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Case Report

Holt-Oram syndrome in an infant presenting with heart failure

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ABSTRACT

Holt-Oram syndrome is an autosomal dominant condition characterized by morphological abnormalities of upper limbs and congenital cardiac defects. We report a case of 6-week-old infant with morphological alterations of upper limbs (absent radius and hypoplastic ulna) since birth and multiple congenital cardiac defects (atrial septal defects and ventricular septal defects), who presented with congestive cardiac failure. This case report illustrates that neonates with anomalies of thumb or upper limbs should be evaluated for possible congenital heart defects.

Key words: *Atrial septal defects, Congestive heart failure, Hand-heart syndrome*

The first description of Holt-Oram syndrome (HOS) dates back to 1960 when Mary Holt and Samuel Oram reported a family with atrial septal defects (ASDs) and congenital anomalies of the thumbs [1]. It is a rare genetic disorder with a prevalence of one case per 100,000 births [2,3]. We report a case of HOS in a 6-week-old infant with right upper limb deformity, failure to thrive and multiple congenital heart defects who presented with congestive heart failure (CHF) and pneumonia. It is probably the first reported case of HOS from India presenting in early infancy with CHF and multiple heart defects.

CASE REPORT

A full-term male baby born to nonconsanguineous parents presented at 6 weeks of life with upper limb deformity (extreme flexion at wrist) since birth and difficulty in breathing for a week. There was a history of suck stop cycles during feeds and not gaining weight. On general examination, right upper limb deformity (extreme flexion at wrist) and failure to thrive was found. Systemic examination revealed tachypnea, respiratory distress, flaring of ala nasi, bilateral crepitations, hepatomegaly, and levine grade 4/6 pan systolic murmurs.

His radiograph revealed an absent radius and hypoplastic ulna. Chest X-ray on posteroanterior view showed cardiomegaly (Cardiothoracic ratio 0.64). Complete blood counts and C-reactive protein were within normal limits. On two-dimensional echocardiography, intramuscular ventricular septal defect (VSD) of 4 mm with the left to right shunt, and multiple small ostium secundum ASDs were found.

A diagnosis of HOS was made on the basis of congenital cardiac and forelimb defects. Parents did not have any family history of limb deformity or cardiac defects. We could not do a genetic analysis due to financial constraints. He was given furosemide, digoxin, and intravenous antibiotics. For limb deformities, orthopedic consultation was taken. He has an uneventful recovery and after clinical improvement sent to higher center for definitive correction of his heart defects.

DISCUSSION

HOS is an autosomal dominant condition (OMIM 142900) with genetic heterogeneity, TBX5 gene located on chromosome 12 (12q24.1) contains 70% of the most common mutations of clinical diagnosis [4]. TBX gene encodes a transcription factor which is important in the development of both the hands and upper limbs [5]. Most of the cases are of familial transmission while new mutations account for 40-85% of cases [3,6].

Clinical manifestations are variable but with complete penetrance, patients always have upper limb abnormalities and about 85-95% have cardiac malformations [2]. Skeletal abnormalities affect only upper limbs, and the presence of lower limb abnormality rules out the diagnosis. Defective development of embryonic radial axis results in varied manifestations ranging from abnormally long thumb to an absent thumb bone or completely absent thumb, underdevelopment or absence of bones in the forearm (radius and ulna), fusion or abnormal development of thumb and wrist bones (thenar and carpal), and abnormal position of the thumb, forearm or shoulders. At minimum, the abnormal carpal bone may be the only manifestation of disease [7].

The majority of the HOS patients have congenital heart malformations of various types; the most common are ASD and VSD. Cardiac conduction defects and multiple structural defects are not uncommon [3]. The condition needs to be differentiated

from Fanconi anemia syndrome, thrombocytopenia-absent radius syndrome, Okihiro syndrome, and long-thumb brachydactyly syndrome [2]. Family screening with X-ray of hands and electrocardiogram should always be done even if no clinical deformity is present and parents should be counseled as it is a genetic disorder with autosomal dominant inheritance with a high degree of penetrance.

CONCLUSION

HOS is a rare autosomal dominant condition. Neonates with anomalies of the thumb or upper limbs should be evaluated for possible congenital heart defects.

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