


Dysgenesis of the inferior vena cava associated with deep venous thrombosis and a partial Protein C deficiency

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ABSTRACT

Dysgenesis of the inferior vena cava is rare but it is being increasingly diagnosed by cross-sectional imaging techniques. Patients are usually asymptomatic with abnormalities detected incidentally. An 11 year old boy presented with a 10 day history of fever, vomiting and abdominal pain, which progressed to his back and lower limbs. Magnetic resonance imaging, computerised tomography and Doppler ultrasonography showed the absence of a suprarenal inferior vena cava with bilateral superficial femoral vein thrombi extending cranially to the end of the aberrant inferior vena cava. Haematological testing revealed a partial Protein C deficiency. The presenting clinical picture in this case is unique within the English literature and highlights that deep venous thrombosis associated with inferior vena cava dysgenesis may not present with typical symptoms in children. Early use of advanced imaging modalities would expedite diagnosis and subsequent treatment.

CASE REPORT

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An 11 year old boy was admitted to hospital after suffering from 10 days of generalized abdominal pain. Two days prior to his admission, he had episodes of vomiting and fever. Physical examination elicited only mild, epigastric pain. There were no signs of meningism or an upper respiratory chest infection but his inflammatory markers and serum bilirubin were raised: white cell count $20.4 \times 10^9/L$ ($3.5-12 \times 10^9/L$), C-reactive protein 253 mg/L (0-7 mg/L), bilirubin 29 $\mu\text{mol/L}$ (3-15 $\mu\text{mol/L}$). An initial, limited ultrasound scan of the biliary system was normal.

From the fourth day of admission, the patient's abdominal pain worsened and he developed non-localised back pain and bilateral leg oedema. He also developed pain in the medial aspects of both thighs with reduced power, diminished lower limb reflexes and an altered gait. Plain radiographs of the pelvis and lumbar spine were unremarkable. Clinical suspicion of a psoas abscess and a possible Tuberculosis paraspinous

collection directed further investigation to a magnetic resonance (MR) image, which was performed on day 13 of his admission. The MR scan showed no collection but did reveal abnormal abdominal venous anatomy. The inferior vena cava (IVC) appeared normal up to the level of the L3 vertebral body, at which point it crossed the midline posterior to the aorta to the region of the left renal vein where it appeared to stop (Figures 1A and 1B). The IVC seemed dilated and the endovascular signal intensity suggested sluggish venous flow and possible thrombus formation. A computerised tomography (CT) scan was performed to clarify the venous anatomy and endovascular characteristics. The non-enhanced CT scan images showed hyperdensity (55 HU) within the proximal abnormal IVC, further suggesting venous thrombus (Figure 2). The intravenous contrast enhanced CT showed that once the IVC had crossed to the left side it narrowed (possibly due to an intravenous web) and then continued cranially. At the level of the IVC narrowing, there was a retroaortic bridge which anastomosed with the right renal vein (Figure 3A). The portion of the IVC remaining on the left side was joined by the left

renal vein then connected with vertebral venous plexus (Figure 3B) shortly before abruptly stopping. The right hand portion of the aberrant IVC also anastomosed with the vertebral venous plexus (Figure 3B). The prominent vertebral venous plexus became the azygos and hemiazygos veins, and these veins were also dilated (Figure 4). Additionally, the inferior mesenteric vein was seen to be abnormally dilated (Figure 5). The right adrenal vein could be seen to anastomose with the hepatic vein to form a small, developed IVC segment, which then drained into the right atrium. Figure 6 shows a schematic of the altered abdominal vessel anatomy in this case.

Duplex Doppler ultrasonography confirmed the presence of a deep venous thrombus (DVT) from both superficial femoral veins extending cranially to the end of the aberrant IVC. Furthermore, haematological studies showed the patient to have a partial protein C deficiency at 64.6 U/dl (72-123 U/dl).

The patient was treated with compression stockings, low-molecular weight heparin and then oral warfarin therapy. When his international normalized ratio was in the therapeutic range he was discharged after spending a total of 18 days in hospital.

DISCUSSION

Dysgenesis of the IVC in the general population has a prevalence of approximately 1% [1]. Young patients who have interruption of their IVC have a 5% chance of DVT of their iliac veins [2]. However, many patients remain asymptomatic and the diagnosis is an incidental finding [3]. Currently, CT and MR are the main diagnostic modalities, however, venography is the best imaging method but is invasive.

Huntington and McClure have theorised that there are potentially 14 different IVC anatomical abnormalities [4]. The most common variations are a left or double IVC and Bass et al. and Malaki et al. present good radiological examples for nine of the different variations (Table 1) [5, 6]. As well as dysgenesis of the IVC, complete agenesis is also possible [7, 8]. The cause of IVC dysgenesis is uncertain but is thought to be either due to embryonic dysontogenesis or thrombosis during intrauterine or perinatal life [2, 9].

The IVC is established through the growth, fusion and degeneration of three sets of paired embryonic veins: posterior cardinal, subcardinal and supracardinal [10]. The posterior cardinal veins develop first but from week six to eight these veins are gradually replaced by the subcardinal and supracardinal veins. The right and left subcardinal veins form an anastomosis at the level of the kidneys and later develop in to the left renal vein, the adrenal veins and the gonadal veins. The right-hand-side subcardinal vein forms the suprarenal IVC. The supracardinal veins develop last and connect with the subcardinal vein anastomosis. The two supracardinal veins subsequently form the azygos and hemiazygos veins with the right-hand-side supracardinal vein forming the infrarenal IVC. As each embryological vein forms different sections of the

adult IVC, anomalies may arise from any of the transformations that take place. In this case, the infrarenal IVC developed normally but the suprarenal IVC did not develop correctly. The resulting increased venous pressure within the embryonic renal-level venous anastomosis maintained the connection between the infrarenal IVC and the developing azygos system. Additionally, due to the aberrant IVC and resultant increased venous pressure, the inferior mesenteric vein was dilated and acted as a collateral vessel for the venous drainage of the lower limbs. There was no evidence to suggest a retrocaval passage of the ureters.

Many studies have identified an anomalous IVC as a potential risk factor for DVT, where an increase in the venous pressure is caused by an inadequate venous return via the collateral circulation [2, 9]. The presence of pro-coagulation abnormalities, such as the partial protein C deficiency in this case, have been identified as risk factors for DVT when found in isolation or in combination with IVC dysgenesis, however, most presentations of IVC dysgenesis reveal no clotting abnormality [11]. Patients are initially treated with low-molecular weight heparin and subsequently with oral anticoagulation. Treatment is recommended for six months but in the presence of other risk factors, lifelong anticoagulation should be considered due to the higher risk for thrombotic recurrence [12]. There are invasive therapeutic treatment options available but they are limited. Within the literature, there is an isolated case of using angioplasty to clear a membranous obstruction within the IVC [13] and two cases of open surgery using prosthetics to reconstruct the venous system [8, 14]. The patients in all three of these cases were affected by chronic venous hypertension.

TEACHING POINT

Initial diagnosis of IVC dysgenesis can be difficult due to the lack of specific symptoms and signs, but MR and CT imaging can be used to clearly diagnose the pathology and may avoid prolonged hospital admissions. Clinicians should remember that when deep venous thrombosis is encountered in young patients, developmental anomalies of inferior vena cava should be considered.

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FIGURES

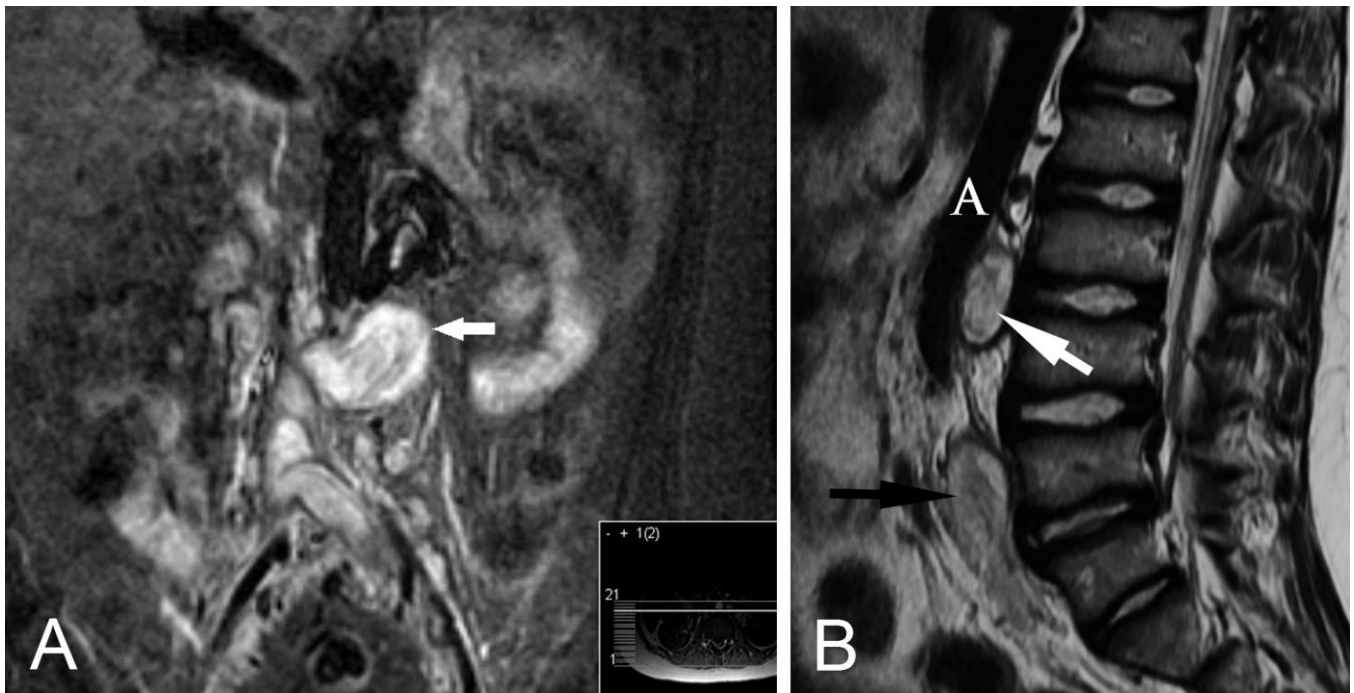


Figure 1: 11 year old male with dysgenesis of the inferior vena cava.

A: Coronal abdominal MR image showing the course of the aberrant inferior vena cava as it crosses the midline from the right to left side (arrow) and then stops. (Protocol: Magnet: 3 Tesla, sequence: Short T1 Inversion Recovery (STIR), slice thickness: 4 mm)

B: Sagittal lumbar spine MR image of showing the point of confluence of the common iliac veins to form the IVC (black arrow) and the subsequent course of the aberrant inferior vena cava as it crosses the midline from the right to left side (white arrow) posterior to the aorta ("A"). (Protocol: Magnet: 3 Tesla, sequence: T2, non-enhanced, slice thickness: 4 mm)

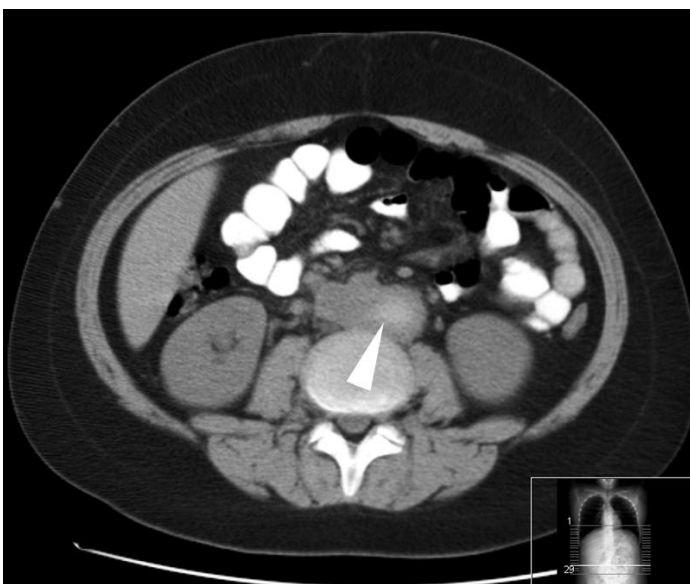


Figure 2 (left): 11 year old male with dysgenesis of the inferior vena cava. Axial abdominal CT image enhanced with oral contrast showing the right to left course of the inferior vena cava with an area of increased density (55 HU) within the aberrant section, suggesting thrombus (white arrow head). (Protocol: 353 mAs, 120 kV, slice thickness: 7.5 mm, contrast material: Gastrografin®, 400 ml volume)

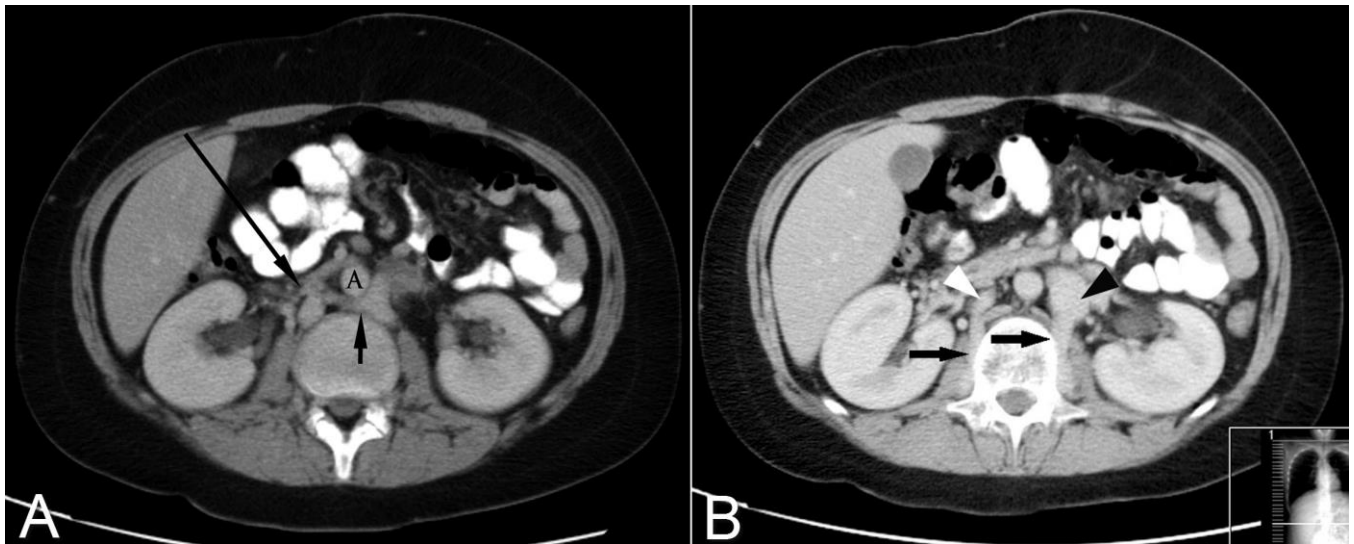


Figure 3: 11 year old male with dysgenesis of the inferior vena cava.

A: Axial abdominal CT image with oral and intravenous contrast enhancement showing the narrowing of the aberrant IVC and the venous bridge as it crosses the midline (small arrow) posterior to the aorta ("A"). The aberrant IVC on the right side joins with the right renal vein (large arrow). (Protocol: 353 mAs, 120 kV, phase: delayed venous, slice thickness: 7.5 mm, contrast material: Gastrografin®, 400 ml volume and Omnipaque™, 300 mgI/ml, 60 ml volume)

B: Axial abdominal CT image with oral and intravenous contrast enhancement showing the continuation of the aberrant IVC on the right (white arrow head) and left (black arrow head) after it has been joined by the renal veins. Both sides of the aberrant IVC then form dilated vertebral collateral veins (black arrows), which later connect with the azygos venous system. (Protocol: 353 mAs, 120 kV, phase: delayed venous, slice thickness: 7.5 mm, contrast material: Gastrografin®, 400 ml volume and Omnipaque™, 300 mgI/ml, 60 ml volume)

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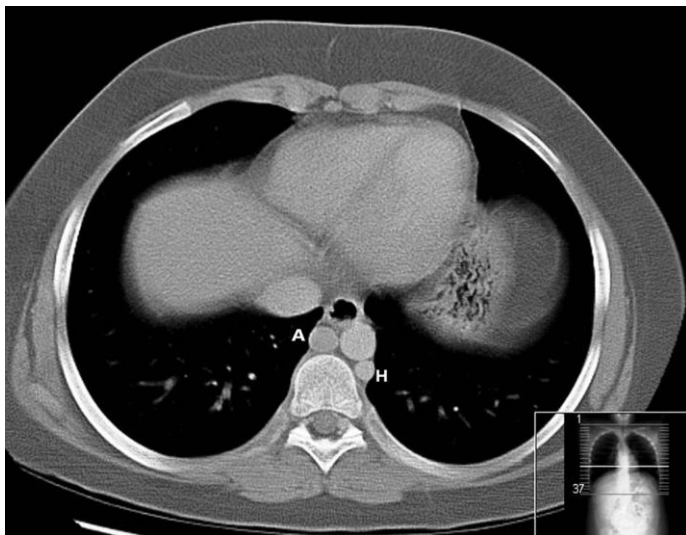


Figure 4: 11 year old male with dysgenesis of the inferior vena cava. Axial chest CT image with oral and intravenous contrast enhancement showing the dilated azygos ("A") and hemiazygos ("H") veins prior to their insertion in to the superior vena cava. (Protocol: 353 mAs, 120 kV, phase: delayed venous, slice thickness: 7.5 mm, contrast material: Gastrografin®, 400 ml volume and Omnipaque™, 300 mgI/ml, 60 ml volume)

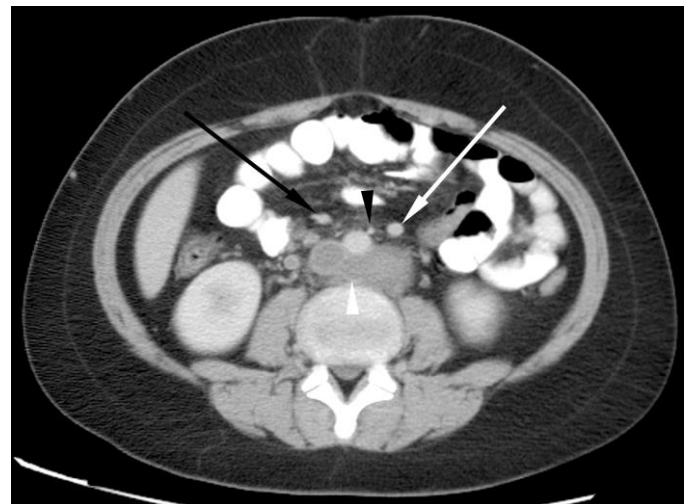


Figure 5: 11 year old male with dysgenesis of the inferior vena cava. Axial abdominal CT image with oral and intravenous contrast enhancement showing the dilated inferior mesenteric vein (large white arrow). The figure also shows the retroaortic path of the aberrant IVC (white arrow head) as well as the superior mesenteric artery as it leaves the aorta (black arrow head) and the superior mesenteric vein (large black arrow). (Protocol: 353 mAs, 120 kV, phase: delayed venous, slice thickness: 7.5 mm, contrast material: Gastrografin®, 400 ml volume and Omnipaque™, 300 mgI/ml, 60 ml volume)

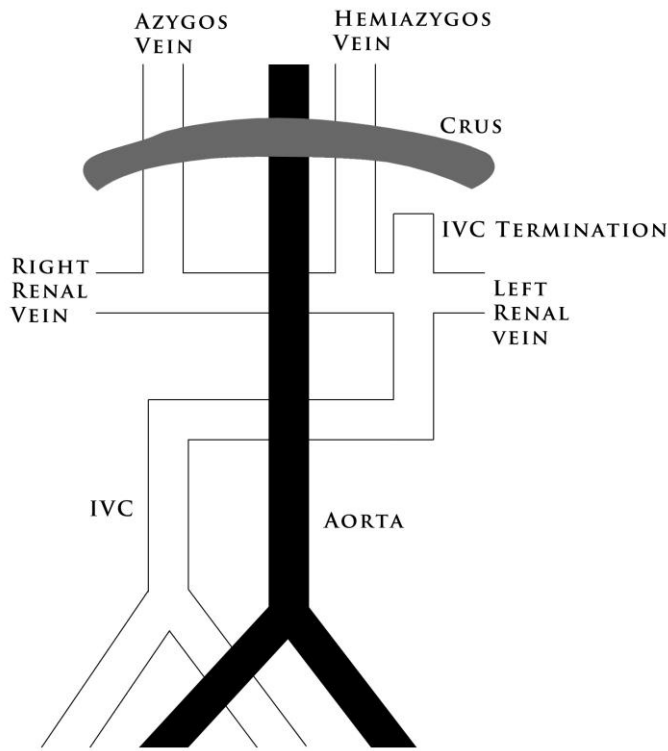


Figure 6 (left): 11 year old male with dysgenesis of the inferior vena cava. Schematic diagram showing the abnormal vessel anatomy of the patient in this case.

Anatomical variations of the Inferior Vena Cava (IVC) and Renal Veins	Known Prevalence
Double IVC	0.2% - 3% [15]
Azygos continuation of the IVC	0.6% [16]
Left IVC	0.2% - 0.5% [15]
Double IVC with retroaortic right renal vein and hemiazygos continuation of the IVC	
Double IVC with retroaortic left renal vein and azygos continuation of the IVC	
Right IVC with azygos and hemiazygos continuation (this case)	
Absent infrarenal IVC with preservation of the suprarenal segment	
Circumaortic left renal vein	8.7% [15]
Retroaortic left renal vein	2.1% [15]

Table 1: Table summarising the more common anatomical variations of the Inferior Vena Cava and the renal veins, with the prevalence of the variation included when known.

Etiology	<ol style="list-style-type: none"> Embryonic dysontogenesis Venous thrombosis during intrauterine life
Incidence	5% chance of developing a DVT in young patients who have dysgenesis of their IVC. General population prevalence of approximately 1%.
Gender Ratio	No specific gender ratio
Age Predilection	Dysgenesis of the IVC is present from birth
Risk Factors	Some childhood risk factors for developing a DVT include: <ol style="list-style-type: none"> Congenital heart or vascular malformations Hypercoagulable states, e.g. Protein C or S deficiency and Factor V Leiden Infective or inflammatory states Malignancy
Treatment	Acute: Compression stockings and low-molecular-weight Heparin Long-term: Oral anticoagulation for 6 months or for life if another risk factor for DVT is present
Prognosis	Recurrent DVT is a risk and patients should avoid preventable risk factors e.g. prolonged immobilization and the oral contraceptive pill. The long-term prognosis of patients with IVC dysgenesis and DVT is not currently known.
Findings on Imaging	<ul style="list-style-type: none"> Plain radiograph of pelvis and lumbar spine: No abnormality detected. Biliary system Ultrasonography: No abnormality detected. Magnetic Resonance: Anomalous path of IVC from right to left, posterior to the aorta. Computed Tomography: Anomalous path of the IVC from right to left, posterior to the aorta. Dilated inferior mesenteric vein. No flow within the IVC. The renal veins joined the aberrant IVC to form large vertebral collateral veins. The collaterals then anastomosed with the azygos and hemiazygos veins, which had become dilated as a result of the increased blood flow. Doppler Ultrasonography: A DVT within both superficial femoral veins, ascending all the way to the end of the aberrant IVC.

Table 2: A summary of clinical information, which is relevant to dysgenesis of the inferior vena cava and also the imaging findings of this particular case.

	Clinical	US	CT	MRI
Appendicitis	Fever, nausea, right lower quadrant abdominal pain	Periappendiceal fluid, noncompressible tubular structure, often unable to visualise normal appendix	Oral or rectal contrast enhanced studies have a sensitivity and specificity of over 98%	Valuable tool for investigating pregnant women with acute appendicitis. Normal and inflamed appendices identified as well as other abdominal pathologies in pregnant women
Mesenteric Adenitis	Fever, nausea, right lower quadrant abdominal pain	Nodes more rounded and hypoechoic than normal. Nodal hyperemia, intestinal hyperperistalsis, mesenteric thickening	Enlarged nodes with or without associated ileal or ileocecal wall thickening. Short axis diameter of at least 5 mm.	Similar findings to CT but MR has no better diagnostic accuracy than CT and has no investigative role for this pathology
Psoas Abscess	Fever, nausea, non-localised abdominal/back pain, limb, knee flexed, hip externally rotated	Fluid filled mass within the muscle, diagnostic in 60% of cases	Focal hypodense lesion, infiltration of surrounding fat, and gas or an air fluid level within the muscle. Supersedes ultrasonography as diagnostic accuracy is 80-100%.	Improved definition of soft tissues and adjacent structures, especially visualization of the vertebral bodies.
Cholecystitis	Upper abdominal pain, peritoneal irritation, referred pain to right shoulder, pain can be colicky in nature, nausea	Pericholecystic fluid, wall thickening >4mm, sonographic Murphy's sign, gall stones >2mm	Pericholecystic fluid, wall thickening >4mm, subserosal edema, intramural gas. Sensitivity and specificity >95%.	Same findings and accuracy as CT. Both modalities lack any therapeutic potential.
IVC dysgenesis and bilateral DVT	Generalized abdominal pain with vomiting and fever	A DVT within both superficial femoral veins, ascending all the way to the end of the aberrant IVC	Anomalous path of the IVC from right to left, posterior to the aorta. Dilated inferior mesenteric vein. No flow within the IVC. The renal veins join the aberrant IVC to form large vertebral collateral veins. The collaterals then anastomose with the azygos and hemiazygos veins, which become dilated as a result of the increased blood flow.	Anomalous path of IVC from right to left, posterior to the aorta.

Table 3: Differential diagnosis for the presentation of Inferior Vena Cava (IVC) dysgenesis and bilateral deep venous thrombosis (DVT).

ABBREVIATIONS

CT: computed tomography
DVT: deep venous thrombus
IVC: inferior vena cava
MR: magnetic resonance
STIR: short T1 Inversion Recovery

KEYWORDS

Dysgenesis; Inferior vena cava; Deep venous thrombosis; Protein C

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