CASE REPORT

A Pitfall in the Diagnosis of Bilateral Deep Vein Thrombosis in a Young Man
Hypoplasia of the Inferior Vena Cava

Yusuke Adachi,1 MD, Kenichi Sakakura,1 MD, Tomohisa Okochi,2 MD, Takaaki Mase,1 MD, Mitsunari Matsumoto,1 MD, Hiroshi Wada,1 MD, Hideo Fujita,1 MD and Shin-ichi Momomura,1 MD

Summary
A 32-year-old man with a history of bronchial asthma was referred for low back pain and bilateral femur pain. Vascular sonography revealed bilateral deep vein thrombosis (DVT) from the femoral veins to the popliteal veins. Computed tomography revealed hypoplasia of the inferior vena cava (IVC) and dilated lumbar veins, ascending lumbar veins, and azygos vein as collaterals. There was no evidence of malignant neoplasm. The results of the thrombophilia tests were within normal limits. Hypoplasia of the IVC is a rare cause of DVT. This anomaly should be considered as a cause of bilateral and proximal DVT, in particular, in young patients without major risk factors.

Key words: Venous thromboembolism, Azygos continuation, Anomaly, Computed tomography

The average annual incidence of deep vein thrombosis (DVT) is estimated about 1 per 1000 in developed countries.1,2 DVT has a multifactorial etiology associated with both acquired and congenital factors, which may induce hypercoagulability or venous stasis.3 When there are no major risk factors for DVT, such as hospital or nursing home confinement, surgery, trauma, malignant neoplasm, chemotherapy, or neurologic disease with paresis,4 further investigation including congenital factors should be implemented, in particular, in young patients. In this case report, we present a young man with DVT, and discuss the cause of his DVT.

Case Report
A 32-year-old man with a history of bronchial asthma was referred for low back pain and bilateral femur pain. He had no fever or dyspnea. His vital signs in the emergency room remained within normal limits with blood pressure of 105/64 mmHg, pulse rate of 85 beats/ min, and pulse-oximetry oxygen saturation of 100% in ambient air. Laboratory data revealed elevated white blood cell counts (12,300/μL), CRP levels (13.6 mg/dL), and D-dimer levels (30.2 μg/mL). The patient had a 12-hour-flight, 1 week before the presentation. Observations revealed bilateral leg edemas with dermatitis and pigmentation of bilateral femurs. Vascular sonography revealed bilateral DVT from the femoral veins to the popliteal veins. Although he revealed a history of bronchial asthma, we performed contrast enhanced computed tomography (CT) with prophylactic administration of intravenous corticosteroids in order to investigate the cause of his bilateral DVT. The CT denied aortic dissection or pulmonary embolism; however, it revealed hypoplasia of the inferior vena cava (IVC) and bilateral DVT. Transverse views of the CT images are presented in Figure 1 (A; Th12 level, B; L1 level, C; L2 level, D; L3 level) and Figure 2A (L4 level), which reveal hypoplasia of the IVC (yellow arrows) and collateral veins (red arrows; dilated lumbar vein, blue arrows; ascending lumbar vein). Figure 2B is a coronal multiplanar reconstruction view of CT images, which emphasizes on the IVC filled with thrombi at the level of L2-L4 (arrows). Figure 2C is a sagittal multiplanar reconstruction view of CT images, which emphasizes on the hypoplastic IVC and collateral veins. Three-dimensional reconstruction of CT images is presented in Figure 3, which demonstrates the dilated ascending lumbar veins (daggers) and azygos vein (asterisks). There was no evidence of malignant neoplasm. The results of thrombophilia tests, including protein C, protein S, antithrombin III, homocysteine, and antiphospholipid antibody were within normal limits. We prescribed warfarin with target PT-INR of 2-3,5 and instructed the patient to use elastic stockings. Both low back pain and femur pain disappeared completely within 3 months. Although we refrained from...
follow-up with contrast enhanced CT due to bronchial asthma, the follow-up vascular sonography revealed increased blood flow in the bilateral femoral veins and popliteal veins. Considering the anomaly of IVC, we should provide lifetime anticoagulation therapy for the patient, because we cannot modify his risk factor for DVT.

**Discussion**

Hypoplasia or absence of the IVC is a rare vascular anomaly, which can be a potential risk for DVT. Historically, Virchow postulated three main causes of thrombosis: stasis of the blood, changes in the vessel wall, and changes in the composition of the blood. Increased venous blood pressure and venous stasis caused by hypoplasia of the IVC presumably affects the development of DVT.

Koc, et al. studied 7972 patients consecutively who underwent routine abdominal multidetector row CT, and reported that the prevalence of interruption or congenital stenosis of the IVC was 0.15% (n = 12). In their study, IVC anomaly associated with the well-developed collaterals is commonly asymptomatic, whereas it is commonly symptomatic if the well-developed collaterals are absent. Ruggeri, et al. studied 75 individuals with DVT aged below 30 years, and reported that the congenital absence of IVC was found in 5.3% (n = 4). Lambert, et al. described 10 consecutive patients with IVC agenesis-associated DVT, and reported that 80% of patients (8/10) with IVC agenesis-associated DVT developed abdominal and/or back pain, which was presumably caused by lumbar DVT. They also conducted a literature review of the previous 62 cases, which revealed that the patients demonstrated quite homogeneous clinical characteristics; young age (< 40 years), male dominant, proximal DVT, and onset after intense physical exertion. The present case also revealed three characteristics (young, male, and proximal DVT).

In patients with hypoplastic IVC and DVT, the occurrence of pulmonary embolism would be rare, because the emboli from DVT would not move into the IVC. Therefore, this case was not complicated by pulmonary embolism; however, there have been a few previous reports, in which the pulmonary embolism occurred even in the presence of IVC anomaly. Lambert, et al. reported that the pulmonary embolism was found in 9.67% (6/62) of the patients with IVC agenesis-associated DVT. In these cases, the emboli from DVT may have migrated through the well-developed collaterals such as hemiazygos and azygos systems to the pulmonary circulation. IVC anomaly with well-developed collaterals may have a lower risk of DVT; however, it may have higher risk of pulmonary embolism once the thrombus is formed.

Surgical treatment for IVC anomaly complicated with DVT has not been established. Dougherty, et al. reported a successful treatment of IVC anomaly with a prosthetic graft from the iliac vein to the intrathoracic azygous vein in a patient with nonhealing pretibial ulceration.

In most of the DVT cases with IVC anomaly, conventional anticoagulation therapy with warfarin has been used to relieve the symptoms. As the patients who experienced thrombosis due to IVC anomaly may have a

---

**Figure 1. Transverse views of CT images.**

**A:** Th12 level, **B:** L1 level, **C:** L2 level, **D:** L3 level. Hypoplastic IVC (yellow arrows), dilated lumbar vein (red arrows), and ascending lumbar vein (blue arrows).
Figure 2. Transverse, coronal, and sagittal views of CT images. A: Transverse view of L4 level (IVC; arrow). B: Coronal multiplanar reconstruction view (IVC; arrows). C: Sagittal multiplanar reconstruction view, which highlights the hypoplastic IVC and collateral veins. Funicular IVC is shown at the level of Th12-L2, and IVC filled with thrombi is shown at the level of L2-L4 (IVC; yellow arrows). Collateral veins are shown as dilated lumbar vein (red arrows), ascending lumbar vein (blue arrows), and azygos vein (asterisk).

Figure 3. Three-dimensional reconstruction of CT images. Left: 30° left anterior oblique view. Right: 70° right anterior oblique view. Dilated ascending lumbar veins (daggers) and azygos vein (asterisks) are shown as collaterals.
higher risk for thrombotic recurrence, lifelong anticoagulation therapy should be considered.\textsuperscript{13,16}

Recently, direct oral anticoagulants (DOACs) have been developed as alternatives to the conventional therapy with warfarin for the treatment of acute venous thromboembolism events.\textsuperscript{7,23} Nevertheless, the clinical efficiency for DOACs for patients with IVC anomalies remains unclear. Further clinical research is warranted.

Although vascular sonography is an effective screening tool for DVT,\textsuperscript{24} it is difficult to describe the whole anatomy including IVC anomaly and collateral veins. The contrast enhanced CT with three-dimensional reconstruction should be considered in order to exclude the IVC anomalies.

In conclusion, we should suspect the presence of IVC anomaly as a cause of DVT, when we see the bilateral and proximal DVT, in particular, in young patients without major risk factors.

Acknowledgments

The authors acknowledge Kyoko Kami, RT, and Hiromi Oka, RT of Saitama Medical Center, Jichi Medical University, for the three-dimensional reconstruction of CT images.

Disclosures

Conflicts of interest: The authors declare that they have no conflict of interest.

References

1. Anderson FA Jr, Wheeler HB, Goldberg RJ, et al. A population-based perspective of the hospital incidence and case-fatality rates of deep vein thrombosis and pulmonary embolism. The Worcester DVT Study. Arch Intern Med 1991; 151: 933-8.
2. Nordstrom M, Lindblad B, Bergqvist D, Kjellstrom T. A prospective study of the incidence of deep-vein thrombosis within a defined urban population. J Intern Med 1992; 232: 155-60.
3. Rosendaal FR. Thrombosis in the young: epidemiology and risk factors. A focus on venous thrombosis. Thromb Haemost 1997; 78: 1-6.
4. Rosendaal FR. Venous thrombosis: a multicausal disease. Lancet 1999; 353: 1167-73.
5. Heit JA, Silverstein MD, Mohr DN, Petterson TM, O’Fallon WM, Melton LJ 3rd. Risk factors for deep vein thrombosis and pulmonary embolism: a population-based case-control study. Arch Intern Med 2000; 160: 809-15.
6. Schneider JG, Eynatten MV, Dugi KA, Duex M, Nawroth PP. Recurrent deep venous thrombosis caused by congenital interruption of the inferior vena cava and heterozygous factor V Leiden mutation. J Intern Med 2002; 252: 276-90.
7. Ruggieri M, Tosetto A, Castaman G, Rodeghiero F. Congenital absence of the inferior vena cava: a rare risk factor for idiopathic deep-vein thrombosis. Lancet 2001; 357: 441.
8. Koc Z, Oguzkurt L. Interruption or congenital stenosis of the inferior vena cava: prevalence, imaging, and clinical findings. Eur J Radiol 2007; 62: 257-66.
9. Lambert M, Marboeuf P, Midulla M, et al. Inferior vena cava agenesis and deep vein thrombosis: 10 patients and review of the literature. Vasc Med 2010; 15: 451-9.
10. D’Aloia A, Faggiano P, Fiorina C, et al. Absence of inferior vena cava as a rare cause of deep venous thrombosis complicated by liver and lung embolism. Int J Cardiol 2003; 88: 327-9.
11. Namisaki H, Nishigami K, Murakami M, Yamamoto T, Ogata Y, Tomita A. Congenital absence of inferior vena cava withazygos continuation revealed by vascular echo in a patient with pulmonary thromboembolism and deep vein thrombosis: a case report. Ann Vasc Dis 2013; 6: 195-7.
12. Dougherty MJ, Calligaro KD, DeLaurentis DA. Congenitally absent inferior vena cava presenting in adulthood with venous stasis and ulceration: a surgically treated case. J Vasc Surg 1996; 23: 141-6.
13. Sakellaris G, Tilenis S, Papakonstantinou O, Bitsori M, Tsetis D, Charisis G. Deep venous thrombosis in a child associated with an abnormal inferior vena cava. Acta Paediatr 2005; 94: 224-4.
14. Shah NL, Shanley CJ, Prince MR, Wakefield TW. Deep venous thrombosis complicating a congenital absence of the inferior vena cava. Surgery 1996; 120: 891-6.
15. Gil RJ, Perez AM, Arias JB, Pascual FB, Romero ES. Agenesis of the inferior vena cava associated with lower extremities and pelvic venous thrombosis. J Vasc Surg 2006; 44: 1114-6.
16. Obernosterer A, Aschauer M, Schnedl W, Lipp RW. Anomalies of the inferior vena cava in patients with iliac venous thrombosis. Ann Intern Med 2002; 136: 37-41.
17. Senoo K, Kondo Y, Miyazawa K, Isogai T, Chun YH, Kobayashi Y. Safety and efficacy of direct oral anticoagulants over warfarin in Japanese patients with acute venous thromboembolism: a meta-analysis. J Cardiol 2016; 69: 763-8.
18. Schulman S, Kearon C, Kakkar AK, et al. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. N Engl J Med 2009; 361: 2342-52.
19. Schulman S, Kakkar AK, Goldhaber SZ, et al. Treatment of acute venous thromboembolism with dabigatran or warfarin and pooled analysis. Circulation 2014; 129: 764-72.
20. Bauersachs R, Berkowitz SD, Brenner B, et al. Oral rivaroxaban for symptomatic venous thromboembolism. N Engl J Med 2010; 363: 2499-510.
21. Agnelli G, Buller HR, Cohen A, et al. Oral apixaban for the treatment of acute venous thromboembolism. N Engl J Med 2013; 369: 799-808.
22. Buller HR, Decousus H, Grosso MA, et al. Edoxaban versus warfarin for the treatment of symptomatic venous thromboembolism. N Engl J Med 2013; 369: 1406-15.
23. Fujino T, Yamazaki Y, Yamazaki A, et al. Efficacy of dabigatran for dissolving deep vein thromboses in outpatients with a deteriorated general condition. Int Heart J 2015; 56: 395-9.
24. Nitta D, Mitani H, Ishimura R, et al. Deep vein thrombosis risk stratification. Int Heart J 2013; 54: 166-70.