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HOLT-ORAM SYNDROME. CLINICAL OBSERVATION FROM THE CARDIOLOGY DEPARTMENT OF THE RABAT CHILDREN'S HOSPITAL

***S. Kebabi, L. Chrakh, L. Chtouki, F. Jabourik and A. Bentahila**

Pediatric Cardiology Department P4 Rabat Children's Hospital, Faculty of Medicine and Pharmacy, Mohammed V Rabat University.

***Corresponding Author: S. Kebabi**
Pediatric Hepato-Gastroenterology and Nutrition Department Rabat Children's Hospital, Faculty of Medicine and Pharmacy, Mohammed V Rabat University.

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ABSTRACT

Holt-Oram syndrome is a rare cardiomelic syndrome with autosomal dominant inheritance. It is clinically characterized by upper limb malformations involving the radial segment, variable rhythm disturbances and congenital heart disease. We report a case, in a 6-month-old patient, revealed by cyanosis and dyspnea on exertion.

KEYWORDS: Holt-Oram; upper limb abnormalities, congenital heart disorder.

INTRODUCTION

Holt-Oram syndrome, also called Heart-Limb or Heart-Hand syndrome, originally described in 1960 by Holt and Oram is defined as a genetic abnormality with autosomal dominant inheritance, rare occurring at an approximate frequency of 1 / 1,000 000 live births, due to a mutation of the TBX5 gene located on chromosome 12. It associates congenital heart disease and skeletal abnormalities of the thoracic limbs.

1. CLINICAL OBSERVATION

This is a 6-month-old male infant; admitted for cyanosis and fatigability during a suckling progressing for a month complicated by respiratory discomfort, the antecedents reveal the existence in the mother of a heart disease type interventricular communication (CIV) and malformations of the upper limb. There is no notion of consanguinity in the parental couple. The personal antecedents note that he was born from a delivery carried out by cesarean section on borderline pelvis with a birth weight: 3kg300, The admission examination notes severe hypotrophy with a weight of 3 kg (3 SD), height of 60 cm, We observed in the left hand: a hypoplastic thumb, a bifid index, a hypoplasia of the thenar eminence. In the right hand, we found hypoplasia of the thenar eminence, a thumb inserted at the same level as the other fingers; giving the appearance of a lack of opposition, the thumb resembling the 5th finger with clinodactyly.

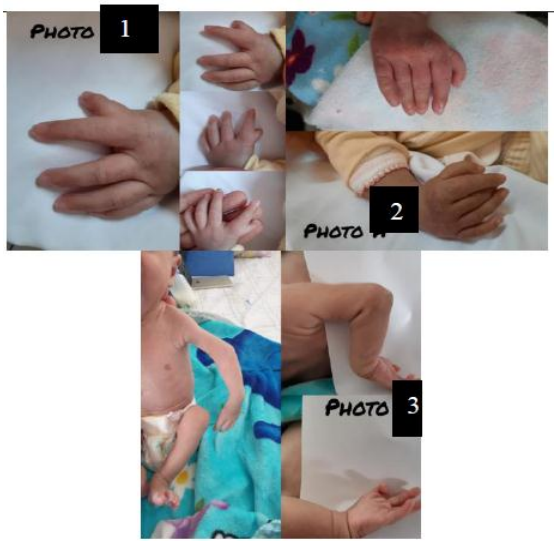

Figure 1: Malformation of the hands in infants.

Figure 2: Hand malformation in the mother.

Cardiovascular examination found galloping noise, femoral pulses present and BP of 80/55 mmgh in both arms. There was no involvement of the lower limbs.

The paraclinical workup performed showed on the chest

x-ray (face) cardiomegaly (RCT = 0.7), and pulmonary hyper vascularization. The ECG showed a sinus rhythm at 71 bpm with a right axial deviation in AVR, a dilation of the right ventricle and a completely right bundle branch block without conduction disorder. Echocardiography showed a complete CAV, trabecular CIV of 6mm, small apical CIV, small high Ciaos, hypoplasia of the LV and horizontal aorta and dilated pulmonary artery with a maximum gradient of 20 mmgh.

The x-rays of the hands and wrists carried out, made it possible to show at the level of the wrist and the left hand: agenesis of the pisiform, a malformation of the scaphoid; agenesis of the first cubital row with a small outline of P1. Examination of the wrist and right hand revealed a tapering aspect of the first right metacarpal, shortening of the third right phalanx (adduction), hypoplasia of P2 (adduction), agenesis of P1.

Figure 3: Hand and wrist radio Right, Left.

Faced with the association of such anomalies, Holt-Oram syndrome has been mentioned especially in the presence of similar cases in the family. A karyotype with a genetic study was performed in the patient and the current mother.

2. GENERAL DISCUSSION

Holt-Oram syndrome is an autosomal dominant genetic disorder that is associated with a mutation in the TBX5 gene. Although this mutation can be inherited, most cases result from a new mutation in patients without a family history of the disease. It affects approximately 1 in 100,000 people and It is characterized by abnormalities of the bones of the upper limb, a family or personal history of congenital heart defect and / or a defective cardiac conduction.

Symptoms of Holt-Oram syndrome vary widely from person to person, even within the same family. Upper limb deformities range from an unusually long thumb that looks like a finger (triphalangia) to an absent thumb bone or absent thumb. Other types of upper l imb malformations may also be present, including underdevelopment or absence of the forearm bones (radius and ulna), fusion or abnormal development of the bones of the thumb and wrist (thenar and carpus), and abnormal position of the thumb, forearm or shoulders. Affected individuals may be unable to fully extend their arms, rotate them inwardly with the palms down (pronation), or rotate them outward. outside with palms up (supination). More severe cases include a deformity in which the hands are attached to the shoulder with absent or shortened arms (phocomelia). In some people with the condition, an abnormality of the wrist bone (carpus) is the only sign of the disease.

Seventy-five percent of those affected have a congenital heart defect. The most common heart defects are interatrial communication ostium secundum (CIA) and interventricular communication (CIA) as observed in our patient.[1]

In some cases, severely affected children exhibit poor growth, shortness of breath, easily fatigable on exertion and / or variable arrhythmias.

The only gene known to be associated with Holt-Oram syndrome is the TBX5 gene. A mutation in the TBX5 gene has been identified in approximately 74% of people with Holt-Oram syndrome. This is probably an underestimate of the true frequency of the TBX5 gene mutation, because genetic tests do not always detect all types of mutations. Currently, there are over 70 known mutations in the TBX5 gene that cause Holt-Oram syndrome. Potential causes for the rest of those affected include incorrect reading and translation of the TBX5 gene during protein production.

The abnormal gene may be inherited from either parent or may be the result of a new mutation in the affected person. About 85% of cases of Holt- Oram syndrome are thought to be due to new mutations in the TBX5 gene. The risk of passing the abnormal gene from the affected parent to their offspring is 50% for each pregnancy. The risk is the same for men and women.[5]

- **Diagnostic**

The diagnosis of Holt-Oram syndrome is based on clinical and family history. X-rays of the hand are taken to check for upper limb deformities. Echocardiography, MRI and other imaging modalities as well as electrocardiography are used to determine the presence and severity of heart defects and / or cardiac conduction disease. Molecular genetic tests using the TBX5 gene are available to confirm the diagnosis. Some people with mild symptoms are not diagnosed until middle age. Prenatal ultrasound of the fetal h eart has been used to diagnose heart defects in children of an affected parent.[2]

Specific treatments for Holt-Oram syndrome are symptomatic and supportive. Depending on the severity of the upper limb abnormalities, treatment may consist of corrective or reconstructive surgery, the use of prostheses for parts of the forearms and hands, and / or physical therapy to help individuals. to improve their motor skills.[3]

In affected individuals who have mild heart conduction abnormalities, treatment may not be necessary. However, in more severe cases, when associated symptoms appear, a pacemaker may be used. The primary treatment for structural heart abnormalities associated with Holt-Oram syndrome is to close the defect (s) with surgery or catheters. In this case, the surgical procedures performed will depend on the location and severity of the abnormalities and associated symptoms. Some people can be treated with drugs and / or other techniques; Early intervention is important so that children with Holt-Oram syndrome can reach their potential.[4]

Family members of those affected should also be carefully evaluated clinically for any symptoms and physical findings that may be associated with Holt-Oram syndrome. Family members with normal clinical evaluations should have x-rays of the wrists and arms as well as echocardiograms to confirm if they have a mild form of the disease.

Genetic counseling is recommended for sufferers and their families.

3. CONCLUSION

Holt-Oram syndrome, an exceptional disease, the early diagnosis of which is possible and the prognosis linked to the existence and severity of cardiac and orthopedic damage, requires multidisciplinary management. Long-term monitoring of conduction is necessary.

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