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CASE REPORT

Holt-Oram syndrome: A case report

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Abstract Holt-Oram syndrome is clinically characterized by morphological abnormalities of the upper limbs and congenital cardiac defects. Although the disease is congenital, the diagnosis may only be made later in life. It is a rare autosomal dominant disorder, caused by a mutation in the *TBX5* gene located on chromosome 12, but sporadic cases have also been reported. We describe the case of a 75-year-old man with known morphological alterations of the upper limbs since birth and congenital cardiac defect (atrial septal defect), who later in life also manifested with advanced atrioventricular block.

PALAVRAS-CHAVE
Síndrome Holt-Oram;
Síndrome mão-coração;
T-BOX;
Defeito septo interauricular

Síndrome Holt-Oram: a propósito de um caso clinico

Resumo A síndrome de Holt-Oram é caracterizada pela associação de defeitos morfológicos dos membros superiores com defeitos cardíacos congénitos. Apesar de ser uma doença congénita, o seu diagnóstico pode só ser feito numa idade mais avançada. É uma doença autossómica dominante rara, devido à mutação do gene T-BX5, localizado no cromossoma 12, mas casos esporádicos também já foram reportados. Descrevemos o caso de um doente de 75 anos, com alterações morfológicas dos membros superiores, presentes desde o nascimento e defeito cardíaco (comunicação inter-auricular) diagnosticado na adolescência, que numa idade mais avançada apresentou bloqueio aurículo-ventricular completo.

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Introduction

Holt-Oram syndrome (HOS), also known as hand-heart syndrome, is a rare genetic disorder clinically characterized by morphological abnormalities of the upper limbs and congenital cardiac defects. Several mutations have been described, but the most frequent is in the *TBX5* gene of the T-box complex, located on chromosome 12. Upper limb abnormalities are always present, and the presence of lower limb abnormalities excludes the diagnosis. Several heart malformations have been described, but atrial septal defect and ventricular septal defect are the most common. Since clinical manifestations may be subtle, the diagnosis may only be made later in life, or even missed.

Case report

We present the case of a 75-year-old man with a previous history of morphological defects of both upper limbs since birth, although no etiological study was ever made. At the age of 15, in the context of tiredness, he was assessed by a cardiologist and an ostium secundum atrial septum defect (ASD) was diagnosed. The patient reported having a low heart rate, around 40 bpm, from a young age, but was always asymptomatic, and so a 24-hour Holter recording was performed annually. From the age of 58 he had documented atrial fibrillation.

At the age of 62, he underwent surgical repair of the ASD, with a continuous suture, in the context of increasing fatigue and dyspnea on exertion and recurrent respiratory infections.

After this surgery he remained asymptomatic from the cardiovascular standpoint, reporting no loss of consciousness, tiredness or breathlessness.

Adding to the described cardiac history, at the age of 55 the patient was diagnosed with Ménière's syndrome, and suffered occasional periods of exacerbation with vertigo, which improved with betahistine treatment.

At the age of 75, he began to have symptoms of dizziness and tiredness, but denied other symptoms, including loss of consciousness, palpitations, dyspnea or chest pain. He was medicated with betahistine, and a 24-hour Holter recording was ordered by his general practitioner. This showed atrial fibrillation as base rhythm, with marked bradycardia (25 bpm); 8909 pauses were registered, predominantly nocturnal, the longest lasting 2.76 seconds in the context of complete atrioventricular block (Figure 1); throughout the recording the patient remained asymptomatic. He was referred for an outpatient cardiology consultation for clinical assessment and treatment in our institution.

After cardiac assessment and additional medical tests, a permanent VVI pacemaker was implanted due to complete atrioventricular block in a patient with atrial fibrillation. During this hospitalization, the physical examination was notable for asymmetry of the upper limbs; morphological changes in the first finger of the right hand, showing similar morphology to the other fingers, and absence of one finger of the left hand (Figure 2); and a central linear scar in the sternum, related to the previous cardiac surgery. No other significant changes were found on physical examination.

The electrocardiogram showed atrial fibrillation with ventricular response of 55 bpm, right bundle branch block and left posterior hemiblock. The chest X-ray after pacemaker implantation (Figure 3) showed a cardiothoracic ratio of >50%, dilatation of the right atrium and of both pulmonary arteries, and pulmonary vasculature enhancement. The transthoracic echocardiogram showed a dilated left atrium; interventricular septal hypertrophy, with preserved left ventricular function, and dilated right chambers with annular dilation of the tricuspid valve, causing moderate tricuspid valve regurgitation, with pulmonary artery systolic pressure calculated at 50 mmHg (moderate pulmonary hypertension); and a dilated pulmonary artery and mild pulmonary regurgitation. No morphological defect of the atrial septum was found, or flow across the atrial septum; the ventricular septum also showed no morphological defect.

The patient also underwent X-ray of the shoulder girdle and upper arm, which showed hypoplasia of the glenoid cavity and bilateral degenerative changes of the gleno-humeral joints; bilateral X-ray of the elbow, fist and hand showed right elbow luxation in the radio-humeral joint, with normal

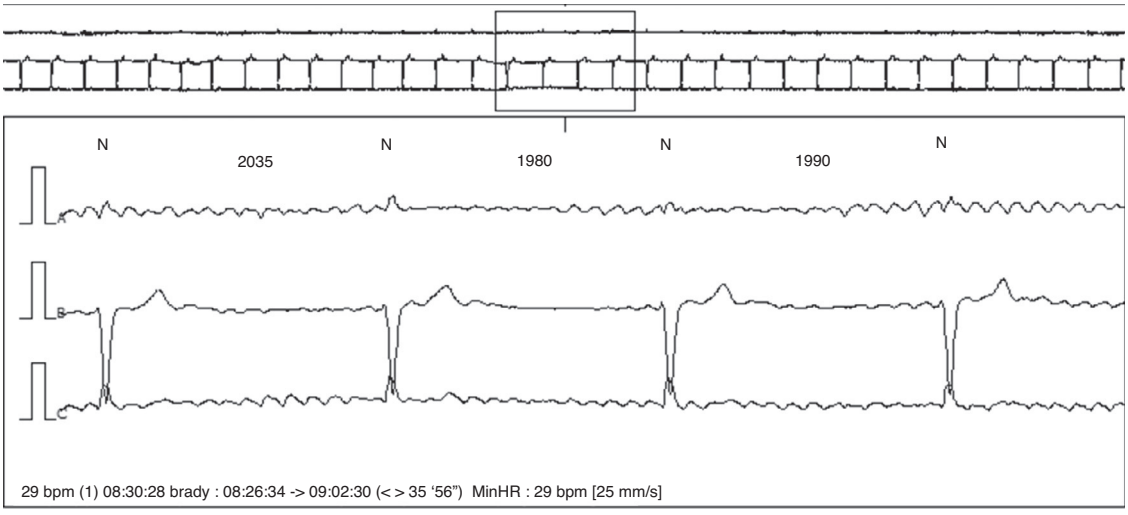

Figure 1 Holter strip showing atrial fibrillation and complete atrioventricular block.