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Case report: Heterotaxy syndrome with polysplenia

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Abstract Heterotaxy syndrome is a rare complex syndrome characterized by cardiac and extra cardiac congenital malformations. The syndrome is divided into two main groups; right isomerism (Ivemark syndrome, asplenia) and left isomerism (polysplenia syndrome). We report a polysplenia syndrome with agenesis of head and uncinate process of the pancreas in a 30-year-old woman who was admitted to our clinic with complaints of loin pain and dysuria.

Introduction:

Heterotaxy syndrome is a condition in which the internal organs are abnormally arranged in the chest and abdomen. The term "heterotaxy" from the Greek words "heteros" means "other than", and "taxis" means "arrangement'.[1]

Most parts of the human body are arranged symmetrically with respect to the sagittal plane. Asymmetric organs develop as midline structures and then become lateralized. The normal position of these organs is called situs solitus [Fig. 1a], while the mirror image layout is called situs inversus [Fig 1b]. Heterotaxy syndrome occurs when embryonic development is arrested to perform normal left-right asymmetry [Fig 2-4].[2-3]

Heterotaxy syndrome is a rare and complex disorder with an incidence of 1/8000- 1/25000 live births.[4] In patients with ***heterotaxy*** syndrome, the spleen is almost always affected, although the reason is not clearly understood. Three types of splenic anomalies have been described: (a) the spleen may be absent; (b) the spleen may be composed of a cluster of smaller splenules, a large spleen may be accompanied by several smaller splenules, or it may be multilobed; and (c) the spleen may be of normal size but located in the right upper quadrant of the abdomen.[5]

Two groups of abnormalities have been identified: aslenia (right isomerism)and polysplenia (left isomerism)- Table 1. Right isomerism is characterized by right lung anatomy on both sides (three-lobed lung, epiarteriel bronchial structure), absence of spleen (or polysplenia in rare cases), midline located liver, right or left sided stomach and gallbladder, adjacent position of abdominal aorta to inferior vena cava, and various frequent cardiac abnormalities [Fig. 3]. Cardiac abnormalities are common in asplenia syndrome, including transposition of great vessels, atrial or ventricular septal defects, truncus arteriosus, stenosis or atresia of pulmonary artery, abnormal venous return and atrioventricular conduction defects [Fig. 4].[4-6]

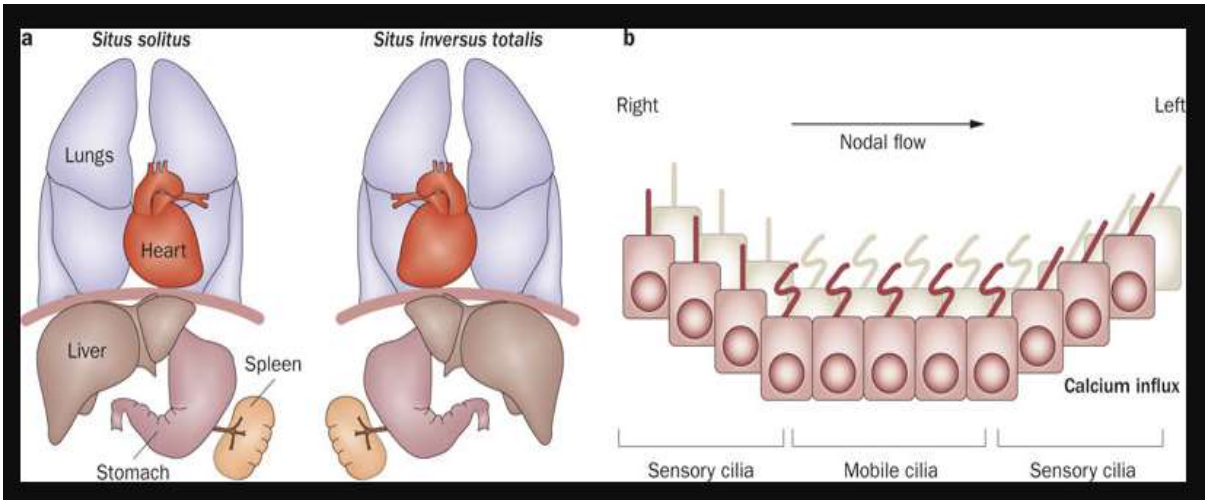


Fig.1: Schematic drawing of normal situs (situs solitus) and situs inversus totalis showing the thoracic and abdominal organs in their left (L) and right (R) positioning

Table 1. Characteristics of polyspenia and asplenia heterotaxy syndromes

Characteristic	Polysplenia (right isomerism)	Asplenia (left isomerism)
Polysplenia	Present	Absent
Asplenia	Absent	Present
Atrial appendages	2 left atrial appendages	2 right atrial appendages
Multiple cardiac defects	Present	More frequent and severe
Congenital heart block	Present	Unlikely
Pulmonary	Bilateral bilobed lungs	Biloateral trilobed lungs
Venous anomalies	Interruption of inferior vena cava with azygous vein continuation	Malposition of inferior vena cava, with inferior vena cava and aorta parallel on the same side of the spine

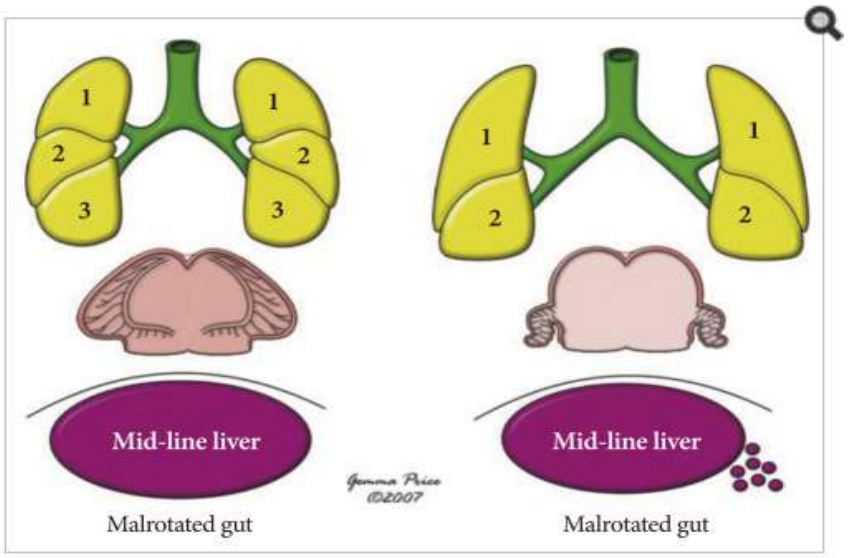


Fig. 2: Typical arrangement of organs within the body in the setting of visceral heterotaxy.

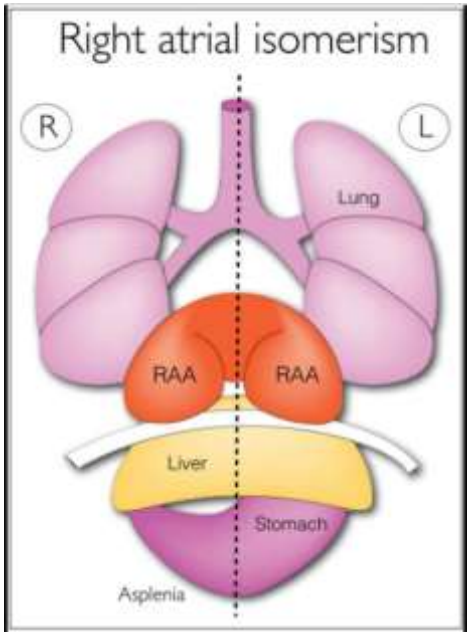


Fig.3: Schematic drawing of thoracic and abdominal organs in right atrial isomerism (asplenia) of heterotaxy syndrome

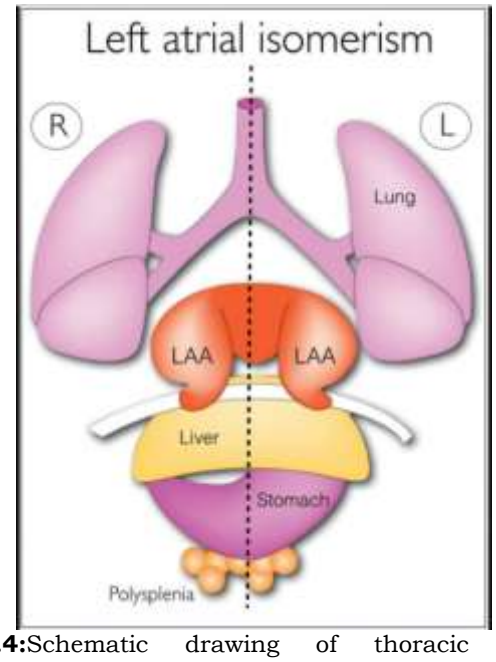


Fig.4: Schematic drawing of thoracic and abdominal organs in left atrial isomerism (polysplenia) of heterotaxy syndrome.

Case Report:

A 30-year-old female attended the medical outpatient department, at Sebha Medical Centre, with pain in the right upper quadrant of the abdomen and dyspepsia. On physical examination, she was 170 cm tall and weighted 80 kg. Apart from tenderness in the right upper quadrant of the abdomen, vital signs and other physical examination findings were normal. Results of the laboratory assessments were normal.

Abdomen ultrasound examination revealed midline liver and five spleens, and stomach in the right side, but the pancreas could not be

observed. Echocardiography findings showed normal heart (Fig. 5).
A CT scan of the abdomen revealed that the liver and gallbladder were settled midline (Fig. 6), whereas, the stomach and the sigmoid colon were on the right side of the midline, whereas the small bowel was primarily left-sided (Fig 7). Similarly, there were five dysmorphic spleens (polysplenia) at the right side of the mid-line (Fig 8). CT scan also identified a short pancreas that could not be seen on ultrasonograhy (Fig 9). The aorta and inferior vena cava were closely sited (Fig 10)

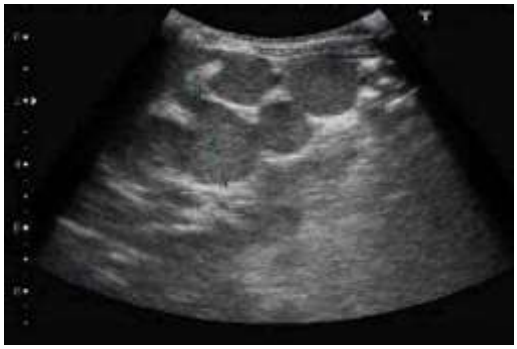


Fig. 5: Ultrasound of abdominal men.

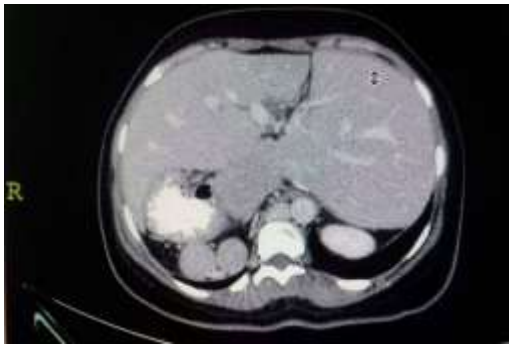


Fig 6. CT showing midline liver and gallbladder

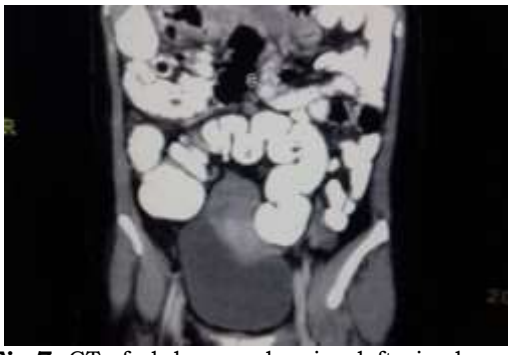


Fig 7. CT of abdomen showing left-sised caecum.

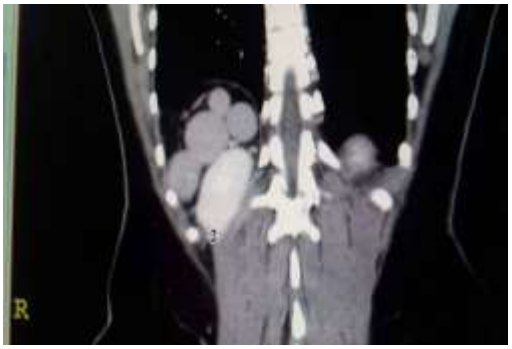


Fig 8. CT of abdomen showing multiple right-sided polysplena.

Fig 9: CT of abdomen with a short pancreas.

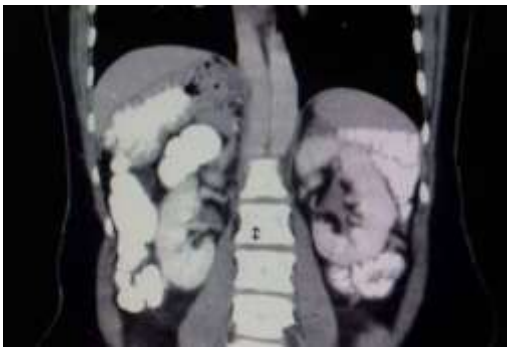
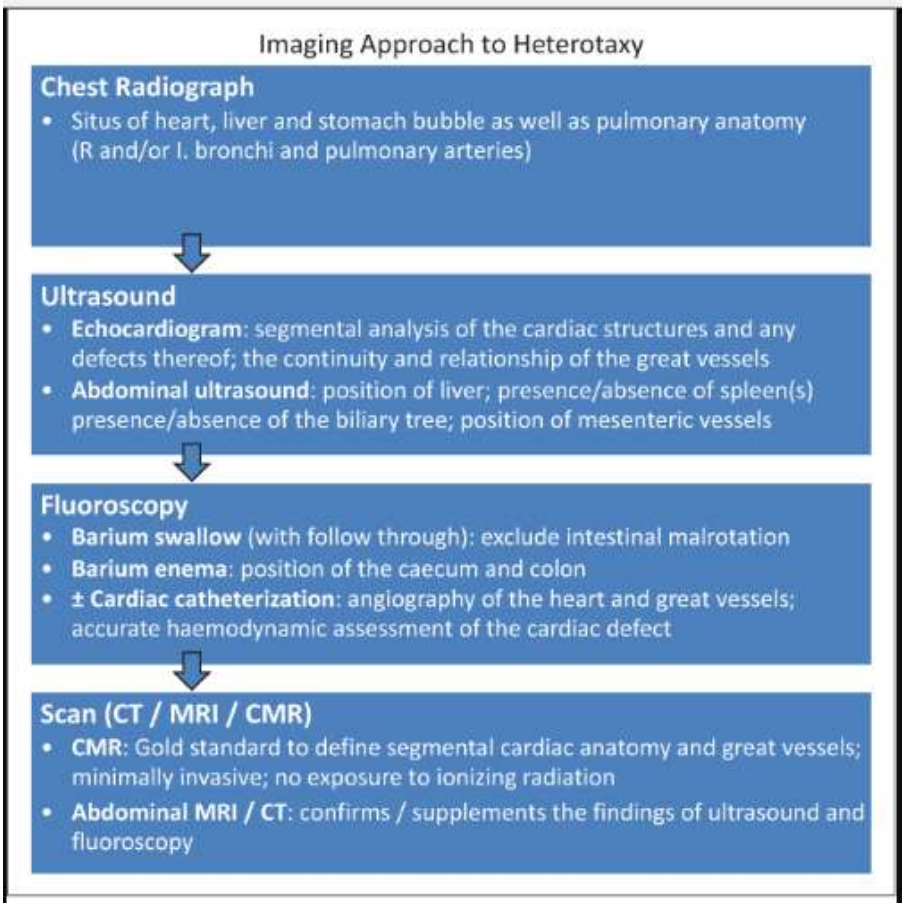


Fig. 10: CT of abdomen revealing closely sited inferior vena cava and aorta.

Table 2: Imaging approach for heterotaxy syndrome



Discussion:

Heterotaxy Syndrome is a complex syndrome that occurs when the axes of the body fail to rotate correctly when developing in the womb. This can affect many different organs of the body systems. It also means that each individual with Heterotaxy is unique.

The present case is consistent with polysplenia syndrome because of multiple dysmorphic spleen located right side of the midline, and reverse type intestinal malrotation. The patient had a midline liver and gall bladder, and right-sided stomach and mall bowel that was on the left side of the abdomen. The pancreas was short. The heart and lungs appeared to be normal.

Most patients with heterotaxy syndrome with polysplenia die at the age of 5, usually due to severe cardiac anomalies.[7] However, our patient was among the estimated 5-10%, who have normal heart or mild cardiac defects and demonstrate no symptoms and survive until adulthood..[8-10] Thus, in the minority of polysplenic patients, with no cardiac anomalies, the syndrome often goes undiagnosed until imaging is obtained for an unrelated reason in adulthood, as for our patient.[11]

In consistence with our case, heterotaxy syndrome with polysplenia is more common in females.[10]

Polysplenia results in 90% of patients to be with left atrial isomerism. Our patient had five dysmorphic spleens. Although patients have many spleens, each is usually ineffective, resulting in functional asplenia. On rare occasions, left atrial isomeric patients have a single, normal, functional spleen.

It is important to remember that although these patients may have several spleens, they spleens may not be functioning. Therefore, the condition of the spleen should be established in all patients with polysplenia syndrome. A blood test called a Howell Jolly Body test can determine whether the patient has a functioning spleen or not. If they do not, they are treated as functionally asplenic who could run a lifetime risk of overwhelming infection.[12]

The liver and gall bladder were midline in our patient, however, the biliary tree defects encountered in the majority of polysplenic patients, was not a feature. If such biliary defects continue without proper treatment, cirrhosis and liver failure become a major concern.[12]

Patients with heterotaxy may have different degrees of intestinal rotation anomalies varying from classic malrotation predisposing to volvulus to non rotation.[13] Gut malrotation are observed in 70% to 100% of cases of polysplenia syndrome.[14]

In this polysplenic patient, the stomach and the sigmoid were in the right side of the midline, whereas the small bowel was mainly on the left

side. The patient had no history of bowel obstruction. Similarly, many patients of intestinal malrotation are asymptomatic due to broader mesentery and they seek medical attention for some other reasons. However, intestinal obstruction in polysplenia syndrome may complicate malrotation with midgut volvulus, intraluminal membrane, annular pancreas, jejunal atresia and preduodenal portal vein.[15] As barium studies may not predict the patients with risk for midgut volvulus, the Ladd's procedure should perhaps be performed in all patients with malrotation.[16]

There is little reference in the literature regarding the morphology of the pancreas in patients with polysplenia.[17] Pediatric patients with polysplenia and other congenital anomalies, were reported to have a short, thick pancreas.[18] The presence of a short pancreas was mostly due to abnormal embryological development of the dorsal bud. The presence of abnormal morphology of both pancreas and spleen is due to the fact that both organs develop in the dorsal mesogastrium.[19]

The clinical significance of this finding relates to a possible relationship to early or late onset diabetes mellitus or the increased incidence of pancreatitis.[20-22] In spite of the small size of the pancreas, our patient did not demonstrate any evidence of diabetes.

Modes of inheritance proposed for heterotaxy include autosomal dominant, autosomal recessive, and X-linked recessive.
The last mode may help to explain the male preponderance of this syndrome. Overall, though, careful genetic study supports a multifactorial inheritance.[2,3,4]

The wide spectrum and variability of presentation of this syndrome is quite broad, and there is no single pathognomonic anomaly that can be cited.

There seems to be no single etiological factor responsible for the development of abnormal lateralization and isomerism. Evidence from human studies and animal models suggests causal heterogeneity. Chromosomal anomalies are only rarely associated with visceral heterotaxy Modes of inheritance proposed for heterotaxy include autosomal dominant, autosomal recessive, and X-linked recessive.
The last mode may help in part to explain the male preponderance of this syndrome. Overall, though, careful genetic study supports a multifactorial inheritance.[23-25]
The wide spectrum and variability of presentation of this syndrome is quite broad, and there is no single pathognomonic anomaly that can be cited.

Assessment of the intra-thoracic contents can be made with plain film, echocardiography, CT and MRI as well as angiography. Below the diaphragm, the abdominal contents can be imaged ultrasound, GI contrast studies, CT and MRI.[23]

Treatment of patients with isomerism should be determined by the nature and severity of the associated cardiac and extracardiac lesions. Most cardiac operations for patients with isomerism are palliative in nature, since normal anatomy is rarely achieved. Not surprisingly, then, mortality rates remain high for patients with heterotaxy syndrome. Factors that have historically been associated with increased operative risk include abnormalities of the systemic venous connection, a partial or total anomalous pulmonary venous connection, a common atrioventricular valve that is incompetent, and a morphologic right ventricle supporting the systemic circulation.[26-29]

The prognosis of patients with complex cardiac lesions and heterotaxy is poor. The 1-year mortality is >85% for patients with asplenia and >50% for patients with polysplenia.[7,30]

Conclusion:

Heterotaxy syndrome with polysplenia is a congenital syndrome that is usually diagnosed in early childhood due to the manifestations of severe cardiac anomalies, which are often part of the syndrome, although cardiac anomalies are less common and complex in polysplenia than in asplenia.
Recent advances in medicine, and in particular, improvements in cardiac surgical skills and techniques worldwide, are likely to result in improvements in survival of these patients.
If there are no cardiac anomalies, the syndrome often goes undiagnosed until imaging is obtained for an unrelated reason in adulthood. Heterotaxy syndrome with polysplenia is more common in females. Genetic studies have found that heterotaxy syndromes are likely to exhibit multifactorial inheritance. Treatment is completely dependant on the malformations (that occur to varying degrees) and the impact that they have clinically.

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