Case Report

Anomalous development of the inferior vena cava: Case reports of agenesis and hypoplasia

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ABSTRACT

We reported the cases of two adult male patients who were admitted to our emergency room with abdominal pain and dyspnea caused by gallstones and pulmonary embolism respectively. During the radiological investigations, as collateral findings, we found two anomalous development of the inferior vena cava. These conditions affect about 4% of population and, although asymptomatic or mildly symptomatic, are associated with thrombotic manifestations as deep vein thrombosis and pulmonary embolism. The prompt recognition of these anomalies is necessary in order to prevent the complications associated with these conditions and to set the best therapy for patients.

1. Introduction

Anomalous embryologic development of the inferior vena cava (IVC) is a rare congenital abnormality that affects approximately 4% [1] of the population [2]. IVC agenesis is one of the less prevalent variants, with an approximate incidence from 0.005% to 1% [3].

These malformations can be unique or can be associated with other abnormalities such as situs inversus, dextrocardia, or polysplenia and asplenia [4].

Thrombotic manifestations such as deep vein thrombosis or pulmonary embolism (PE) are the most common clinical occurrence in these patients but usually this condition is completely asymptomatic.

We report a series of two cases of anomalous development of IVC in a patient with PE and in an asymptomatic patient.

2. Cases presentation

2.1. Patient #1

An abdominal magnetic resonance imaging (MRI) examination was performed to assess the diameter of the primary
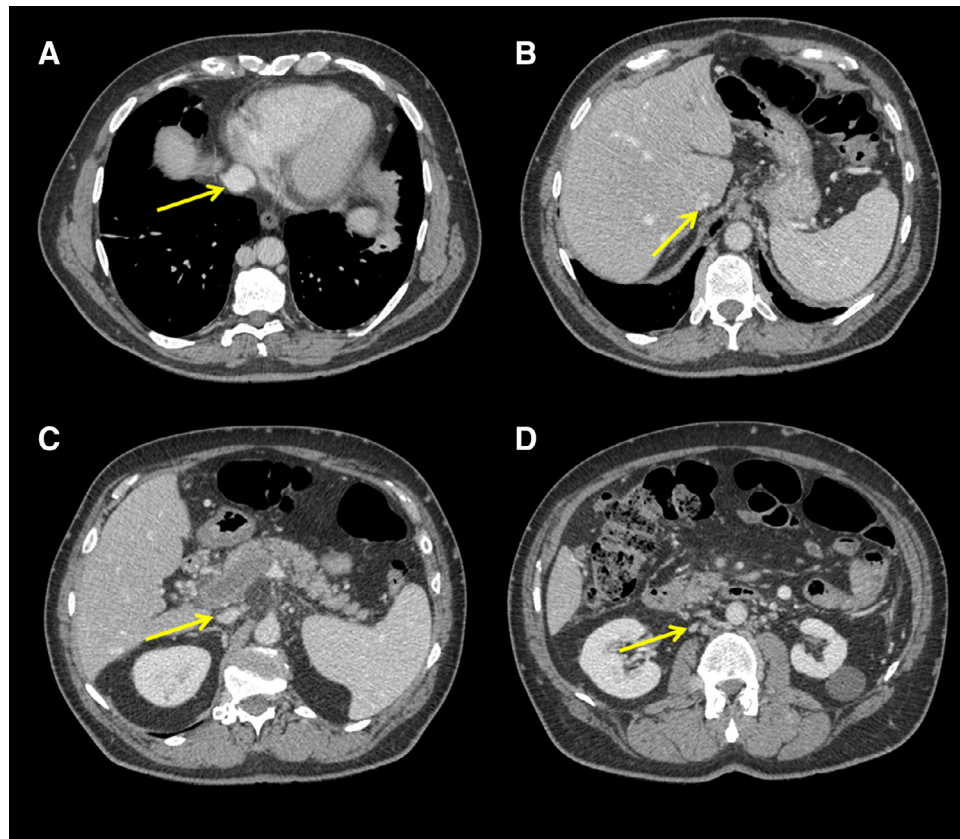

Fig. 1 – – Computed tomography, portal phase, axial sections; (A) regular aspect of suprahepatic inferior vena cava (IVC) (yellow arrow); (B) intrahepatic IVC (yellow arrow); (C) reduction caliber of infrahepatic IVC (yellow arrow); (D) hypoplasic aspect of infrarenal IVC (yellow arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

biliary duct. MRI was performed by an MR scan operating at 1.5 T (Intera 1.5 T; Philips Healthcare, Best, The Netherlands) with four channels phased array coil. The imaging protocol included a T2-weighted axial (with breath-hold, repetition time [TR] shortest, echo time [TE] 80 ms, slice thickness 7 mm, slice gap 1 mm), T2-weighted axial spectral presaturation with inversion recovery (TR shortest, TE 80 ms, slice thickness 7 mm, slice gap 1 mm), T1-weighted axial (TR shortest, TE 4.6 ms, slice thickness 8 mm, slice gap 1 mm), DUAL (spoiled gradient echo, within and out-phase echoes time; out of phase: TR shortest, TE 2.3 ms, slice thickness 5 mm, slice gap 1 mm; in-phase: TR shortest, TE 4.6 ms, slice thickness 5 mm, slice gap 1 mm), T2-balance on coronal plane (TR shortest, TE shortest, slice thickness 7 mm, slice gap 1 mm), T1-high resolution isotropic volume excitation (TR shortest, TE shortest, slice thickness 2 mm at 0 in, 30 in, 90 in, and 150 in after administration of contrast medium intravenous (Gadobenato dimeglumina 0.5 M; volume: 15 mL; flow rate: 2.5 mL/s). The examination was completed by a T1 post Gadolinium Contrast (Gd) (TR shortest, TE 4.6 ms, slice thickness 8 mm).

The examination confirmed the gallstone disease, showing a normal diameter of the primary biliary duct and, additional finding, IVC agenesis with dilated paravertebral vein system (Fig. 1).

In order to assess the structure and the diameter of the abdominal venous vessels a contrast-enhanced CT examination was performed by a 64-slice CT scanner (Lightspeed; General Electric Healthcare, Waukesha, WI). The protocol included a noncontrast CT scan, with 5 mm of thickness, and dynamic acquisition at 35 and 90 seconds after administration of iodine contrast medium (Iobitridol; volume: 120 mL; flow rate: 2.5 mL/s), slice thickness: 2.5 mm.

In addition to IVC agenesis and dilation of paravertebral vein system, CT showed deep venous ectasia and specifically of azygos and hemiazygos veins (Fig. 2), renal veins (Fig. 3), external iliac veins, pudendal veins, obturator veins, testicular veins, gluteal veins, and lumbar ascending veins (Fig. 4), caused by blood flow redistribution (Fig. 5).

2.2. Patient #2

A 65-year-old male was admitted to the Emergency Department for upper quadrants abdominal pain and dyspnea. Pulmonary embolism was suspected and a contrast-enhanced chest CT was performed.

At the moment of the CT examination blood laboratory tests showed: Creatinine: 0.9 mg/dL (normal value (nv): 0.7-1.3 mg/mL); Fibrinogen: 632.00 mg/dL (nv: 200-400 mg/dL), D-
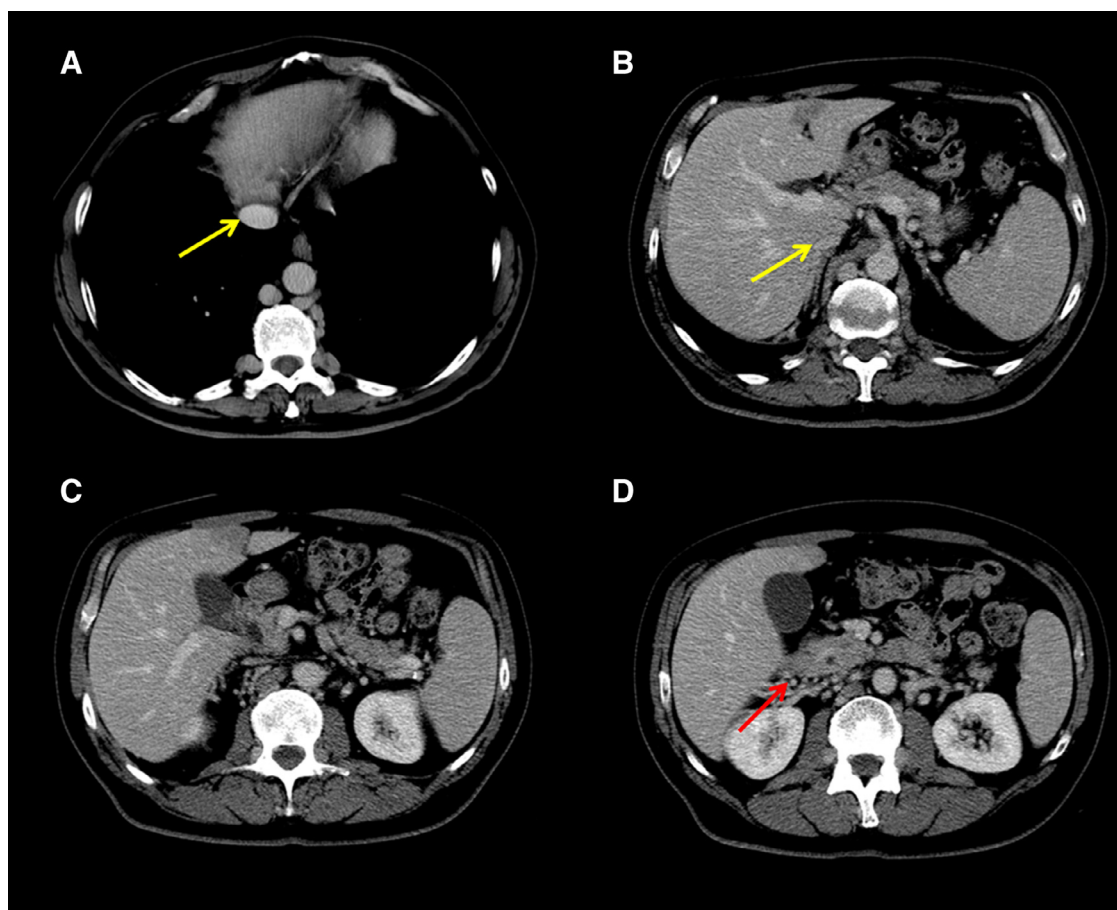
Fig. 2 – – Computed tomography, portal phase, axial sections; (A) regular aspect of suprahepatic inferior vena cava (IVC) (yellow arrow); (B) intrahepatic IVC (yellow arrow); (C) reduction caliber of infrahepatic IVC (yellow arrow); (D) infrarenal tract IVC absent (red arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

dimer: 5260.00 ng/mL (nv: 0-500 ng/mL); international normalized ratio (INR) 1.4 (nv: 0.8–1.2); NT - Pro Brain natriuretic peptide (BNP): 208 pg/mL (nv: 0-125pg/mL); C-Reactive Protein (CRP): 101.11 mg/mL (nv: 0-3 mg/mL); α-amylase: 50 UI/L (nv: 25-115 UI/L); lipase: 144 U/L (nv: 73-393 U/L); Aspartate Amino-transferase (GOT) 17 U/L (nv: 6-32 U/L); Alanine Aminotrans-ferase (GPT) 38 U/L (nv: 15-56 U/L); Gamma-Glutamyl Trans-ferase (GGT) 66 UI/L (nv: 15-85 UI/L); Alkaline phosphatase test (ALP): 94 UI/L (nv: 40-129 UI/L); total bilirubin: 1.62 mg/dL (nv: 0.20-1.10 mg/dL); direct bilirubin: 0.51 mg/dL (nv: 0.01-0.20 mg/dL); Lactic Acid Dehydrogenase (LDH): 186 U/L (nv: 85-245 U/L), ferritin: 541.90 ng/mL (nv: 22-322 ng/mL).

CT exam showed multiple filling defect of subsegmental branch of the right inferior lobar pulmonary artery. As additional finding, the scans through the upper abdomen revealed a hypodense mass in the portal vein lumen. In order to assess the site of origin of pulmonary embolism the CT exam was extended to the abdomen showing extensive thrombosis causing complete occlusion of the portal vein and proximal superior mesenteric vein lumen. Furthermore, it showed IVC hypoplasia (Fig. 6), with superficial collateral circulation and

ectasia of azygos and hemiazygos systems, left femoral vein, superficial epigastric vein, thoraco-epigastric vein, paraumbil-ical vein, and superior epigastric veins to make up for IVC hy-poplasia (Fig. 7). The CT scanner was a 64-slices Lightspeed (General Electric Healthcare, Waukesha, WI) and the scan protocol included a noncontrast CT scan, with 5 mm of thickness, and two dynamic acquisitions with thickness of 2.5 mm, the first performed 15 seconds after the administration of the iodine contrast medium (for the thoracic imaging) and the second with a delay of 75 seconds to the first (for the evaluation of the thoracic and abdominal venous system). It was administrated 115 mL of Iobitridol; flow-rate 2.5 mL/s).

3. Discussion

The normal adult right-sided IVC is completely developed by the eighth week of fetal life. The infrahepatic IVC develops as a composite structure from these three pairs of veins: the posterior cardinal veins, the subcardinal veins, and the supracardinal veins.
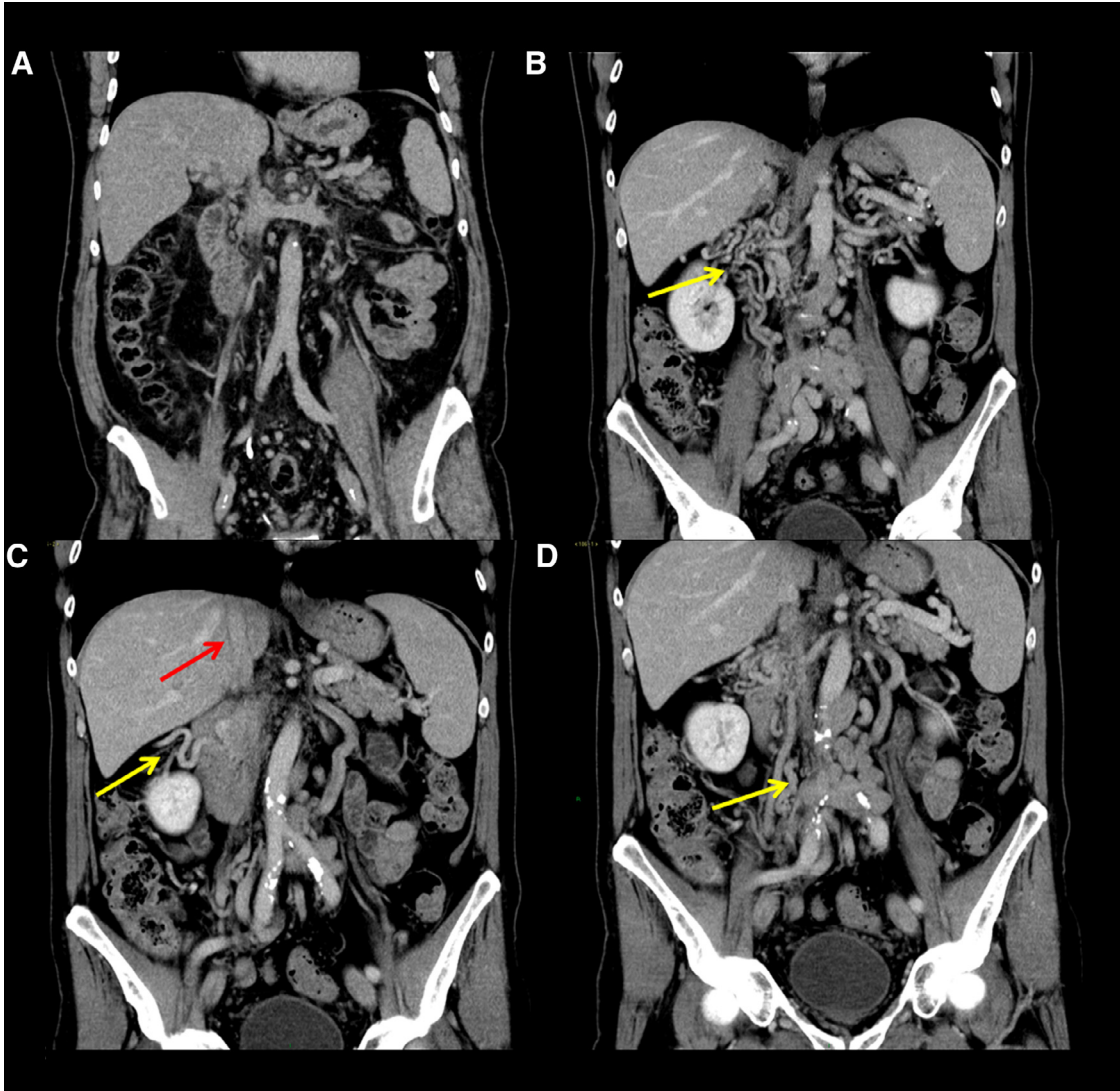
Fig. 3 – – Computed tomography, portal phase, coronal sections; (A) absence of infrarenal tract of inferior vena cava; (B) dilated, tortuous, collateral vessels (yellow arrow); (C) detail of collateral vessels communicating with right renal vein (yellow arrow). The section showing low contrast enhancement of intrahepatic inferior vena cava (red arrow); (D) dilated collateral vessels, particularly ascending lumbar veins (yellow arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).

Persistence or regression of these embryonic veins can lead to numerous rare congenital anomalies such as IVC hypoplasia, left IVC, double IVC, and agenesis of infrarenal IVC [1,5].

The posterior cardinal veins are the earliest to form and are the dominant system.

During the seventh week of embryonic life, the subcardinal veins, ventromedial and parallel to the posterior cardinal veins start to predominate.

Ultimately, the right subcardinal vein forms the prerenal and suprarenal segment of the IVC.

The supracardinal veins start to develop at 6 weeks and predominate at 8 weeks. They are dorsomedial to the regressing posterior cardinal veins and lateral to the subcardinal veins. They extend above the diaphragm to become azygos and hemiazygos veins.

The left supracardinal vein regresses, instead the right supracardinal vein forms the post renal and infrarenal segment of the IVC.

Anastomotic channels between the supracardinal and subcardinal veins form the intervening renal segment of the IVC [5].

Main anatomic anomalies and variation of IVC:

(a) *IVC hypoplasia:* has a very low incidence (<1%) in the general population and higher in young patients with deep venous thrombosis (DVT) and no other predisposing factor (5%) [6].
(b) *Left IVC:* occurs in 0.2% and 0.5% of the population.
(c) *Double IVC:* occurs in <3% of the population.
(d) *Agenesis:* is a rare congenital abnormality, with a probably underestimated incidence estimated in less than 1% [1,5].

Fig. 4 – – Balanced Turbo Field Echo – Breath Hold (BTFE-BH) sequence magnetic resonance imaging, coronal section; ectasic and tortuous paravertebral and ascending lumbar vessels.

The main venous variants related to the agenesis are: absence of suprarenal IVC, absence of the infrarenal IVC with preservation of the suprarenal segment [7–9] and absence of the entire IVC [7–18].

Due to these abnormalities blood flow is redistributed in four different pathways:

1. *Deep pathways*

From ascending lumbar vein to intervertebral veins, finally in azygos vein, or as an alternative, from intercostal vein to hemiazygos vein.

2. *Portal pathway*

From the hemorrhoidal plexus in hemorrhoidal veins then to inferior mesenteric vein finally in portal vein, or from superficial abdominal veins to paraumbilical veins.

3. *Median pathway*

From gonadal vein to renal vein finally in renal and azygos anastomosis.

4. *Superficial pathway*

From epigastric vein to internal mammary vein then to subclavian vein, or as an alternative, from epigastric vein to iliac vein, thoracoabdominal vein then to lumbar vein and finally in axillary vein [19,20].

IVC agenesis is a rare condition and the physiopathologic mechanism is unclear, although some authors have proposed an acquired etiology in which IVC agenesis is secondary to a possible intrauterine or perinatal thrombosis [7].

In patients with agenesis of the infrarenal IVC collateral circulation development is common, usually through the four large ways above mentioned: the gonadal venous system, which drains to the suprarenal cava; the paravertebral venous plexus, which drains to the superior vena cava through the azygous–hemiazygous system; the hemorrhoidal plexus, draining to the portal vein; and the superficial pathway, which drains to the subclavian veins and superior cava through superficial abdominal veins [4,5].

Most patients with infrarenal IVC agenesis are asymptomatic. The typical presentation is the isolated DVT especially at the iliofemoral segment in young male patients [21].

Despite the incidence of proximal venous thrombosis, the probability of PE is very low because the migration of thrombi is prevented by the extensive network of compensatory collateral circulation [1,2].

Symptoms associated to collateral pathways are uncommon, however lower extremity neurologic symptoms, resulting from compression of the lumbosacral nerve roots [4,22,23], and abdominal symptoms, caused by compression of visceral structures related to the gonadal venous system, are frequently observed [4,24].

Maintenance therapy with vitamin K antagonist (VKA) is considered the best approach. The duration of anticoagulant treatment is debated and there is no clear scientific evidence. Most authors agree on the need of life-long low-molecular-weight heparin (LMWH) therapy because of the irreversible nature of the risk factor and high incidence of recurrence when therapy is interrupted [25,26]. Other authors claim the use of this approach only in patients with further associated risk factors and in those whose symptoms reoccur when LMWH are withdrawn [21].

The best treatment strategy of DVT associated with agenesis of inferior vena cava (AIVC) is unclear, due to the uncommon occurrence of this condition and the absence of clinical trials to determine the optimal therapeutic strategy.

Although, conservative treatment, such as LMWH and VKA therapy, combined with elastic stockings, is sufficient in many cases [21].

Lambert et al. [19] described 72 patients with AIVC-associated DVT treated with long-term oral VKA anticoagulation, and none developed DVT recurrence during treatment [19,25]. The venous thrombectomy and/or replacement of IVC seems to prevent the deterioration of the chronic venous insufficiency over time and should be considered in patients with acute DVT of the iliofemoral veins, which causes a complete collapse of the collateral system [21,27].

Other therapeutic approaches include thrombolytic treatment and venous bypass surgery [25,28] but their use is not common because of the high rate of thrombolysis-related recurrence and low rate of venous bypass experienced surgeons.

Because of the low incidence of PE in these patients, a prophylactic IVC filter would not be recommended [5]. However, in these two cases we did not place an IVC filter because both the patients had ectasia of the veins azygos and hemiazygos, condition that would not protect the embolism despite the IVC filter.
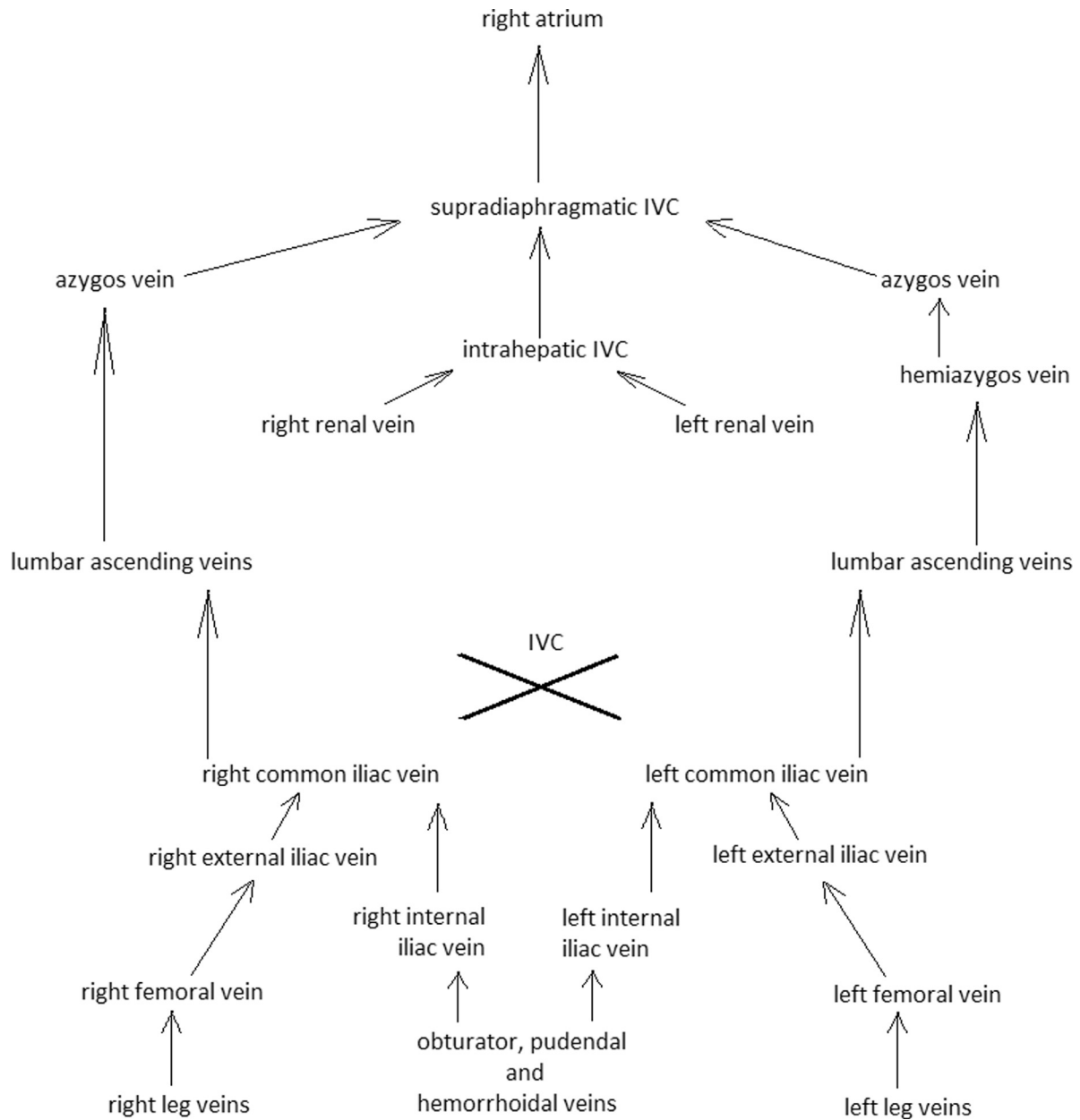
right atrium

supradiaphragmatic IVC

azygos vein

intrahepatic IVC

azygos vein

hemiazygos vein

right renal vein

left renal vein

lumbar ascending veins

IVC

lumbar ascending veins

right common iliac vein

left common iliac vein

right external iliac vein

left external iliac vein

right internal
iliac vein

left internal
iliac vein

right femoral vein

left femoral vein

right leg veins

obturator, pudendal
and
hemorrhoidal veins

left leg veins

Fig. 5 – – Blood flow redistribution in patient with inferior vena cava agenesis.
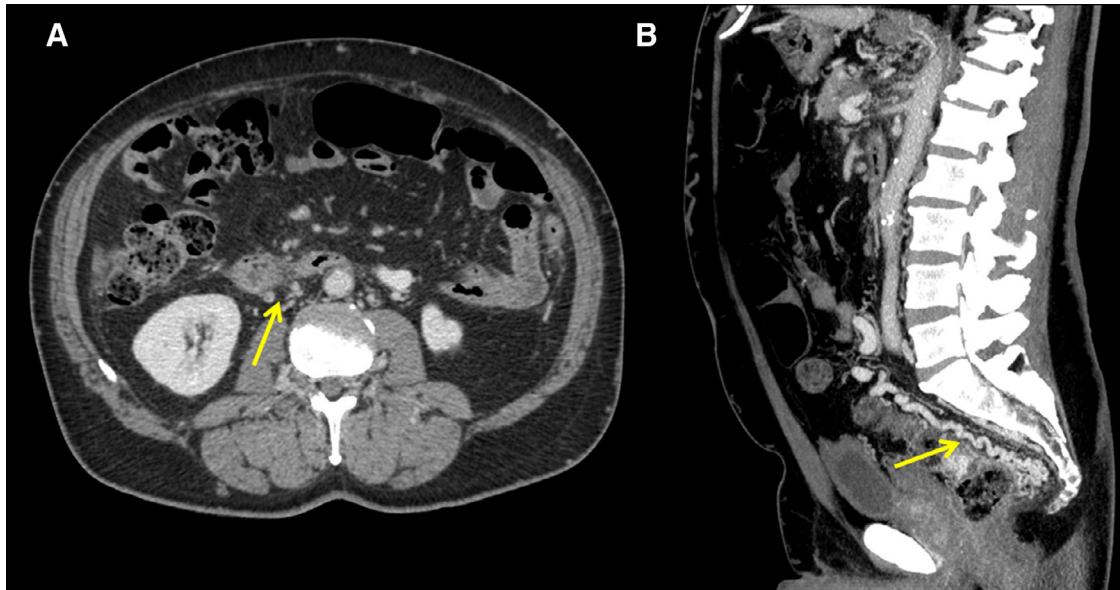
Fig. 6 – – (A) Computed tomography, portal phase, axial section; hypoplasic infrarenal inferior vena cava (yellow arrow); (B) Computed tomography, portal phase, sagittal section; dilated and tortuous hemorrhoidal vein (yellow arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.).
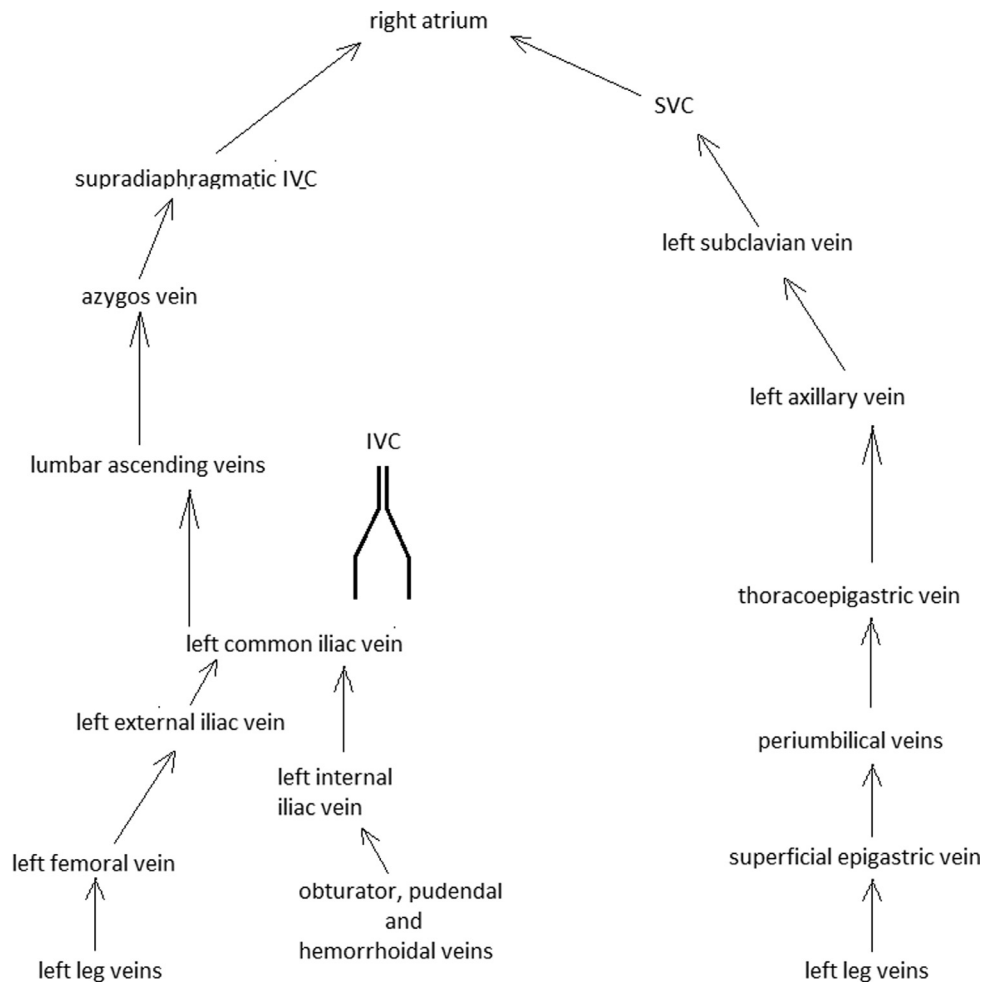

Fig. 7 – – Blood flow redistribution in patient with inferior vena cava hypoplasia.

4. Conclusion

LMWH followed by VKA is currently considered the best treatment option for this condition, but it should be patient tailored. The need for long-term anticoagulation therapy should also be evaluated in each patient [4]. Patients with AIVC have a high risk of developing long-standing asymptomatic clot with a resultant high risk of DVT and recurrence. A prompt identification of IVC abnormalities may allow an early intervention although there are no data about long-term morbidity and mortality [29,30].

CT and MRI play a pivotal role in the evaluation and follow-up of patients with IVC anomalies and CT is especially useful in the evaluation of collateral pathways such as superficial and deep abdominal venous vessels. Moreover, although the embolism from anomalous venous system is a rare condition it should be carefully investigated and excluded in order to set the best therapy for the patient (LMWH or VKA).

Conflicts of interest

None.

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