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Sinus Venosus Atrial Septal Defect with Hemianomalous Right Upper Pulmonary Venous Drainage in Holt-Oram Syndrome

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ABSTRACT

Holt-Oram syndrome (HOS), an autosomal dominant genetic condition, is characterized by congenital heart defects, upper limb abnormalities and heart block. HOS is associated with *TBX5* mutation. The condition is often associated with ostium secundum type of ASD. We present here the case of a 2-year-old child with sinus venosus atrial septal defect with hemianomalous right upper pulmonary venous drainage in HOS.

Keywords: Holt-Oram syndrome, hemianomalous pulmonary venous drainage, atrial septal defect - sinus venosus, preimplantation genetic diagnosis

Holt-Oram syndrome (HOS) is an autosomal dominant genetic condition characterized by congenital heart defects, upper limb abnormalities and heart block and is associated with *TBX5* mutation. During surgical correction of atrial septal defects (ASDs), problems encountered from the Anesthetist's perspective include difficulty in placing vascular lines, tracheal intubation, ventilation and problems in invasive arterial monitoring. Association with sinus venosus ASDs with hemianomalous pulmonary venous drainage is rare. Surgical correction with rerouting is reported here.

CASE REPORT

A 2-year-old child presented with failure to thrive, excessive sweating and feeding difficulty. Associated features were absent right thumb and imperforate vagina. There was no family history of congenital heart disease. Right radial pulse was absent. The right arm was short and the left arm was normal. X-ray of right arm showed absent radius. Chest X-ray showed cardiomegaly and electrocardiogram (ECG) showed incomplete right bundle branch block. Evaluation showed situs solitus, levocardia, atrioventricular and ventriculoarterial concordance, normal systemic and pulmonary venous drainage, a large sinus venosus ASD measuring 15 mm × 12 mm with right upper hemianomalous pulmonary venous drainage, and tricuspid regurgitation (PG = 20 mmHg). Lab evaluation was within normal limits. Inhalational anesthetic induction was given to facilitate endotracheal intubation. Femoral artery and internal jugular venous cannulation were done under ultrasound guidance. ASD closure and rerouting of hemianomalous pulmonary venous drainage was done under mild hypothermia (32°C) and cardioplegic cardiac arrest by autologous nonfixed pericardial patch closure. Weaning from cardiopulmonary bypass (CPB) was smooth in normal sinus rhythm and no residual shunt was detected on epicardial echocardiography.

DISCUSSION

Effective prenatal genetic diagnosis of Holt-Oram syndrome (HOS) is limited by factors that modify clinical manifestations and confound prediction of an individual's phenotype. Familial ASDs are often

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associated with *GATA4* and *NKX2-5* mutations. Abnormalities in genes essential to cardiac septation have been associated with ASDs, including mutations in the cardiac transcription factor gene *NKX2-5*, *GATA4* and *TBX5, MYH6* located on chromosome 14q12 and other mutations. HOS is often associated with ostium secundum type of ASD. Ostium primum ASDs are often associated with DiGeorge syndrome and Ellis-van Creveld syndrome. Cardiac defects in HOS include ASD (34%), ventricular septal defect (VSD, 25%), patent ductus arteriosus (PDA), ECG changes (35%) and asymptomatic conduction disturbance with variable degree of AV block. Heart-hand syndrome type II (Tobatznik syndrome), Heart-hand syndrome type III (OMIM 140450) do not include ASD and do not map to band 12q2. Those with HOS may have additional bone abnormalities such as a missing thumb, a long thumb, partial or complete absence of bones in the forearm, underdeveloped bone of the upper arm, and abnormalities of the collar bone or shoulder blades. The manifestations of HOS are dysplasia of upper limb, ranging from minor radiographic abnormalities to phocomelia and cardiac abnormalities. The associated skeletal deformities include triphalangeal thumbs, carpal bone dysmorphism, shortness of ulna, short humerus, aplasia of the radius and phocomelia.

In addition to anomalous pulmonary venous drainage, inferior vena caval interruption and persistent left superior vena cava may be associated. Hypoplastic peripheral vessels add on to difficulty in catheterization and invasive monitoring. Individuals may present at birth with sinus bradycardia and first-degree atrioventricular (AV) block. AV block can progress unpredictably to a higher grade including complete heart block with and without atrial fibrillation. Pre-pregnancy history of arrhythmia and maternal age more than 30 years have been noted as risk factors for maternal cardiac complications. By comparison with the general population, women with unrepaired ASDs had an increased risk of pre-eclampsia, fetal loss and low birth weight. By contrast, the outcome for offspring of women with a repaired defect was similar to that of the general population. Pregnancy should be avoided in women with an ASD and severe pulmonary hypertension.

In a contemporary study, maternal mortality was prohibitively high (28%) in women with congenital heart disease and pulmonary hypertension, despite use of pulmonary vasodilator therapy in more than half of the patients.

CONCLUSION

Sinus venosus, primum and coronary sinus septal defects need surgical closure. Secundum defects can be closed by either surgery or by a percutaneous route using an occluding device delivered by a catheter. Transcatheter closure might not be feasible in some large secundum defects or small infants. Status of peripheral vessels needs evaluation before transcatheter procedures are planned. A variety of cardiac anomalies may be associated with conduction problems and other system involvement in HOS, which may make both device closure and surgical approaches to be meticulously planned well in advance with appropriate investigations and diagnosis of all associated lesions. As we go on to identify more genetic etiologies for congenital heart defects, preimplantation genetic diagnosis, as an adjunct to *in vitro* fertilization, will help prevent transmission of such diseases from parents to their children.

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