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Nonbacterial thrombotic endocarditis mimics acute infective endocarditis in a woman with endometrial cancer



KEYWORDS

Blood culture negative endocarditis;
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Dear Editor,

Blood culture-negative endocarditis (BCNE) is a formidable cardiac condition, and the survey of the etiology is a clinical challenge. It is a crucial decision to make the diagnosis of noninfective endocarditis after detailed inspection. Here we present a case of cancer-associated nonbacterial thrombotic endocarditis (NBTE) with a favorable outcome.

A 63-year-old woman had clear cell endometrial cancer, International Federation of Gynecology and Obstetrics (FIGO) stage IVB, diagnosed a year ago, which was classified as a stable disease after an optimal debulking surgery and adjuvant chemotherapy. She presented with left arm and neck swelling for ten days due to catheter-related thrombosis. The local swelling subsided after removal of port catheter and anticoagulant therapy. Two weeks later, there was a transient episode of left hemiparesis and dysphagia. Brain *magnetic resonance imaging* revealed scattered infarction in right hemisphere (Fig. 1a). Carotid ultrasound, Holter monitor, and transthoracic echocardiography (TTE) were performed to investigate embolic source, but results showed no explicable abnormality. However, another embolic event with mainly right middle cerebral artery occlusion recurred two weeks later. Emergent endovascular thrombectomy (EVT) was performed with successful total reperfusion. The pathological examination of the retrieved emboli showed fibrinous material. Fever up to 38.1 °C

developed right after EVT, and transesophageal echocardiography (TEE) disclosed a fluttering material, 0.79 cm in length (Fig. 1b). Empirical cefepime and vancomycin were parenterally administered for suspected infective endocarditis (IE). She had no prior antibiotic exposure or animal contact within two weeks before admission. Except for a markedly elevated serum level of D-dimer (>7,650 ng/mL; normal range: 0–500 ng/mL), her hemogram and biochemical studies for liver and renal function were within normal limits. Three sets of blood cultures with prolonged incubation, polymerase chain reaction (PCR) detection of bacterial via 16S ribosomal RNA in blood, and phase II species-specific immunoglobulin M and PCR for *Coxiella burnetii* in blood, all failed to find an etiological pathogen. Moreover, no microorganism could be identified in the emboli by Gram staining. During hospitalization, chest and abdomen computed tomography revealed pulmonary embolism (Fig. 1c), renal and spleen infarctions (Fig. 1d), peritoneal carcinomatosis, and pulmonary nodules, which were pathologically confirmed by CT-guided biopsy to be clear cell carcinoma of gynecologic origin. With the clinical diagnosis of cancer-associated NBTE, she received chemotherapy for endometrial cancer afterwards and continued anticoagulants. There was no vegetation in TTE performed two months later. There was no sign or evidence of infection in the following three months after discontinuation of antibiotic therapy.

There are several causes of BCNE, which should be surveyed comprehensively.¹ Bloodstream infections due to atypical pathogens, molecular testing and prolonged incubation of blood cultures, and pathological and microbiological surveys in resected cardiac valve or emboli should be conducted, if available. If the etiological assays fail to identify any causative pathogen, non-infectious causes should be considered. Antinuclear antibodies, anti-phospholipid antibodies, and peripheral eosinophil counts could be tested to exclude Libman-Sacks or Löeffler endocarditis. NBTE is not uncommon accounting for the

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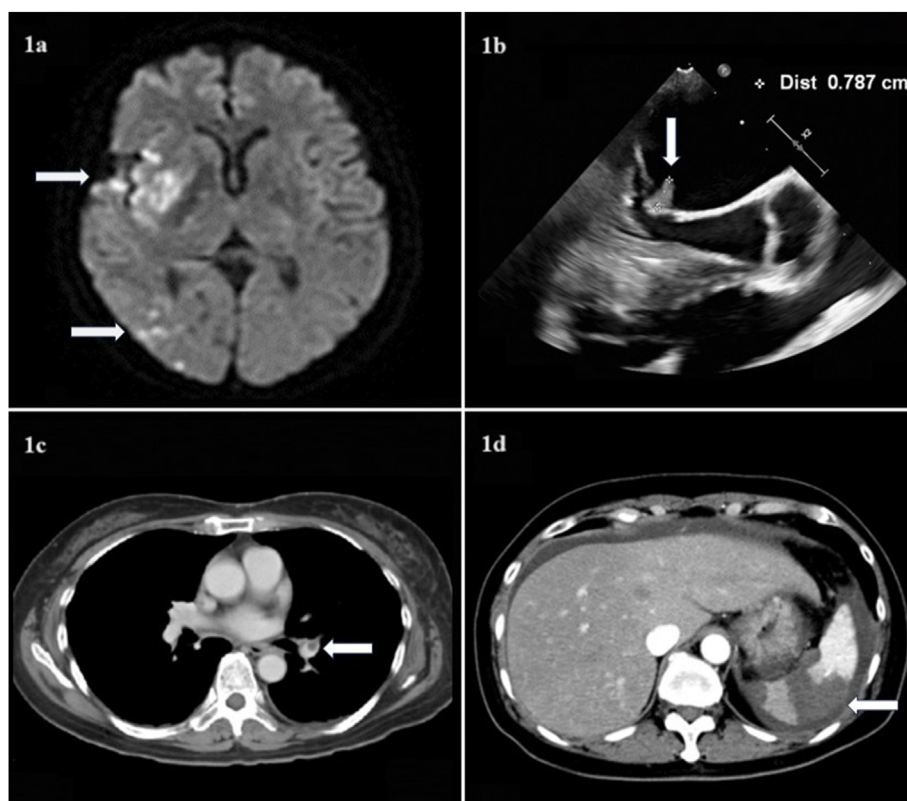


Figure 1. Image studies of the present case of nonbacterial thrombotic endocarditis. Infarction of right insular cortex, temporal and occipital lobes on brain *magnetic resonance imaging* (1a), a fluttering material, 0.79 cm in length, in the mitral valve noted in transesophageal echocardiography (1b), pulmonary embolism in a left segmental pulmonary artery on chest computed tomography (1c), and splenic infarction on abdominal computed tomography (1d).

prevalence of 0.61%–1.08% in published autopsy studies, and is commonly associated with pancreas, lung cancer, or lymphoma.^{2,3} As for gynecologic cancers, NBTE commonly occurs in the cases of mucin-producing adenocarcinomas but is rarely described among those with clear cell carcinoma.^{4,5} Since no organism was identified after a comprehensive evaluation, the presence of elevated serum D-dimer level, multiple systemic embolisms, concurrent pulmonary embolism, and advanced malignancy could serve as potential indicators of NBTE.^{3,4} Current recommended management of NBTE includes targeted therapy of underlying illness, anticoagulants, and cardiac surgery, if there is severe valvar dysfunction or a large vegetation. In conclusion, NBTE represents a diagnostic challenge for clinicians because of its clinical and echocardiographic overlap with those of infective endocarditis. Especially concurrent pulmonary and multiple systemic embolisms, awareness of variable and clueful characteristics of NBTE is vital for timely intervention and appropriate management to improve patient outcomes.

Declaration of competing interest

There are no conflicts of interest to be declared by the authors.

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References

1. Lin KP, Yeh TK, Chuang YC, Wang LA, Fu YC, Liu PY. Blood culture negative endocarditis: a review of laboratory diagnostic approaches. *Int J Gen Med* 2023;16:317–27.
2. González Quintela A, Candela MJ, Vidal C, Román J, Aramburo P. Non-bacterial thrombotic endocarditis in cancer patients. *Acta Cardiol* 1991;46:1–9.
3. Llenas-García J, Guerra-Vales JM, Montes-Moreno S, López-Ríos F, Castelbón-Fernández FJ, Chimeno-García J. [Nonbacterial thrombotic endocarditis: clinicopathologic study of a necropsy series]. *Rev Esp Cardiol* 2007;60:493–500.
4. Oueida Z, Scola M. Ovarian clear cell carcinoma presenting as non-bacterial thrombotic endocarditis and systemic embolization. *World J Oncol* 2011;2:270–4.
5. Lin YK, Lee JT, Yang FC, Sung YF, Kao HW, Lin CC, et al. Systemic embolic events with nonbacterial thrombotic endocarditis as manifestations of recurrent ovarian clear cell carcinoma. *Taiwan J Obstet Gynecol* 2015;54:625–8.

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