Unilateral Hypoplastic Kidney in a Case of Holt-Oram Syndrome

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Abstract

Holt-Oram syndrome (HOS) is characterised by skeletal abnormalities of the upper limb & congenital cardiac defects. Here we report a case of one day old male baby with skeletal abnormalities of forearms and hands, atrial septal defect of ostium secundum type and unilateral hypoplastic kidney. Till date, other associated anomalies like extra-hepatic portal hypertension, renal artery malformations etc have been reported with Holt-Oram syndrome, but it is the first case to be reported in association with hypoplastic kidney.

Key words: Holt-Oram Syndrome, Ultrasonography, Hypoplastic kidney.

Introduction

Holt-Oram syndrome (HOS) is characterised by skeletal abnormalities of the upper limb with mild to severe congenital cardiac defects. It has autosomal dominant inheritance and near complete penetrance with variable expression[1]. A mutation in TBX5 gene located on chromosome 12 (12q24.1) has been associated with variable phenotypes[2,3]. This syndrome, first described in 1960[1], is also referred to as Hand-Heart syndrome. About 350 cases have been reported worldwide and some of them were associated with other anomalies. We find it interesting to present this case since there is no reported case of Holt-Oram Syndrome associated with unilateral hypoplastic kidney.

The Case

A one-day-old, 2.4 kg, Hindu male baby, born out of non consanguineous marriage & delivered normally of a 25-year-old mother, was admitted in our nursery with several congenital anomalies of the upper limbs. The baby had radially curved & short left forearm with absent thumb, index & middle fingers of the left hand and hypoplastic thumb attached to the palm by a thin thread-like pedicle in the right one [Figure 1]. Other anthropometric parameters were within normal limits. There was no facial dysmorphism. Thorough systemic examination didn't reveal any abnormality.

X-ray of upper limbs showed absent radius with absent 1st, 2nd and 3rd metacarpal in left side and absent 1st metacarpal on the right side. Remaining skeletal survey did not reveal any abnormality. Hemogram, renal function and serum electrolytes were normal. ECG was normal. Echocardiography showed ostium secundum ASD (6.4mm in size). Abdominal ultrasongraphy showed hypoplastic kidney in the right side (1.53cc) with normal volume of left one (4.36cc) [Figure 2].

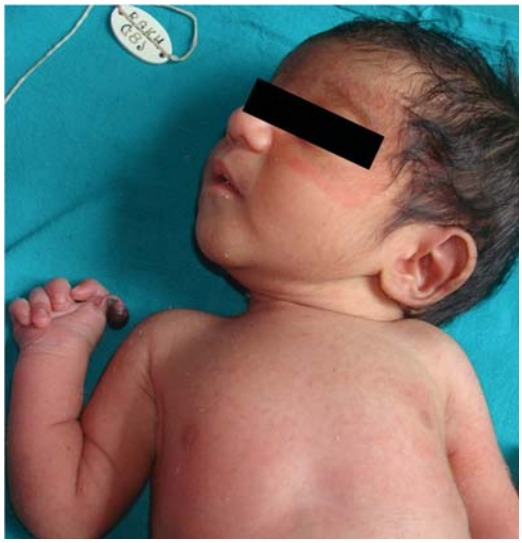

Fig 1: Picture of the baby showing radially curved and short left forearm with absent thumb, index & middle fingers of the left hand with hypoplastic thumb attached to the palm by thin thread-like pedicle in the right one.

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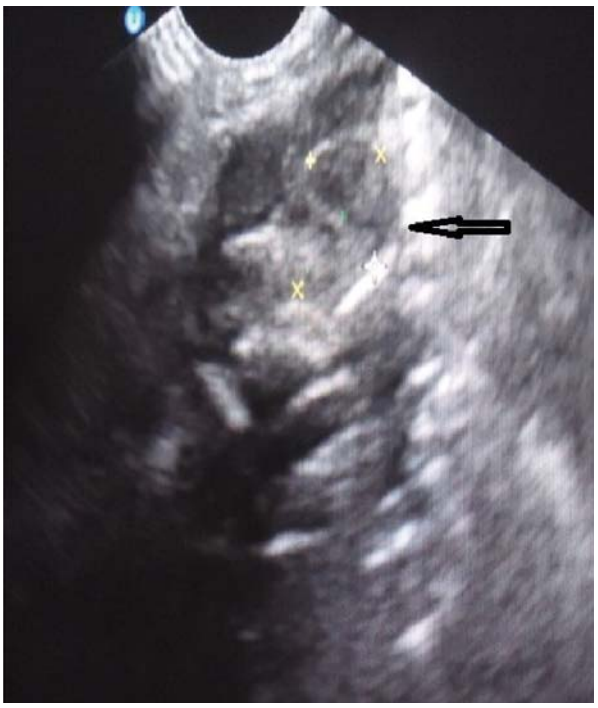

Fig 2: Abdominal ultrasonography showing hypoplastic kidney in the right side (Volume:1.53cc).

Discussion

Holt-oram syndrome is a rare genetic disorder. Its prevalence is calculated as 0.95 in 1, 00,000 births. It is characterised by skeletal dysplasia of upper limb and congenital cardiac malformation. The responsible gene is reported to be localized in long arm of chromosome 12 (12q24.1) which encodes human transcription factor TBX5[2]. Mutation of the gene produces abnormal expression of the limb and cardiac development. It has autosomal dominant inheritance. Forty percent of cases are associated with new mutations.

Upper extremity abnormalities may be unilateral or bilateral, but left side is mostly involved like our case. These abnormalities are ranging from mild hypoplasia of radius or ulna to phocomelia[3]. This baby had absence of thumb, index & middle fingers of the left hand with hypoplastic thumb on the right side.

Secundum-type atrial septal defect (ASD) and ventricular septal defect (VSD) are the most common heart defects. Other cardiac anomalies are conduction defect, truncus arteriosus, mitral valve defect, patent ductus arteriosus, tetralogy of Fallot, persistent left superior vena cava, abnormal left coronary artery ostium, atrioventricular canal defect and hypoplastic left heart[4,5,6,7]. In our case, ostium secundum ASD was present.

Differential diagnosis considered in the present case was Fanconi anaemia (FA), Thrombocytopenia – absent radius (TAR) syndrome, VATER / VACTERL syndrome & Trisomy 18. Fanconi anaemia had been excluded as there were no characteristic physical malformations or hematologic manifestations in this baby[8]. In TAR, in which radii are absent, the thumbs are always present, not so for our case. It presents at birth with severe thrombocytopenia with bleeding manifestations and radial ray defects[9]. Trisomy 18 can rarely have radial ray defects and eye anomalies. However trisomy 18 has host of different physical abnormalities and a typical facies[8]. Holt-oram syndrome has considerable overlap in the physical abnormalities with VATER /VACTERL syndromes, but the present case had no vertebral anomaly though there was hypoplastic kidney in the right side.

In literature there is a case report of ectopic kidney with radial dysplasia only[10]. Holt-oram syndrome with extrahepatic portal hypertension and renal artery malformation has been reported previously[11], but no report associated with hypoplastic kidney has been done till date.

Conclusion

Holt-oram syndrome itself is a rare syndrome and among all the previously reported cases, none of them was associated with hypoplastic kidney. Thus, USG abdomen may be considered as a screening investigation in patients with Holt-oram syndrome to rule out this association and thereby to prevent its future complications.

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