



CASE REPORT

Ivemark Syndrome: Syndrome of Right Isomerism, a Case Report and Review of Literature

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Abstract

Right isomerism (Ivemark syndrome) is a rare disorder associated with multiple congenital malformations. It is the result of embryological anatomical disturbances, characterized by absence of spleen, malformations of the heart and abnormal arrangement of the internal organs of the chest and abdomen.

This case report describes a rare occurrence in a newborn, presented at 4 hours of age with bluish discoloration of the extremities and low oxygen saturation and diagnosed with complex cyanotic congenital heart defect with situs ambiguous, which was undetected in the antenatal period.

Keywords: Asplenia; Heterotaxy; Isomerism; Ivemark; Situs ambiguous.

Introduction

Right isomerism (Ivemark syndrome) is a very rare embryological disorder. The incidence is approximately 1:10,000 - 1: 40,000 live births with a male predominance.¹in a large series of patients with right atrial isomerism, factors associated with mortality. Background. Right atrial isomerism is associated with complex congenital heart disease and high morbidity and mortality. Method. All data from patients diagnosed with right atrial isomerism between January 1970 and March 1996 were reviewed. Results. A total of 91 consecutive patients (54 male It is characterized by a tendency towards bilateral right sidedness (trilobed) lungs with bilateral “right” atria, asplenia and situs ambiguous.²

In 1826, Martin Ivemark first observed heterotaxy syndrome consisting of splenic agenesis with congenital cardiac malformation and partial situs inversus. Then in 1955, he reported an occurrence rate of 0.1 percent of asplenia syndrome in 7,032 necropsies.

The genetic inheritance of right isomerism is poorly understood. Genetic and environmental factors play a role. Diagnosis of this syndrome is usually made in the neonatal period.³

For comparison, left isomerism has an incidence of 1: 10,000 to 1: 20,000 live births and a female predominance.³ It is characterized by a tendency towards bilateral left sidedness (bilobed) lungs with bilateral “left” atria and multiple spleens.

Case presentation

A single-term, female infant was born to parents of a non-consanguineous marriage, with maternal age of 35 years and paternal age of 43 years, by spontaneous vaginal delivery at 40+5 weeks of gestation, with a birth weight of 3.660 kg with no obvious external dysmorphic features. Antenatal period was uneventful, and the fetal anomaly scan was normal. The newborn established spontaneous respiration at birth, thus no resuscitation was needed. Within four hours the newborn was noted to have a dusky skin color with low oxygen saturation on pulse oximetry. There was no respiratory distress, or hypothermia. With the possible clinical diagnosis of cyanotic congenital heart disease, the newborn was admitted in the neonatal intensive care unit (NICU) for further evaluation.

Diagnostic Assessment

Electrocardiogram (ECG) showed regular rhythm and superior QRS axis deviation. Chest and abdomen x-ray (Figure 1) showed a midline cardiac shadow, the orogastric tube directed towards the right side and the umbilical venous catheter directed towards the left side.

X-ray findings were confirmed with abdominal ultrasound which revealed a midline liver with absent spleen, fundus of the stomach on the right side of the body cavity, agenesis of the gall bladder, a short pancreas, and juxtaposition of the inferior vena cava.

Computerized tomography (CT) scan of the chest and heart showed a single ventricle and dilated right atrium (Figure 1 A & B), trilobed left lung and multiple cardiovascular anomalies, absent gall bladder (Figure 1C), absent spleen and right sided stomach (Figure 1D).

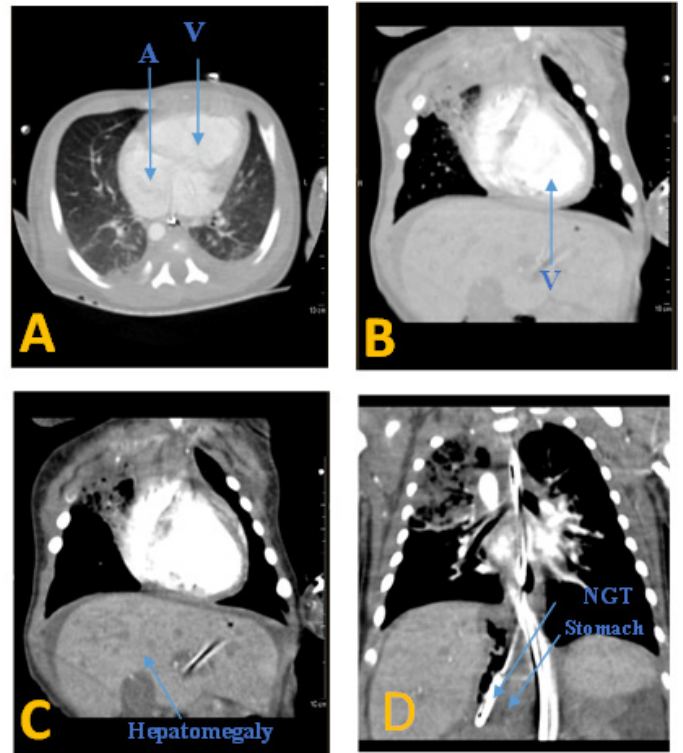


Figure 1: Computerized tomography (CT) Angiography of the chest and abdomen. (A) Axial view shows single ventricle “V” and dilated right atrium “A”. (B) Coronal view shows single ventricle. (C) Coronal view show hepatomegaly with absent gallbladder. (D) Coronal view shows right side stomach with inserted nasogastric tube.

An Echocardiography (ECHO) done showed a complex cyanotic heart disease with the following features: Univentricular heart (Right atrial isomerism/ unbalanced Atrioventricular Septal Defect (AVSD)) (Figure 2A), pulmonary valve atresia, hypoplastic pulmonary artery branches, Patent ductus arteriosus (PDA)/ Major aortopulmonary collateral arteries (MAPCA’s) (Figure 2B), large ventricular septal defect (VSD), single atrium (Figure 2C), Total anomalous pulmonary venous connection (TAPVC) to right heart side (RHS) of common atrium, AV valve regurgitation and RHS

aortic arch. ECHO also revealed a dilated right ventricle (systemic ventricle) with good systolic function and a normal aortic valve with no signs of stenosis and regurgitation.

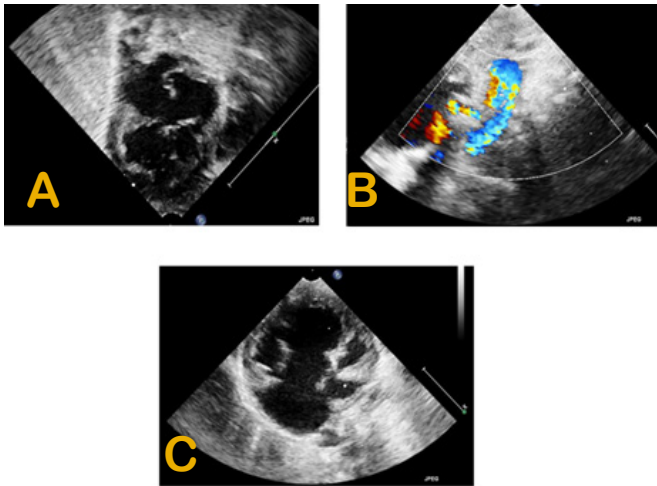


Figure 2: Echocardiography. (A) Subcostal view. Univentricular heart (Right atrial isomerism/unbalanced atrioventricular septal defect). (B) Suprasternal view Patent ductus arteriosus/Major aortopulmonary collateral arteries (MAPCA's) (Aortic pulmonary collateral). (C) Parasternal four chamber view. Single atrium. Arrows and legends

Treatment

The neonate was initiated on oxygen via nasal cannula. However, the clinical condition of the newborn rapidly deteriorated, required intubation and mechanical ventilation. Prostaglandin infusion at 0.05mcg/kg/minute was started, for the duct dependent cardiac lesion (pulmonary atresia) in order to maintain the duct patency as bridge therapy till the surgical intervention. Subsequently the newborn required inotropic support due to hemodynamic instability. Unfortunately, the neonate did not respond to the conventional therapy and succumbed on postnatal day 45.

Discussion

Situs ambiguous refers to an abnormal positioning of the internal organs in comparison to the normal. It is divided into two: right isomerism (situs ambiguous with asplenia) and left isomerism (situs ambiguous with polysplenia).

Ivemark syndrome or right isomerism is a rare syndrome. An estimated prevalence of 1/600,000 to

0.51 per million births was reported in one study.⁴

Ivemark syndrome is a sequence in which the left side of the body is identical to the right. There are several characteristic features of this syndrome. These include misplacement centrally positioned liver, intestinal malrotation that can lead to incarceration and perforation of the small bowel, and underdevelopment (hypoplasia) or absent (asplenia) spleen.⁵ There have been no specific risk factors identified; it is thought that the underlying etiology is a primary defect in lateralization, which occurs around day 28 of gestation, leading to a deviation from the normal position of viscera. A study identified a genetic correlation with Ivemark syndrome supported an autosomal recessive inheritance for a non-sense mutation or abnormal insertion in the GDF1 gene in chromosome location 19 p13.11.⁶

Infants with Ivemark syndrome often have congenital heart defects that can be diagnosed antenatally or present with cardiac symptoms at birth. They might present with cyanosis, desaturation, hypoxia, and signs of heart failure. These cardiac defects include transposition of the great vessels, atrial or ventricular septal defect and double outlet right ventricle. This case study also had similar presentations in regard to cyanosis and desaturation at 4 hours of birth and were diagnosed postnatally with complex congenital heart defects. Truncus arteriosus is a rare congenital heart disease (CHD) with an incidence of 0.03–0.056/1000 live births, comprising <1% of congenital cyanotic heart disease (truncus). The association of truncus arteriosus with a single ventricle has been reported in literature but the associations with single atrium, single ventricle, and situs inversus is rare and have been reported in very few cases.⁷

Similar to this case, most infants with right isomerism experience obstruction of the pulmonary outflow tract, pulmonary atresia, and common mixing situations of oxygenated and deoxygenated blood. Right isomerism usually presents in two-fifths of cases that share this clinical picture. Kumar et al. reported a case of Ivemark syndrome with acyanotic heart disease: AVSD with normal (RV) and (LV) outflow tract which is a rare condition.⁸

The abnormal arrangement of internal organs in right isomerism leads to malrotation of the intestine, volvulus and thus leads to a clinical picture of acute abdomen. Another characteristic feature of Ivemark syndrome other than a midline positioned liver is atresia of the bile duct which can lead to yellowish discoloration due to the accumulation of bilirubin. The syndrome can be associated with alterations of the form, size and position of the pancreas or aplasia of the pancreas. This can lead to pancreatic insufficiency and a decrease in insulin and gastric hormone secretion.⁴

Hashmi A, et al, found 62% of infants presented at birth. Among the complex cyanotic congenital heart defects, ventricular hypoplasia or single ventricle was found in 73% of infants. The overall mortality rate was reported as 69%. In their study, the independent risk factors for decreased time to death included the absence of pulmonary outflow obstruction, the presence of major AV valve anomaly and obstructed pulmonary veins.^{1,2}

Infants with Ivemark syndrome are more susceptible to fulminant septicemia due to asplenia. Waldman et al. reported a greater frequency of fulminant and fatal septicemia produced by encapsulated bacteria in patients with asplenia syndrome compared with appropriate controls; therefore, prophylactic antibiotics should be given for congenitally asplenic patients.⁹

In conclusion, Ivemark syndrome is a non-curable, rare syndrome that should always be managed by a multidisciplinary team to decrease the risk of morbidity and mortality.

Footnotes:

Competing interests

None declared.

Ethical approval

The case report was approved by the Head of Scientific Research department in King Hamad University Hospital.

Authors' Contributions

Razan drafted the initial manuscript of the case report. James J, Ahmed F, Abdulaziz A edited and wrote the final manuscript. Emad S and Neale K

supervised the aspects of the work.

Conflict of Interests

None declared.

Acknowledgments

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