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A Rare Case Report of Newborn with Holt-Oram Syndrome

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ABSTRACT

Holt-Oram syndrome or heart-hand syndrome is a multisystem congenital disorder, characterized by distinctive malformations of bones of the thumb and forearms and associated abnormalities of the heart. Here we report a rare case of newborn with morphological alterations of upper limbs (absent radius and hypoplastic ulna) and 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 always be evaluated for possible congenital heart defects.

Key words: Atrial septal defects, newborn, Congestive cardiac failure, Hand-heart syndrome.

INTRODUCTION

Holt-Oram syndrome or heart–hand syndrome is a multisystem congenital disorder. [1] 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. [1,2] It is a rare genetic disorder with a prevalence of 1 case per 100,000 births. [2,3] Since then, about a few hundred cases have been reported worldwide. It is characterized by distinctive malformations of bones of the thumb and forearms and associated abnormalities of the heart. Here we report a case of HOS in a newborn with right upper limb deformity and respiratory distress.

CASE REPORT

A full-term (39+4 weeks) male newborn was born to a 23 year old Primigravida by vaginal route with birth weight of 2.345kg with uneventful postnatal transit with APGAR score of 7 and 8 at 1 and 5 minutes of life respectively. All maternal serology were negative with uneventful antenatal history. There was no history of consanguinity in parents. Head circumference was 33.7cm (noted after 24 hours of life) and length 48 cm at birth. Both fontanelles were normal. All the external orifices were patent. Newborn passed meconium and urine within 24 hours of life.

On general examination, Newborn had upper limb deformity of left side forearm. There was presence of abnormally long thumb in bilateral hands with absence of bones of left forearm (radius and ulna).Both thumbs were triphalangeal. There was restriction of supination and pronation in left forearm. Both lower limbs were normal. Rest head to toe examination was normal. Newborn developed respiratory distress on day 2nd of life. Examination in NICU revealed tachypnoea and subcostal and intercostal retractions. Downes score was 3/10. Examination showed bilateral crepitation, hepatomegaly and Levine grade 4/6 pan systolic murmurs. Baby was admitted to NICU and received oxygen, antibiotics, diuretics, digoxin initially as possibility of pneumonia/acyanotic heart disease was kept. Gradually RDS settled

over next 3 days of life.

His radiograph revealed an absent radius and hypoplastic ulna on left side. Chest X-ray on postero-anterior view showed cardiomegaly (Cardiothoracic ratio 0.67). Complete blood counts and C-reactive protein were within normal limits. Platelet count was normal. Thyroid profile was normal. Neurosonogram, USG abdomen and KUB were normal. On two-dimensional echocardiography, intramuscular ventricular septal defect (VSD) of 5 mm with the left to right shunt, and multiple small ostium secundum ASDs were found.

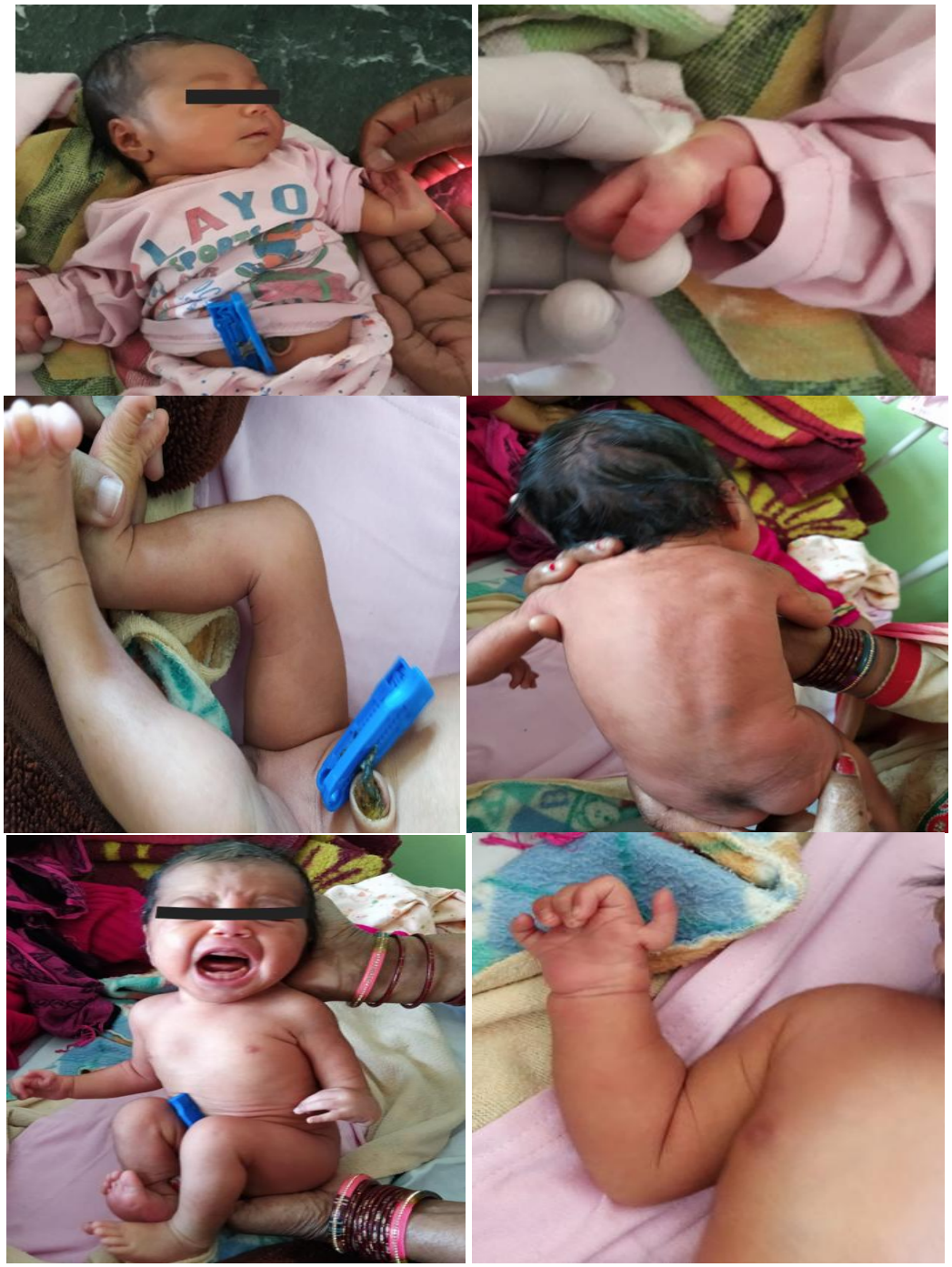

FIGURE 1-6 showing features of newborn with Holt-Oram Syndrome:

1. **Showing absence of radius and ulna in left forearm**
2. **Showing long thumb in both hands**
3. **Rest of images showing normal lower limbs, genitalia and back.**

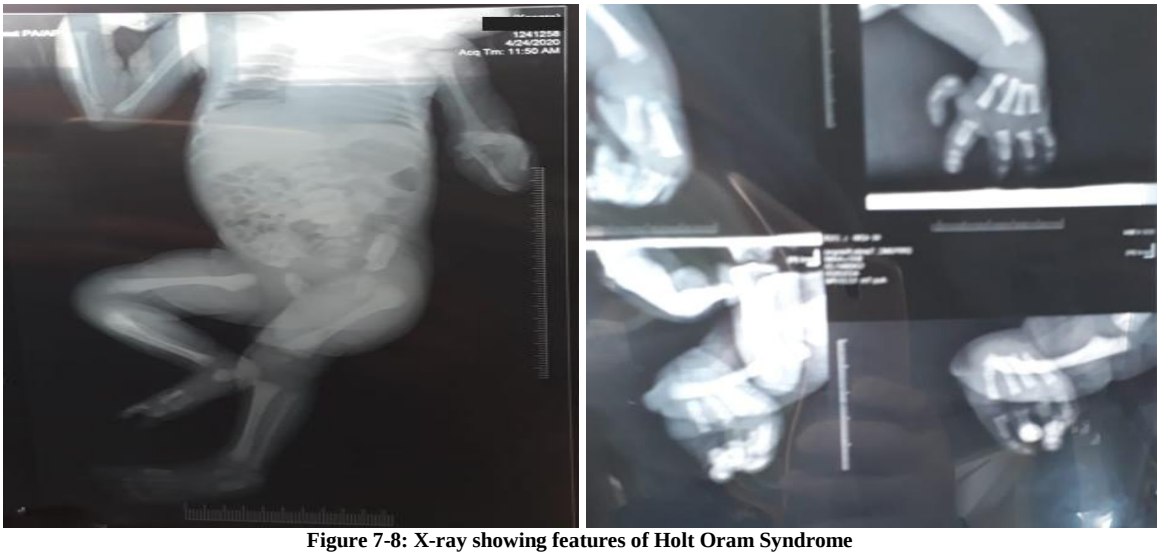

Figure 7-8: X-ray showing features of Holt Oram Syndrome

A diagnosis of Holt Oram Syndrome 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 and non-availability in our institute. New born received given furosemide, digoxin, and intravenous antibiotics. For limb deformities, orthopaedic consultation was taken. New born was kept on follow up for cardiac defects .Orthopaedic consult was taken for corrective surgery but parents refused.

DISCUSSION

Holt-Oram Syndrome is also called as the Heart-Hand Syndrome or Atrio-Digital Dysplasia. HOS is an autosomal dominant condition (OMIM 142900) with genetic heterogeneity, TBX5 gene located on chromosome 12 (12q24.1) which 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. [5,6] The symptoms and physical findings associated with Holt-Oram Syndrome may vary greatly, the severity being greater in succeeding generation.

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. It does not affect lower limbs because of the fact that mutant gene affects the embryogenesis during the 4^{th} and 5^{th} week of intrauterine life when the lower limbs are not differentiated. 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. Others include PDA, endocardial cushion defects, hypoplasia of left ventricle or conduction disturbances (1st degree heart blocks). [8-10] Cardiac conduction defects and multiple structural defects are not uncommon. [3] There may be associated renal anomalies. [10] Prognosis depends on the severity of cardiac and orthopaedic lesions.

Differential diagnosis include

1.Fanconi anaemia syndrome

2. Thrombocytopenia-absent radius (TAR) syndrome
3. Okihiro syndrome
4. long-thumb brachydactyly syndrome [2]
5.VACTERL association
6. Radial ray choanal atresia.

Family screening with X-ray of hands and electrocardiogram should always be done even if no clinical deformity is present and parents should be counselled as it is a genetic disorder with autosomal dominant inheritance with a high degree of penetrance. The main aim of management includes the physical therapy to at least provide some function to the deformed upper limbs and primarily the detection of the cardiac abnormalities so that they can be corrected at an early stage to prolong the longevity of patients. [11]

CONCLUSION

The Holt-Oram syndrome is a rare disorder with a constellation of upper-limb deformities and cardiac defects. The aim of this article was to present the classic findings of Holt-Oram syndrome to look for any structural cardiac defects for early detection and management as these children can stay a normal life if cardiac part and orthopaedic part is managed early. Thus, all the newborns with upper-limb deformities should be evaluated for cardiac defects so that early management is planned.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms regarding images and other clinical information to be reported in the journal.

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