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Granulomatosis with Polyangiitis (Wegener Granulomatosis) Mimicking Infective Endocarditis

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Abstract

Introduction

Infective endocarditis (IE) has been reported to mimic granulomatosis with polyangiitis (GPA) and to test positive to antineutrophil cytoplasmic antibodies (ANCA), which may lead to a misdiagnosis and inappropriate treatment.

Case presentation

We report a case of a 59-year-old man admitted for purpura, gangrenous digital infarcts and glomerulonephritis. The diagnosis of IE was initially considered on the basis of heart murmur and two positive haemocultures to corynebacterium. Ineffectiveness of antimicrobial therapy and further neurological and nasal manifestations supported the diagnosis of GPA.

Conclusions

IE should be ruled out before initiation of immunosuppressive treatment. If the disease progresses despite antimicrobial treatment, vascular diseases should be rapidly taken into account in differential diagnosis and treated early to avoid fatal complications.

Keywords: Granulomatosis with polyangiitis, endocarditis, haemocultures, antineutrophil cytoplasmic antibody (ANCA)

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Introduction

Infective endocarditis (IE) may present with a variety of immunologic phenomena, including small vessel vasculitis such as cutaneous purpura and glomerulonephritis. These may mimic the clinical manifestations of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, especially granulomatosis with polyangiitis (GPA) [1].

We report a case of GPA that presented initially with gangrenous digital infarcts, purpura, general signs and glomerulonephritis with positive haemocultures, mimicking IE.

Case report

A 60-year-old male with a past medical history of chronic sinusitis was admitted for alteration of general state, prolonged fever, vascular purpura and Raynaud's phenomenon. He was a cigarette smoker (80 pack years) and did not take any medication. He reported having a fever, weakness, weight loss and Raynaud's phenomenon for a month and leg oedema, inflammatory arthralgia and macroscopic haematuria for 15 days. Physical examination showed blood pressure of 150/90 mmHg and fever (*T*=39°C). The following were observed: bilateral low extremities oedema, digital necrosis (*Fig. 1*) and extensive vascular purpura on the legs (*Fig. 2*).

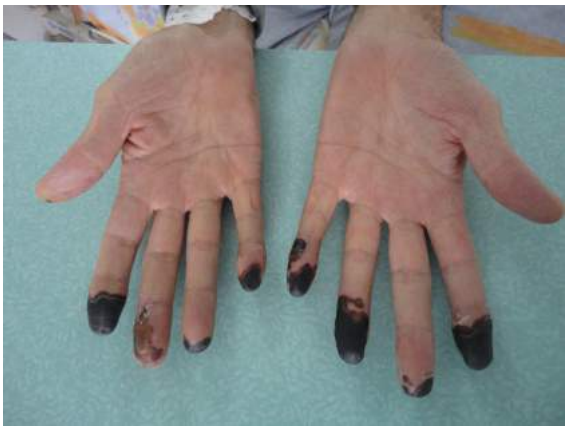

Figure 1: Digital necrosis

Heart examination revealed an aortic murmur. Urinary sediment analysis showed occult blood of 3+ and protein of 3+.

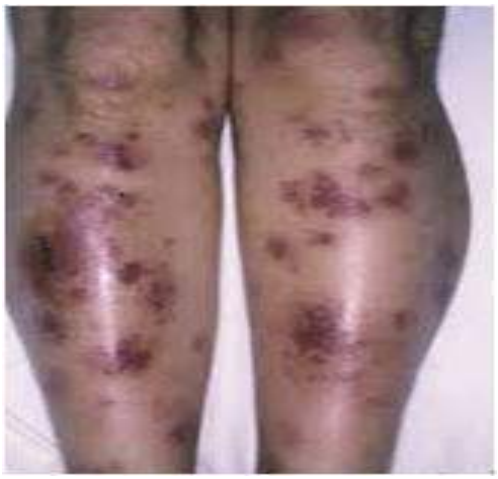

Figure 2: Vascular purpura

The other systems were unchanged. Laboratory values showed anaemia (Hb 10.7 g/dl, VGM 82 fl), leukocytosis (white blood cells 15,000/µl, neutrophils 9000/µl), increased inflammatory indices (C-reactive protein 175 mg/l, erythrocyte sedimentation rate 117 mm), low prothrombin ratio 55% (80%–100%) and renal insufficiency (urea 7.9 mmol/l, creatinine 120 µmol/l). Electrophoresis showed serum protein at 65 g/l and serum albumin at 27.3 g/l. Urine analysis revealed proteinuria at 4.5 g/day and cytobacteriological examination of urine showed a haematuria at 900/mm3 and leukocyturia at 25/mm3 with negative culture. C3 level was normal (1.3 g/l) and C4 level was consumed (0.07 g/l). Cryoglobulinaemia was negative. Hepatitis B, hepatitis C and HIV serologies were negative. Two blood cultures were positive to corynebacterium. Chest X-ray and electrocardiogram were without abnormalities. Transthoracic and transoesophageal echocardiography did not show any vegetations. Skin biopsy revealed leukocytoclastic vasculitis. Kidney biopsy was impossible because of the low prothrombin rate.

The diagnosis of IE was made based on general signs, cardiac murmur, vascular purpura, glomerulonephritis, inflammatory biological syndrome and positive haemocultures. The patient was treated with antibiotics: vancomycin i.v. 500 mg/day and gentamycin i.v. 80 mg/day adapted to renal function and antibiogram.

Two weeks later, the patient had persistent fever and developed odynophagia and paraesthesia. The oto-rhino-laryngological examination revealed mucosal abnormalities of the nose .Tendon reflexes were abolished. Inflammatory indices and creatinine levels (640 µmol/l) had increased. A head scan revealed chronic pansinusitis. Electromyography revealed severe mono-neuropathy multiplex. Nerve and muscle biopsy showed vasculitis. Capillaroscopy showed specific microangiopathy. His serum tested strongly positive for ANCA against PR3 at 847 UI/ml (normal <5 U/ml). The diagnosis of GPA was retained. We started appropriate induction therapy with a three-pulse dose of methylprednisolone at a dose of 1 g/day relieved with oral corticosteroids at a dose of 1 mg/kg/day for 4 weeks. He received a six-pulse dose of cyclophosphamide every 15 days for the first three pulses and every three weeks. Four months after the onset of symptoms, clinical signs of active disease were absent. Inflammatory indices, creatinine levels (80 µmol/l) and proteinuria (1.5 g/24 h) had declined.

Discussion

We reported a male patient with two positive cultures to corynebacterium and c-ANCA/PR3. Clinical features including cardiac murmur, purpura and glomerulonephritis associated with positive blood culture for corynebacterium enabled an initial diagnosis of IE. The characteristic abnormalities seen during nasal endoscopy, together with neuropathy and ineffectiveness of antibiotic therapy, suggested a diagnosis of GPA, and this was corroborated by the results of the immunological tests and the pathological findings from nerve and muscle biopsy.

The diagnosis of GPA may be a challenge and it is difficult to distinguish it from other diseases like IE [2–4]. Some clinical features of GPA and IE overlap, including vegetations detectable by echocardiography, inflammatory signs and renal involvement [5]. Organ involvement in IE is usually limited to the skin and kidneys. Proteinase-3/c-ANCA (PR3/C-ANCA) is highly associated with GPA, with a sensitivity and specificity of >90%, as reported in our case. IE may also manifest with positive ANCA [6–8]. It has been suggested that the induction of ANCA in infectious diseases, more specifically in IE, may occur through non-specific B-cell activation or autoimmunization after the release of PR3 or MPO from neutrophils, and PR3/C-ANCA is the most common ANCA type [9].

Some pertinent differentiating features including splenomegaly, hypocomplementaemia, elevated RF, cryoglobulinaemia, positive antinuclear and anticardiolipin antibodies and positive blood cultures, were found to be more indicative of IE than GPA [4]. Our case fulfilled one major (two positive cultures of blood samples drawn >12 h apart) and three minor (fever of >38°C, immunologic and vascular phenomena) Duke's criteria. These findings, associated to hypocomplementaemia, were highly suggestive of a clinical diagnosis of IE.

On the other hand, initially, there was no convincing evidence of GPA. Biopsies of affected tissues are important to confirm a diagnosis of GPA and to rule out other diseases. Unfortunately, in our case, kidney biopsy was impossible because of the low prothrombin ratio, and skin biopsy showed leukocytoclastic vasculitis. The diagnosis of GPA was retained after two weeks on the basis of the ineffectiveness of antibiotics, neurological and nasal manifestations, rapidly

progressive renal failure and the results of nerve and muscle biopsies. In our case, one possible reason for the positive blood culture may have been a contamination.

Considering the initial diagnosis of IE, our patient was treated with antibiotics. It is essential to distinguish GPA from IE as the immunosuppressive treatment used to treat it is potentially toxic; it could aggravate the infection and have life-threatening consequences. So, before the initiation of effective therapy of GPA, IE must be ruled out rapidly. In fact, the mean duration of survival of adults with untreated GPA was merely 5 months, with 82% of the patients dying within the first year and 90% within the second year [10]. The cause of death is usually acute renal failure or severe pulmonary manifestations with haemoptysis. Long-term survival became possible following the introduction of prednisone and cyclophosphamide [10].

Conclusion

In summary, this case of GPA is presented because of the differential diagnostic problems that arose. A correct diagnosis and prompt treatment are crucial, since the untreated disease is frequently fatal.

Learning Points

- IE may closely mimic the clinical manifestations of GPA.
- IE should be ruled out in any patient with vasculitis.
- ANCA can be positive in IE.
- Correct diagnosis and early treatment of GPA are crucial.

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