported.
Case report: In a 55-year-old female with a family history of MD1 and a personal history of a single syncope, palpitations, and hyperCKemia, 70 CTG repeats were detected in the *DMPK* gene. Her brother had presented atypical clinical, electromyographic, and muscle biopsy features since the age of 35 but had been diagnosed with MD1 after he later developed typical distal myotonia. He died suddenly during an episode of syncope at the age of 53. A sister with clinical myotonia died suddenly during sleep at the age of 45 and a second sister with quadriparesis died from complications of intestinal rupture at age 52. A third sister committed suicide at age 40 after developing recurrent syncopes, while a fourth sister had hyperCKemia and foot-extensor weakness. The mother of these five affected children died suddenly from myocardial rupture.
Conclusions: MD1 with <100 CTG repeats may exclusively manifest cardiologically. Family screening for MD1 is important even in asymptomatic patients. MD1 may initially manifest without typical features, while muscle biopsy may be misleading and indicate glycogenosis. Close cardiac follow-up is important if MD1 manifests cardiologically to prevent syncope or sudden cardiac death.

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PALAVRAS-CHAVE
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Envolvimento cardíaco;
Arritmias ventriculares

Síncope e hiper CKemia como manifestações mínimas de expansões *short CTG-repeat* na distrofia miotónica 1

Resumo
Introdução: Na distrofia miotónica tipo 1 (DM1) devido a expansão CTG 50-100 não foram reportadas até ao momento síncope e palpitações como manifestações iniciais da mesma.
Caso clínico: Numa mulher de 55 anos com história familiar de DM 1 e antecedentes de um único episódio síncopal, palpitações e hiper CKemia, foi detetada uma expansão de *CTG-repeat* de 70 no gene DMPK. O irmão apresentava desde os 35 anos características clínicas, eletromiográficas e nas biópsias musculares atípicas tendo-lhe sido diagnosticada DM 1 após ter desenvolvido mais tarde miotonia distal típica. Morreu subitamente no contexto duma síncope aos 53 anos. Uma irmã com miotonia clínica morreu subitamente aos 45 anos durante o sono. Uma segunda irmã com quadriparesia morreu de complicações de rotura do intestino aos 52 anos. Uma terceira irmã cometeu suicídio aos 40 anos após ter desenvolvido síncopes recorrentes. Uma quarta irmã tinha hiper CKemia e fraqueza muscular nos pés. A mãe destes 5 filhos afetados morreu subitamente de rotura do miocárdio.
Conclusão: A DM1 com CTG-repeat expansão < 100 pode manifestar-se exclusivamente do ponto de vista cardiológico. O rastreio familiar para DM1 é importante mesmo nos doentes assintomáticos. A DM1 pode manifestar-se inicialmente sem características típicas de DM1. A biópsia muscular na DM1 pode ser enganadora e indicar glicogenose. Um seguimento cardíaco rigoroso é importante se a DM1 se manifesta sob o ponto de vista cardiológico para prevenir a síncope ou morte súbita.

Introduction

Clinical manifestations in patients with myotonic dystrophy type 1 (MD1) carrying a CTG expansion of 50–100 repeats are usually mild and include ptosis or cataract.[1–3] Syncope has occasionally been described as a manifestation of MD1[4,5] but syncope and palpitations as the only initial manifestations of MD1 due to a CTG expansion of 50–100 repeats have not been reported.

Case report

The index patient (II/1) is a 55-year-old female, height 165 cm, weight 58 kg, with a history of a single syncope four years earlier and recurrent early morning palpitations since then, treated by beta-blockers (Figure 1). She had a family history of MD1 and was referred for assessment of genetic status. She reported daytime sleepiness but her clinical neurologic and cardiological exam was completely normal. Blood tests, however, revealed hyperCKemia of 264 U/l (normal 26–145 U/l). Work-up for the syncope in 2014, including cerebral magnetic resonance imaging, carotid ultrasound, and electroencephalogram, was normal. Cardiologic examination including telemetry and echocardiography was uninformative. On standard ECG incomplete right bundle branch block was recorded once. Genetic testing by PCR revealed a heterozygous CTG expansion of 70 repeats in the *DMPK* gene.

Her family history was noteworthy for at least five sibs affected out of a total of six (Figure 1). Her brother (II/2) manifested at onset in 1991 (age 35) with reduced motility of the tongue and difficulty with chewing and closing his mouth. Following these abnormalities he developed myotonia of both hands, daytime sleepiness, easy fatigability, and adynamia. Starting in 1998 (age 42) he reported permanent tiredness and aching muscles after exercise. A clinical neurologic exam at that time revealed wasting of the tongue edges, tongue fasciculations, clinical myotonia, and wasting of the thighs. Blood tests revealed hyperlipidemia, mild hyperCKemia of 204 U/l (normal <172 U/l), and mild elevation of gamma-glutamyl-transpeptidase (57 U/l; normal <55 U/l). Ischemic exercise testing and lactate stress testing were normal. Needle electromyography (EMG) showed marked myopathic alterations but no spontaneous activity. Muscle biopsy revealed a myopathic syndrome with accumulation of fat and particularly glycogen, which was interpreted as indicative of glycogenosis (Figure 1). Biochemical investigations revealed normal activity of respiratory chain complexes. Visually evoked potentials were noninformative. Echocardiography was indicative of hypertrophic cardiomyopathy, the left ventricular myocardium having abnormal texture. The 24-hour ECG was normal. In 2004 (at age 48) he presented with mild dysarthria and clinical myotonia but no muscle weakness. This time needle EMG revealed myotonic discharges in the thenar muscles. MD1 was diagnosed genetically on detection of a heterozygous CTG repeat expansion of 500. Colonoscopy in 2006 (age 49 years) revealed a cecal tubular adenoma and gastroscopy in 2008 (at age 52) revealed Barrett esophagus. He died suddenly during an episode of syncope in 2009 at age 52.

Three sisters (II/3, II/4, and II/5) were also affected. One sister (II/3) manifested marked myotonia and died