

## Multiple Thrombi in the Heart in Trousseau Syndrome Caused by Pancreatic Carcinoma

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A 65-year-old woman presented to our emergency room because of sudden onset of right hemiparesis with severe fatigue. Neurological examination revealed right hemiparesis with right facial numbness and an extensor planter response on the right side. Magnetic resonance imaging with diffusion-weighted imaging revealed multiple high-intensity areas in both cerebral hemispheres and the right cerebellum. A diagnosis of acute stage of multiple brain infarctions caused by emboli was made. An abdominal computed tomography showed a pancreatic tumor with multiple liver metastases. High D-dimer and serum carbohydrate antigen 19-9 concentration strongly suggested Trousseau syndrome associated with pancreatic cancer. The patient had another large embolic stroke and died on day 47. Autopsy was performed. There were large thrombi in the left ventricular apex and in the left atrial appendage. There was also a papillary-shaped vegetation on the aortic valve that consisted mainly of fibrin without any inflammatory cells or destruction of the valve, these findings being characteristic of NBTE. This case is remarkable in that the patient had 3 different types of cardiac thrombi in her heart associated with Trousseau syndrome. **Key Words:** Nonbacterial thrombotic endocarditis—pancreatic cancer—Trousseau syndrome—cerebral infarction.  
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Trousseau syndrome, which is characterized by a hyperactive coagulation state resulting in various types of thromboembolism, may be associated with concomitantly diagnosed malignancy, often in the form of mucin-

positive carcinomas. However, this type of coagulopathy can occur in association with any type of malignancy. Although thrombi originating in the heart may cause ischemic stroke in patients with Trousseau syndrome, appropriate investigations do not always reveal intracardiac thrombi. It has been reported that around a quarter of patients with malignancy-related coagulation disorder have coexisting nonbacterial thrombotic endocarditis (NBTE),<sup>1</sup> which is characterized by nonbacterial vegetation without valvular destruction.<sup>2</sup> Because NBTE is rarely diagnosed in living patients, autopsy studies report a higher than expected frequency of NBTE in patients with malignancy.<sup>3</sup> Here, we report a patient with cardioembolic stroke who was eventually diagnosed as having Trousseau syndrome. An autopsy revealed 3 different types of thrombus in the heart.

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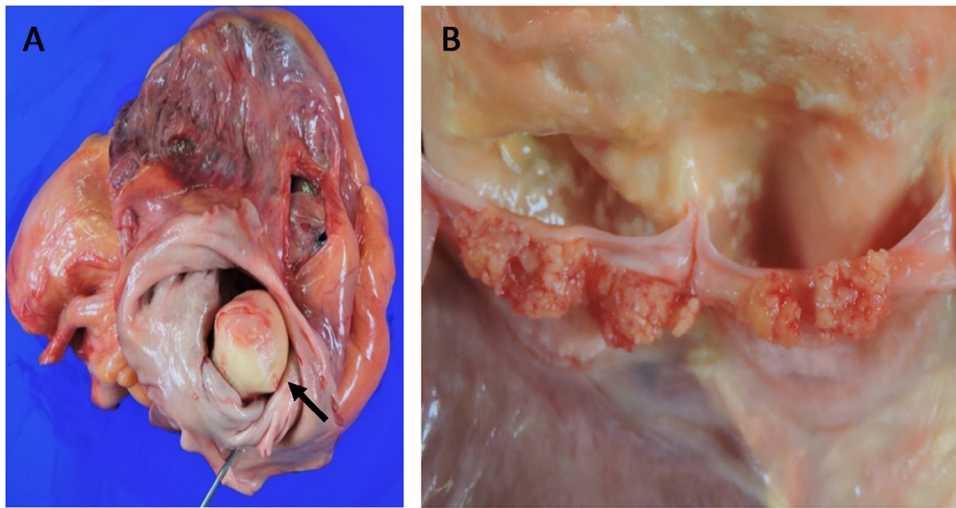
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**Figure 1.** (A) Large thrombus in the left atrial appendage that is organized and mainly composed of fibrin. (B) Papillary-shaped fragile vegetations with no associated inflammation on the aortic valve.

A 65-year-old woman presented to our emergency room because of sudden onset of right hemiparesis with severe fatigue. Neurological examination revealed right hemiparesis with right facial numbness and an extensor planter response on the right side. Magnetic resonance imaging with diffusion-weighted imaging revealed multiple high-intensity areas in both cerebral hemispheres and the right cerebellum. A diagnosis of acute stage of multiple brain infarctions caused by emboli was made and the patient was admitted to our stroke unit. Because the patient also reported abdominal discomfort, an abdominal computed tomography (CT) was performed, which showed a pancreatic tumor with multiple liver metastases. Blood concentrations of fibrinolytic markers such as D-dimer and fibrin degradation product were very high, as was the patient's serum carbohydrate antigen 19-9 concentration, strongly suggesting Trousseau syndrome associated with pancreatic cancer.

Despite treatment with intravenous heparin (15,000 units/day), further embolic strokes occurred. Chest and abdominal CT showed asymptomatic thromboemboli in the patient's lungs and kidneys, and an ultrasound examination revealed deep venous thrombus in her right leg. Because of the advanced stage of the pancreatic cancer, the patient received palliative care rather than curative treatment.

On day 23, the patient had another embolic stroke, which resulted in disturbance of consciousness, conjugate eye deviation to the right, and left hemiplegia. Brain CT revealed fresh infarction throughout the right middle cerebral artery territory. The patient died on day 47 and autopsy was performed 18 hours after her death.

Macroscopically, there was extensive neuromalacia in the right hemisphere. On microscopic examination, multiple small infarcts were found throughout the cerebral hemispheres, brain stem, and cerebellum. Ischemic lesions

were also seen in both lungs, the spleen, and kidneys, indicating general thromboembolism. The patient's heart weighed 465 g. There were large thrombi in the left ventricular apex (Supplemental Fig S1) and in the left atrial appendage (Fig 1, A) accompanied by rich neovascularization, suggesting that the thrombi were not fresh ones. There was also a papillary-shaped vegetation on the aortic valve (Fig 1, B) that consisted mainly of fibrin without any inflammatory cells or destruction of the valve, these findings being characteristic of NBTE. A 4-cm tumor was found in the tail of pancreas; this was thought to be a primary cancer. Histological examination showed proliferation of atypical epithelial cells forming irregular ducts, accompanied by abundant fibrous stroma (Supplemental Fig S2). These findings are consistent with invasive pancreatic carcinoma. Additionally, multiple cancerous lesions in the liver had similar pathological features on microscopic examination, indicating they were metastases from the pancreatic cancer. Hence, the patient had Trousseau syndrome with the characteristic thromboembolism in multiple organs.

NBTE may result in paradoxical cerebral embolism, tumor embolism, and sinus thrombosis.<sup>1</sup> NBTE can induce both cerebral infarction and asymptomatic systemic emboli causing, for example, splenic and renal infarction. Cerebral infarction may also result from the hypercoagulable state associated with malignancy known as Trousseau syndrome. Our patient developed multiple cerebral infarctions and had pancreatic cancer with liver metastases, consistent with a diagnosis of Trousseau syndrome.<sup>3</sup>

This case is remarkable in that the patient had 3 different types of cardiac thrombi in her heart associated with Trousseau syndrome. The thrombus on her aortic valve was likely responsible for her initial stroke because it was granular and fragile and thus likely to produce emboli, whereas the other thrombi in her left appendage

and apex were relatively large and had smooth surfaces, so these thrombi were less likely to have induced multiple small embolic strokes. The patient developed neurological symptoms resulting from multiple small cerebral infarctions, which is characteristic of Trousseau syndrome. The patient's hypercoagulable state with malignancy played important roles in this case. Thus, when a patient with small, multiple cerebral infarctions is encountered, the whole body should be carefully checked for any evidence of malignancy to enable establishment of an early diagnosis.

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### Appendix: Supplementary Material

Supplementary data to this article can be found online at [doi:10.1016/j.jstrokecerebrovasdis.2017.12.005](https://doi.org/10.1016/j.jstrokecerebrovasdis.2017.12.005).

### References

1. Graus F, Rogers LR, Posner JB. Cerebrovascular complications in cancer patients. *Medicine (Baltimore)* 1985;64:16-35.
2. Asopa S, Patel A, Khan OA, et al. Nonbacterial thrombotic endocarditis. *Eur J Cardiothorac Surg* 2007;32:696-701.
3. El-Shami K, Griffiths E, Streiff M. Nonbacterial thrombotic endocarditis in cancer patients: pathogenesis, diagnosis and treatment. *Oncologist* 2007;12:518-523.