

## Pauci-immune crescentic glomerulonephritis in a patient with B-lymphocyte poly/autoreactivity

Sirs,

A 55-year-old female was referred for evaluation of haematuria (>100 red blood cells/optic field) and mild proteinuria (1022 mg/24 hour urine collection). Review of systems, use of medications, family history and habits were unrevealing. Physical examination revealed mild hypertension (150/95mmHg) and trace oedema (+1) in the lower extremities. Laboratory testing was significant only for the presence of hypergammaglobulinaemia, positive ANA titres (1:1280, diffuse pattern) as well as anti-myeloperoxidase (58U; n.v. <6U), anti-dsDNA (389U; n.v. <60 U) and anti-Ro-60 autoantibodies. Serum C3 and C4 levels were in the upper normal levels. Renal biopsy showed focal segmental necrotising glomerular lesions (staining red with the Masson trichrome stain; Fig. 1a, x400, white arrow) as well as cellular crescents in 50% of the 44 glomeruli (Fig. 1a, black arrows), some of which were concentric (Fig. 1b, arrows, silver methenamine, x400). The non-necrotic glomerular segments were unremarkable without hypercellularity. The rest of the glomeruli appeared normal without mesangial, endocapillary hyperplastic lesions, subendothelial or subepithelial deposits. The interstitium showed mild focal lymphocytic infiltration mainly periglomerularly. Extra-glomerular necrotising arteritis was not detected. Immunofluorescence for immunoglobulins (IgG, IgA, IgM), complement components (C3, C1q, C4) and light chains ( $\kappa$  and  $\lambda$ ) was negative. Immunohistochemistry against C4d, IgG & IgG4 was also negative. The patient was treated with enalapril (5 mg/daily), as well as, for six months with monthly intravenous pulses of cyclophosphamide (1 gr/m<sup>2</sup> body surface) and 1 gr methylprednisolone. With this therapeutic regimen all findings (hypertension, haematuria and proteinuria) abated and the patient was placed on maintenance immunosuppressive treatment (azathioprine 1.5 mg/kg/body weight daily). Three years later, while the patient was free of symptoms and findings, hypergammaglobulinaemia and autoantibodies were still present. Sporadic cases of patients with connective tissue disorders, primarily Sjögren's syndrome and systemic lupus erythematosus who develop pauci-immune crescentic glomerulonephritis have been presented in the literature (1, 2). To the best of our knowledge this is the only case of pauci-immune crescentic glomerulonephritis presented in a patient who expresses only autoantibodies specific for systemic autoimmune

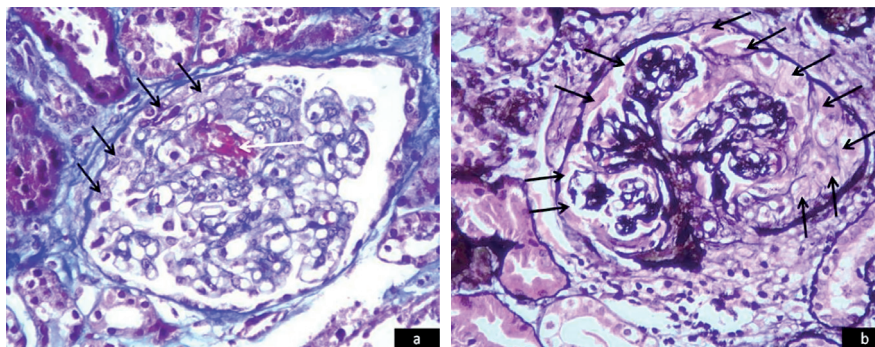


Fig. 1.

disease in the absence of clinical disease manifestations, even after a 3-year follow-up. Circulating anti-cellular autoantibodies, however, can be detected, in the serum of individuals many years prior to clinically apparent disease (3). The renal histopathological findings observed in our patient can be attributed to antibodies to myeloperoxidase. This is supported from studies in mice which provide strong evidence for a direct role of anti-myeloperoxidase autoantibodies in the pathogenesis of pauci-immune, necrotising glomerulonephritis through activation of neutrophils and monocytes (4). The reason for which serum anti-dsDNA autoantibodies and/or the anti-Ro60 did not deposit in this patient's kidneys and has not produced renal disease is an intriguing question. Patient serum complement levels were normal, implying that the patient's anti-ds-DNA and anti-Ro-60 autoantibodies were not able to activate and consume complement. It would be of interest to study if circulating anti-idiotypic antibodies against the autoantibodies or the autoantibody immunoglobulin class could account for inability of these autoantibodies to induce pathology.

*H.M. Moutsopoulos drafted the manuscript, conception and design of the manuscript, acquisition, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, approved the version to be published, agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.*

*H. Gakiopoulos dealt with the acquisition, analysis and interpretation of the data, approved the version to be published; agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.*

*The present study was approved by the Ethical-Scientific Committee of the Laikon Hospital (12/20-4-2016) and the patient provided informed consent in accordance with the declaration of Helsinki.*

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