Vasculitis with mesangial IgA deposits complicating relapsing polychondritis

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Reprints will not be available from the authors.

Received on March 5, 2001; accepted in revised form on May 31, 2001. © Copyright CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 2002.

Key words: Systemic vasculitis, mesangial IgA deposits, relapsing polychondritis.

ABSTRACT

The authors report the case of a patient presenting with cutaneous, renal and neurologic vasculitis in the course of relapsing polychondritis (RPC).

A 78-year-old man presented with a palpable purpura of the lower limbs, high fever, arthralgias, delirium, and nephrotic syndrome. He had a history of relapsing polychondritis treated by corticosteroids. Renal biopsy showed diffuse endo- and extracapillary proliferative glomerulonephritis with mesangial IgA deposits. A spectacular regression of the symptoms was observed in response to pulse intravenous methylprednisolone.

Relapsing polychondritis is complicated by vasculitis in 25% of the cases. This vasculitis is characterized by cutaneous, neurologic and renal manifestations, usually occurring in elderly patients. Renal involvement is characterized by segmental and focal or diffuse necrotizing glomerulonephritis. The mesangial IgA deposits observed in our patient are rarely present in the course of RPC.

Renal manifestations identify severe forms of RPC, justifying systematic screening for renal complications.

Introduction

Relapsing polychondritis (RPC) is a rare autoimmune disease, characterized by recurrent episodes of inflammation followed by progressive destruction of the nasal, auricular and laryngotracheal cartilaginous structures. We report a case of relapsing polychondritis accompanied by cutaneous, neurologic and renal manifestations of systemic vasculitis.

Case report

A 78-year-old man was admitted for investigation of purpura of the lower limbs, present for the previous fortnight. He had a history of insulin-requiring diabetes for 8 years, and transurethral resection of a prostatic adenoma. The diagnosis of relapsing polychondritis was made at the age of 70, when he presented with arthralgias, auricular chondritis, erythema nodosum and sicca syndrome. He was treated with systemic corticosteroids and finally prednisolone 10 mg/day as a long-term treatment. No other treatment was used except insulin.

Clinical examination of this patient showed purpuric popular lesions associated with hemorrhagic vesicles and skin necrosis on the lower limbs, suggestive of skin vasculitis. The patient reported arthralgias affecting the knees and ankles without any local inflammatory signs. During the following days, he presented with fever (39°C), confusion, agitation, and disorientation with regard to time and space. His blood pressure was within the normal range and his neurologic examination showed no focal neurologic deficit.

Laboratory evaluation revealed nonspecific increased inflammatory activity (ESR: 83 mm at 1 hour; C-reactive protein: 126 mg/l); a polyclonal elevation of serum IgA to 7.14 g/l was also observed. A nephrotic syndrome was diagnosed with a proteinuria of 7 g/24 hours, hypoproteinemia of 54 g/l, hypoalbuminemia of 25 g/l, microhematuria (6 x 10^3/mm^3) and mild renal failure [serum creatinine increasing from 73 to 110 μmol/l]. Serum and urinary protein electrophoresis did not reveal any monoclonal immunoglobulins. Hepatitis B and C, HIV, parvovirus B19, and cytomegalovirus serologies were negative. Blood and urcultures were sterile and chest X-rays showed no sign of bronchopulmonary infection. Antinuclear and anti-DNA antibodies were negative. Cryoglobulinemia, anticardiolipid, antarticilag, anticollagen II and antineutrophil cytoplasmic antibodies (ANCA) were negative. Circulating immune complexes were at the upper limit of normal (3.8 μg/ml for a normal value less than 3.5 μg/ml) and complement levels were within the normal range. The cerebral CT scan showed age-related cortical atrophy. Cerebrospinal fluid analysis was normal apart from isolated raised CSF protein of 0.84 g/l. Cerebral MRI revealed non-specific white substance abnormalities which could be related to cerebral vasculitis or to age.

Skin biopsy specimens demonstrated a leukocytoclastic vasculitis with the presence of IgM and C3 deposits along the walls of the dermal capillaries.
Renal biopsy showed nearly 50% obsolescent glomeruli. Diffuse endocapillary proliferative glomerulonephritis was evidenced with segmental lesions, crescent formation and necrotic lesions in 6 of the 12 remaining glomeruli. Light microscopy also showed thrombotic occlusions and marked endarteric fibrosis of the small interlobular arteries. Immunofluorescence studies revealed mesangial IgA and C3 deposits.

The patient’s general, cutaneous and neurologic condition improved greatly after daily injections of methylprednisolone (1 g/day for 3 days), followed by prednisone 1 mg/kg/d. Ten days after beginning the treatment, he was no longer confused and feverish, the purpuric lesions had entirely disappeared and a slight laboratory inflammatory syndrome was observed (CRP: 50 mg/l). Three weeks later, the nephrotic syndrome had regressed and urinalysis revealed a moderate proteinuria of 1 g/24 h with no haematuria and this renal function was stable with a serum creatinine level of 100 µmol/l. During a 2-year follow-up the patient remained well on regular treatment with insulin and 10 mg/day prednisolone. No relapse has been observed during this follow-up (haematuria negative, proteinuria 0.39 g/l and serum creatinine level 109 µmol/l).

Comments
Relapsing polychondritis is an autoimmune disease characterised by recurrent inflammatory disorders of the cartilaginous structures, resulting in their fibrous degeneration (1). It has now been clearly established that this disease may be either isolated or associated with manifestations of other systemic diseases, such as rheumatoid arthritis, systemic lupus erythematosus and especially systemic vasculitis (2, 3). The manifestations of vasculitis are observed in approximately 25% of cases (2).

The diagnosis of systemic vasculitis was made in our patient because of evidence of multisystemic involvement: vesicular and necrotic purpuric skin lesions, arthralgias, confusion and nephrotic syndrome with impaired renal function revealing a diffuse proliferative glomerulonephritis with mesangial IgA deposits. Clinical and biological exams failed to reveal trigger factors (infections, drugs) explaining the release and symptoms improved on corticosteroids alone.

Cutaneous manifestations are observed in 35% to 62% of the cases of RPC (1). They often consist of inflammatory erythematous nodules on the limbs, resembling erythema nodosum, oral aphthous ulcers, and pseudofolliculitis similar to the mucocutaneous lesions of Behçet’s disease. The skin lesions of RPC are frequently due to a skin vasculitis, associated with skin nodules, livedo reticularis, palpable purpura, or a maculopapular, urticarial, or vesicular rash.

Neurologic manifestations have rarely been described during RPC (1, 4) and consist of acute or subacute neurologic symptoms such as headache, confusion, seizure, hallucinations, cranial or peripheral neuropathy and focal neurologic deficit. These neurological complications, more frequent during RPC with vasculitis, are probably related to a cerebral vasculitis. Rupture of a cerebral aneurysm or a cerebral vascular thrombosis may otherwise explain the neurologic abnormalities (1, 4).

Renal involvement is reported in 10% to 22% of the cases of RPC and generally affects elderly patients with systemic vasculitis (1, 5).

The most common renal manifestations are mild proteinuria, microscopic haematuria and rapidly progressive renal failure. The serum complement level is usually normal and antinuclear antibodies are negative. Circulating immune complexes are detected in rare cases (1,5,6). Renal biopsies show segmental and focal or diffuse glomerulonephritis with extracapillary crescents and necrotic lesions, resembling the histologic disorders observed during polyarteritis nodosa (PAN) and Wegener’s granulomatosis (1,5-7). Mesangial proliferation, glomerulosclerosis and more rarely, tubulo-interstitial nephropathy may also be observed in the course of RPC (1,5-7). Immunofluorescence microscopy of kidney biopsy specimens inconstantly shows IgM, IgG and complement deposits in the baseline membrane, capillary walls and mesangium, suggesting that immune complexes may play a role in the pathogenesis of the glomerular lesions of RPC (1,5-7).

We report a case of systemic vasculitis with necrotic and proliferative glomerulonephritis and mesangial IgA deposits, an association rarely reported in the course of RPC. Only 6 cases of diffuse proliferative glomerulonephritis with mesangial IgA deposits were found in the literature (5, 6,8). The role of circulating IgA in the pathogenesis of mesangial IgA deposit nephropathy has never been confirmed. The responsibility of IgA circulating immune complexes in the development of these nephropathies has also been suggested (6, 9, 10).

The presence of mesangial IgA deposits associated with a renal vasculitis, arthralgias and vesiculo-bullous purpura of the limbs is also suggestive of the diagnosis of Schönlein-Henoch purpura, a systemic vasculitis which has already been reported in the literature to be associated with RPC. Several arguments are in favor of this diagnosis: the combination of arthralgias, ‘palpable’ purpura, and nephrotic syndrome revealing a mesangiproliferative glomerulonephritis with IgA deposition and elevated serum IgA. Our patient did not present any gastrointestinal symptom, present in 75% of the cases of Schönlein-Henoch purpura. Furthermore, granular IgA deposits in dermal vessels, frequently observed in Schönlein-Henoch purpura, were also absent in our patient. However, these IgA deposits, although sensitive, are not specific for the diagnosis of Schönlein-Henoch purpura and their absence does not exclude this diagnosis. Chronic liver diseases and systemic lupus erythematosus, which sometimes show IgA deposits in the glomeruli, were excluded by the anamnesis and their specific tests in our patient.

Another differential diagnosis in this case of relapsing polychondritis is Wegener’s granulomatosis, a systemic vasculitis with articular, ocular, tracheobronchial, cutaneous and renal involvement (1). In fact, several cases of chondritis of the external ear have
been reported in the course of Wegener’s granulomatosis (WG) and a possible association between the two diseases has not been formally excluded (5, 11). Antineutrophil cytoplasmic antibodies giving a diffuse granular labelling of the cytoplasm (D-ANCA), Wegener’s granulomatosis, are also very manifestaions, the negative ANCA ence of mesangial IgA deposits.

In conclusion, the development of a systemic vasculitis in the course of RPC is a serious complication of the disease. It represents the third cause of death from RPC after respiratory and cardiovascular complications (13). The presence of renal involvement during RPC identifies a subset of patients with more severe disease reflected in a worse survival, whether or not they present signs of extrarenal vasculitis (2, 5). The insidious nature and diversity of renal manifestations justifies screening for proteinuria and/or haematuria during the course of relapsing polychondritis. The detection of renal complications reflects the severity of the disease and could justify the introduction of high-dose systemic corticosteroids, possibly combined with immunosuppressants and plasmapheresis (2, 6, 14, 15).

References
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