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Case Report

Polysplenia with situs inversus totalis, azygos continuation of the inferior vena cava, and duplication of the superior vena cava in a healthy adult: A case report ☆

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ABSTRACT

Polysplenia syndrome is an embryological disorder whereby the usual left-right asymmetry of thoracic and abdominal viscera fails to develop. It is a rare entity, estimated to occur at a frequency of 1 in 40,000, and is often associated with cardiac and biliary abnormalities. More than 75% of patients die before the age of 5 years, and even in the absence of cardiac anomalies, only 5%-10% of patients are expected to survive into adulthood without complications. Although polysplenia syndrome encompasses a wide range of anatomic abnormalities, there is no single pathognomonic feature. Hence, the prognosis of patients with polysplenia depends on their anatomy, thus necessitating radiology in their management. Here we present a case of a 56-year-old man with polysplenia syndrome and situs inversus totalis. This presentation is atypical because polysplenia is usually considered a form of situs ambiguus, and cases with situs inversus totalis are exceedingly rare. Also noted in our patient are variations in the great vessels, including aortic arch branches and the venae cavae which are features not typically associated with either polysplenia syndrome or situs inversus totalis. The patient is healthy and asymptomatic at baseline, with his diagnosis being made incidentally. Our case report is the first to describe this unique combination of cardiothoracic and cardiovascular anatomy. It also emphasizes the importance of radiologists in caring for patients with laterality defects. As these disorders are uncommon, more data on their anatomic variations may help provide better medical care to this patient population.

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Introduction

Laterality defects are alterations in the left-right axis of thoracoabdominal viscera [1]. Their prevalence is estimated at 1.1 per 10,000 live births [2]. As outlined in a review by Lin et al., 2014, the positioning of thoracoabdominal viscera along the left-right axis can be classified in 3 broad categories: situs solitus, which is the normal positioning of viscera; situs inversus totalis (SIT), which involves a mirror image reversal of all viscera; and situs ambiguus, also known as heterotaxy syndrome, which involves thoracoabdominal organs being positioned along the left-right axis in any way that differs from situs solitus or situs inversus totalis [2]. All 3 arrangements are considered mutually exclusive to one another. Moreover, both SIT and heterotaxy syndrome are laterality defects, but SIT does not typically impair organ function because the viscera are still in concordant positions relative to one another. As a result, SIT patients are asymptomatic and diagnosis is usually incidental [2].

In contrast, heterotaxy syndrome can be clinically concerning [3]. It involves any abnormal arrangement of thoracoabdominal viscera across the left-right axis, and therefore there are a range of clinical outcomes depending on each patient's unique anatomy. Two broad categories of heterotaxy syndrome exist: polysplenia syndrome (PS) and asplenia syndrome (AS). In PS, also known as left isomerism, both atria resemble the left atrium, both lungs are bilobed like the left, the liver is midline, and multiple splenules are present, among many other associated features [4]. In AS, or right isomerism, both atria resemble the right atrium, both lungs are trilobed like the right, the liver is midline, and no spleen is present [4].

Although heterotaxy syndrome and SIT are considered mutually exclusive laterality defects, here we present a case of a 56-year-old male patient who has cardiothoracic anatomy characterized by features of PS and SIT. We also describe additional vascular anatomic variants, including a retroesophageal origin of the left subclavian artery, duplication of the superior vena cava, and a retroaortic left renal vein, which are not typically associated with either PS or SIT.

Case presentation

Our patient is a 56-year-old male from Asia with a past medical history of venous thromboembolism and a diagnosis of SIT from decades prior. In 2013, he had an episode of unexplained right flank pain and received a CT scan of his abdomen to investigate for nephrolithiasis. No organic cause was found for the pain, however his diagnosis of SIT was brought into question since the imaging demonstrated multiple splenules in the right upper quadrant and an unusual configuration of the pancreas, both of which are associated with PS (Fig. 1). Since splenules in PS are usually in the left upper quadrant, this patient was given a combined diagnosis of SIT and PS. Despite the high prevalence of congenital heart disease in PS, a screening echocardiogram did not reveal any clinically significant abnormalities, which fits with his avid lifelong involvement in sports. Otherwise, the only significant concern in his medical history has been 2 episodes of venous thromboembolism; one deep vein thrombosis in his left arm following immobilization from a broken limb in 2011, and pulmonary emboli during an episode of COVID-19 pneumonia in 2021.

During his pneumonia episode, the patient's bloodwork was within normal limits for a COVID-19 infection, demonstrating mildly elevated AST, ALP and significantly elevated CRP and D-dimer; no other abnormalities were found. A CT pulmonary angiogram at the time confirmed a mirror arrangement of his thoracic viscera as well as several vascular anatomic variants including azygos interruption of the inferior vena cava, a retroesophageal origin of the left subclavian artery, duplication of the superior vena cava, and a retroaortic left renal vein (Fig. 2). The patient's azygos vein was also enlarged at 24 mm, which is above the 10 mm upper limit of normal [5].

The patient's physical exam findings were unremarkable, and none of his medical records discussed any significant concerns. Regarding his diagnoses of PS and SIT, he has been asymptomatic for most of his life, with both having been discovered incidentally. He continues to work a nonsedentary job in the automotive industry with minimal limitations to his daily activities. Currently, he is not receiving thrombosis prophylaxis or follow-up care with a hematologist for venous thromboembolism and has not received any surgery or pathology.

Discussion

Situs ambiguus or heterotaxy syndrome is a broad classification of laterality defects whereby the cardiovascular system and thoracoabdominal viscera attempt to develop with a bilateral left-sidedness, in the case of polysplenia syndrome (PS), or right-sidedness, as in the case of asplenia syndrome (AS). Both result in a wide range of birth defects [6]. PS occurs in approximately 1 in 40,000 live births and characteristically presents with 2 or more splenules in the left upper quadrant, instead of a single large spleen [7,8]. Another anatomic abnormality almost as commonly associated with PS is azygos interruption of the abdominal inferior vena cava in the thorax [9]. Several other anatomic features that are variably associated with PS include dextrocardia, abnormal pulmonary and portal venous return, various congenital heart diseases, bilateral bilobed lungs, midgut malrotation, dorsal pancreatic agenesis, gallbladder agenesis or atresia, and a large midline liver [6]. In some cases, patients with a single large spleen but other anatomic characteristics PS may still be classified as having the disorder [10]. Given their discordant thoracoabdominal anatomy, patients with PS are rarely asymptomatic, and 1-year mortality is greater than 50% due to severe congenital heart disease [4].

AS has a slightly higher incidence at approximately 1 in 22,000 live births [11]. Characteristically, there is no spleen, but like PS it is associated with several other anatomic abnormalities of the cardiovascular system and thoracoabdominal viscera [12]. These include complex congenital cyanotic heart disease such as total anomalous pulmonary venous return, endocardial cushion defects, transposition of the great

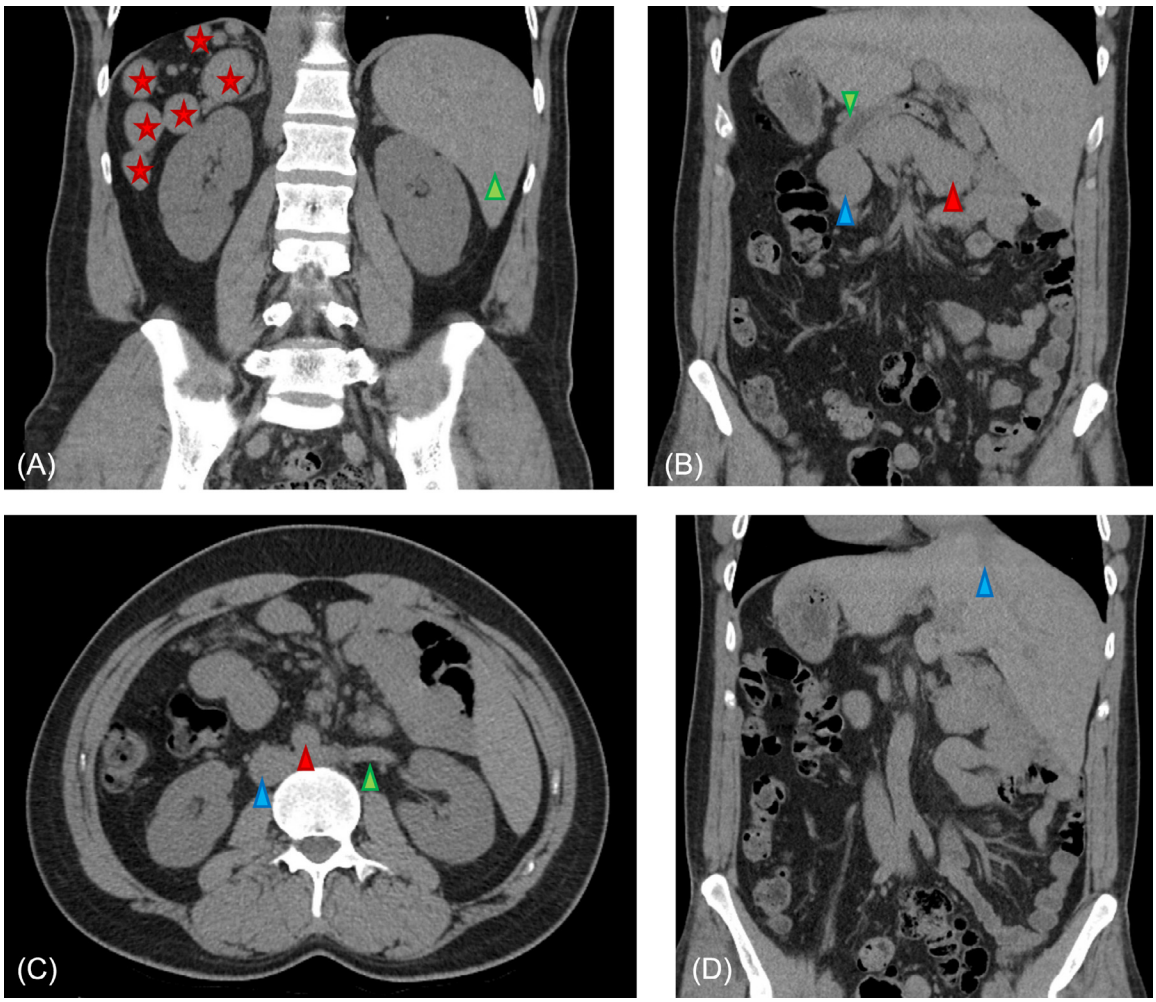

Fig. 1 – CT of the abdomen and pelvis without contrast conducted in 2013. (A) Coronal section demonstrates multiple splenules in the right upper quadrant (red stars) and a left sided liver (green arrowhead). (B) Another coronal section demonstrates a short pancreas (red arrowhead). Although the lack of contrast makes tissue differentiation poor, the pancreas seems to have an enlarged head and body but lacks a tail. The duodenum (green arrowhead) and colon (blue arrowhead) can be seen surrounding the pancreas, highlighting its borders. (C) Axial section demonstrates a retroaortic left renal vein (green arrowhead). The aorta (red arrowhead) is anterior to the inferior vena cava (blue arrowhead) and left renal vein. (D) Coronal section labels hepatic vein (blue arrowhead), which appears to be draining into the right atrium.

arteries, as well as vascular abnormalities like superior vena cava duplication and anterior positioning of the inferior vena cava relative to the abdominal aorta. Regarding thoracoabdominal viscera, AS is also associated with intestinal malrotation, bilateral trilobed lungs, bilateral right atria, and a midline liver. AS is more strongly associated with congenital heart disease than PS, with the 1-year mortality being greater than 85% [4]. Overall, HS is clinically important but poorly understood.

In contrast, situs inversus totalis (SIT) is a more commonly known and more benign laterality defect, with an incidence of approximately 1 in 10,000 [13]. This developmental defect is characterized by a total mirror-image arrangement of thoracoabdominal viscera in comparison to its usual left-right layout. SIT is mutually exclusive to either type of HS. Patients with SIT are asymptomatic since their organs are in concordant positions to one another, although they do have slightly higher rates of congenital heart disease than the general population [1]. Due to their lack of symptoms, SIT is primarily diagnosed incidentally.

Anatomic features of case patient

Our patient presented with anatomic features of both PS and SIT, which is exceedingly rare. Only 5 case reports have described a similar combination of findings [14–18]. His anatomic features in keeping with PS include multiple splenules, a shortened pancreas without a tail, azygos interruption of his inferior vena cava, and hepatic vein drainage into the right atrium. His remaining thoracoabdominal anatomy is in keeping with SIT, including dextrocardia, a bilobed left-sided lung, a trilobed right-sided lung, a left-sided liver, and a complete mirror-image reversal of his gastrointestinal tract including the splenules, which are in the right upper quadrant instead of the left. Moreover, our pa-

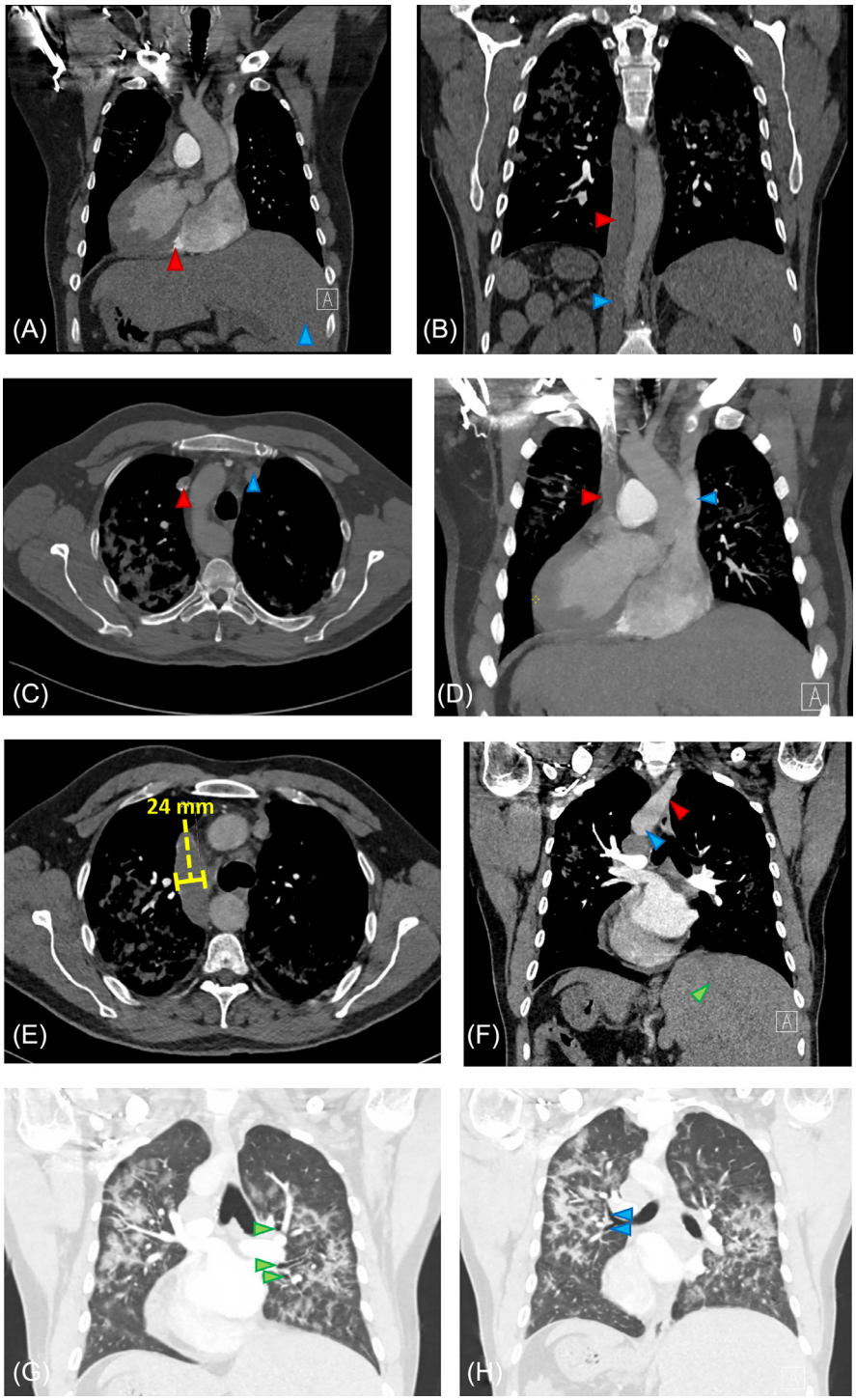

Fig. 2 – CT pulmonary angiogram conducted during episode of COVID-19 pneumonia in 2021. (A) Coronal view demonstrates dextrocardia (red arrowhead) with a left-sided liver (blue arrowhead). (B) Deeper plane on coronal view shows a right-sided inferior vena cava in the abdomen (blue arrowhead), continuous with the azygos vein in the thorax (red arrowhead). Axial (C) and coronal (D) views of thoracic cavity demonstrate duplicated superior vena cavae, with contrast-enhancement in the right branch (red arrowhead) and none in the left branch (blue arrowhead). (E) Axial view reveals an enlarged azygos vein (yellow bar) draining into the heart, measuring 24 mm in diameter, in comparison to the usual <10 mm diameter. (F) Coronal view highlights retroesophageal origin of the left subclavian artery (red arrowhead) from the aortic arch (blue arrowhead). This view also demonstrates the hepatic vein (green arrowhead), which was questioned to be draining directly into the right atrium. Lung windows of coronal section demonstrate (G) 3 secondary bronchi (green arrowheads) in the left lung and (H) 2 secondary bronchi (blue arrowhead) in the right lung. The images also demonstrate extensive ground-glass changes, in the context of COVID-19 pneumonia and sequelae of pulmonary thromboembolic disease.

tient presented with cardiovascular anatomic variations of the great vessels that are not typically associated with either PS or SIT, including a retroesophageal left subclavian artery, a duplicated superior vena cava, and a retroaortic left renal vein. These cardiovascular variants are benign and occur in the general population at frequencies of 0.4%-1.8%, 0.3%, and 3% respectively [19–21]. However, only case report described PS and SIT in the context of aortic arch branch variations [15], and the occurrence of the retroesophageal left subclavian artery and the duplicated superior vena cava has not yet been reported to occur in the context of PS and SIT.

Nonetheless, this patient's SIT and the absence of congenital heart disease discovered on his echocardiogram may explain his survival into adulthood without significant medical complications, as well as his incidental diagnosis. His medical history is only significant for venous thrombosis and right flank pain, which have both been reported in patients with laterality defects. Venous thromboembolism occurs at a higher rate in patients with laterality defects, most likely because of their cardiovascular malformations [22]. Although both episodes of our patient's venous thrombosis were provoked (his deep vein thrombosis followed immobilization from an orthopedic surgery on his left arm, and his pulmonary emboli occurred in the context of COVID-19 pneumonia), this does not rule-out the possibility of anatomic abnormalities that increased his chance of venous thrombosis. For instance, his subclavian artery and vena cavae anomalies could have respectively contributed to his upper-extremity deep vein thrombosis and pulmonary emboli, potentially through altering his blood flow pattern. Moreover, our patient may have had other vascular anatomic abnormalities that were not captured on CT, which could better explain his increased venous thromboembolism. Regarding his flank pain, it has been the presenting complaint leading to an incidental diagnosis of PS in several case reports [10,23]. Flank pain in patients with PS is suspected to occur due to intestinal ischemia [24], however given his history of venous thrombosis, there may have been underlying vascular anatomic abnormalities responsible for both presentations. However, the patient's risk of venous thrombosis was not deemed above average by his care providers, given that both episodes were provoked, and therefore he has not required prophylactic anticoagulation or follow-up with a hematologist.

Preferred imaging modalities for laterality defects

There is no single best imaging modality for laterality defects, as each type has its own advantages and disadvantages for different body systems [25]. Since heterotaxy patients often present with symptoms of congenital heart disease, the first imaging they might receive is chest radiography. Similarly, patients with abdominal pain may receive abdominal radiography during their initial workup. Radiography can identify major anatomic defects like a midline heart and liver, symmetric bronchial branching, or a right-sided stomach, but fails to provide finer anatomic characterization of cardiac chambers, the pancreas and spleen, or the intestines [25].

Other imaging modalities that should be included in patients' initial workup include echocardiography, abdominal ultrasounds, and upper GI series [26]. Echocardiography can diagnose and characterize congenital heart disease, while abdominal ultrasounds assess intra-abdominal contents. Likewise, upper GI series can rule-out malrotation of the intestines, which predisposes patients to volvulus. Patients also commonly receive contrast-enhanced CT imaging, which provides information about vascular anatomy [6,9]. This was particularly useful in our patient, who received a CT pulmonary angiogram, since it highlighted his unique vascular anatomy, including the suspected hepatic vein drainage into the right atrium. MRI is also a valuable modality especially in fetal patients, since it has no associated radiation and provides significant detail on soft-tissue anatomy [27]. Specifically, MRI helps determine prognosis in fetal patients since it can diagnose biliary atresia or intestinal malrotation, which cannot typically be detected on fetal ultrasound [27].

Conclusion

To conclude, our case report is the first to describe this unique combination of thoracic, abdominal, and cardiovascular anatomy. This report expands the literature on cases involving the cooccurrence of PS with SIT and describes new cardiovascular anatomic variations that may be associated with both. Since laterality defects are uncommon, more data on their anatomic variations may help provide better medical care to this patient population going forwards. Going forwards, further research may be needed to investigate vascular abnormalities in patients with laterality disorders.

Patient consent

Written informed consent for publication of their details was obtained from the patient.

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