Study on Holt Oram Syndrome – examination and results

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Introduction

Holt-Oram syndrome (HOS) also known as Hand- Heart syndrome is a very rare autosomal dominant disease caused by a mutation in the *TBX5* gene located on chromosome 12. Clinically it manifests with morphological abnormalities of the upper limbs and congenital cardiac defects leading to variety of complications. Cardiac malformations go undiagnosed till late in life. With routine antenatal checkup, external physical deformities can be found out with high suspicion of congenital heart malformations as well, which can lead to early effective management. We here by describe a case of 20 year-old female with known morphological alterations of the upper limbs since birth presented with Right heart failure diagnosed to have atrial septal defect.

The congenital cardiac and upper limb deformities occurring together are known as heart- hand syndrome. The most common among them is HOS with incidence of 1 in 100,000 live births. It is an autosomal disorder occurring due to the mutation in chromosome 12q24.1, which codes for the human transcription factor TBX5 gene. Mary Clayton Holt and Samuel Oram in 1960 described HOS as a triad of ASD, Conduction disturbances and digital malformations. Our patient also has ASD along with left distal phocomelia and digital anomalies on both hands.

A 20-year-old girl was referred to the department of cardiology, with the history of dyspnea (NYHA grade 2) and palpitation for the past 1 year. Her past medical and family history was unremarkable. On musculoskeletal examination, she had obvious bilateral upper limb deformities. The left upper limb was abnormally short with absent forearm and hand arising from the arm, which falls under type III distal phocomelia and with oligo-dactyly The right upper limb also had hypo plastic thumb with syndactyly of the thumb and index finger Skeletal radiographs of the left upper limb depicted absent radius, ulna, 1st and 2nd metacarpals along with the phalanges of the first two digits. There were no obvious lower limbs or spine deformities.

Physical examination revealed elevated Jugular venous pressure, blood pressure of 110/70mmHg, pulse rate of 96 beats/min and O2 saturation was 98% in room air On cardiovascular examination, right parasternal heave of grade 2 was present; auscultation revealed wide fixed split of the second heart sound with loud pulmonary component was noted along with Ejection systolic murmur of grade III, best heard over the pulmonary area.

Electrocardiogram demonstrated normal sinus rhythm and right axis deviation with incomplete right bundle branch block. Chest X ray showed cardiomegaly due to right atrial and ventricular dilatation with dilated pulmonary trunk. Two-dimensional transthoracic echocardiography in four chamber view revealed a large ostium secundum type of ASD (32mm) with left to right shunt right atrial and ventricular dilatation, severe pulmonary artery hypertension (58 mmHg), and an left ventricular ejection fraction of 55%. Tricuspid annular plane systolic excursion (TAPSE) was 15 mm suggesting mild Right ventricular (RV) systolic dysfunction. All other laboratory investigations were normal. Hence the diagnosis of HOS was formulated based on clinical, radiographic and echocardiographic evidence. She was stabilized with medical management (ACE inhibitors, diuretics and beta blocker) and was referred to cardiovascular surgery for complete intracardiac repair with pericardial patch closure of the septal defect.

CONCLUSION

In conclusion, we report a case of HOS associated with distal phocomelia and oligodactyly of left upper limb and syndactyly of the right hand along with ostium secundum type ASD in heart failure. Due to its high degree of cardiac complications and recent advancements in fetal echocardiogram, all patients with upper limb deformities in antenatal checkup should have cardiac evaluation with recent for early detection and effective management to have a better prognosis.