

## PHOTOCLINIC



**A** 6-year-old female child was consulted for repeated respiratory infections. She was the fourth child of apparently normal parents born as normal delivery. She had normal IQ and no complaint till fifth year of age. There was no family history of any disease and her other siblings were also normal. On P/E, pulse rate was 115 / minute and regular with normal BP, but a right ventricular heave without thrill. S1 was normal but S2 was widely splitted and fixed. A grade 3/6 systolic murmur was audible at the upper left sternal border. There was no positive clinical finding in the respiratory system. P/E of the skeletal system revealed the lack of first fingers in both upper limbs and the lower extremities were normal.

ECG showed a normal sinus rhythm with a regular heart rate of 115/minute, right axis deviation, right ventricular hypertrophy; a prominent tall p wave of 3 mm, and incomplete RBBB. Chest radiography showed increased cardiothoracic ratio, enlargement of the right

atrium and right ventricle; with increasing pulmonary vascular marking.

In radiography of the upper extremities, bony shadows of the first digit in the right and the left hands were not seen. Scaphoid was absent on the right side. Humerus shadow did not appear on both sides. Above-mentioned radiological evidences suggested radial side defect. Doppler echocardiography showed a large atrial septal defect of 22 mm, paradoxical interventricular septal motion and mild pulmonary stenosis, with a pressure gradient of 20 mm per Hg, prolapse of anterior mitral leaflet without any regurgitation. Enlargement of the right atrium and ventricle were seen.

Cardiac catheterization and ventriculography confirmed atrial septal defect of secundum type, along with dilatation of the main pulmonary artery and enlargement of the right atrium and ventricle.

**Your Diagnosis?**

See next page for diagnosis

## Photoclinic Diagnosis: Holt-Oram syndrome

Holt-Oram syndrome (HOS) is a rare genetic disorder characterized by distinctive malformations of the bones of the thumbs and forearms (upper limbs) and/or abnormalities of the heart.<sup>1</sup> This is an autosomal dominant condition first elaborated in 1960, which shows marked variability. The cardinal manifestations are dysplasia of the upper limbs and atrial septal defect.<sup>2</sup> In many infants with the disorder, the thumbs may be absent, hypoplastic or even have an extra bone (triphalangy). Affected infants may also have additional upper limb malformations such as underdeveloped (hypoplasia) or extra bones in the wrist; malformations of certain bones of the hands, and/or underdeveloped radius, ulna or humerus. Scapula, clavicles and/or other bones may also be abnormal.<sup>3</sup> In most cases, infants with HOS have cardiac abnormalities that may include anatomical malformations of the heart and/or electrocardiographic conduction defects. In individuals with the disorder, atrial or ventricular septal defects (ASDs or VSDs) or both are the most common structural heart defects.<sup>2</sup> Individuals with HOS may have electrocardiographic conduction defects as a separate finding or in association with septal defects. The effects of such defects are highly variable, ranging from asymptomatic in some to serious complications in the others.<sup>2</sup> HOS is an autosomal dominant disorder. In approximately 60% of cases, it is inherited from an affected parent. In about 40% of cases, the disorder is the result of a spontaneous genetic change. The atrial involvement ranges from none to a large secundum defect with early severe hemodynamic abnormality. Other cardiac malformations have also been reported<sup>4</sup> with VSDs being the most frequent. Other manifestations include dermatoglyphic abnormalities, pectus excavatum, hypoplastic peripheral arteries, and cardiac conduction disturbance, the last usually involves the AV node and presents in patients with septal defects.<sup>2</sup>

The diagnosis of HOS is most likely to be missed in a patient with an unknown or unremarkable family history of a secundum septal defect and minimal or no thumb anomaly. In any sporadic case of ASD, the patient and the parents should be carefully examined for limb malformations.<sup>5</sup> Detection of a subtle limb defect alters the recurrence risk in offspring of the proband from

the empirical risk of an isolated septal defect of 3 percent to nearly 50 percent of an autosomal dominant trait.<sup>6</sup>

Prenatal echocardiography is suggested for all the pregnant ladies having family history of congenital heart or limb defect. The severity of the reduction defect varies widely, from a proximally placed thumb to near total absence of the arm. Upper extremity deformity is usually bilateral, as it was in our case. Only about fifty percent of patients have the cardiac defect.<sup>2</sup> In the presented case the patient had atrial septal defect along with the absence of both thumbs. The skeletal and cardiac manifestations are not correlated in individuals and how a parent is affected is not a reliable predictor of effects on offspring.<sup>5</sup> Presumably a large septal defect could be detected as well. Although the HOS bears some resemblance to the VATER association, the clear mendelian nature and lack of more extensive organ system involvement of the Holt-Oram indicate that the two conditions do not represent a pathogenetic spectrum.

## References

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