

THE CLINICAL PICTURE

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Trousseau syndrome

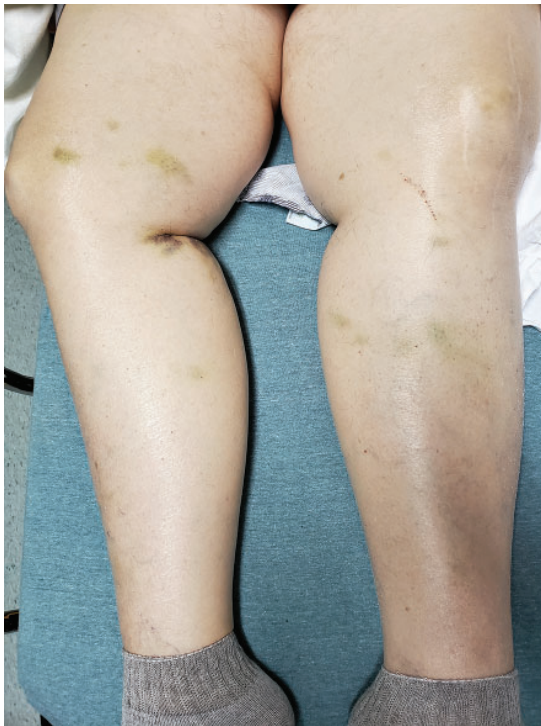


Figure 1. Multiple bluish macules were scattered on both legs, the sequelae of migratory thrombophlebitis.

A PREVIOUSLY HEALTHY 75-year-old man presented to the clinic with memory loss, lightheadedness, and new-onset headaches. He also reported fatigue, anorexia, and epigastric abdominal pain, but no slurred speech or focal weakness.

Physical examination confirmed he had no focal neurologic deficit, but examination of the skin revealed multiple bluish macules scattered over both legs (**Figure 1**). Closer inspection revealed extensive discoloration in the right popliteal fossa, with 2 palpable thrombosed superficial veins (**Figure 2**). With these findings suggesting Trousseau syndrome,

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Figure 2. Closer inspection revealed extensive discoloration in the right popliteal fossa, with two palpable thrombosed superficial veins.

anticoagulation was started immediately and imaging was ordered to look for deep vein thrombosis and an underlying malignancy.

■ IMAGING GIVES A FULLER PICTURE

Although the patient had no leg pain or tenderness, Doppler ultrasonography confirmed deep vein thrombosis bilaterally, extending from the common femoral veins through the popliteal veins. Abdominal computed tomography showed a 2.8-cm pancreatic body mass, and endoscopic biopsy confirmed pancreatic adenocarcinoma.

Magnetic resonance imaging of the brain revealed multifocal acute infarcts that raised the concern for embolic disease. However, transthoracic echocardiography revealed no vegetations, valvular disease, or patent foramen ovale that could have been the source of embolism. Computed tomographic angiogra-

phy of the head and neck showed no evidence of vascular disease.

The patient was discharged on extended anticoagulation with low-molecular-weight heparin (LMWH) and was referred for palliative chemotherapy.

THE SPECTRUM OF THROMBOEMBOLIC DISEASE

The syndrome of migratory thrombophlebitis as a sign of malignancy bears the name of Armand Trousseau, who in 1865 published the first clinical record associating undiagnosed visceral malignancy and unexpected thrombosis. In a twist of fate, Trousseau diagnosed the syndrome in himself 2 years later and died of gastric cancer.^{1,2}

Today, Trousseau syndrome covers a spectrum of disease including chronic disseminated intravascular coagulation, microangiopathic hemolytic anemia, nonbacterial thrombotic endocarditis, and arterial thrombosis.

Thrombosis in malignancy is complicated and represents an intersection of hematology and oncology. Mucin-producing carcinomas are commonly linked with the syndrome,³ but this is not an exclusive association. The pathophysiology is complex, and tissue factor, tumor hypoxia, tumor-associated cysteine proteinase, and most recently, oncogene activation have been implicated.^{4,5}

MANAGEMENT

Intuitively, one would think that the clinical focus should be on diagnosing and treating the underlying malignancy. However, thrombosis is an uncommon presentation of cancer, and if provoking factors are present, thrombosis should not routinely trigger a search for cancer beyond age-appropriate screening. Nevertheless, Trousseau syndrome is not a benign thrombophlebitis, and when diagnosed it requires immediate treatment.

Until recently, LMWH was the only anticoagulant recommended for cancer-associated thrombosis, based on comparisons with vitamin K antagonists. Now, with data from recent clinical trials, guidelines have been updated and the direct-acting oral anticoagulants edoxaban and rivaroxaban have been added to LMWH as preferred options because they have better efficacy than vitamin K antagonists.⁶ On the other hand, a higher risk of major bleeding was seen with direct-acting oral anticoagulants, mainly in patients with luminal gastrointestinal malignancies, which have a high risk of mucosal bleeding.⁶

Therefore, when recommending therapy, clinicians should consider bleeding risk, renal function (edoxaban and rivaroxaban should be given in lower doses or not at all in patients with renal impairment), drug interactions (which are common with vitamin K antagonists), and patient preference.

REFERENCES

1. **Trousseau A.** Phlegmasia alba dolens. Lectures on clinical medicine, delivered at the Hotel-Dieu, Paris. London, England: New Sydenham Society; 1865:281–332.
2. **Khorana AA.** Malignancy, thrombosis, and Trousseau: the case for an eponym. *J Thromb Haemost* 2003; 1(12):2463–2465. doi:10.1111/j.1538-7836.2003.00501.x
3. **Pineo GF, Brain MC, Gallus AS, Hirsh J, Hatton MW, Regoeczi E.** Tumors, mucus production, and hypercoagulability. *Ann N Y Acad Sci* 1974; 230:262–270. doi:10.1111/j.1749-6632.1974.tb14458.x
4. **Varki A.** Trousseau's syndrome: multiple definitions and multiple

mechanisms. *Blood* 2007; 110(6):1723–1729. doi:10.1182/blood-2006-10-053736

5. **Boccaccio C, Comoglio PM.** A functional role for hemostasis in early cancer development. *Cancer Res* 2005; 65(19):8579–8582. doi:10.1158/0008-5472.CAN-05-2277
6. **Key NS, Khorana AA, Kuderer NM, et al.** Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO clinical practice guideline update. *J Clin Oncol* 2019; JCO1901461. doi:10.1200/JCO.19.01461. Epub ahead of print.

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