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Case Report
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Holt Oram Syndrome: Complete AV Block Treated with LBBAP

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Abstract

Holt Oram Syndrome is a hereditary disease with autosomal dominant inheritance. The most common mutation occurs in the T-box complex TBX5 gene located on chromosome 12. It is characterized by disorders of the upper limbs and disorders of the heart. This syndrome has a broad clinical spectrum and can range from subclinical radiologic findings to life-threatening disease. Although the heart can be affected in many ways, atrial and ventricular septal defects are common. In some rare cases, the conduction system is affected. Our case had no history of chronic disease or drug usage. ECG at presentation showed sinus bradycardia. We report a patient who was diagnosed with Holt Oram syndrome in childhood and presented with a high degree of atrioventricular block and was treated with conduction system pacing.

Keywords: Holt Oram syndrome

Introduction

Holt Oram Syndrome (HOS) is a rare genetic disorder, also known as hand-heart syndrome. It was described in 1960 by Mary Clayton Holt and Samuel Oram. In 4 generations of family members, morphologic defects of the upper extremities and atrial septal defect (ASD) were found. Although many mutations have been identified, the most frequent mutations were found in the TBX5 gene on chromosome 12. This syndrome consists of a triad of hand malformations, cardiac conduction defects and ASD. Upper limb defects are always present and lower limb defects exclude the diagnosis.

The prevalence of congenital heart disease (CHD) varies between 75 and 95%, with ventricular septal defect (VSD) being the most common. Sinus bradycardia and atrioventricular (AV) block of varying degrees develop in some patients [1-3]. Although sinus bradycardia and first degree AV block are seen at birth, in individuals with HOS, regardless of CHD, these AV blocks may unpredictably progress to a higher degree of complete AV block with atrial fibrillation.

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Case Presentation

A 47-year-old woman presented to our cardiology clinic with dyspnea, fainting and exertional chest pain. At the age of 9 years, she underwent surgery for radius aplasia and ASD. On admission, blood pressure was 117/85 mmHg and arterial blood gas analysis was unremarkable. Other biochemistry, hemogram and hormone tests were also normal. ECG showed sinus bradycardia (Figure 1). On the next day's control ECG, complete AV block was observed (Figure 2). Echocardiography was performed and no significant valvular pathology and enlargement of the cardiac chambers were observed. Left ventricular ejection fraction (LVEF) was normal.

Since the patient had exertional chest pain and intermittent episodes of AV block, coronary angiography was performed and slow flow was observed in the left anterior descending artery and right coronary artery. During coronary angiography, a significant decrease in heart rate (35 bpm) was observed and Mobitz type 2 AV block developed. However, hemodynamic deterioration did not develop. After the procedure, the patient was followed up in the coronary intensive care unit and intermittent episodes of Mobitz type 2 and complete AV block were observed during monitoring and ECG follow-up.

DDD-R pacemaker implantation was scheduled because of the patient's history of syncope and episodes of high-degree AV block. A permanent pacemaker with left bundle branch pacing was implanted because of the patient's young age and to prevent the development of heart failure

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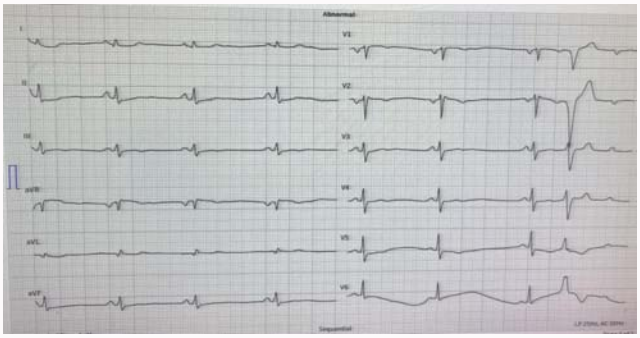

Figure 1: ECG on admission.

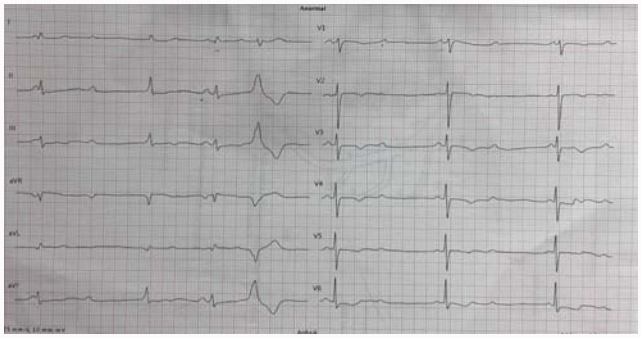

Figure 2: ECG of the patient one day after hospitalization.

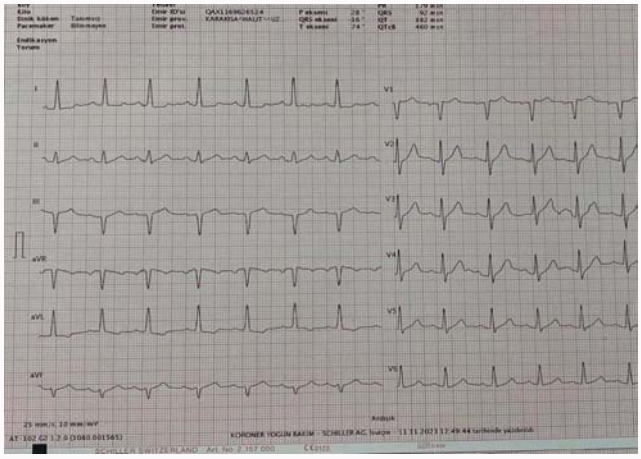

Figure 3: ECG after pacemaker implantation with LBBAP.

(Figures 3 and 4). During hospitalization, physical examination was normal and the pacemaker was interrogated with the programmer one day after implantation. Treshold, sensing and lead impedance values were within normal range. The patient was asymptomatic during clinical follow-up after discharge. Pacing rate was over 60% and there was no decrease in LVEF.

Discussion

In the United States, HOS is observed in 1 in 100000 births [4]. Although clinical manifestations are variable, upper limb abnormalities are always present. Developmental defects in the embryonic radial axis cause a wide spectrum of phenotypes [5,6]. Defects may be unilateral or bilateral, symmetrical and may involve the radial carpal and thenar bones. Left-sided hand and arm disorders are more severe than right-sided ones.

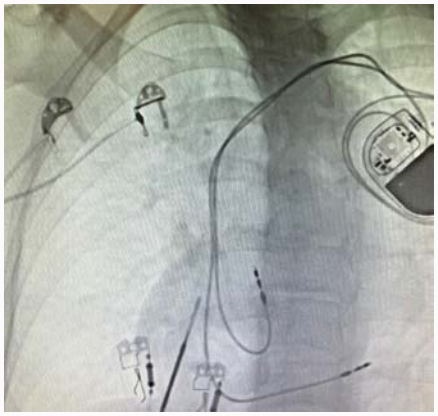

Figure 4: Fluoroscopic view after left bundle branch pacing.

Most HOS patients have cardiac malformations and all types of cardiac anomalies have been reported [5]. ASD and VSD are the most commonly detected anomalies [7]. VSDs are localized to the muscular trabeculated septum [6]. Morphologic abnormalities are sometimes accompanied by rhythm disorders including AV block, bradycardia and atrial fibrillation [8]. In 39% of patients, only ECG abnormalities can be observed without anatomical cardiac anomaly [9]. Sudden cardiac death may occur due to advanced AV block. Our patient had ASD and was repaired surgically. She had no cardiac symptoms after ASD operation and presented to our cardiology clinic with symptomatic high-grade AV block years after surgery. After coronary angiography and clinical follow-up, DDD-R implantation was scheduled.

In this report, we present a patient with HOS and high degree AV block who was scheduled for permanent pacemaker implantation. Our case is the first report of an HOS patient with advanced AV block and treated with LBBAP. She was young and exercising regularly. Due to the patient's concerns about decreasing physical activity, she was proposed the LBBAP. LBBAP has recently emerged as a suitable alternative to traditional and His bundle pacing (HBP). By stimulating the cardiac conduction system physiologically, LBBAP can result in a more homogeneous left ventricular contraction and relaxation. Similarly, in the case of Skwarek-Dziekanowska et al, the patient was implanted pacemaker with with HBP technique [10]. In our case, we decided to perform DDD-R pacemaker-using LBBAP, which provides physiological pacing, compared to HBP.

LBBAP offers several potential advantages over HBP, including lower pacing thresholds, lack of atrial capture/far field atrial oversensing, and similar degrees of electrical and mechanical synchrony despite longer QRS duration. LBBAP seems to be comparatively easier from a technical standpoint than HBP, with a shorter learning curve, attributed to a larger target area and implantation deeper in the right ventricle, further away from atrial myocardium [11]. In addition, right ventricular pacing may induce electromechanical dyssynchrony [12]. Physiological pacing reduces the risk of heart failure. LBBAP enables the preservation or restoration of electromechanical synchrony, which makes this method particularly interesting for patients with decreased ejection fraction and congenital heart disease (CHD) [13] and little is known about the use of this type of therapy in CHD.

The treatment of HOS requires a multidisciplinary approach involving genetics, cardiology, orthopedics and hand surgery.

Arrhythmia treatment may require medication, surgical intervention or pacemaker implantation. Affected individuals should be followed up annually with ECG, Holter and echocardiography. The spectrum of cardiac involvement is very important in the prognosis of HOS. Patients with ASD have a very good prognosis after ASD closure.

So far, there is no report on which pacing methods are more appropriate in patients with HOS and congenital AV block, as in our case. The LBBAP technique is a new physiologic pacing method that may prevent heart failure.

Critical heart complication in our case suggests need for thorough cardiological monitoring, because of risk for sudden cardiac death resulting from the progressive conduction impairment. In summary, cardiac involvement is important for prognosis. Our present data indicate the importance of careful management and monitoring for CHDs in patients with Holt–Oram syndrome, especially in those with cardiac conduction abnormalities.

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