American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2020; 21: e923341
DOI: 10.12659/AJCR.923341

Received: 2020.02.07
Accepted: 2020.04.18
Available online: 2020.05.08
Published: 2020.06.03

Rare Extracardiac Anomalies Presented with Right Heterotaxy Syndrome in a Newborn Baby: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABEFG 1 Roya Huseynova
AEG 1 Latifa A. Bin Mahmoud
AEFG 1 Eman AlJohani
AEF 2 Oqtay Huseynov
AEF 1 Adli Abdelrahim
AEFG 3 Khalid A. AlOmran

1 Department of Neonatology, King Saud Medical City, Riyadh, Saudi Arabia
2 Azerbaijan Medical University, Baku, Azerbaijan
3 Department of Cardiology, King Saud Medical City, Riyadh, Saudi Arabia

Corresponding Author: Roya Huseynova, e-mail: huseynova_roya@yahoo.com, r.huseynova@ksmc.med.sa
Conflict of interest: None declared

Patient: Female, 1-day-old
Final Diagnosis: Right heterotaxy syndrome with complex heart disease • annular pancreas • radius aplasia • partial syndactyly of the thumb and index finger
Symptoms: Feeding problems • tachypnea
Medication: —
Clinical Procedure: —
Specialty: Cardiac Surgery • Cardiology • Orthopedics and Traumatology • Pediatrics and Neonatology • Radiology • Surgery

Objective: Unusual clinical course
Background: Heterotaxy is a syndrome of abnormal arrangement of the internal thoracic-abdominal structures across the left-right axis of the body. It is a primary disorder with 2 main settings – bilateral left sidedness (polysplenia syndrome) or right sidedness (asplenia syndrome) – although some overlapping or uncertainties may occur. Patients with right heterotaxy typically present with asplenia, complex heart disease, and other thoracoabdominal organ situs abnormalities.
Case Report: We present a unique case of congenital asplenia syndrome with complex heart disease, annular pancreas, and other extra-heterotaxic anomalies (e.g., musculoskeletal) in the form of a radius aplasia and partial syndactyly of the thumb and index finger of the left hand. These associated anomalies have not been reported before.
Conclusions: This case shows the need for paying increased attention to the implications of other extracardiac anomalies that can be associated with heterotaxy syndrome.

MeSH Keywords: Heterotaxy Syndrome • Infant, Newborn • Isomerism

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/923341

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Background

Heterotaxy is a syndrome of abnormal arrangement of the internal thoracic-abdominal structures across the left-right axis of the body. It is a primary disorder with 2 main settings – bilateral left sidedness (polysplenia syndrome) or right sidedness (asplenia syndrome) – although some overlapping or uncertainties may occur [1]. Although the syndrome occurs sporadically, some genetic abnormalities have been also reported [2,3]. The reported incidence of heterotaxy syndrome (HT) is 1–1.5/10 000 live births [4]. Patients with complex cardiac lesions and heterotaxy have a poor prognosis, with mortality of over 85% for patients with asplenia, and over 50% for patients with polysplenia [5]. Around 40–70% of patients with heterotaxy syndrome have shown involvement of various systems [6], many of them with various congenital gastrointestinal anomalies, but only a few of them have presented other systemic involvement such as respiratory, genitourinary, central nervous system, and skeletal anomalies.

The appearance of the muscle-skeletal type anomalies presented in this index case has not been reported previously.

Case Report

The female infant was born of first-degree consanguineous marriage to a 29-year-old mother at 38 weeks of gestation by a cesarean section after a failed induction at a peripheral hospital. The mother was healthy, with no history of radiation exposure or drug intake during pregnancy. No similar conditions were reported in the family. At 20 hours of age, the newborn was referred to the tertiary neonatal intensive care unit for surgical intervention as a suspected case of duodenal atresia.

On admission, weight was 2400 g (in the 10th centile), length was 55 cm (in 97th centile), and head circumference was 35 cm (in the 50th centile). The infant appeared stable and had acceptable ranges of vital signs and blood gases. She was afebrile, with heart rate 130/minute, respiratory rate 55/minute, not distressed, with oxygen saturation 95–96% at room air. Routine blood investigations, including the level of platelets, were normal during the whole hospital stay.

Musculoskeletal system assessment revealed deformity of the left upper limb, with radial flexion and partial syndactyly between her left thumb and index finger. Radiography of the left limb showed complete radial aplasia, with abnormal flexion of the wrist (Figure 1). A skeletal survey of the whole body did not show any other osseous anomalies. The abdomen was soft and the infant was passing stool. She was kept nil per os orally. However, persistent dilated stomach on serial abdomen radiography findings (Figure 2) and residual gastric greenish aspirate raised the suspicion of a duodenal web; therefore, on postnatal day 2, a laparotomy was performed. During surgery, an annular pancreas was found to be obstructing part of the duodenum. The stomach and first section of duodenum were grossly dilated.

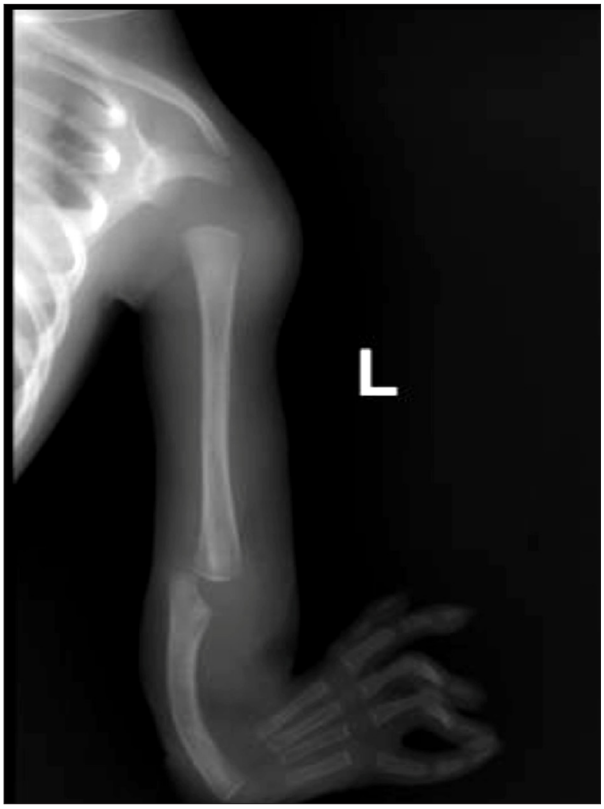

Figure 1. Radiograph of left upper limb shows the complete radial aplasia with persistent flexion of the wrist.

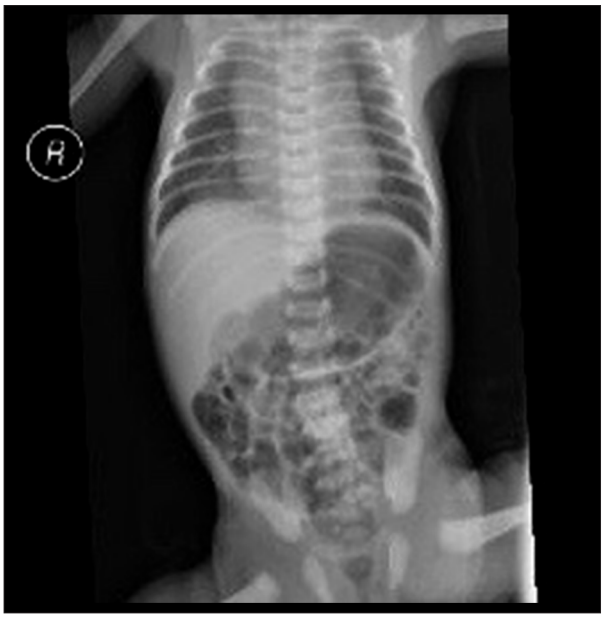

Figure 2. Abdomen radiography shows dilated stomach bubble.

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

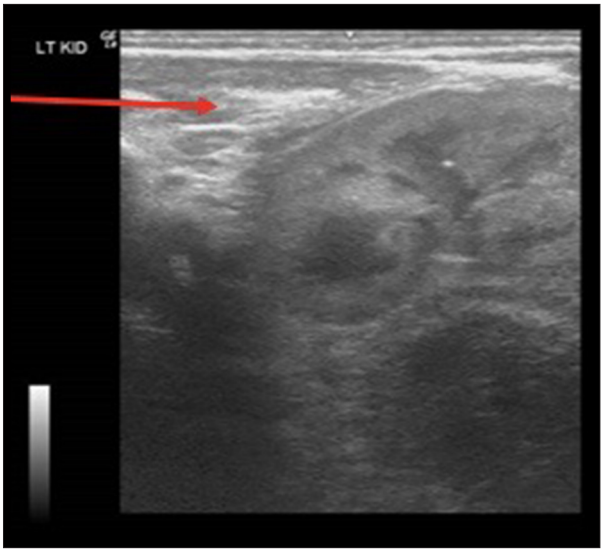

Figure 3. Abdominal ultrasound shows non-visualized spleen.

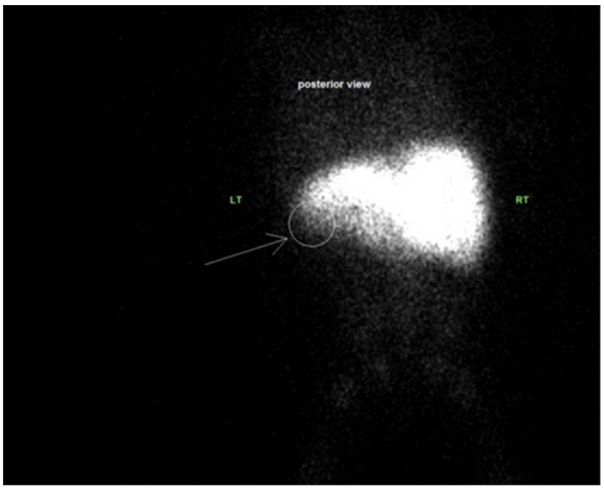

Figure 4. Standard spleen and liver scan using 99mTc-Sulfur-colloid demonstrated the normal anatomical location of the liver and non-visualized spleen.

Ultrasound of the abdomen revealed normal parenchymal echogenicity of the liver, patent hepatic veins, gall bladder, and normal size of both kidneys, with preserved cortical medullary differentiation. No ascites was found. The spleen could not be visualized (Figure 3). Repeated abdomen ultrasound revealed the same findings. The absence of the spleen raised a high suspicion of the possibility asplenia syndrome, which was supported by the presence of Howell-Jolly bodies on the peripheral blood smear report.

A standard spleen and liver scan using 99mTc-Sulfur-colloid showed normal anatomical location of the liver, but the spleen was not visualized in normal anatomical location or in ectopic location (Figure 4).

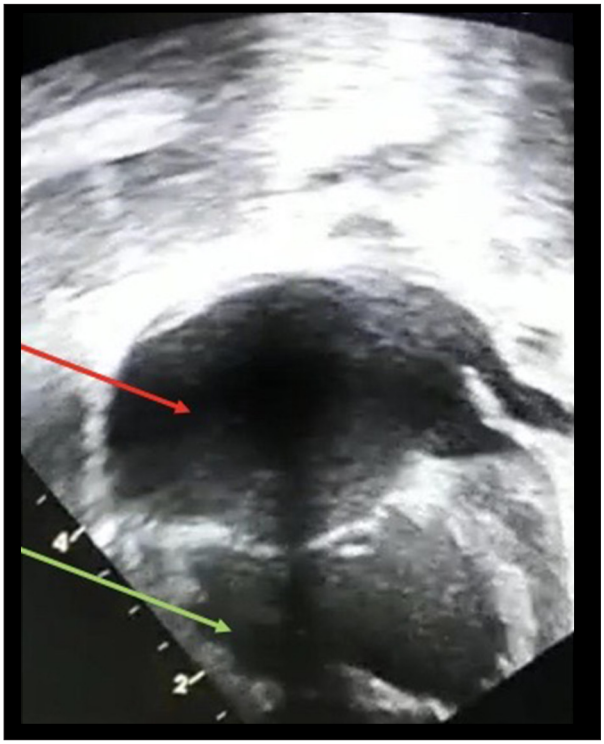

Figure 5. Parasternal view shows single common atrium, single AV valve, and single ventricle.

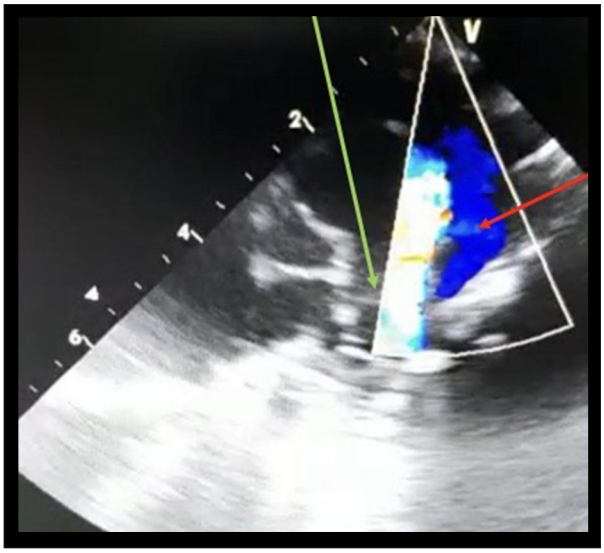

Figure 6. Short axis view shows aorta is parallel to pulmonary artery (d-TGA).

An echocardiography done on the 2nd day of life showed: levocardia, complex congenital heart disease, single atrium right atrium morphology, with large pyramidal appendages, single ventricle with right ventricle morphology (good function), single atrioventricular (AV) valve, dextro-transposition of the great arteries (d-TGA) with moderate pulmonary valve stenosis, and small patent ductus arteriosus (PDA) (Figure 5 and 6).

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

A head ultrasound showed normal visualized parenchymal echogenicity with no evidence of intraparenchymal hemorrhage, except for a small focus of increased parenchymal echogenicity with the central hypoechoic component, which could be related to the choroid plexus cyst.

At 3 weeks of age, the infant developed persistent late-onset staphylococcus sepsis that required prolonged treatment. During the hospital stay, the condition of the infant gradually improved. She reached full feeding and was extubated to nasal continuous positive airway pressure (nCPAP) with oxygen requirement 30%. She received prophylactic antibiotic therapy due to asplenia, and anti-heart failure medications.

The patient continued to have follow-up with cardiology, orthopedic, and plastic surgeons.

Owing to the unavailability of corrective neonatology cardiac surgical services in the hospital, the patient was accepted for further management at a higher-level cardiology center.

Discussion

Based on the findings, the presented case was diagnosed as asplenia syndrome (right isomerism) with congenital complex heart disease (right morphology atrium and ventricle, single AV valve, d-TGA with moderate pulmonary valve stenosis, small PDA), annular pancreas, left-side upper-limb anomalies of the radial aplasia, and partial syndactyly of the thumb and index finger.

Asplenia was supported by the existence of Howell-Jolly bodies, small fragments of DNA revealed by the peripheral blood smear [7], and confirmed by the spleen scan report.

Ivermark syndrome, known as asplenia or right isomerism of internal organs, is characterized by gastrointestinal anomalies like midline liver, inverted duodenal loop, right-sided gastric fundus, and complex heart diseases. It usually occurs in males, where severe complex heart disease is complicated by the increased susceptibility to fatal infections due to immune-compromised conditions as a result of asplenia [8].

Almost all infants with congenital asplenia have manifestation of visceral heterotaxia in which a mild form may be present with normal or close to normal location of liver, non-retroperitoneal location of the pancreas, and partial common gastrointestinal mesentery, while the more severe form has nonrotation of the intestines and common gastrointestinal mesentery [9]. There is various systemic involvement in heterotaxy syndrome. Approximately 70% of babies with heterotaxy syndrome have some degree of intestinal rotation [10]. Most defects are common to both asplenia and polysplenia syndromes, although biliary atresia and extra-hepatic portosystemic anastomosis is mainly detected with polysplenia syndrome.

Patients with polysplenia have less severe heart defects compared to patients with asplenia, in which typical cardiac findings such as unbalanced atrioventricular defect, double outlet right ventricle, pulmonary atresia, and bilateral 'right atria like' appendages are present [11].

This index case echocardiography findings of single right morphology atrium and ventricle, are typical cardiac findings suggestive of right isomerism accompanied by AV canal, TGA, and moderate pulmonary valve stenosis. Because newborn babies with complex heart disease can be asymptomatic in the first hours of life, as in our index case, they may be discharged early without sufficient diagnosis, increasing the risk of deterioration or mortality. Wren et al. reported that approximately 25% of neonates with serious heart diseases were discharged without being diagnosed [12]; therefore, early recognition and timely intervention are crucial for improving outcomes in these neonates. Patients with asplenia are immunocompromised and hence have an increased risk of sepsis due to overwhelming infections in the absence of a functioning spleen [13]. The index case developed persistent late-onset staphylococcus sepsis and was treated with a prolonged course of antibiotics.

Although there are many reported cases of asplenia syndrome, few have had associated extra-heterotaxic anomalies. Association of the musculoskeletal anomalies with asplenia syndrome were reported in 2 cases, where one case was described to have clubbing of hands with overlapping toes and another case had absence of radii [9]. To the best of our knowledge, this is the first report of a patient with asplenia with unilateral absence of radius and partial syndactyly.

The common syndromes associated with radii anomalies and congenital heart diseases include Holt-Oram syndrome (HOS) and thrombocytopenia absent radius (TAR).

HOS is an inherited disorder characterized by upper-limb defect and cardiac anomalies. In most cases, the abnormality is either an atrial septal defect or a ventricular septal defect. The presence of a complex heart defect is rare in HOS and was recently reported by Baban et al. to include bilateral hypoplastic thumbs, brachydactyly, radioulnar synostosis, and intermediate atrioventricular canal defect (AVD) with aortic coarctation, but these findings were not associated with heterotaxy syndrome, as is reported in this index case [14].

TAR syndrome is a genetic disorder associated with absent radii and episodes of thrombocytopenia in the neonatal period [15]. Association of TAR syndrome with annular pancreas was

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

described by Karaman et al. [16]. The observed unilateral absence of radius could be considered as an atypical type of TAR syndrome, but the normal level of platelets in the index case rule out the possibility of this syndrome.

Conclusions

This case study is unique in that the association of congenital asplenia syndrome (right heterotaxy), complex congenital heart disease, annular pancreas and other extra-heterotaxic involvement as skeletal anomalies has not been reported previously. The nature of cardiac disease is the most important causal factor of survival and is well described, but can be easily missed if presented initially as asymptomatic; therefore, early prompt assessment and timely intervention are needed.

This index case supports that asplenia syndrome can be associated with other congenital anomalies, and indicates the importance of screening for extra-heterotaxic anomalies that may affect the general course of these infants' health and development.

Conflict of interest

None.

References:

1. Cohen MS, Anderson RH, Cohen MI et al: Controversies, genetics, diagnostic assessment, and outcomes relating to the heterotaxy syndrome. Cardiol Young, 2007; 17(Suppl. 2): 29–43
2. Hwang MS, Su WJ, Lin JL: Asplenia syndrome in a pair of monozygotic twins. Acta Paediatr, 2006; 95: 500–1
3. Haaning AM, Quinn ME, Ware SM: Heterotaxy-spectrum heart defects in Zic3 hypomorphic mice. Pediatr Res, 2013; 74: 494–502
4. Lin AE, Krikov S, Riehle-Colarusso T et al., National Birth Defects Prevention Study: Laterality defects in the national birth defects prevention study (1998–2007): Birth prevalence and descriptive epidemiology. Am J Med Genet A, 2014; 164A: 2581–91
5. Kim SJ: Heterotaxy syndrome. Korean Circ J, 2011; 41(5): 227–32
6. Ticho BS, Goldstein AM, Van Praagh R: Extracardiac anomalies in the heterotaxy syndromes with focus on anomalies of midline-associated structures. Am J Cardiol, 2000; 85: 729–34
7. Working Party of the British Committee for Standards in Haematology Clinical Haematology Task Force. Guidelines for the prevention and treatment of infection in patients with an absent or dysfunctional spleen. BMJ, 1996; 312: 430–34
8. Christopher GL: Ivermark syndrome. J Behav Neurosci, 2019; 2(1): 17–23
9. Freedom RM: The asplenia syndrome: A review of significant extracardiac structural abnormalities in 29 necropsied patients. J Pediatr, 1972; 81(6), 1130–33
10. Borenstein SH, Langer JC: Heterotaxia syndromes and their abdominal manifestations. Curr Opin Pediatr, 2006; 18: 294–97
11. Van Praagh S: Cardiac malpositions and the heterotaxy syndrome. In: Keany JF, Lock JE, Fyler DC (eds.), Nadas's Pediatric Cardiology. 2nd ed. Philadelphia, Saunders Elsevier, 2006; 589–608
12. Wren C, Reinhardt Z, Khawaja K: Twenty-year trends in diagnosis of life-threatening neonatal cardiovascular malformations. Arch Dis Child Fetal Neonatal Ed, 2008; 93: F33–35
13. Rubin LG, Schaffner W: Care of the asplenic patient. N Engl J Med, 2014; 371: 349–56
14. Baban A, Pitto L, Pulignani S et al: Holt-Oram syndrome with intermediate atrioventricular canal defect, and aortic coarctation: functional characterization of a *de novo* TBX5 mutation. Am J Med Genet A, 2014; 164A (6): 1419–24
15. Toriello HV: Thrombocytopenia-absent radius syndrome. Semin Thromb Hemost, 2011; 37(6): 707–12
16. Karaman I, Ozalevli S, Karaman A, Erdogan D: TAR syndrome with annular pancreas and anal atresia – a case report. Eur J Pediatr Surg, 2004; 14(2): 123–25

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]