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Case report

A classic and fatal case of *Streptococcus mutans* subacute bacterial endocarditis; A now potentially underappreciated disease

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ABSTRACT

Acute bacterial endocarditis is now common and easily suspected and recognized in the setting of prosthetic valves, injection drug use, or bacteremia with virulent organisms. Conversely, subacute bacterial endocarditis has drastically decreased in incidence, and recognition may be further hampered by the indolent non-specific presentation. Delayed diagnosis is common and can lead to serious complications and fatalities. We describe a patient found to have *Streptococcus mutans* subacute bacterial endocarditis, who presented with classic risk factors and findings, and who died shortly after presentation due to hemorrhagic conversion of an embolic stroke in the setting of anticoagulation. It is critical that all cases of streptococcal bacteremia be appropriately evaluated and treated, and that *Streptococcus* spp. not ever be routinely considered a blood culture 'contaminant'.

Introduction

Endocarditis is characterized by a vegetation composed of platelets, fibrin, and microorganisms on the endocardial surface [1,2]. Vegetations usually are localized to a valve but can be found on any damaged portion of the endocardium. While acute bacterial endocarditis is common in the era of prosthetic valves and intravenous drug use, the incidence of subacute bacterial endocarditis (SBE) has drastically decreased [3,4]. SBE is caused by organisms with low virulence, such as the viridans streptococci, which exist as normal oral flora. Persistent bacteremia is characteristic, and constitutional symptoms such as low-grade fevers, chills, night sweats, malaise, fatigue, loss of appetite, weight loss, and anemia predominate. Serious complications result from circulating immune complexes and embolism/infarction rather than the infectious organism itself. The course is protracted, with diagnosis often delayed [1,2].

'Vascular phenomena' are the result of emboli; common sites include the spleen, kidneys, coronary vessels, lungs, brain, and digits (Janeway lesions). Most are clinically insignificant except those involving the coronary and cerebral circulations. Osler nodes, Roth spots, subungual hemorrhages, petechia, splenomegaly, and arthritis represent immune complex deposition or 'immune phenomena'. In the kidneys, this deposition causes a vasculitic glomerulonephritis, and hematuria is nearly universal. Deposition in small vessels can cause a leukocytoclastic vasculitis that manifests as cutaneous purpura. Rheumatoid factor, cryoglobulins, and macroglobulins may be present [1,2].

The Duke criteria were originally developed in the era of subacute bacterial endocarditis, and describe and create criteria for the diagnosis of endocarditis; the major Duke criteria include evidence of bacteremia and endocardial involvement. Minor criteria include the vascular and immune phenomena noted above, fever, a predisposing condition, and other microbiological or echocardiographic evidence not meeting the major criteria [1,2]. Given that vascular and immune phenomenon take time to develop, they are not seen in acute cases of endocarditis (those typically caused by more virulent pathogens), making Duke criteria less likely to be positive in clinically suspected cases of acute endocarditis.

The mainstays of treatment for all infectious endocarditis cases are antimicrobials and surgery if indicated. Anticoagulation was tried as an adjunct treatment in the past as a way to improve penetration of antimicrobials into the vegetation. It was later learned that anticoagulation provides no benefit, increases risk of intracranial hemorrhage, and is inadvisable unless a separate indication exists. Use in prosthetic valve endocarditis remains controversial [5]. Mortality of SBE was 100 % in the pre-antimicrobial era and remains so in the absence of antimicrobials.

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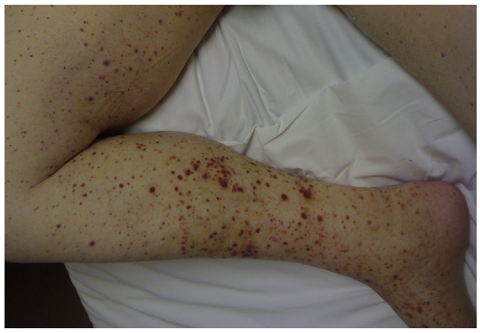

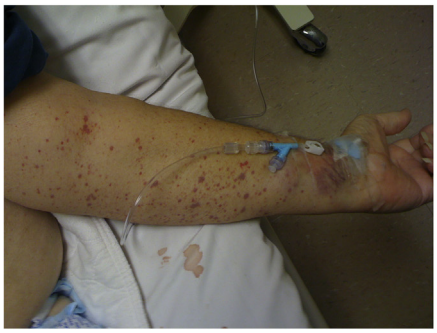

Figs. 1 and 2. Petechial and purpuric rash on extremities.

Mortality has dropped to 15–30 % since the introduction of antimicrobials but survival rates decrease with delays in recognition and treatment [2].

Subacute bacterial endocarditis causes significant morbidity and mortality when left untreated. We describe a patient found to have *Streptococcus mutans* subacute bacterial endocarditis, who presented with renal failure, heart failure, and vasculitic rash, and who died shortly after presentation due to hemorrhagic conversion of an embolic stroke in the setting of anticoagulation.

Case

A 64 year old man presented with six months of intermittent chills, night sweats, fatigue, dyspnea on exertion, leg swelling, arthralgias, vomiting, diarrhea, unintentional 115-pound weight loss and a painful purple rash (Figs. 1 and 2). Evaluation six weeks earlier revealed acute kidney injury and rhabdomyolysis after a fall; the patient attributed the fall to profound weakness. Esophagogastroduodenoscopy, colonoscopy, computed tomography (CT) of chest, abdomen, and pelvis, and routine blood work during that hospitalization revealed only acute kidney injury caused by rhabdomyolysis and corrected by intravenous fluids.

Past medical history included hypertension, arthritis, venous thromboembolic disease and an uncharacterized heart murmur. The patient was on life-long warfarin. On physical examination, vital signs included temperature 37 °C, blood pressure 99/63 mmHg and pulse 70 bpm. The patient appeared chronically ill. Oral examination revealed poor dentition and dry mucous membranes. Lungs were clear and the abdomen was benign without organomegaly. A 3/6 holosystolic murmur was heard best over the cardiac apex with radiation to the left axilla. No jugular venous distention was seen. Peripheral pitting edema and non-blanching, palpable petechiae and purpura were present on all extremities. Full neurologic examination was unremarkable except for generalized weakness.

Laboratory studies revealed normocytic anemia with hemoglobin 8.4 g/dl and renal insufficiency with blood urea nitrogen 95 mg/dl and creatinine 5.2 mg/dl. Other abnormal laboratory values included sodium 130 meq/L, prothrombin time 23 mg/dL, partial thromboplastin time 34.1 mg/dL, erythrocyte sedimentation rate 98 mm/hr, albumin 2.5 g/dL, trace cryoglobulins, C3 88 mg/dl, and C4 22 mg/dl. Free kappa and lambda were elevated at 56.2 mg/dl and 218 mg/dl respectively. Peripheral blood smear showed microcytic red cells with anisopoikilocytosis, burr cells, elliptocytes, and few schistocytes. Urine studies showed a protein to creatinine ratio 0.57 and 80–90 RBC/hpf, consistent with glomerulonephritis. Serum protein electropheresis revealed an abnormal broad band of IgA lambda; urine protein electropheresis showed no spike. CT of the abdomen showed only splenomegaly (Fig. 3). In preparation for renal and skin biopsies, intravenous heparin was substituted for warfarin.

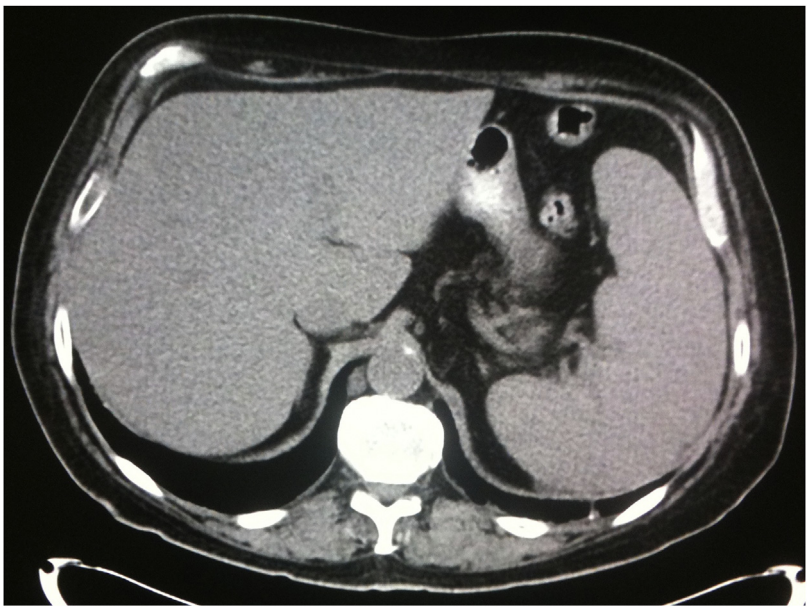

Fig. 2. {([Fig. 3])} CT abdomen: splenomegaly.

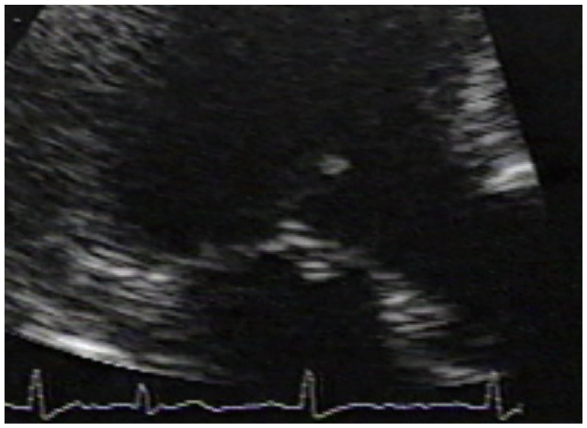

Fig. 3. {([Fig. 4])} TTE: vegetation on mitral valve (echodensity in center).

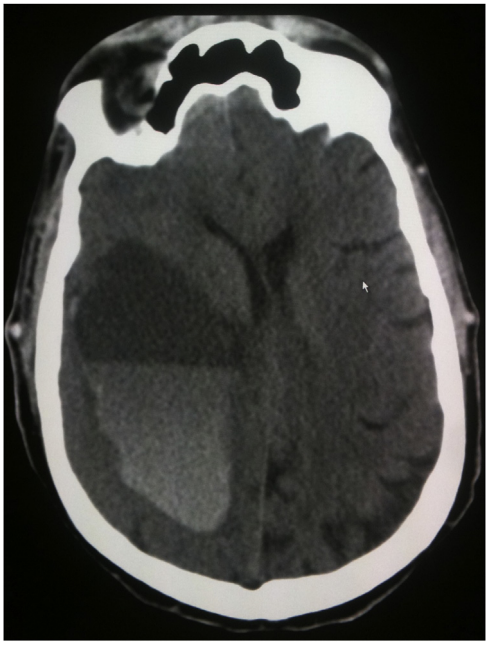

Fig. 4. {([Fig. 5])} CT head: massive intracranial hemorrhage with edema and midline shift.

Transthoracic echocardiogram revealed normal biventricular size and systolic function, a 0.5 × 0.4 cm echodensity on the mitral valve (Fig. 4) and moderate pulmonary hypertension with right ventricular systolic pressures of 45–50 mmHg. Blood cultures subsequently were reported as growing *Streptococcus mutans*, and further inquiry into the prior admission revealed blood cultures positive for a microaerophilic *Streptococcus*, which was described at the time as a 'probable contaminant' by the medical team. Soon after initiation of antimicrobials, the patient suffered a fatal intracranial hemorrhage (Fig. 5).

Discussion

Subacute bacterial endocarditis is now uncommon, but fatal if unrecognized. In this patient's case, the diagnosis was not initially pursued during his first hospital admission despite bacteremia, a heart murmur, and classic symptoms. He met both major clinical Duke criteria, and four of five minor criteria (he could not meet the fifth criteria 'positive blood culture not meeting major criteria'). The vegetation was found on the atrial side of the mitral valve, the expected site of a regurgitant jet in mitral insufficiency, which was consistent with his examination findings and history of murmur. His poor dentition and known history of murmur provided an ideal setting for SBE to develop.

This patient was prescribed life-long anticoagulation for history of venous thromboembolic disease; discontinuation of anticoagulation for suspicion of SBE would increase risk for pulmonary embolus, while use of anticoagulation in the setting of endocarditis would increase risk of intracranial bleeding. Unfortunately continuation of anticoagulation lead to a fatal intracranial hemorrhage, which appeared to be in the setting of previous infarct, likely from a septic emboli.

This case highlights both embolic and immune complex mediated complications of subacute bacterial endocarditis including heart failure, renal failure, presumed leukocytoclastic vasculitis, and cerebral embolism, as well as propensity for intracranial bleeding in the setting of anticoagulation. This case also serves to provide an unfortunate example of the dangers of delayed diagnosis in SBE and in use of anticoagulation in this setting.

Informed consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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CRediT authorship contribution statement

SA Schmalzle: Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

None.

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