CASE REPORT

Double venous compression due to duplicated inferior vena cava-induced right common iliac vein thrombosis

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SUMMARY

Venous compression syndromes are caused by extrinsic venous compression of anatomical structures, such as the adjacent arteries and bones. Chronic venous compression and pulsative vibratory arterial pressure accelerate the development of deep vein thrombosis. Herein, we report the first case of double venous compressions due to a duplicated inferior vena cava-induced right-sided common iliac vein thrombosis. The thrombus was induced by left-sided inferior vena cava entrapment and right-sided common iliac vein compression, resembling nutcracker syndrome and May-Thurner syndrome, respectively. Bypass flow of the right inferior vena cava rendered the right lower extremity asymptomatic. Once daily anticoagulation edoxaban was effective. Congenital venous anomalies and bypass formations should be considered when a common iliac vein thrombus without symptoms in the lower extremities is observed, and a lifelong periodical follow-up is mandatory, even after remission.

BACKGROUND

Venous compression syndromes are caused by extrinsic venous compression of anatomical structures, such as the adjacent arteries, ligaments, muscles, bones and any pathological masses.^{1–3} Chronic venous compression leads to venous flow stasis and hypertension. Pulsative vibratory arterial pressure accelerates repetitive microtrauma, endothelial injury and inflammation, predisposing the deposition of platelets and fibrin, and hence, the development of deep vein thrombosis.

Left-sided common iliac vein (CIV) compression by the right common iliac artery and lumbosacral spine can induce left-sided CIV thrombosis, known as May-Thurner syndrome.⁴ Venous stasis of the left lower extremity results in leg swelling, varicose veins, venous eczema, hyperpigmentation, exertional pain, venous ulcers and pulmonary thromboembolism.² Left-sided renal vein entrapment caused by a narrowed angle between the superior mesenteric artery (SMA) and aorta is known as nutcracker syndrome. Left-sided renal vein hypertension usually leads to increased venous and capillary pressure, resulting in haematuria and reflux of the left testicular vein or the ovarian and parametric venous plexus.³

Duplicated inferior vena cava (IVC) is a congenital IVC anomaly, which occurs when symmetrical

pairs of the supracardinal veins do not fuse during the fourth to eighth week of gestation.^{5–7} Duplicated IVC is mostly discovered incidentally, and its prevalence is estimated as 0.3%–0.4%. The management of duplicated IVC is complicated, as recurrent IVC thrombosis may develop, especially in the presence of additional predisposing factors, such as thrombophilia and endothelial trauma.⁶ Anticoagulation is the mainstay treatment for IVC thrombosis. Adjunctive therapeutic modalities, such as IVC filters, catheter direct therapy, percutaneous transluminal angioplasty, stenting and surgical thrombectomy are considered in selected patients; however, evidence-based treatment guidelines have not yet been established.⁸

Herein, we report the first case of double venous compression due to a duplicated IVC-induced right-sided CIV thrombosis, which was resolved by once daily anticoagulation therapy alone.

CASE PRESENTATION

A 62-year-old woman was referred to our hospital with bilateral chest pain resistant to antibiotics. Initially, she had experienced 3 days of left-sided chest pain and shortness of breath and had visited her regular physician; she was diagnosed with left pneumonia with pleuritis, and antibiotics were administered for 5 days. One week later, she experienced additional right-sided chest pain and was referred to our hospital for further examination and treatment. She had never experienced swelling of the lower extremities. She had been treated with oral esomeprazole (20 mg daily) for chronic gastritis and was taking raloxifene (60 mg daily) for the prevention of postmenopausal osteoporosis. She did not consume any alcohol and did not smoke. She had no history of recent immobilisation or dehydration.

INVESTIGATIONS

On physical examination, she was afebrile and her other vital signs were normal. Respiratory sounds were also normal; however, left-sided chest pain was induced on deep inhalation. Other examinations were unremarkable. Routine laboratory tests revealed moderate inflammation and mild macrocytic anaemia with vitamin B₁₂ deficiency. Her laboratory results were as follows: white cell count, $4.96 \times 10^9/L$; C reactive protein level, 6.60 mg/dL; haemoglobin level, 10.3 g/dL; mean corpuscular

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Figure 1 High-resolution CT (HRCT) of the lungs; day of admission. HRCT shows bilateral consolidations in both lower lobes.

volume, 119.8 fL; mean corpuscular haemoglobin concentration, 35.5 pg; serum vitamin B₁₂ concentration, 122 pg/mL and serum folate level, 22.0 ng/mL. Chest radiography showed consolidations in both lung fields. High-resolution CT showed consolidations in both lower lobes, with mild pleural effusion (figure 1).

On the basis of a tentative diagnosis of recurrent pneumonia, antibiotics were restarted. In addition, periodical parenteral vitamin B₁₂ treatment was added for the macrocytic anaemia. Further laboratory tests were negative, including tests of antinuclear and antineutrophil cytoplasmic antibodies. Although her chest pain was slightly relieved, it remained after 10 days of antibiotics. She was afebrile, without any symptoms such as cough and sputum during the course of treatment. Her D-dimer level was slightly increased (5.4 µg/mL).

On day 20 of hospitalisation, contrast-enhanced whole-body CT revealed a duplicated IVC and right-sided CIV thrombus (figure 2A–D). The branched left IVC was entrapped by the SMA and abdominal aorta. The left renal vein was joined to the left IVC. The CIV was bifurcated at the left-side of the abdominal aorta, and the right CIV was compressed between the left

Figure 2 Contrast-enhanced CT. (A) Reconstruction image of the duplicated IVC in blue and abdominal aorta in red. Of note, the right IVC is merged with the right CIV (dotted circle). (B–D) The left IVC is entrapped between the SMA and aorta. The narrowed angle of the SMA is 23°. The right CIV is approximately 50% compressed between the left CIA and fourth vertebral body at the level of CIV bifurcation. The thrombus is locally found in the right CIV (arrowhead). (E–G) Complete resolution of the thrombus 4 weeks after anticoagulant therapy. CIA, common iliac artery; CIV, common iliac vein; IVC, inferior vena cava; Lt, left side; Rt, right side; SMA, superior mesenteric artery.

common iliac artery and fourth lumbar vertebral body. The right IVC was merged with the right CIV. The thrombus had formed locally in the right CIV. No findings of congenital cardiac defects or pulmonary hypertension were observed on cardiac ultrasonography. A diagnosis of pulmonary thromboembolism with right-sided CIV thrombosis was made.

TREATMENT

Oral anticoagulant edoxaban (30 mg once daily) was introduced; a reduced dosage was used because the patient's body weight was less than 60 kg (48 kg). Raloxifene was discontinued. Further screening tests of thrombophilia, including proteins C and S, were within normal limits. Lupus anticoagulant and anticardiolipin antibodies were also negative. Without aggravation of respiratory symptoms, she was discharged on day 24 of hospitalisation.

OUTCOME AND FOLLOW-UP

One-month postdischarge, repeat contrast-enhanced whole-body CT showed complete remission of the right-sided CIV thrombosis (figure 2E–G) and bilateral consolidations in the lungs. Her D-dimer level was 0.2 µg/mL. As she had an uneventful course, without any complications, edoxaban was continued with periodical follow-up.

DISCUSSION

The present case highlights two interesting clinical issues.

First, the present case demonstrates that double venous compression due to a duplicated IVC can induce right-sided CIV thrombosis with an asymptomatic right lower extremity. Unfortunately, the confirmed diagnosis of right-sided CIV thrombosis was delayed, as the patient did not present with any symptoms related to the right lower extremity. Considering the location of the thrombus in the right CIV, the collateral bypass of the right IVC may help explain the lack of symptoms in the right lower extremity (figure 3). Furthermore, the double venous compression due to a duplicated IVC rendered the venous flow stasis more complex. The downstream left-sided IVC entrapment, resembling nutcracker syndrome of the left renal vein in normal individuals, occurred between the SMA and aorta. Although many variants of congenital IVC anomalies have been reported, including those in the left IVC alone, the left IVC mostly branches

Figure 3 A diagram depicting the venous flow in the duplicated IVC with right-sided CIV thrombus. Double venous compression (arrowhead a, b) can induce right-sided CIV thrombosis. The collateral bypass of the right IVC can explain the lack of symptoms in the right lower extremity. CIV, common iliac vein; IVC, inferior vena cava; Lt, left side; Rt, right side.

at the level of the left renal vein.⁵ A narrowed SMA angle can induce venous stenosis, resulting in venous flow stasis and hypertension, while a normal SMA branches perpendicular to the aorta.^{3,9} Considering the larger diameter of the IVC, chronic left-sided IVC entrapment may have been the prothrombotic factor in the present case. In addition, an upstream right-sided CIV compression was observed, similar to that in May-Thurner syndrome. Although left-sided CIV thrombosis can occur due to anatomical left-sided CIV compression in individuals with a normal IVC, asymptomatic left-sided CIV compression itself may not be uncommon.^{3,10,11} Kibbe *et al* examined 50 CT scans of asymptomatic patients and found that 24% had compression of the left CIV greater than 50%.¹⁰ Similarly, Nazzal *et al* reviewed 300 CT scans and found that 19.6% and 44.7% of the patients had compression greater than 70% and 50%, respectively, with higher incidences in women. The authors concluded that CIV stenosis is not associated with clinical symptoms similar to deep vein thrombosis.¹¹ Furthermore, Gayer *et al* observed interactions between congenital IVC anomalies and prothrombotic backgrounds in seven of nine young patients.¹² Although the present case had some prothrombotic factors, such as oral raloxifene and vitamin B₁₂ deficiency, there were no strong causes of right-sided CIV thrombosis beyond the double venous compression. An English-language literature search using relevant keywords in the PubMed database yielded some reports of thrombosis with a congenital IVC anomaly.^{9,13–19} However, no reports of right-sided CIV thrombosis with double venous compression due to a duplicated or left IVC were found. Thus, we believe that the present case is the first of its kind to be reported.

Second, the present case demonstrates that once daily anticoagulant edoxaban can resolve subacute to chronic right-sided CIV thrombus on the background of double venous compression. CIV thrombosis should be treated based on the phase, severity and background.⁴ The present case was treated conservatively with oral anticoagulant edoxaban alone, considering the subacute/chronic phase and relatively mild symptoms, without respiratory dysfunction. Several reports of venous compression-induced thrombosis treated with oral anticoagulant alone exist, in which the anticoagulant was discontinued in 6–12 months.^{20–22} Although the thrombus was resolved in 4 weeks on high-resolution CT in the current case, the double compression remains anatomically present. Thus, lifelong anticoagulant therapy and periodical evaluation is preferred to prevent recurrent thrombosis. Other adjunctive therapies, including endovascular treatments and surgical interventions, should be carefully selected, as a change in venous flow dynamics can induce another venous flow stasis.

As mentioned above, some other prothrombotic factors were observed in the present case. Raloxifene is mildly associated with venous thromboembolism.²³ In addition, some reports suggest a relationship between vitamin B₁₂ deficiency and thromboembolism.^{24,25} Although these potential risks of thrombosis remain unconfirmed, the discontinuation of raloxifene and the continuation of parenteral vitamin B₁₂ treatment are considered favourable.

Pneumonia is the most frequent incorrect diagnosis in undiagnosed pulmonary thromboembolism. The diagnosis of pulmonary thromboembolism by the lung CT alone remains presumptive in the present case. According to a risk evaluation for deep vein thrombosis, such as the Wells scoring system, the risk score was low in the present case.²⁶ Thus, it is important to differentiate pulmonary thromboembolism and deep vein thrombosis, especially in low-risk patients with pneumonia following an atypical clinical course.

In conclusion, congenital venous anomalies and bypass formations should be considered when CIV thrombus is observed without symptoms of the lower extremities. Lifelong periodical follow-up is mandatory in such cases, even after remission.

Learning points

- Double venous compression due to a duplicated inferior vena cava can induce right-sided common iliac vein thrombosis.
- The collateral bypass of the right inferior vena cava may mask symptoms of the right lower extremity, delaying the diagnosis of right-sided common iliac vein thrombosis.
- Once daily anticoagulant edoxaban can resolve subacute to chronic right-sided common iliac vein thrombus with double venous compression; however, lifelong periodical follow-up is mandatory.

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Reminder of important clinical lesson

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