Holt- Oram syndrome: a case report

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Abstract

Background: Holt-Oram syndrome (HOS) is mainly an autosomal dominant condition characterized by upper limb abnormalities and in 85 – 95% of cases, congenital cardiac malformations. It may occur as a result of new mutations in 40% of cases.
Methods: We reviewed the case notes of a neonate.

Results: We present a case of HOS in a one week old male with an absent radius but no congenital cardiac abnormality born to apparently normal parents.
Conclusion: HOS is a rare disease and highlights the need for parental counseling.

Key words: Holt-Oram, Congenital Malformations, Phocomelia, Oligodactyly,

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Introduction

Holt-Oram syndrome (HOS) is a rare hereditary disease estimated to affect 1 in 100,000 individuals, and is characterized by skeletal dysplasia of upper extremities in all patients and congenital cardiac anomalies in 85-95% of cases[1,2]. A broad clinical spectrum is associated with this syndrome and ranges from subclinical radiological findings to life threatening disease. The case reported is one of the few reported cases of HOS in the West African sub region.

Case Report

A one week old male neonate referred to our facility with complaints of upper limb deformity from birth and jaundice. He was a product of a term gestation delivered via spontaneous vaginal delivery to a 21 year old para 2+0 mother. The pregnancy was booked at 28 weeks gestation in a private hospital in Jos and mother had received her routine haematinics and one dose of tetanus toxoid. Mother was treated with Artesunate and Sulfadoxine-Pyrimethaminefor Malaria in her first trimester before she became aware she was pregnant. There was no indiscriminate use of drugs, exposure to radiation, rash suggestive of viral prodromes or ingestion of herbal or traditional medication during the pregnancy. Child did not cry at birth and had to be resuscitated vigorously at birth and had a birth weight of 2.83kg. Examination findings were those of grossly malformed upper limbs; severe phocomelia, oligodactyly (three fingers) and absent thumb on the right upper limb, and mild phocomelia, syndactyly and absent thumb were observed on the left upper limb. The pulse rate was 140 beats per minute and with first and second heart sounds only with no murmurs. Other examination findings were normal. X-rays of the upper limbs showed absent radius and carpal bones with a deformed and fractured ulnar on the left with a shortened radius and ulnar, dislocated at the elbow and absent carpal bones on the right. Chest radiograph showed normal pulmonary vascular markings and normal cardiothoracic ratio of 0.52. Electrocardiograph showed low voltages with normal axis deviation and while echocardiography showed no abnormalities. Platelet count remained between 130x 10^9 and 160x10^9. He currently stable on follow up at the neonatology clinic.

Discussion

Holt–Oram syndrome(HOS)was first described in 1960 as coexistence of ASD, conduction disorders on ECG and hand malformations[1]. It is popularly called the heart-hand syndrome. HOS is transmitted mainly by autosomal dominant inheritance. Other cases of Holt-oram syndrome are sporadic, and result from new mutations in the TBX5 gene on chromosome 12q24 that occurs in people with no history of the disorder in their family[1,3]. With no family history of similar illness in the family and no physical evidence of limb deformities in the parents, the index case may be sporadic as radiologic evaluation of the parents' upper limbs was not performed. Although autosomal dominant HOS has near complete penetrance and variable expression, subtle limb involvement may not become clinically apparent without radiographic studies[4,5].

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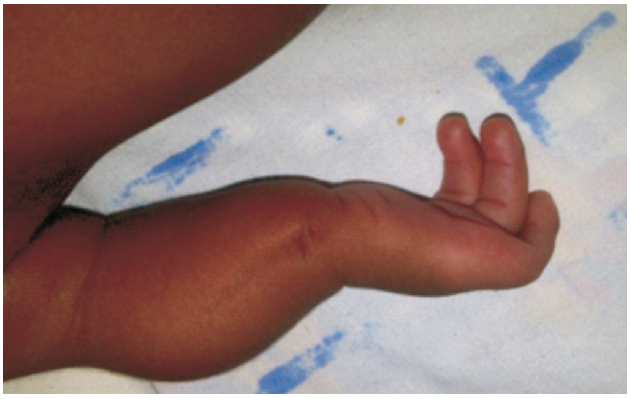
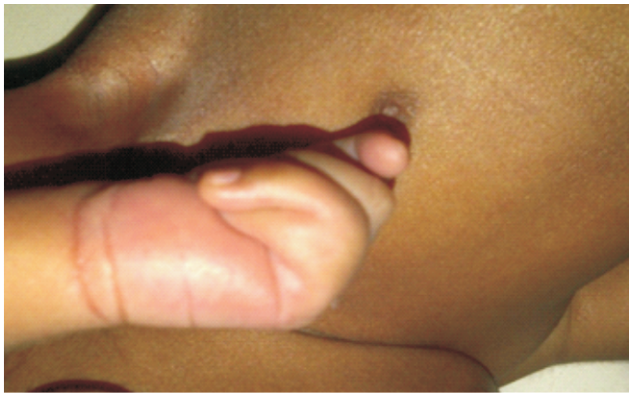
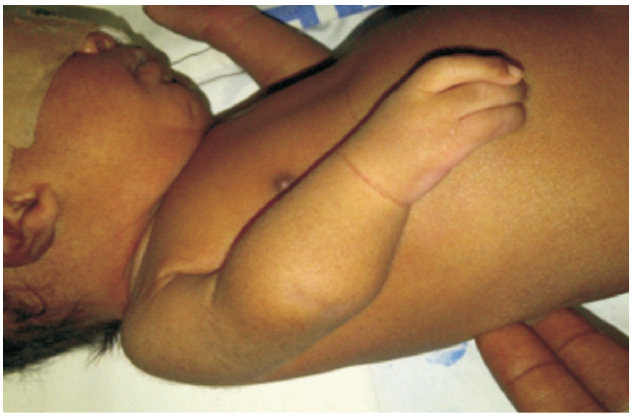


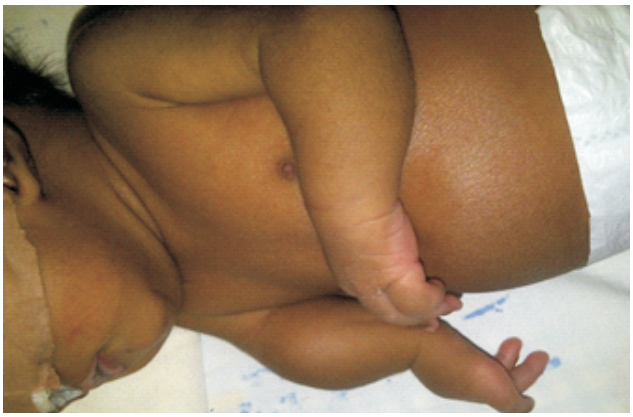
1a. Right upper limb



1b. Left upper limb



1c. Right upper limb



1d. Both upper limbs

Figure 1. Upper limb deformities in a neonate with the Holt-Oram syndrome at the Jos University Teaching Hospital

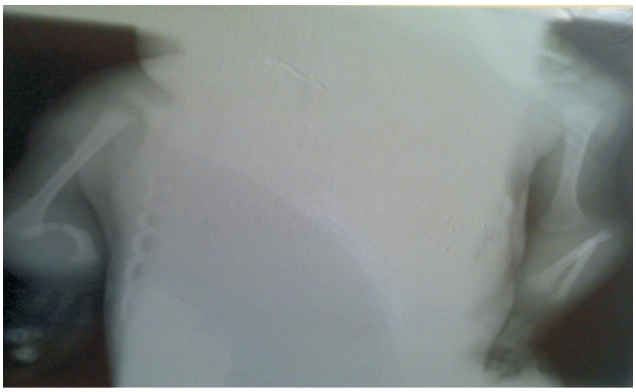


Figure 2.Absent radius on and fractured ulnar on left forearmin a neonate with the Holt-Oram syndrome at the Jos University Teaching Hospital

Upper limb deformities occur exclusively and are usually bilateral and frequently asymmetrical as seen in index case. Sometimes, only one upper limb is affected. The spectrum of limb defects ranges from mild (slight carpal bones abnormalities) to severe (phocomelia). Partial or complete absence of one of the forearm bones usually the radius occurs. However, abnormalities of the ulnar bone are said to be indicative of other diagnoses. Also, the thumb may either be triphalangeal (finger-like), hypoplastic or absent[6]. The thumb on the right upper limb was absent in the case reported.

Cardiac abnormalities occur in approximately 75% of patients with HOS (95% of familial cases). Cardiac abnormalities may occur singly or as complex heart defects and almost any kind of abnormality may occur. The most common cardiac abnormalities are ostiumsecundum atrial septal defect (ASD) and ventricular septal defect (VSD)[5,7]. Conduction defects such as atrioventricular block and right bundle branch block, and arrhythmias like atrial flutter, fibrillation, supraventricular tachycardias (SVT) and Wolf Parkinson White (WPW) syndrome may be present.[8]In this case reported, there were no abnormalities detected on ECG though low voltages were present which can be a normal finding in new-born babies. A 24 hour holter ECG monitor may have picked up episodic arrhythmias such as SVT and WPW syndrome. Echocardiography revealed no abnormality in the index case.

The main differential diagnosis is Thrombocytopaenia-Absent Radius (TAR) syndrome, an autosomal recessive condition characterized by bilateral radial agenesis and thrombocytopenia in which cardiac involvement is present in up to 33% of cases. [9] The diagnosis of TAR syndrome was considered in this case study, specifically because the parents had no phenotypic abnormalities, making the possibility of an autosomal recessive condition (as in TAR syndrome) more likely. However, the findings of absent thumb made the diagnosis of TAR syndrome very unlikely because in this condition as the thumbs are invariably present in TAR syndrome. Moreover, thrombocytopenia was not seen in the haematologic assessment of this child even at third day of life which is one of the main criteria for TAR syndrome diagnosis. Other conditions with upper limb abnormalities include Fanconi anaemia, Kaufman-mcKusick syndrome, SC phocomelia, Nager syndrome, Roberts syndrome and Edwards syndrome (Trisomy 18).

This paper presents a rare disease and highlights the need for parental counselling.

References

1. Holt M, Oram S. Familial heart disease with skeletal malformations. Br heart J 1960; 22:236-246.
2. Sletten LJ, Pierpont ME.Variation in severity of cardiac disease in Holt-Oramsyndrome.Am J Med Genet 1996, 65:128-132.
3. Newbury-Ecob RA, Leanage R, Raebun JA, Young ID. Holt-Oram syndrome: A Clinical genetic study. J Med Genet 1996;33:300-307
4. Basson CT, Cowley GS, Solomon SD.The clinical and genetic spectrum of the Holt-Oram syndrome (heart-hand syndrome).N Engl J Med 1994; 330: 885-891.
5. Hurst JA, Hall CM, Baraitser M.The Holt-Oram syndrome.J Med Genet 1991; 28:406-410.
6. Huang T. Current advances in Holt-Oram Syndrome.Pediatr 2002; 14:691–695
7. Bossert T, Waither T, GummertJ, Hubald R et al. Cardiac malformations associated with Holt-Oram syndrome: Report on a family and review ot the literature. ThoracCardiovascSurg 2002; 50: 312-314.
8. Bruneau BG, Logan M, Davis N, Levi T et al. Chamber-specific cardiac expression of Tbx5 and heart defects in Holt-Oram syndrome. DevBiol 1999; 11:100-108.
9. Newbury-Ecob RA, Leanage R, Raeburn JA, Young IDl. Holt-Oram syndrome: A clinical genetic study. J Med Genet 1996; 33:300-307.