Case Report

MPO antibody-positive vasculitis in a patient with psoriatic arthritis and gold-induced membranous glomerulonephritis

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Introduction

Psoriatic arthritis is an inflammatory arthropathy associated with psoriasis and characterized by the absence of rheumatoid factor [1]. Renal involvement is not common during the course of psoriasis or psoriatic arthritis, apart from some cases of membranous [2] or IgA nephropathy [3]. It is also well known that membranous glomerulonephritis can complicate gold salt therapy [4], which is sometimes used for the treatment of joint symptoms in psoriatic arthritis. Although 8% of patients affected by psoriasis without vasculitic manifestation are positive for p-ANCA [5], to our knowledge there is no report of p-ANCA-positive crescentic glomerulonephritis with focal necrosis complicating psoriatic arthritis.

We describe a patient affected by psoriatic arthritis who developed membranous nephropathy after oral gold therapy. Occasionally, positive p-ANCA were detected. Nephrotic syndrome disappeared after discontinuation of oral gold preparations. A second renal biopsy, performed after 6 months because of reappearance of proteinuria and development of renal failure, disclosed focal necrotizing glomerulonephritis with extracapillary proliferations.

Case

In January 1993, a 52-year-old man with a 22-year history of psoriasis and a 10-year history of psoriatic arthritis was referred to our Department of Nephrology for proteinuria in nephrotic range (5.2 g/24 h). In the previous 3 years he had been successfully treated with non-steroidal anti-inflammatory drugs and oral gold therapy because of joint symptoms.

On admission physical examination was unremarkable. Blood pressure was 140/80 mmHg. Laboratory analysis revealed normal renal function (serum creatinine 1.03 mg/dl with n.v. <1.25 mg/dl, BUN 45 mg/dl with n.v. 15–50 mg/dl), total serum protein 7.9 g/dl (n.v. 6.4–8.0 g/dl), total serum albumin 3.8 g/dl (n.v. 3.66–4.8 g/dl), hypergammaglobulinaemia (serum gamma-globulins 2.01 g/dl with n.v. 0.84–1.34 g/dl) with elevated serum IgG (2297 mg/dl with n.v. 840–1660 mg/dl) and IgA (759 mg/dl with n.v. 90–359 mg/dl), elevated ESR (57 mm/h with n.v. <15 mm/h), Ra test 61 UI/ml (n.v. <50 UI/ml). Haemochrome, C-reactive protein, complement C3 and C4, antinuclear antibodies were normal. Urinalysis revealed haematuria (+++), proteinuria (1.8 g/24 h) and 10–20 erythrocytes/field. Testing for ANCA by indirect immunofluorescence revealed perinuclear staining (+++) and autoantibodies to myeloperoxidase were detected by radioimmunoassays (839 UI/ml with n.v. <10 UI/ml) [6]. Sonogram of the kidney was normal.

Percutaneous renal biopsy was performed. Light microscopy revealed seven glomeruli with thickened capillary walls containing discontinuous segmental subepithelial deposits, mild mesangial proliferation and mesangial deposits (Figure 1a). The interstitium and blood vessels were normal. Direct immunofluorescence showed diffuse granular staining with IgG (+) in glomerular basement membranes (Figure 1b), mesangial deposits with IgA (+/−) and IgM (+) and negative staining for C3, C4, C1q, and fibrinogen. Electron microscopy demonstrated small, intramembranous immune deposits localized to the epithelial side of the basement membrane. These findings were compatible with stage I–II membranous glomerulonephritis.

We did not prescribe any therapy because of the normal renal function and the disappearance of proteinuria after discontinuation of the gold-salts.

In June 1993 the patient was again admitted to our Department because of non-nephrotic proteinuria (1.8 g/24 h), microhaematuria and renal failure (serum creatinine...
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Fig. 1 a,b. First renal biopsy. (a) Capillary walls with stick appearance and with segmental subepithelial deposits (tric × 312.5). (b) Small segmental granular IgG deposits along capillary walls (I.F. × 312.5).

Fig. 2 a,b. Second renal biopsy. (a) Glomerulus almost completely filled by inflammatory infiltrate; partial destruction of Bowman’s capsule (argentic × 312.5). (b) Positive staining for fibrinogen in crescents and in an area of segmental intracapillary necrosis (I.F. × 312.5).

Creatinine 1.65 mg/dl. He did not report any joint symptoms and he was not taking any anti-inflammatory drug or oral gold therapy. Blood pressure was 130/90 mmHg. Laboratory analysis showed renal failure (serum creatinine 1.83 mg/dl, BUN 58 mg/dl), elevated ESR (80 mm/h) and C-reactive protein (21.6 mg/dl with n.v. <6 mg/dl), anaemia (Hb 9.8 g/dl with n.v. 12–18 g/dl) with normal leukocyte and platelet count and elevated serum IgG (2537 mg/dl) and IgA (783 mg/dl). Urinalysis showed haematuria (+++ + ) and proteinuria (2.5 g/24 h) with hyaline-granular casts. The result of the Ra test was double (114 UI/ml) compared to the time of the first biopsy. Positive p-ANCA were still present (ANCA I.F. ++ + + , antimyeloperoxidase 570 UI/ml). Thoracic radiography was normal.

Light microscopy of the second renal biopsy revealed eight glomeruli. Two glomeruli were almost completely obliterated by periglomerular inflammatory infiltrate with partial destruction of Bowman’s capsule (Figure 2a). Three glomeruli showed florid segmental crescents and in one there was an area of intracapillary necrosis. Direct immunofluorescence demonstrated weak discontinuous staining with IgG (+/−) and C3 (+) in the glomerular basement membrane and positive fibrinogen (+ +) in crescents and necrotic areas (Figure 2b). Electron microscopy showed that the membranous nephropathy had almost completely disappeared. These data allowed us to make a diagnosis of focal necrotizing glomerulonephritis with extracapillary proliferation.

Immunosuppressive therapy was started with intravenous pulse methylprednisolone (750 mg/day for 3 days), followed by prednisone (1 mg/kg/day) and oral cyclophosphamide (2 mg/kg/day), resulting in improvement of renal function (after 3 month-follow-up serum creatinine was 1.36 mg/dl) and reduction of p-ANCA (antimyeloperoxidase 117 UI/ml).

Discussion

In our patient there was a clear temporal relationship between oral gold therapy and onset of proteinuria as well as between its discontinuation and proteinuria disappearance. Therefore membranous nephropathy was probably related to gold salts therapy. Renal failure is unusual in gold nephrotoxicity [7,8] and indeed serum creatinine was normal at the time of the first renal biopsy.

Six months after the first renal biopsy the clinical picture changed. Renal failure and anaemia occurred
and indexes of acute phase increased. These data, together with the presence of positive p-ANCA, suggested that the patient had developed vasculitis. As expected the second renal biopsy revealed pauci-immune focal necrotizing glomerulonephritis with extracapillary proliferation. The membranous nephropathy had almost completely disappeared.

P-ANCA have been described in 8% of patients affected by psoriasis and in 19% of patients affected by rheumatoid arthritis (RA) without any vasculitic manifestation [5]. Although the prognostic significance of these positive ANCA tests is still unknown, the detection of ANCA in some patients may not be coincidental, but related to the development of vasculitis. Microscopic polyarteritis (MP) and Wegener’s granulomatosis (WG) have been rarely reported to occur during the course of RA [9–11]. Moreover, it is well known that RA can be complicated by vascular inflammation involving small and medium-sized vessels, probably because of the deposition of immune complexes in the vessel walls [12]. Interestingly, RA vasculitis has been associated with increased concentration of rheumatoid factor and with the need to intensify treatment with anti-rheumatic drugs, such as D-penicillamine or gold salts [13]. Both drugs have been described as causing membranous glomerulonephritis with immune complex deposition, probably after inducing autoimmunity [14–16]. D-penicillamine has also been associated with ANCA-positive crescentic glomerulonephritis [17]. It has been suggested that toxicity from gold or penicillamine treatment may be under genetic control related to HLA-DR antigens [18]. Although gold salts therapy has never been previously described in association with ANCA-positive crescentic glomerulonephritis, we suggest that this drug is able to cause systemic vasculitis after the exposure of neoantigens in the kidney and the induction of a nephritis in subjects likely to develop autoimmunity.

In conclusion we report a case of p-ANCA-positive crescentic glomerulonephritis complicating psoriatic arthritis and gold induced membranous glomerulonephritis. Although we cannot exclude the possibility that the occurrence of p-ANCA-positive crescentic glomerulonephritis in our patient was simply coincidental or related to psoriatic arthritis per se, we propose that crescentic glomerulonephritis was a consequence of gold therapy.

References


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