Case report

Tetralogy of Fallot with Holt-Oram syndrome

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KEYWORDS

Arrhythmias
Atrial septal defect
Holt-Oram syndrome
Tetralogy of Fallot

ABSTRACT

Holt-Oram syndrome (HOS) is characterised by mild to severe congenital cardiac defects and skeletal abnormalities of the upper limb. This syndrome is also referred to as Hand-Heart syndrome. The most common cardiac disorder is an ostium secundum detected an atrial septal defect (ASD), followed by ventricular septal defect (VSD) and ostium primum ASD. We report a case of HOS with tetralogy of Fallot (TOF). This association is very rare and is hardly reported in the literature.

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Introduction

Holt-Oram syndrome (HOS) was first reported in 1960 by Mary Clayton Holt and Samuel Oram, who detected an atrial septal defect (ASD) in members of four generations of a family. Detected an ASD which was associated with a congenital anomaly of the thumbs which lay in the same plane as the fingers.

The most common congenital heart defect is the ostium secundum ASD, seen in 60% of patients with HOS followed by the ventricular septal defect (VSD). The other associated findings include hand malformations and conduction disturbances, originally described by Holt and Oram. The other complex congenital cardiac malformations, like VSD with infundibular pulmonary stenosis, complete atrio-ventricular (AV) canal defect, mitral valve prolapse, hypoplastic left heart syndrome, coarctation of aorta, subaortic stenosis, patent ductus arteriosus, etc. have rarely been reported in HOS.

Recently, we came across a case of hand malformation with cyanotic congenital heart disease, which was later identified as tetralogy of Fallot (TOF). This association is rarely described in patients with HOS.

Case report

A 2-year-old female child presented with fatigability, bluish discolouration (cyanosis), and growth retardation, since 6 months of age (Figure 1). Patient also had right hand malformation in the form of radial deviation at wrist and cubitus valgus deformity of right upper limb and hypoplastic right

Figure 1 Cyanosis of lips while crying.

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thumb being at the same plane as fingers (distally located than the opposite thumb) (Figure 2). One of her family members had congenital cardiac malformation. Her father's sister had medium size perimembranous VSD, but she had no anomaly related to either of the hands. None of the other family members are affected.

General examination

Patient had cyanosis, which increased on crying and did not improved on 100% oxygen inhalation. Grade II clubbing was also present.

Figure 2 (A, B) Showing right hand deformities (radial deviation of wrist and cubitus valgus deformity of the right elbow). (C) Left hand deformity.

Cardiovascular system examination

Apex beat was within midclavicular line at the fifth intercostal space. A systolic thrill was present at the upper left intercostal space. Grade I left parasternal heave was present. Ejection systolic murmur was heard at mid and upper left intercostal space. A single second heart sound (S2) was heard.

Musculoskeletal system examination

Right thumb was hypoplastic and located distally in the plane of fingers, in comparison to the left thumb. Right hand was deviated radially at the wrist. Rest of the systemic examination did not reveal any abnormality.

Investigations

Haemoglobin (Hb)—19.8 g/dL, total count—10,100/mm³, differential count—N40 L52 E3 M5, platelet count—1,14,000/mm³, haematocrit—60.9%, mean corpuscular volume (MCV)—75.0 fl, red blood cells (RBC) count—8.13 × 10⁶/mm³.

Figure 3 Forearm and hand radiograph showing hypoplastic radius and triphalangeal thumb.

Figure 4 Chest radiograph showing boot-shaped heart and pulmonary oligemia.

Radiograph right hand: triphalangeal thumb, distally located, hypoplastic radius, radial deviation of the right wrist (Figure 3).

Chest radiograph posterior–anterior view: No cardiomegaly (cardiothoracic ratio <50%), boot-shaped heart (Coeur en sabot), main pulmonary artery inconspicuous (concave), decreased pulmonary vascularity (Figure 4).

Electrocardiogram (ECG): Right ventricular hypertrophy, right axis deviation, no arrhythmia detected (Figure 5).

Two-dimensional echocardiography with colour Doppler: Situs solitus, levocardia, large perimembranous VSD with 40% aortic override with right to left shunt, hypoplastic and confluent main, right, and left pulmonary artery, predominantly infundibular pulmonary stenosis with peak gradient

of 80 mmHg, interatrial septum is intact, no patent ductus arteriosus or any other defect seen (Figure 6).

We concluded from the above findings that this was a case of TOF associated with HOS.

Discussion

Holt–Oram syndrome is a rare syndrome with one in 1,00,000 live births affected.¹ About 300 cases have been published revealing a wide spectrum of clinical signs. Association of TOF is very rare. We could find only one study which included 18 patients of HOS, conducted in China, which showed some association between these two findings.²

Figure 5 Right ventricular hypertrophy; right axis deviation.

Figure 6 (A) Parasternal long axis view showing overriding of aorta and large perimembranous ventricular septal defect. (B) Parasternal short axis view showing hypoplastic and confluent PA. (C) Continuous Doppler showing infundibular pulmonary stenosis with pressure gradient of 80 mmHg. AO: ascending aorta, PA: pulmonary artery, RA: right atrial, RV: right ventricle.

Holt-Oram syndrome is an autosomal dominant disorder. The underlying genetic defect was found on the long arm of chromosome 12. Mutation in the TBX-3 and TBX-5 genes lead to a wide range of phenotypes typical of HOS.^{1,3}

The review of orthopaedic sign in the literature remains poor.⁴ Frequent signs are radial ray abnormalities, absent or abnormal radius, upper limb-transverse elements missing, and various thumb anomalies. Occasional signs are scoliosis, abnormal ribs, hypertelorism, scapula anomalies, and pectus excavatum, which were absent in our patient.

Arrhythmias have also been reported in HOS. Most of the patients who present with arrhythmias have anatomical heart anomalies. Around 39% of the patients with HOS show no anatomical heart anomalies but only ECG abnormalities. Electrocardiogram abnormalities include right bundle branch block (RBBB), wandering pacemaker, sinus node dysfunction, atrial fibrillation/flutter, paroxysmal supraventricular tachycardia (PSVT), and Wolff-Parkinson-White syndrome (WPW).

Ostium secundum ASD is the most common in patients with HOS⁵ followed by VSD. The severity of the cardiac spectrum is not always proportional to that of the upper limb deformity. Anomalies of the great vessels have also been associated with HOS (vena cava, subclavian artery, coarctation

of aorta, and hypoplastic aortic arch). But, it is worth emphasising that the spectrum of this syndrome is still growing as there are miles to go because this is a relatively rare syndrome with only about 300 cases been reported till date worldwide. Hence, it is rather too premature to say that the above association (HOS with TOF) is really a rare association. The whole aim of publishing this case is to add on to the present spectrum of this syndrome.

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Obituary

Dr. A.K. Thakur, Patna

Dr. A.K. Thakur, the doyen of cardiology in the state of Bihar died on 19th December 2011. He is considered the father of modern cardiology in Bihar. He is closely associated with the establishment and development of Indira Gandhi Institute of Cardiology, Patna. He was instrumental in developing the cardiology training programme at the same institute. Born in 1937, Dr. Thakur did his MBBS and MD at Patna and received Cardiology training at Manchester, UK. After his retirement from government service he established a Private Hospital for Cardiology called the “Heart Hospital” and continued his services to public. He actively participated in CSI activities throughout. He is survived by wife, two children and two grandchildren.

Compiled by
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