

# Vascular anomalies in a case of *situs inversus*

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*Situs inversus is a developmental condition in which the thoracic and abdominal organs fail to negotiate their normal migration patterns and the result is a mirror-image arrangement of these viscera. The literature provides evidence that individuals with this condition have a higher incidence of other congenital malformations (e.g. heart anomalies). Here we describe the dissection of a 71 year-old female cadaver with situs inversus, in which we discovered multiple anomalous vessels associated with the coeliac trunk directed toward the liver. In addition, we identified the inferior vena cava on the left side and a persistent supracardinal vein on the right, constituting a double inferior vena cava. Finally, we identified multiple abnormal venous channels associated with the sub-renal inferior vena cava. These vascular patterns are indeed a rare finding and have surgical implications but may indicate a higher incidence of vascular anomalies in cases of situs inversus.*

**Key words:** gross anatomy, development, inferior vena cava, supracardinal vein

## INTRODUCTION

Developing and migrating mammalian cells recognise and interpret a myriad of signalling molecules and growth factors. If the viscera are to develop in a normal fashion, these signals must be present in sufficient quantities and must be recognised and properly interpreted by the developing cells of the embryo. The mammalian body plan demonstrates many asymmetries and the signals required for “sidedness” (namely lefty, nodal, sonic hedgehog and the genes *inversus viscerum* (IV) and inversion of embryonic turning (INV) [2] begin their expression early in development, prior to gastrulation. Interestingly, it appears that on the molecular level there are left-to-right signalling discrepancies that contribute to the visceral asymmetries observed in the body cavities. When the correct gradients are not present, visceral anomalies can result. *Situs inversus* is a rare condition, occurring in roughly 1 in every 10,000

individuals, where the proper folding of the heart and rotation of the gut are reversed [20]. As a result, the asymmetries of the viscera in the body cavities are a mirror image of the normal arrangement [8]. It is not surprising that this condition has been attributed to errors in left-to-right signalling [4, 11, 13].

The condition of *situs inversus* is of clinical significance: it is important for the physician to be aware of the possibility of this condition, as more common conditions will present uncharacteristically (appendicitis, for instance, will present as pain in the left lower quadrant). Notably, it has been reported that approximately 20% of patients with *situs inversus* have Kartagener syndrome, an abnormality affecting the respiratory cilia and often accompanied by infertility [3]. *Situs inversus* also carries an elevated incidence of congenital heart disease, anomalies involving the abdominal viscera and an association with vascular anomalies [9, 10, 12, 16]. Here we report

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multiple vascular anomalies discovered during the dissection of a cadaver with *situs inversus*.

### METHODS

This report is based on the dissection and observations made of a 71 year-old female cadaver that was previously diagnosed with *situs inversus*; the cause of death was pneumonia. The cadaver was dissected by the departmental faculty using traditional methods and techniques. A complete digital photography log was kept during the dissection.

### RESULTS

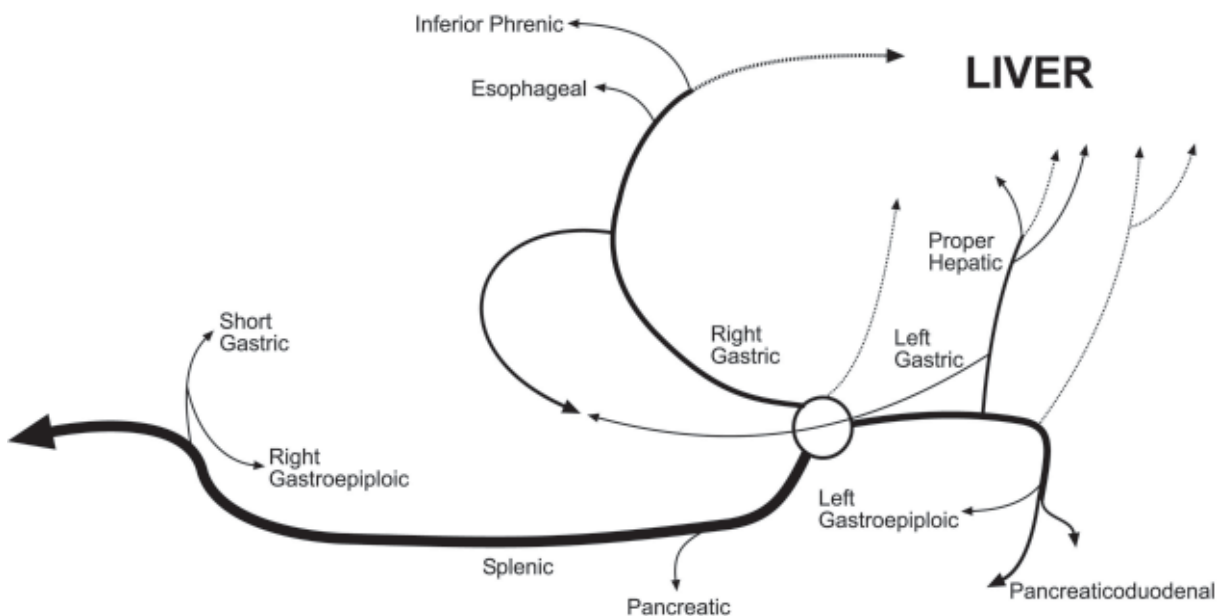
#### Arrangement of the viscera

The arrangement of the viscera in our cadaver is in general agreement with previous reports of *situs inversus*. Specifically, the apex of the heart was directed toward the right side and the "right ventricle" gave rise to the aorta. The right lung had only two lobes with a prominent cardiac notch and lingula, while the left lung had three lobes. The oesophagus was found on the right side of the thorax, where it pierced the right crus of the diaphragm at about the level of the 10<sup>th</sup> thoracic intervertebral disc. The stomach and spleen were found on the right side, while the first part of the duodenum was directed toward the left and the tail of the pancreas to the right. The liver was found on the left side and

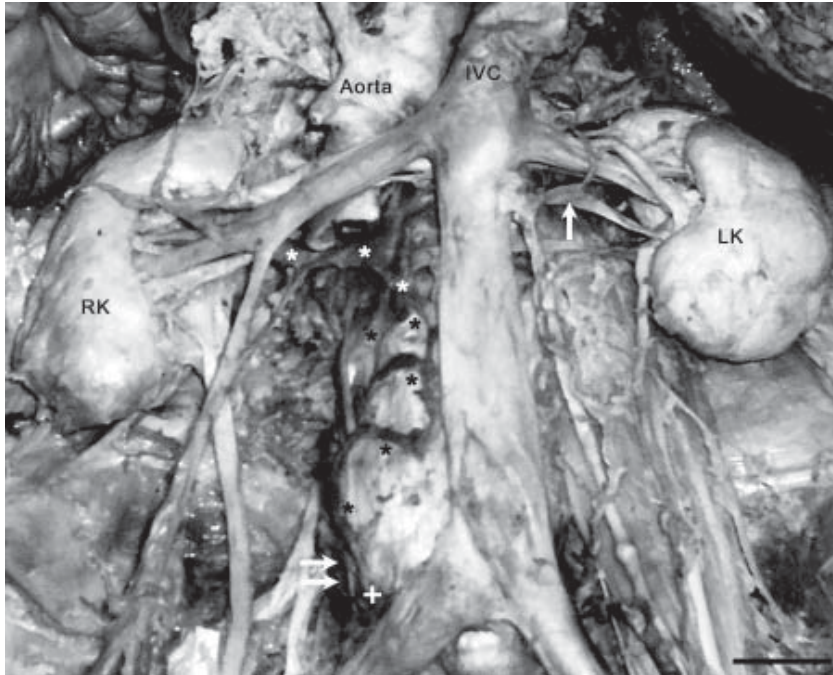
the caecum was found in the left iliac fossa; the ascending colon ascended the left side to the liver, where it turned medially to become the transverse colon. On the right, the transverse colon turned inferiorly and descended toward the right iliac fossa, where it became peritonealised and continued into the pelvis.

#### Visceral branches from the abdominal aorta

For the most part, the major arterial trunks in the abdomen, namely the coeliac, superior mesenteric and inferior mesenteric arteries, corresponded to the expected mirror-image pattern. However, we did observe anomalous branching from the coeliac trunk (Fig. 1; anomalous branches are shown with dashed lines). The coeliac trunk had three major branches that corresponded to the splenic, right gastric and common hepatic arteries. The course and branching of the splenic artery was unremarkable. Closely associated with the origin of the right gastric artery was a small accessory hepatic artery that arose from the coeliac trunk and entered the porta hepatis. The right gastric artery supplied the lesser curvature of the stomach and oesophagus and sent a branch to the diaphragm and finally gave rise to an aberrant hepatic artery that pierced the right lobe of the liver. The common hepatic artery was directed towards the left side, where it gave rise to a left gastric artery that coursed to the right along the lesser



**Figure 1.** Schematic of the coeliac trunk. In our specimen, the coeliac trunk had a branching pattern that was a mirror image of the normal pattern. However, there were numerous accessory branches to the liver (indicated by dashed lines) and a branch that served the territory of a right inferior phrenic artery.

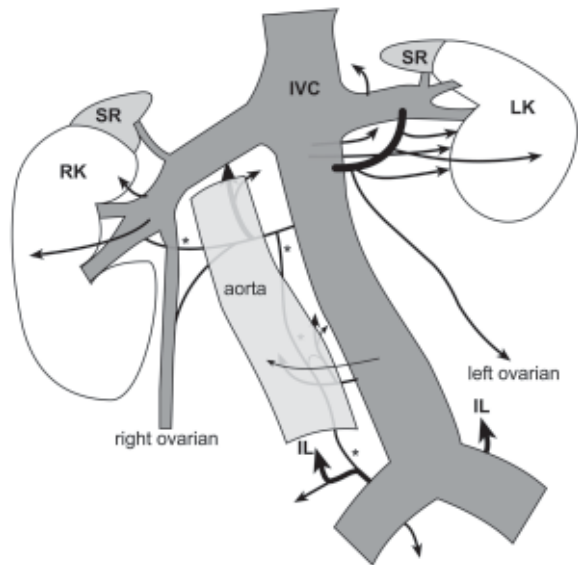


**Figure 2.** Venous anomalies associated with the inferior vena cava (IVC). The IVC was situated on the left side of the abdominal cavity and the aorta was found on the right side. Note the numerous renal vessels and the venous collar associated with the left kidney (single arrow). On the right, the iliolumbar vein arose from the common iliac vein. The origin of the common vessel is indicated by a “+” and the iliolumbar vein is indicated by the double arrows. On the right side a common vessel arose from the common iliac vein (indicated by the “+”). This vessel gave rise to an iliolumbar vein (double arrows) and a venous channel that connected the common iliac and right renal vein; the course of this vessel is indicated by asterisks. The scale bar equals 3.3 cm; RK — right kidney; LK — left kidney.

curvature of the stomach toward the oesophagus. The common hepatic artery divided, giving rise to a proper hepatic artery and a gastroduodenal artery. The proper hepatic artery divided into three branches as it approached the substance of the liver. Also arising from the common hepatic artery was another vessel, distal to the proper hepatic artery, that supplied the left lobe of the liver.

### Inferior vena cava and tributaries

In our dissection of the abdominal cavity we observed the aorta on the right side of the abdomen and the inferior vena cava (IVC) on the left side, as expected, and both vessels seemed of normal calibre. Interestingly, we noticed numerous venous anomalies associated with the drainage of the kidneys, gonads and the body wall (Fig. 2); a schematic of the venous patterns described below is shown in Figure 3. The drainage of the right kidney and suprarenal gland was unremarkable, although we noticed two smaller veins arising from the renal fascia emptying into the right renal vein. The right renal vein received the right ovarian vein, which was of a much larger calibre than the left ovarian vein. The



**Figure 3.** Schematic of the venous anomalies associated with the inferior vena cava (IVC). This figure completely documents the anomalies found in relation to IVC. The black asterisks indicate the path of the channel connecting the common iliac and the right renal vein. Note also the venous collar associated with the left renal vein; SR — suprarenal gland; RK — right kidney; LK — left kidney; IL — iliolumbar vein.

substance of the left kidney was drained by two large veins that joined to form the left renal vein. The left renal vein also received a single suprarenal vein. The substance of the left kidney was also drained by three smaller veins, two of which emptied into an abnormal venous "collar" that provided a communication between the subrenal IVC and the left renal vein. This venous collar also received a vein that drained the renal fascia on the left side and the left ovarian vein. The third of the small accessory renal veins emptied into the posterior-most aspect of IVC. The left renal vein also received a small vessel that appeared to be draining a small region of the posterior body wall. From the right common iliac vein arose an iliolumbar vein that could be traced through the substance of the psoas major muscle along the vertebral column. From this vessel arose a medially directed venous channel that ascended posterior to the aorta and communicated with at least two lumbar veins. As this channel approached the right renal vein, it divided into an ascending branch and a lateral branch. The ascending branch continued to ascend behind the aorta along the vertebral bodies and could not be traced further. The lateral branch was directed toward the right side and split into two branches, one that joined the renal vein and one that joined the right ovarian. Thus there exists in this specimen a vertical venous channel that formed a communication between the common iliac and the right renal vein (asterisks in Figures 2 and 3).

## DISCUSSION

The literature provides solid evidence that *situs inversus* is associated with multiple congenital defects [14]. Numerous visceral anomalies have been associated with this condition, namely atrial and ventricular septal defects, tetralogy of Fallot, Kartagener syndrome, duodenal atresia, biliary atresia, and gastroschisis [12, 14]. Recently, however, it has become apparent that there may be a higher incidence of vascular anomalies associated with *situs inversus* [9]. Therefore it seems worthwhile to document the appearance of vascular anomalies in cases where the organs may be malpositioned (including dextrocardia and malrotation of the gut).

The finding of multiple vascular variations in our cadaver provides further support for an association of vascular anomalies with *situs inversus*. Indeed, the disorganisation or absence of midline signals has influenced the position of the organs in these persons. Thus it appears that path-finding signals may also be awry in *situs inversus*. It is therefore worth-

while for the physician to be aware of the increased incidence of neurovascular variation in patients with *situs inversus*, especially in procedures that are normally regarded as routine (such as appendectomy).

The development of IVC is complex and includes posterior cardinal, subcardinal and supracardinal venous channels and a hepatic segment contributed by the vitelline channels. Proper formation of IVC requires a complicated pattern of fusion and regression of these venous channels so that IVC is really a composite of these channels [15]. Because of this complex developmental pattern anomalies of IVC occur, albeit rarely. One of the potential anomalies associated with development of IVC is the persistence of both supracardinal veins. Normally, on the right side of the developing embryo, the supracardinal vein contributes extensively to IVC; on the left side this channel largely regresses and contributes only to the hemiazygos vein in the thorax. If both right and left supracardinal channels persist, the result is two vertical channels in the abdomen: this is referred to in the literature as a double IVC or persistent left IVC. It is estimated that this arrangement occurs in 0.2–3% of individuals [5, 6]. In the instance of double IVC, the abnormal (left) IVC arises from the left common iliac and empties into the left renal vein. It has been noted that the duplicated IVC is typically smaller than the normal channel [17]. Additionally, it appears that there is significant variation (across cases) in the size of the two IVC [1].

The communication between the common iliac vein and right renal vein constitutes, in our opinion, the persistence of the supracardinal vein and corresponds to the persistence of a "left IVC". Typically in cases of double IVC the normal IVC is situated on the right side of the abdomen and the double vessel is found on the right. In this case of *situs inversus* the normal IVC is found on the left side and the double vessel is found on the right posterior to the aorta. In a review of the literature, it has been observed that a double IVC typically terminates by joining the left renal vein [1]. So in a case of *situs inversus* it follows that the double IVC should join the right renal vein, as it does in our specimen. To the best of our knowledge, this is the first report of a double IVC in *situs inversus*. It is worth noting that, because of the small calibre of the double IVC in our specimen and the fact that it was almost completely covered by the aorta, this channel could have easily gone unrecognised.

We present here a case of *situs inversus* accompanied by numerous venous anomalies involving

duplication of IVC and accessory renal veins. The occurrence of a double IVC has been shown to be clinically relevant. A double IVC may contribute to recurring pulmonary emboli in patients who have received an IVC filter [17]. In addition, a double IVC may be misdiagnosed as lymphadenopathy, even with modern imaging techniques [6, 7]. The ability to recognise and distinguish a double IVC from lymphadenopathy in a patient with suspected testicular or ovarian cancer is significant. Moreover, it has been noted that venous anomalies, such as those described above, may result in unexpected bleeding during surgery, especially when this involves the retroperitoneal region (as in aortic reconstruction or sympathectomy) [6, 18]. Finally, numerous visceral anomalies, particularly involving the kidney and ureter, have been associated with a double IVC [19]; we observed no such defects in our specimen.

Interestingly, duplication of IVC has been associated with anomalies of the renal veins [6]. This observation is certainly in line with our findings. However, the venous collar observed on the left side of our specimen is peculiar. Venous collars have been observed in relation to the left renal vein in patients with a normal, right-sided aorta. In these cases the renal vessels form a collar that surrounds the aorta en route to IVC. In *situs inversus* the aorta is on the right side and so the origin of a venous collar involving the left renal vein is puzzling.

## REFERENCES

1. Bass JE, Redwine MD, Kramer LA, Huynh PT, Harris JH (2000) Spectrum of congenital anomalies of the inferior vena cava: cross-sectional imaging findings. *Radiographics*, 20: 639–652.
2. Casey B, Hackett BP (2000) Left-right axis malformations in man and mouse. *Curr Op Genet Dev*, 10: 257–261
3. Cowan MJ, Gladwin MT, Shelhamer JH (2001) Disorders of ciliary motility. *Am J Med Sci*, 321: 3–10.
4. Ferrero GB, Gebbia M, Pilia G, Witte D, Peier A, Hopkin RJ, Craigen WJ, Shaffer LG, Schlessinger D, Ballabio A, Casey B (1997) A submicroscopic deletion in Xq26 associated with familial situs ambiguus. *Am J Hum Genet*, 61: 395–401.
5. Friedland GW, deVries AP, Nino-Murcia M, King BF, Leder AL, Stevens S (1992) Congenital anomalies of the inferior vena cava: embryogenesis and MR features. *Urol Radiol*, 13: 237–248.
6. Giordano JM, Trout HH (1986) Anomalies of the inferior vena cava. *J Vasc Surg*, 3: 924–928.
7. Hunter JD, Callaway MP, Wakely CJ (1998) Double and nothing. *Br J Radiol*, 71: 99–100.
8. Gruber W (1865) über das vorkommen eines Mesenterium commune für das Jejunum-Ileum und die größere Anfangshälfte des Dickdarmes bei seitlicher Transposition der Viscera aller Rumpfhöhlen. Resultate aus den bis jetzt gemachten Beobachtungen seitlicher Transposition der Viscera aller Rumpfhöhlen zugleich, oder jener der Bauch- und Beckenhöhle. *Arch Anat Physiol Wissen Med*, pp. 558–569.
9. Kamitani S, Tsutamoto Y, Hanasawa K, Tani T (2005) Laparoscopic cholecystectomy in situs inversus totalis with “inferior” cystic artery: a case report. *World J Gastroenterol*, 11: 5232–5234.
10. Kleinfeld M, Rozanski JJ, Brumlik JV, (1976) Situs inversus, subaortic and subpulmonic stenosis, ventricular septal defect and single coronary artery. *Chest*, 70: 391–393
11. Kosaki K, Casey B (1998) Genetics of human left-right axis malformations. *Semin Cell Dev Biol*, 9: 89–99.
12. Lee SE, Kim HY, Jung SE, Lee SC, Park KW, Kim WK (2006) Situs anomalies and gastrointestinal abnormalities. *J Pediatr Surg*, 41: 1237–1242.
13. Levin M, Pagan S, Roberts DJ, Cooke J, Kuehn MR, Tabin CJ (1997) Left/right patterning signals and the independent regulation of different aspects of situs in the chick embryo. *Dev Biol*, 189: 57–67.
14. Marta MJ, Falcao LM, Saavedra JA, Ravara L (2003) Um Caso de *Situs Inversus Total*. *Rev Port Cardiol*, 22: 91–104.
15. Moore KL, Persaud TVN (2003) The cardiovascular system. In: *The developing human: Clinically oriented embryology*. Saunders, Philadelphia, PA.
16. Murayama H, Maeda M, Sakurai H, Watanabe T (2006) Absent left superior vena cava with persistent right superior vena cava in viscerotransposition. *Pediatr Cardiol*, 27: 293–296.
17. Nirupama A, Pallapothu R, Holmes R, Johnson MD (2005) Inferior vena cava duplication and deep vein thrombosis: case report and review of literature. *Ann Vasc Surg*, 19: 740–743.
18. Shindo S, Kubota K, Kojima A, Iyori K, Ishimoto T, Kobayashi M, Kamiya K, Tada Yusuke (2000) Anomalies of inferior vena cava and left renal vein: risks in aortic surgery. *Ann Vasc Surg*, 14: 393–396.
19. Tore GT, Tater I, Celik HH, Oto A, Aldur MM, Denk CC (2005) Two cases of inferior vena cava duplication with their CT findings and a review of the literature. *Folia Morphol*, 64: 55–58.
20. Torgensen J (1949) Genetic factors in visceral asymmetry and in the development and pathologic changes of the lungs, heart and abdominal organs. *Arch Path (Chicago)*, 47: 566–593.