

Microscopic polyangiitis following recurrent *Staphylococcus aureus* bacteremia and infectious endocarditis.

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ABSTRACT

Secondary vasculitis resulting from unusual pathologic expressions of infections has been described and has important clinical significance. Infectious agents have also been implicated in the pathogenesis of different primary systemic necrotizing vasculitides. Infectious endocarditis is of particular importance in the differential diagnosis of a patient presenting with ANCA associated vasculitis. We report a well-documented case of a patient with recurrent Staphylococcus aureus bacteremia who developed bacterial endocarditis and also fulfilled the Chapel Hill Conference definitions for microscopic polyangiitis. To the best of our knowledge, it is the second case of bacterial endocarditis associated with both pANCA and anti-MPO specificity that fulfilled definitions for systemic necrotizing vasculitis. We emphasize the potential pathogenic role of infection as the trigger factor for the development of systemic vasculitis.

Introduction

Secondary vasculitis resulting from unusual pathologic expressions of infections has been described and has important clinical significance (1-3). Infectious agents may also contribute to the activity and possibly to the mechanisms associated with the so-called "idiopathic" primary vasculitic syndromes (1, 2). Although, *Staphylococcus aureus* (*S. aureus*) has been implicated in the pathogenesis of Wegener's granulomatosis (4), the specific role of bacterial infections in other forms of ANCA-associated vasculitides such as Churg-Strauss syndrome and microscopic polyangiitis (MPA) is unknown. We describe a patient with recurrent *S. aureus* bacteremia who developed infectious endocarditis and MPA.

Case report

A 71-year-old woman was admitted to the hospital because of fever, abdominal pain and palpable purpura. Three weeks before admission, she had been diagnosed as having gangrenous cholecystitis and *S. aureus* bacteremia. Due to this, she was engaged on antibiotic treatment. Surgery to remove the gall-

bladder was also performed. At the time of admission, the physical examination showed fever (temperature 37.8°C), abdominal distention and palpable purpura in the lower extremities and buttocks. Also, a systolic murmur and paresis on dorsiflexion of the left foot were found. The erythrocyte sedimentation rate was 55 mm/h (normal value: < 20 mm/h). C-reactive protein was 23.5 mg/L (normal value: < 5 mg/L). Blood cell count showed 3,530,000/mm³ erythrocytes (normal value: 4,200,000-5,400,000/mm³), hemoglobin 10.6 g/dl (normal value: 14.0-16.0 g/dl), hematocrit 31.9% (normal value: 37%-47%), 9,700/mm³ leukocytes (normal value: 4,800-10,800/mm³) with 76.6% neutrophils, and platelet count 214,000/mm³ (normal value: 130,000-400,000/mm³). Fibrinogen was 456 mg/dl (normal value: 170-400 mg/dl) but coagulation parameters were normal. Serum creatinine level was 1.31 mg/dl (normal value: 0.40-1.30 mg/dl). Antinuclear antibodies, anti-native DNA, C3, C4, rheumatoid factor, serum IgA, cryoglobulins, anti-cardiolipin antibodies, and hepatic function tests were negative or normal. Hepatitis B and C serology was also negative. Indirect immunofluorescence disclosed p-ANCA testing positive at a titer of 1:160, and anti-MPO antibodies were also found by ELISA at a concentration of 134 U/ml. Urinalysis showed microscopic hematuria and red blood cell casts. Chest radiograph was normal. Electromyography showed left axonal neuropathy with spontaneous activity, which was consistent with mononeuritis multiplex. A skin biopsy disclosed a necrotizing arteritis involving small and medium sized arteries with fibrinoid necrosis and neutrophil infiltration. No IgA immune-deposits were found. Tissue biopsy cultures were sterile. A gastroscopy showed an edematous, inflamed, and erythematous hemorrhagic petechial mucosa. A duodenal biopsy showed neutrophil infiltration accompanied by hematic extravasation. Six blood cultures were positive for *S. Aureus*. A routine transthoracic echocardiography disclosed mobile vegetation on the mitral valve. Transesophageal echocardiography

confirmed this finding (Fig. 1).

The patient fulfilled the Duke criteria and also the Chapel Hill Consensus Conference definitions for bacterial endocarditis and MPA (5, 6) respectively. Intravenous cloxacillin (3 g/every 6 hours), oral rifampicin and steroid therapy (initially 15 mg of methylprednisolone every six hours) were started. Two weeks later, because of clinical improvement, methylprednisolone therapy was switched to oral prednisone. Antibiotic therapy was maintained for 6 weeks. The patient's condition progressively improved with total resolution of symptoms and clinical manifestations. Normalization of renal function and urinalysis was also achieved. No valve surgical replacement was required. Steroid therapy was tapered until complete discontinuation 12 months later. At that time, ANCA antibodies were negative by immunofluorescence and ELISA.

Discussion

In the clinical practice, a combined positivity for ANCA using both immunofluorescence and ELISA testing and the presence of pathological findings of vasculitis on a tissue biopsy (7) are required to establish a diagnosis of ANCA-associated primary systemic necrotizing vasculitis.

Infections have been considered to be one of the potential triggering factors for ANCA-associated vasculitides (1, 4, 8). Bacterial endocarditis can mimic clinical vasculitis (3, 9, 10) and, due to this, it is of particular importance the consideration of this entity in the differential diagnosis of idiopathic systemic necrotizing vasculitides. In this regard, bacterial endocarditis has also been reported to be associated with ANCA antibodies (2, 4, 8). However, to the best of our knowledge only a single case of bacterial endocarditis associated with both p-ANCA and anti-MPO specificity that also fulfilled definitions for systemic necrotizing vasculitis has previously been reported (11).

In this report we describe a well-documented case of recurrent *S Aureus* bacteremia that fulfilled both the Duke cri-

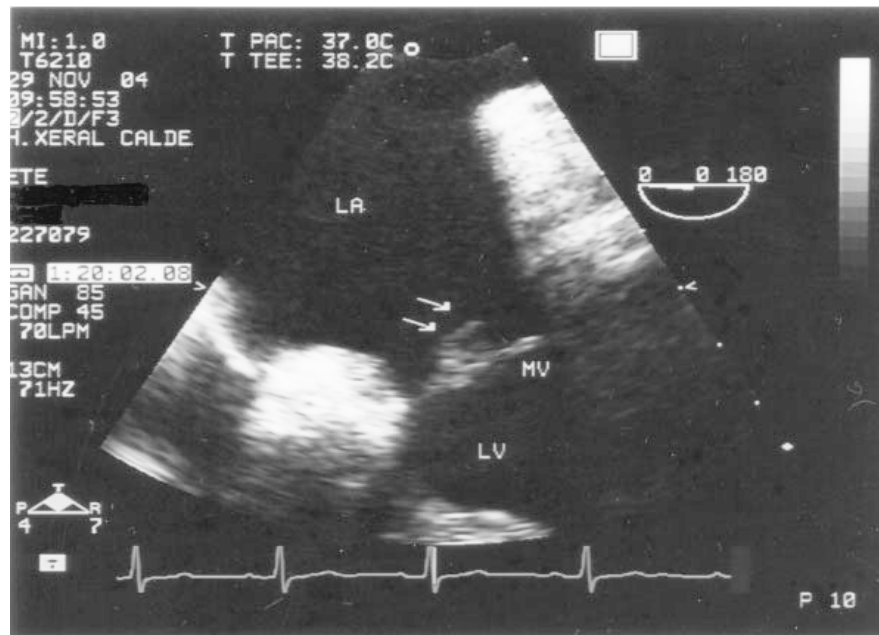


Fig. 1. Transesophageal echocardiogram showing mobile vegetation attached to the anterior leaflet of the mitral valve (arrows).

LA: left atrial; LV: Left ventricle; MV: mitral valve.

teria for bacterial endocarditis (5) and the Chapel Hill Consensus Conference definitions for MPA (6). In our case, the close relationship between both diseases could support a potential etiological role of infection as the triggering factor for the development of systemic necrotizing vasculitis.

Chronic stimulation of staphylococcal superantigen reactive T cells may lead to induction or stimulation of ANCA-production by B cells. A marked increase in the expression of the variable region genes of the B chain of the T-cell receptor was found in patients with MPA compared to controls and other forms of vasculitis (11).

In conclusion, our case constitutes a good example of potential association between infection and systemic necrotizing vasculitis. Further reports on similar cases are needed to improve our knowledge on the potential implication of infection in the pathogenesis of systemic vasculitides.

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