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Nonbacterial Thrombotic Endocarditis

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INTRODUCTION

Nonbacterial thrombotic endocarditis (NBTE) is an uncommon condition that describes aseptic lesions of the heart valves.[1] Historically, NBTE has been synonymous with marantic endocarditis, Libman-Sacks endocarditis, and verrucous endocarditis. NBTE differs from culture-negative endocarditis, which describes infectious origins based on clinical history and symptomatology that have not been readily identified or difficult to culture.[2] It is most commonly a postmortem finding (autopsy series 0.9 - 1.6%) and seen in advanced malignancy.[2]

Based on autopsy reports, patients with an underlying malignancy are six times more likely to develop NBTE compared to the general population (1.25% vs. 0.2%).[2] Solid tumor cancers are associated more commonly with NBTE, with mucin-secreting adenocarcinomas having the highest observed rates. The pathogenesis of NBTE is unclear, but endothelial injury plus hypercoagulability are thought to work synergistically. Interestingly, heart valve vegetations in NBTE have been discovered to be distinctly different from infectious vegetations. Due to the lack of an inflammatory reaction at the site of deposition, NBTE valvular vegetations are dislodged easily, explaining their higher rates of embolization and end-organ infarction.[2] This report presents a rare case of NBTE in a patient with newly diagnosed cancer.

CASE REPORT

A 29-year-old female with a history of alcohol abuse and recurrent pancreatitis presented to her primary care physician complaining of severe dyspnea on exertion, fatigue, and pallor. The patient was referred to the emergency department for further evaluation after outpatient laboratory work revealed significant pancytopenia. She reported subjective fever, chills, sore throat, and productive cough. She denied any symptoms of bleeding at the time. The patient never used tobacco products and quit drinking alcohol several years prior to hospital admission.

Family history was remarkable for a maternal grandfather with history of leukemia and Hodgkin's lymphoma. Her vital signs on admission were remarkable for tachycardia. Physical examination was significant for skin pallor and dry mucosal. Complete Blood Count on presentation showed hemoglobin of 4 g/dl, platelets of 56x109/L, and white blood cells of 14x109/L with 40% peripheral blasts, but the Disseminated Intravascular Coagulopathy panel was negative. Peripheral blood flow cytometry was concordant with a diagnosis of acute myelomonocytic leukemia (AMML). She was admitted to the hospital for transfusions and further workup.

A bone marrow biopsy confirmed the diagnosis of AMML with complex karyotype t (16;16) as well as negative NPM1 and CEBPA mutations. An initial echocardiogram revealed an ejection fraction of 55% with no valvular abnormalities. She was started on broad spectrum antibiotics and blood cultures were collected on admission. Induction chemotherapy was initiated with cytarabine and daunorubicin. Subsequent to chemotherapy treatment, her respiratory status rapidly deteriorated, eventually requiring intubation with worsening bilateral infiltrates on chest x-ray. Bronchoscopy done shortly after intubation was consistent with diffuse alveolar hemorrhage (DAH).

The patient developed neutropenic fever requiring her antibiotics to be expanded to vancomycin, meropenem, acyclovir, and voriconazole. Multiple sets of blood cultures were negative even though she continued to be persistently febrile with no source of infection.

A week after being intubated, she suddenly developed signs of neurological damage including not withdrawing to pain and absent brainstem reflexes; a head CT could not be done to due respiratory instability. She quickly developed multi-organ failure and required continuous renal replacement therapy (CRRT). The patient also developed left leg ischemia caused by an arterial clot in the deep femoral artery.

Family discussion led to comfort care. Autopsy revealed a massive non-hemorrhagic infarct involving left frontal, left parietal, and left occipital lobes of the brain resulting from an embolus originating from fibrin vegetation on the aortic valve (Figure 1A). There was pulmonary hemorrhage involving primarily the right and left lower lung lobes (Figure 1B). In addition, fibrin vegetations on the tricuspid valve were noted (Figure 1C). Multiple infarcts in the left and right kidney, as well as the spleen, were noted (Figure 1D). Fibrin thrombi within capillaries of both kidneys and lungs was compatible with disseminated intravascular congestion.

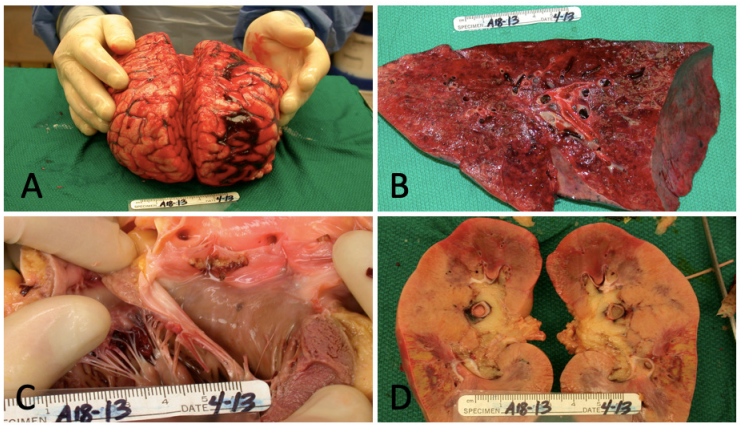

Figure 1. Postmortem evidence of nonbacterial thrombotic endocarditis symptomatology. A) Whole brain exam showing massive non-hemorrhagic infarct affecting multiple territories. B) Pulmonary hemorrhage. C) Fibrin vegetation on the aortic valve. D) Infarcts in bilateral kidneys.

DISCUSSION

NBTE is a rare condition describing sterile thrombi deposition on heart valves in the absence of bacterial growth in blood cultures.[1] NBTE is clinically significant as it increases the risk of systemic embolic events including stroke (a rare event).[3] This case is unusual in that the embolic phenomenon was fatal, as most cases are discovered incidentally post-mortem and are not well described in the literature. Microscopically, NBTE results from agglutinated platelets mixed with strands of fibrin, which is unusual in this case of severe thrombocytopenia.[4] NBTE is most commonly associated with advanced malignancy (80% of cases), systemic lupus erythematosus, and antiphospholipid syndrome. The most common symptom of NBTE is embolic phenomena in up to 50% of patients rather than valvular dysfunction.[5] In this case, NBTE led to significant morbidity and mortality from kidney failure requiring CRRT and massive stroke. Even though NBTE has a low incidence, when cultures yield negative results and significantly thrombogenic patients are not responsive to empirical antibiotic treatment, the possibility of NBTE should be considered.[6]

CONCLUSION

This report described a rare case of NBTE in a young patient with a new diagnosis of Acute Myeloid Leukemia (AML). NBTE is a rare condition associated with high mortality and morbidity rates. It is uncommonly reported in patients with AML and is often a postmortem diagnosis but can present with organ failure from infarction. Diagnosis of NBTE requires a high degree of clinical suspicion especially in patients with malignancy who have clinical features suggestive of endocarditis with a negative workup for an infectious etiology.

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