

Malposition of internal organs: A case of situs ambiguous anomaly in an adult*

İç organların malpozisyonu: Erişkinde bir situs ambiguous anomalisi

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Situs ambiguous anomaly is a rarely encountered condition in clinical practice that is characterized by the presence of multiple congenital anomalies relevant to intraabdominal organs and the cardiovascular system. While this syndrome is mostly diagnosed as a serious cyanotic cardiac disease in the first year of life, only 5% may survive beyond five years of life, and it can be a diagnostic challenge. In this report, we present an adult case of situs ambiguous anomaly which was diagnosed incidentally. The patient had centrally located liver, multiple splenules, interrupted inferior vena cava with azygos continuation, and bilateral bilobed lungs. Furthermore, she had a history of an atrial septal defect operation 20 years previously. These congenital anomalies were found to be compatible with situs ambiguous anomaly (its polysplenia variant). The interesting points of this patient are that she reached an advanced age without complaint in spite of congenital heart disease, and that the diagnosis was made incidentally during routine examination.

Key words: Situs, situs ambiguous, anomaly, malposition, congenital

Situs ambiguous anomalisi, intraabdominal organlara ve kardiyovasküler sisteme ait multipl konjenital anomalilerin varlığı ile karakterize, klinikte uygulamada nadir rastlanılan bir durumdur. Bu sendrom çoğu kez yaşamın ilk 5 yılında ciddi siyanotik kalp hastalığı nedeniyle ortaya çıkmasına rağmen, vakaların %5'i daha ileri yaşlara kadar yaşayabilir ve teşhiste zorluklara neden olabilir. Bu makalede, rastlantısal olarak teşhis edilen bir situs ambiguous vakası sunuyoruz. Hastada santral olarak yerleşmiş bir karaciğer ile birlikte multipl splenüller bulunuyordu, inferior vena cavanın subhepatik kısmı kesintiye uğramıştı ve azygos veni ile devam ediyordu, her iki akciğerde de iki lob bulunuyordu. Ayrıca, hastanın 20 yıl önce atrial septal defekt operasyonu öyküsü mevcuttu. Sayılan bu anomaliler situs ambiguous anomalisinin polispleni varyantı ile uyumlu bulundu. Bu vakanın ilginç tarafı, konjenital kalp hastalığına rağmen herhangi bir şikayeti olmaksızın ileri yaşlara kadar yaşayabilmesi ve rutin muayene esnasında rastlantısal olarak tespit edilmesidir.

Anahtar Kelimeler: Situs, situs ambiguous, anomal, malpozisyon, konjenital

INTRODUCTION

Position of the viscera (heart, lungs, liver, spleen and bowels) is defined very early in embryogenesis. Normally, an asymmetry exists between the left and the right side of the human body, as the liver is on the right and the spleen on the left side. However, defects in asymmetry may occur during embryogenesis and there is a spectrum of malformations ranging from reverse asymmetry (situs inversus) to a complete lack of physiologic asymmetry (situs ambiguous) (1). Serious cyanotic

heart diseases are the most often encountered manifestations of the situs anomalies in the first year of life, and 95% of the patients die before the fifth year. The remainder of the patients are generally detected with abnormal physical or radiological findings as described below (2).

In this report, we present a case of situs ambiguous anomaly (polysplenia syndrome, bilateral left-sidedness) that was diagnosed incidentally at an advanced age.

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CASE REPORT

A 62-year-old female patient was admitted to our gastroenterohepatology department in April 2002 with complaints of fatigue and abdominal discomfort. In her past medical history, there was an operation for atrial septal defect (ASD) 20 years previously. Physical examination revealed an enlarged liver, but the other findings were unremarkable. Laboratory examination revealed elevated transaminases and HCV-RNA positivity. Chest radiography and electrocardiographic examination were normal. On plain abdominal radiography, gastric air bubble was on the right side.

Abdominal ultrasonography (US) revealed hepatomegaly with prominent left lobe and normal appearance of the spleen. The texture of the parenchyma was coarse granular pattern suggesting chronic parenchymal disease. Furthermore, paraaortic round solid homogeneous masses, initially reported as lymphadenopathies or metastatic lesions, were noted.

Abdominal computed tomography (CT) scan which was performed to delineate the masses revealed enlarged and centrally located liver with its left lobe filling the entire left hypochondrium, but interestingly the spleen was not present in its normal region. In addition, the stomach was located on the right side (Fig. 1). Thus, it was seen that the enlarged left lobe of the liver was erroneously

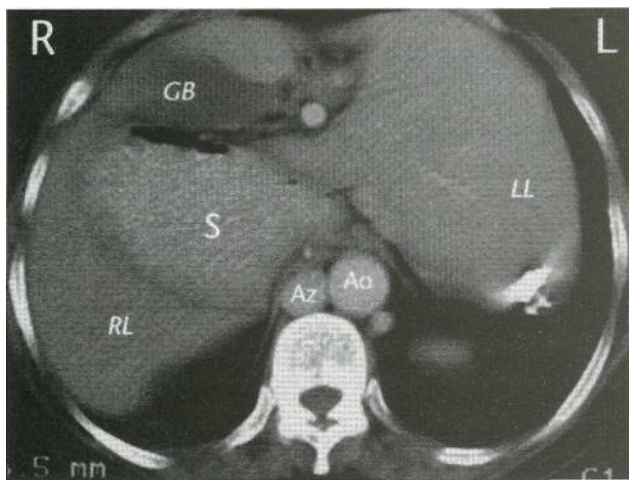


Figure 1. Contrast-enhanced computed tomography scan at the level of upper abdomen. Anomalies that were determined at this level include centrally located liver with absent spleen (RL, right lobe of the liver; LL, left lobe of the liver), right-sided stomach (S), retrocrurally located and partially dilated azygos vein (Az) right of aorta (Ao). Gallbladder (GB) was in normal position

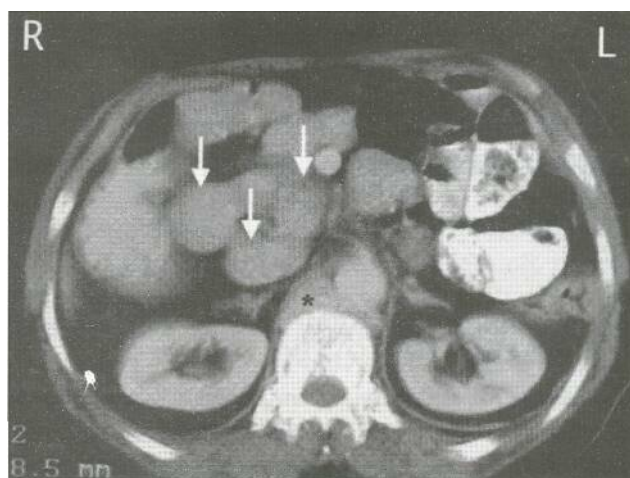


Figure 2. Contrast-enhanced computed tomography scan image at the level of kidneys demonstrates multiple round solid masses, located in paraaortic region (arrows). Tc-99m heat-denatured red blood cell selective splenic scintigraphy revealed splenules (Asteriks: azygos vein)

reported as normal spleen on US and that there was an intestinal malrotation. Furthermore, there were multiple round-to-ovoid solid paraaortic masses (Fig. 2).

In addition to these findings, interruption of inferior vena cava (IVC) and azygos/hemiazygos continuation anomaly (azygos/hemiazygos vein replaced IVC) were noted. Right renal vein drained into the IVC, whereas the left renal vein drained into the azygos vein through a retrocrural course. From here, the IVC was replaced by azygos and hemiazygos veins in the retrocrural space showing some degree of dilation. At the level of

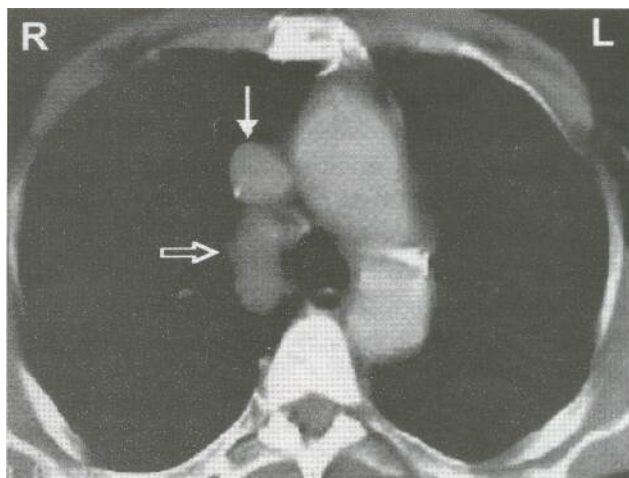


Figure 3. Contrast-enhanced computed tomography scan image at the level of the aortic arch demonstrates joining of azygos vein (open arrow) with superior vena cava (white arrow)

diaphragmatic hiatus, the hemiazygos vein crossed to the right side anterior to the aorta to join the azygos vein that drained into the superior vena cava at the level of tracheal bifurcation (Fig. 3).

Centrally located liver with absent spleen and azygos/hemiazygos continuation anomaly with interruption of intrahepatic portion of IVC are usually associated with polysplenia syndrome. Thus, the multiple paraaortic solid masses that were demonstrated on abdominal US and CT scan were thought to represent multiple splenules (polysplenia syndrome). To exclude the possibility of paraaortic lymphadenopathy or metastases and to verify the splenic nature of these masses, Tc-99m heat-denatured red blood cell selective spleen scintigraphy was performed. On this examination, multiple round hyperactive regions with the same appearance and shape of the masses seen on CT scan were determined (Fig. 4). These findings confirmed that the masses were multiple splenules (not lymphadenopathies or metastases). With these findings, the diagnosis of polysplenia syndrome (left isomerism of situs ambiguous anomaly, or bilateral left-sidedness) was made.

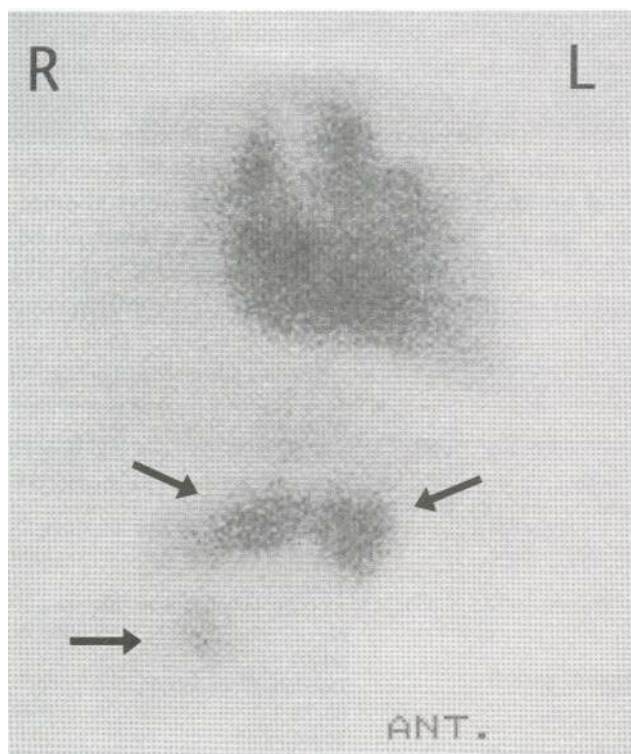


Figure 4. Tc-99m heat-denatured red blood cell selective splenic scintigraphy, anterior projection. Notice midline hyperactive round foci consistent with splenules (arrows)

Thorax CT scan and echocardiographic examination were performed to determine other anomalies related to this syndrome. It was found that the lungs had two lobes on each side representing bilateral left lung morphology. The hepatic veins drained directly into the right atrium. The patient's echocardiographic examination showed only mild pulmonary hypertension and there was no atrial abnormality. These abnormalities were compatible with polysplenia syndrome.

Because the patient's complaints were not relevant to polysplenia syndrome, and the transaminases were elevated in addition to HCV-RNA positivity, a percutaneous liver biopsy was performed and chronic hepatitis C infection was diagnosed. Combination therapy with interferon alpha and ribavirin was started.

DISCUSSION

During the third week of embryogenesis, the thickness, known as primitive streak, appears caudally to the embryonic disc. As soon as the primitive streak appears, it is possible to identify the embryo's craniocaudal axis, its dorsal and ventral surfaces and its right and left sides. The first major break in symmetry during development is seen in the fourth week when the heart tube loops to the right followed by the initial 90 degree clockwise rotation of the stomach in the fifth week (1). This determination of left-right asymmetry is non-random and highly conserved among humans (3).

The term "situs" describes position of the viscera. In situs solitus, the viscera are in their normal position (stomach and spleen are on the left, liver is on the right, the three-lobed right lung is on the right, and the two-lobed left lung is on the left). When the intraabdominal organs, lungs and heart chambers are reversed (like a mirror-image), this arrangement is termed situs inversus (the liver is on the left, the spleen and fundic air bubble are on the right). If the situs of viscera cannot be readily determined, the condition is termed situs ambiguous or situs indeterminus (4).

The incidence of situs inversus and of situs ambiguous syndromes has been estimated to occur in 1 and 0.25 per 10,000 live births, respectively (5, 6).

Situs ambiguous has two major variations: (1) asplenia syndrome (right isomerism or bilateral right-sidedness), associated with a centrally located liver, absent spleen, and two morphologic

three-lobed right lungs; and (2) polysplenia syndrome (left isomerism, or bilateral left-sidedness), associated with multiple small spleens, interruption of the intrahepatic portion of IVC, and bilateral two-lobed left lung morphology (7). There are some sub-variations between these two forms.

Situs ambiguous anomaly is a more severe disorder than situs inversus. The majority of patients with situs inversus have no significant clinical problems, with only 3-9% having cardiac abnormalities and 25% suffering from primary ciliary dyskinesia (PCD). In PCD, cilia in the respiratory epithelium are either immotile or dyskinetic. This leads to chronic respiratory infection and sinusitis. Also, as a result of immotile sperm flagella, affected males are usually infertile (8).

However, in situs ambiguous, 90-99% of the patients have severe congenital heart anomalies: atrial septal defect, ventricular septal defect, atrioventricular septal defect, pulmonary stenosis or atresia, and anomalous systemic venous or pulmonary venous return (Table 1) (7). These complex cardiac anomalies are largely responsible for the high mortality rate in these patients. Mortality rate in asplenia syndrome (79% in the first year of life) is slightly higher than in polysplenia syndrome (61% in the first year) (5). In a review of 146 polysplenia syndrome cases, 50% of the cases died by four months and only 5% survived to adolescence (9). In a recent comprehensive study, 19 adult patients with situs anomalies were investigated. In this study, eight patients had polysplenia syndrome and none of them had congenital heart disease, which in part explains their survival into adulthood (10). For these reasons, patients are generally identified in the newborn or infant period with severe cyanosis, and

survival beyond five years of age is seen in under 5% of cases. Furthermore, asplenia syndrome increases the risk of serious infections such as bacterial sepsis, which further increases the mortality rate in infancy (11). The interesting point in our patient is that she could reach such an advanced age without complaint because her cardiac abnormality, ASD, was not so severe and had been surgically corrected 20 years earlier.

The existence of a situs abnormality should be suspected if there is an abnormal finding during physical examination. For example, in patients with dextrocardia (30%-40% of patients with situs ambiguous), heart sounds and an apical impulse will be on the right rather than the left. In these patients chest radiography will show that the heart shadow is on the right, and electrocardiographic and echocardiographic findings will support the cardiac anomalies related to abnormal situs(12).

Transposition of visceral organs, though more difficult to detect on physical examination than dextrocardia, can be detected by palpating the liver on the left and the spleen on the right in situs inversus or the large transverse liver in situs ambiguous. Right-sided gastric air bubble may be a clue for the diagnosis of a situs anomaly syndrome. Further radiological investigation should be performed to delineate these abnormal physical findings. For this purpose, it is thought that abdominal CT scan is more reliable than abdominal US in determining malpositions of the internal organs and anomalies of the vessels. When intraabdominal masses, suggesting splenules, are determined, Tc-99m heat-denatured red blood cell selective spleen scintigraphy can be used for confirmation (13).

Table 1. Features of polysplenia and asplenia variants of situs ambiguous anomaly

Feature	Polysplenia	Asplenia
Spleen	Multiple	Absent
Lungs	Bilateral bilobar with hyparterial bronchi	Bilateral trilobar with eparterial bronchi
Right-sided stomach	Less common	Yes
Symmetric, centrally located liver	Yes	Yes
Partial intestinal rotation	Yes	Yes
Interrupted inferior vena cava with azygos continuation	Characteristic	No
Dextrocardia (%)	30-40	30-40
Pulmonary blood flow	Increased (usually)	Decreased (usually)
Transposition of great arteries (%)	15	60-75
Total anomalous pulmonary venous return (%)	Rare	70-80
Other common defects	Partial anomalous pulmonary venous return, ventricular septal defect	Pulmonary atresia, pulmonary stenosis
Risk of sepsis	No	Yes
Absent gallbladder; biliary atresia	Yes	No

In summary, situs ambiguous anomaly is an embryologically and anatomically well known condition. However, we presume this condition is not well known among physicians not specialized in pediatrics because it is encountered more fre-

quently in children. But, the diagnosis of situs ambiguous anomaly should be kept in mind when the aforementioned abnormal physical findings are encountered, even in patients of advanced age.

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