

## Dual positivity for cytoplasmic and perinuclear anti-neutrophil antibodies in a patient with Henoch-Schönlein purpura

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### ABSTRACT

We herein describe the case of a 60-year-old man who presented clinical and histopathological evidence of Henoch-Schönlein purpura. Antineutrophil antibodies (ANCA) showed positive results on an enzyme-linked immunosorbent assay and immunofluorescence for anti-myeloperoxidase and anti-proteinase 3 antibodies. Dual positivity for both cytoplasmatic (C-ANCA) and perinuclear (P-ANCA) antineutrophil antibodies has been found previously in a small number of reports, but to our knowledge this is the first time the simultaneous presence of C-ANCA and P-ANCA has been observed in Henoch-Schönlein purpura.

### Introduction

Since the description of both P and C-ANCA (anti-neutrophil cytoplasmic antibodies) in the late 1980s (1, 2), there have been many reports about their pathogenic and clinical implications in rheumatic diseases. The presence of ANCA has been described in Wegener's granulomatosis, microscopic polyangiitis, idiopathic necrotizing glomerulonephritis (pauci-immune glomerulonephritis) and Churg-Strauss syndrome (3). They may also be seen in a variety of gastrointestinal and other rheumatic disorders and after the administration of certain drugs (4). Although ANCA have occasionally been described in patients with Henoch-Schönlein purpura, other studies have not confirmed this association. We report here the case of a man who presented with clinical and histopathological features of Henoch-Schönlein purpura with both patterns of ANCA concurrently: a perinuclear staining pattern with anti-myeloperoxidase specificity, and a cytoplasmic staining pattern with anti-proteinase 3 specificity.

### Case report

A 60-year-old man presented with a 2-week history of upper respiratory tract infection, transient arthralgias in the knees and ankles and palpable purpura in the lower extremities with occasional fever. He did not report any cough, dysnea, hemoptysis, chest pain, abdominal pain or visual complaints, and no

possible offending drug that might have a temporal relationship to the symptoms was given. His previous medical history was unremarkable and he did not exhibit otitis, sinusitis symptoms or asthma. He was a farm worker who did not smoke or drink alcohol.

Physical examination disclosed purpura in lower extremities, thighs and inferior part of abdomen. The patient's blood pressure was 120/75 mm Hg and he was afebrile. Hemoglobin was 14.2 mg/dl, the white cell count 8,400/mm<sup>3</sup> and C-reactive protein was elevated at 7 mg/dl. IgA was 751 mg/dl (normal value < 450) and Singer-Plotz, Waaler-Rose, VDRL and Mantoux tests were negative. Complement, plasma creatinine and urea were normal. Urine analysis revealed proteinuria of 3.14 g/24h with a benign urinary sediment.

Antinuclear antibodies were negative and ANCA were positive by indirect immunofluorescence (anti-human IgG-AM as secondary antibody) at a 1/40 titration showing both a perinuclear and a cytoplasmic pattern. This was confirmed by a positive enzyme-linked immunosorbent assay (ELISA wells coated with MPO and PR3 from Wielisa® commercial kits, alkaline phosphatase labelled anti-human IgG and peroxidase labelled anti-human IgA, five calibrators from 320 units to 10 units, positive and negative controls were run each time) for anti-myeloperoxidase antibodies [IgG 40 U and IgA 45 U (negative < 10 Units)] and anti-proteinase 3 antibodies [IgG 37 U and IgA 43 U (negative < 10)]. Anti-glomerular basement membrane, cryoglobulins and hepatitis C and B serology were negative. Occult bleed tests were negative and clotting studies were normal as well. Blood cultures were negative and sepsis was excluded.

Chest X-ray was normal. Paranasal sinus X-rays did not show opacifications or other alterations. High resolution thoracic scanning was performed without pathological findings and a paranasal scanning was also normal. A biopsy specimen from the cutaneous purpura showed leukocytoclastic vasculitis with vascular IgA deposition. Renal biopsy revealed globular deposits of IgA (accompanied by C3 and IgG) in the me-

sangium and the glomerular capillary wall with focal diffuse mesangial proliferation and matrix expansion. Prednisone (1 mg/kg) was initiated on the day of renal biopsy. Four weeks later clinical improvement was observed, proteinuria began to decrease and corticosteroids were tapered gradually. At the one-year follow-up no proteinuria was detected and treatment with corticosteroids was suspended. At the moment of this report the patient remains asymptomatic and ANCA antibodies are negative.

## Discussion

Henoch-Schönlein purpura is a systemic vasculitis with a prominent cutaneous component that is characterized by the tissue deposition of IgA-containing immune complexes (5). The characteristic tetrad of rash, arthralgias, abdominal pain and renal disease is virtually pathognomonic in children once clotting disorders and sepsis are excluded. In adults it must be distinguished from other systemic autoimmune diseases (such as hypersensitivity vasculitis and systemic lupus erythematosus) that can produce similar symptoms. Our patient had negative antinuclear antibodies and did not show any other features of lupus. Although IgA nephropathy has rarely been described in Wegener's disease (6), this association may be fortuitous and reflect the high incidence of IgA nephropathy. In our patient no other clinical or histopathological findings suggested any other systemic vasculitis such as Wegener's granulomatosis. The evidence of IgA deposition in the skin and kidney, palpable petechiae, arthralgias and IgA nephropathy supports our diagnosis of Henoch-Schönlein purpura.

ANCA has occasionally been noted in

patients with Henoch-Schönlein purpura (7), but other studies have failed to demonstrate this association (8,9). This controversy has been especially sharp regarding the role of the isotype expressed by these autoantibodies. Some authors (10) have suggested that IgA ANCA is not an important serologic marker in Henoch-Schönlein purpura because the presence of serum IgA rheumatoid factor may produce weak false-positive results for IgA ANCA, but others (11) have concluded that they are closely associated with this disease and they may be directed against a different autoantigen than the one recognized by IgG ANCA. The fact that both the anti-myeloperoxidase and proteinase 3 specificities found in this patient belong to IgG and IgA isotypes clearly distinguishes this case from those previously described. To our knowledge, this is the first time the simultaneous presence of C-ANCA and P-ANCA has been observed in Henoch-Schönlein purpura. Dual positivity for both antibodies has been reported previously in a patient with concurrent Churg-Strauss syndrome and giant cell temporal arteritis (9) and in a patient with a antiglomerular basement membrane disease (12).

The role of ANCA in Henoch-Schönlein purpura remains controversial and future studies could elucidate the nature of the association of both P and C-ANCA in this and other diseases.

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## References

- DAVIES DJ, MORAN JE, NIALLJF, RYAN GB: 1. DAVIES DJ, MORAN JE, NIALLJF, RYAN GB: 1.
- JENNE DE, TSCHOPP J, LUDEMANN J, UTECHT B, GROSS WL: Wegener's autoantigen decoded (letter). *Nature* 1990; 346: 520.
- FALK RJ, JENNETTE JC: Anti-neutrophil cytoplasmatic autoantibodies with specificity for myeloperoxidase in patients with systemic vasculitis and idiopathic necrotizing and crescentic glomerulonephritis. *N Engl J Med* 1988; 318: 1651-7.
- CHOI HK, MERKEL PA, WALKER AM, NILES JL: Drug-associated anti-neutrophil cytoplasmic antibody-positive vasculitis: prevalence among patients with high titers of antimyeloperoxidase antibodies. *Arthritis Rheum* 2000; 43: 405-13.
- KAUFFMANN RH, HERRMANN WA, MEYER CJ, DAHAMR, VAN ES LA: Circulating IgA-immune complexes in Henoch-Schönlein purpura. A longitudinal study of their relationship to disease activity and vascular deposition of IgA. *Am J Med* 1980; 69: 859-66.
- VRTOVSNICK F, QUEFFEULOU G, SKHIRI H et al.: Simultaneous IgA nephropathy and Wegener's granulomatosis – overlap or coincidence (the role of renal biopsy). *Nephrol Dial Transplant* 1999; 14: 1266-7
- ESNAULT VL, RONDA N, JAYNE DR, LOCKWOOD CM: Association of ANCA isotype and affinity with disease expression. *J Autoimmun* 1993; 6: 197-205.
- ROBSON WL, LEUNG AK, WOODMAN RC: The absence of anti-neutrophil cytoplasmic antibodies in patients with Henoch-Schönlein purpura. *Pediatr Nephrol* 1994; 8: 295-8.
- GUARDIOLA JM, RODRÍGUEZ-PLA A, LÓPEZ-CONTRERAS J et al.: Simultaneous presence of C-ANCA and P-ANCA in a patient with concurrent Churg-Strauss syndrome and giant cell temporal arteritis. *Scand J Rheumatol* 2000; 29: 68-9.
- SAULSBURY FT, KIRKPATRICK PR, BOLTON WK: IgA anti-neutrophil cytoplasmic antibody in Henoch-Schönlein purpura. *Am J Nephrol* 1991; 11: 295-300.
- RONDA N, ESNAULT VL, LAYWARD L et al.: Anti-neutrophil cytoplasm antibodies (ANCA) of IgA isotype in adult Henoch-Schönlein purpura. *Clin Exp Immunol* 1994; 95: 49-55.
- MEISELS IS, STILLMAN IE, KUHLIK AB: Anti-glomerular basement membrane disease and dual positivity for anti-neutrophil cytoplasmic antibody in a patient with membranous nephropathy. *A J Kidney Dis* 1998; 32: 646-8.