Large Non-Bacterial Vegetation Causing Acute Aortic Regurgitation
— Unexpected Finding at Autopsy —

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Figure. (A) Chest X-ray showing cardiomegaly and pulmonary edema. (B–D) Transthoracic echocardiography: (B) short-axis view and (C) parasternal long-axis view showing thickening of the aortic valve due to vegetation. (D) Color Doppler imaging showed severe aortic regurgitation. (E–H) Autopsy findings. (E,F) Gross photographs of aortic valve: (E) short-axis view showing large vegetations involving the aortic valve, which restricted the ability of the valve leaflets to close; (F) long-axis view showing large vegetations that extended to the left ventricle (arrowhead). (G,H) Hematoxylin-eosin stain histological section through the aortic leaflet. (G, original magnification ×40; H, ×200). The vegetations consisted of fibrin-rich thrombi with slight inflammatory cells and did not show any evidence of bacteria or tumor tissue. No destruction of the aortic valve (asterisk) was detected.
A 53-year-old woman who had undergone surgery and chemotherapy for stage IA ovarian serous adenocarcinoma 1 ½ years previously, was admitted for acute left hemiparesis. Magnetic resonance imaging showed multiple cerebral infarctions, and computed tomography indicated a metastatic liver tumor and ascites. Venous ultrasonography showed acute thrombosis in the left lower leg, but blood analysis was negative for hematological disorders. The patient was therefore diagnosed with Trousseau’s syndrome combined with recurrent ovarian cancer. Unfractionated heparin infusion was initiated immediately, and rivaroxaban was given on day 7 of hospitalization. Anticoagulation therapy had to be stopped, however, because of intracranial bleeding.

On day 26, the patient developed acute heart failure (Figure A). Transthoracic echocardiography showed severe aortic regurgitation with vegetations (Figure B-D). This had not been detected before the surgery for ovarian cancer. Infective endocarditis was suspected, and an antibiotic was initiated. On day 29, superior mesenteric artery thrombus developed, and anticoagulation therapy with heparin was re-administered, but multiple organ failure developed rapidly, and the patient died on day 38. Autopsy showed recurrent ovarian cancer; multiple renal, and splenic infarctions; and bowel necrosis. The ability of the aortic valve to close was restricted by the large vegetations (Figure E,F). Microscopy indicated non-bacterial thrombotic endocarditis (NBTE), including a fibrin-rich thrombus, preservation of the architecture of the cusp, and the absence of bacteria or tumor tissue (Figure G,H). Based on the autopsy results, it was concluded that NBTE associated with recurrent ovarian cancer had caused acute aortic regurgitation and heart failure.

NBTE is most commonly associated with malignancy and occurs in 4% of all advanced-stage cancers.1 NBTE-related vegetation is more friable and prone to systemic embolization compared with the vegetations associated with infective endocarditis.2 Embolization of the brain, kidneys, spleen, extremities, and coronary artery are the most common, occurring in up to 40% of cases.3 Malignancy-associated NBTE-related vegetation mostly affects the mitral and aortic valves, and such lesions are typically small (<1 cm in diameter).3 On histology such vegetation is composed of fibrin and platelet aggregates and is free from bacteria and tumor tissue.6 Anti-tumor therapy and systemic anticoagulation with heparin are crucial for preventing recurrent embolization in NBTE and Trousseau’s syndrome.7 Vitamin K antagonists are less effective at preventing recurrent thromboembolization.8 The effects of direct oral anticoagulants have not yet been examined in sufficient detail. Unfortunately, in the present case, anticoagulation therapy induced intracranial bleeding; therefore, the interruption of the anticoagulation therapy resulted in excessive enlargement of the vegetation and systemic embolization. On autopsy, an unexpected large vegetation was found, which had induced acute aortic regurgitation and heart failure. The current report describes a very rare case of large aortic vegetation discovered on autopsy.

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References