Case report

"A Rare Bond: Exploring the Heart-Hand Connection in Holt-Oram Syndrome"

Abstract

Holt-Oram syndrome is an autosomal dominant disorder characterized by upper limb abnormalities in association with congenital heart lesions. We present you a 42 years old female having ostium secundum atrial septal defect (OS-ASD) and congenital upper limb deformity. Her X-ray of hands showed bilateral abnormal carpal bones with underdeveloped thumb. This study highlights the importance of recognizing the heart-hand connection in Holt-Oram syndrome and presents the need for multidisciplinary care and early intervention.

Key Words: Holt-Oram Syndrome, ASD, Hand Deformity.

Introduction

Holt-Oram syndrome also referred to as the heart-hand syndrome, is an autosomal dominant disorder that is characterized by upper limb abnormalities in association with congenital heart lesions (1). First described in 1960 by Holt and Oram, the syndrome was identified when thumb anomalies and atrial septal defects (ASD) were observed in family members across four generations (2, 7. 8). Since then, the identification of more cases and advances in technology has allowed for a greater understanding of the syndrome (3, 6). However, there is still a significant proportion of individuals who are being born with the disorder in both industrialized and underdeveloped countries (4 - 6).

Case Presentation

A 42 years old female born of non-consanguineous marriage with full term normal vaginal delivery without any perinatal complications referred to our hospital with chief complaints of breathlessness since 3 years and palpitations since 1 year. Patient was a known case of Ostium secundum atrial septal defect (OS-ASD) since childhood and has upper limb deformity since birth. Dyspnea was of NYHA Class III and was not associated with orthopnea, paroxysmal nocturnal dyspnea or any seasonal variation. Patient had strong family history of similar features through three generations in father, brother & her elder son. On clinical examination pulse rate was 78 beats/minute, irregularly irregular and blood pressure of 100/60 mmHg. She had deformed hands (Hypoplastic and triphalangeal thumb) (Image 1). On Auscultation she had normal first heart sound with wide split and fixed second heart sound. There was a grade III systolic murmur in pulmonary area and short, rumbling mid-diastolic murmur in mitral area. Her routine blood investigations were within normal limit. Her X-ray of hands showed bilateral abnormal carpal bones with

underdeveloped thumb (Image 2). Electrocardiogram was showing atrial fibrillation with controlled ventricular rate, right axis deviation with right atrial enlargement with right ventricular hypertrophy. Echocardiography was suggestive of OS-ASD of size 40 mm with adequate rims and left to right shunt across it with grossly dilated right heart (Image 3). Cath study was suggestive of reversible pulmonary arterial hypertension with PVR of 1.24 and Qp: Qs of 6.61. Genetic analysis revealed a heterozygous mutation in TBX5 gene on chromosome 12q24.1. Percutaneous closure of ASD with a 44 mm Life-Tech ASD closure device was successfully done under TEE guidance. Long term follow up revealed great recovery without short term or long term complications.

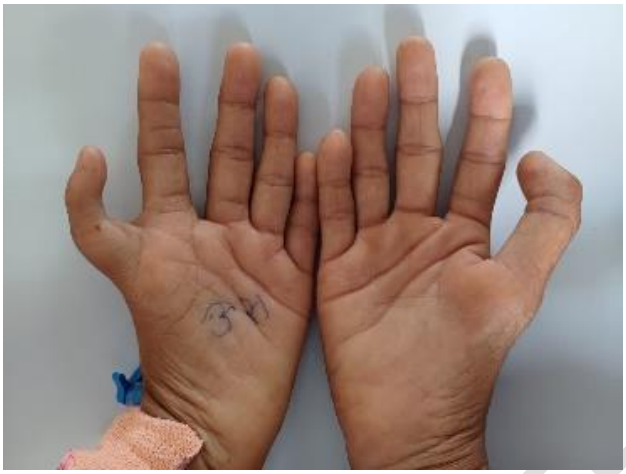

Image 1. S/O Hypoplastic and triphalangeal thumb

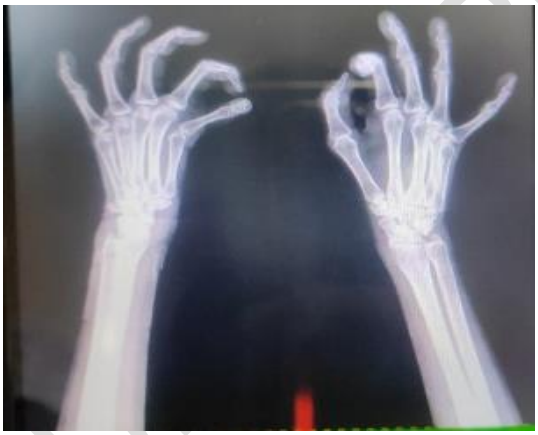

Image 2. bilateral abnormal carpal bones with underdeveloped thumb

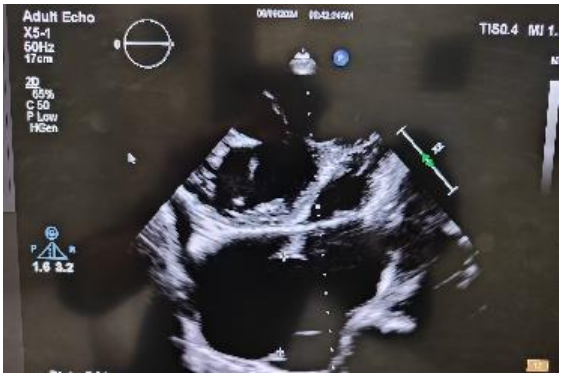

Image 3. OS-ASD of size 40 mm with adequate rims

Discussion

Holt-Oram syndrome also referred to as the heart-hand syndrome, is an autosomal dominant disorder that is characterized by upper limb abnormalities in association with congenital heart lesions (1). First described in 1960 by Holt and Oram, the syndrome was identified when thumb anomalies and atrial septal defects (ASD) were observed in family members across four generations (1, 2). The syndrome affects approximately 1 in 100,000 births, with a slight female preponderance (2). The heterozygous mutation in the TBX5 gene on chromosome 12q24.1 confirms the diagnosis of Holt-Oram syndrome (2). TBX5 is a transcription factor essential for cardiac and limb development. Mutations in TBX5 disrupt normal development, leading to the characteristic features of the syndrome (2, 7, 8).

Our patient presented with classical features of Holt-Oram syndrome with upper limb deformity (hypoplastic and triphalangeal thumb), congenital heart defect (ostium secundum atrial septal defect, OS-ASD) and cardiac conduction abnormality (atrial fibrillation). Upper-limb malformations can involve the carpal bones, thenar bones, and radial bones (1-3). These abnormalities may be unilateral or bilateral and symmetric or asymmetric. Most cases are unilateral and affect the left side (5). The strong family history of similar features across three generations highlights the autosomal dominant inheritance pattern of Holt-Oram syndrome in our case (6, 8). The diagnostic approach included physical examination, imaging studies (X-ray, echocardiography), electrocardiography, cardiac catheterization and genetic analysis (4, 5). Untreated, Holt-Oram syndrome can lead to pulmonary hypertension, congestive heart failure, arrhythmias and sudden cardiac death (3-5). Timely management and follow-up can improve quality of life and prevent complications (1-5).

Conclusion

Holt-Oram syndrome should be suspected in individuals with Upper-limb malformation, atrial septal defect, cardiac conduction disease and family history of congenital heart defects**.** This case highlights the importance of recognizing the heart-hand connection in Holt-Oram syndrome and emphasizes the need for multidisciplinary care and early intervention.

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