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CASE REPORT

Natural history of Brugada syndrome in a patient with congenital heart disease

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Abstract Risk stratification of sudden death in patients with Brugada syndrome (BrS) is a controversial issue, and there is currently no consensus on the best method. Examination of data from the natural history of the disease is of fundamental importance and may help to identify relatives at risk. At the same time, study of the genetic mutations responsible for the disease may also contribute to risk stratification of the syndrome, enabling identification of asymptomatic relatives carrying mutations.

This paper presents the case of a young man, aged 26, monitored as a pediatric cardiology outpatient from birth for a simple structural heart defect not requiring surgery. Analysis of the evolution of the patient's electrocardiogram revealed the appearance, at the age of 20, of a pattern compatible with type I BrS. Following an episode of syncope and induction of polymorphic ventricular tachycardia in the electrophysiological study, a cardioverter-defibrillator was implanted. One year later, a single shock terminated an episode of ventricular fibrillation. A molecular study of the *SCN5A* gene identified a rare mutation, c.3622G>T (p.Glu1208X), recently described and associated with more severe phenotypes in patients with BrS, as in the case presented.

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História natural da síndrome de Brugada num doente com cardiopatia congénita

Resumo A estratificação do risco de morte súbita nos doentes com síndrome de Brugada (SB) é um assunto controverso, não existindo atualmente consenso sobre a forma ideal de o fazer. O estudo da história natural da doença é fundamental e pode ajudar a identificar os familiares em risco. Por outro lado, o estudo das mutações genéticas responsáveis pela síndrome pode contribuir para a estratificação do risco, identificando os familiares assintomáticos portadores de mutação.

Este artigo apresenta o caso de um jovem de 26 anos de idade, seguido na consulta de Cardiologia Pediátrica desde o nascimento por um defeito cardíaco estrutural simples, que resolveu espontaneamente. A análise evolucionária do eletrocardiograma do doente documentou o aparecimento, aos 20 anos de idade, de um padrão compatível com SB de tipo 1. Após um episódio de síncope e indução de taquicardia ventricular polimórfica no estudo electrofisiológico, foi implantado um cardioversor-desfibrilador. Um ano depois, um episódio de fibrilhação ventricular foi terminado por um choque único. O estudo molecular do gene SCN5A identificou uma mutação rara [c.3622G>(p.Glu1208X)], recentemente descrita e associada a fenótipos mais graves nos doentes com SB, tal como no caso por nós apresentado.

Case report

We present the case of a young man, aged 26, monitored as a pediatric cardiology outpatient from birth for a perimembranous ventricular septal defect. The patient's family history included sudden death of his maternal grandfather in the fifth decade of life, and ''arrhythmia'' in his father, controlled with propranolol. The initial electrocardiogram (ECG), at age one month, presented a predominance of R waves and ST depression in the right precordial leads (Figure 1). During follow-up, the ventricular septal defect was observed to become restrictive and eventually closed spontaneously. The patient progressed without complications until the age of 20, at which time the ECG pattern changed, with the appearance of complete right bundle branch block and ST-segment elevation in the right precordial leads (Figure 2), suggesting type I Brugada syndrome (BrS). The patient was monitored irregularly, due to his good health and failure to attend appointments. He appeared to remain asymptomatic until the age of 24, when he presented a first episode of syncope, at rest, during the night, not preceded by prodromal symptoms or fever and accompanied by tonic-clonic movements and sphincter incontinence. This episode was initially interpreted as a seizure, leading to a brief hospitalization. Following this episode and in view of the ECG features, an electrophysiological study was conducted, during which sustained polymorphic ventricular tachycardia was induced. A single-chamber implantable cardioverter-defibrillator (ICD) was implanted. Three months later, the patient suffered an episode of syncope followed by a shock. Interrogation of the device revealed that the shock was appropriate and due to ventricular fibrillation. The current monitoring period (subsequent to ICD implantation) has lasted for two years, with no new episodes of arrhythmia to date, and without drugs. The patient and his family were referred to the cardiogenetics clinic for genetic counseling prior to the decision to conduct the molecular study, and neuropsychological support was initiated. As well as genetic counseling, all family members underwent an ECG, with normal results. The patient's genetic study was conducted on the *SCN5A* gene, which is responsible for 15–30% of BrS mutations.[1,2] A pathogenic mutation in heterozygosity, c.3622G>T (p.Glu1208X), and the polymorphisms c.87A>G (p.Ala29Ala) in homozygosity and c.3183A>G (p.Glu1061Glu) and c.5457T>C (p.Asp1819Asp) in heterozygosity were identified. The variant c.3841-24C>T was also identified, without clinical significance to date. Molecular study of first-degree relatives is currently under way.

Discussion

BrS is an autosomal dominant hereditary heart disease with incomplete penetrance and a mean prevalence of 5:10 000 in Europe.[3] The syndrome occurs more frequently in patients of Asian origin, in particular in Japan and south-east Asia, especially Thailand and the Philippines, where prevalence is estimated at up to 12:10 000.[4] BrS is characterized by the presence of electrocardiographic changes (incomplete right bundle branch block and ST-segment elevation in the right precordial leads) and a tendency for sudden cardiac death caused by polymorphic ventricular tachycardia or ventricular fibrillation.[3] The ECG alterations may not be always present, surfacing as a result of fever, the use of sodium channel blockers, vagolytic agents, beta-blockers and others.[3] BrS is responsible for over 4% of all sudden deaths and 20% of sudden deaths in patients with structurally normal hearts.[3] It is more frequent among males, and the mean age for the first manifestations is 40, although it can occur at younger ages, as shown by the case under examination, or older ages.[3] The risk of sudden death in these patients over a 24-month period has been estimated at 8%.[3]

Molecular studies conducted in the late 1990s demonstrated a relationship between mutations in genes which encode ion channels and the existence of hereditary lethal