IgA-mediated anti-glomerular basement membrane disease. A case report

Enfermedad mediada por autoanticuerpos IgA anti-membrana basal glomerular

Dear Editor,

Anti-glomerular basement membrane disease (anti-GBM) is a rare disease usually mediated by IgG autoantibodies. It usually presents as rapidly progressive glomerulonephritis, often accompanied by pulmonary hemorrhage.[1] The hallmark of anti-GBM disease are the blood circulating and tissue-bound autoantibodies that target antigenic sites within the glomerular basement membrane (GBM) and sometimes alveolar basement membranes.[2]

We present a rare case of anti-GBM disease mediated by IgA autoantibody. A 65-year-old-man presented with gross haematuria and nephrotic range proteinuria and was admitted to the hospital.

His medical history included meningitis in childhood, obesity (BMI 47.53 kg/m^2), glucose intolerance, hypertension, hypercholesterolemia, duodenal ulcers, liver hemangioma and rectal polyps. He lost 12 kg during the last 3 months and suffered from dysuria, pollakiuria and nocturia. Medications were: amlodipine and valsartan, moxonidine, torasemide, nebivolol, atorvastatin, meloxicam and tramadol with paracetamol.

Upon admission his blood pressure was 150/80 mmHg. He had pretibial edemas. Ultrasound examinations showed normal kidneys. Laboratory investigation revealed negative cANCA, pANCA, ANA, ENA, anti-dsDNA and antiphospholipid antibodies along with normal C3 and C4 levels. Urine and serum electrophoresis showed no monoclonal IgA, kappa or lambda light chains. Routine enzyme-linked immunosorbent assay (ELISA) targeting IgG circulating anti-GBM autoantibodies were negative. Urine examination revealed proteinuria of nephrotic range (11.8 g/day), haematuria with dysmorphic erythrocytes and leukocyturia. His serum creatinine level raised from 98 to 313 μmol/L in two months and serum proteins were low. Chest X-ray showed bilateral pleural effusion and voluminous hiluses. He had partial respiratory insufficiency with SO_2 94%.

Renal biopsy was performed. Light microscopy demonstrated focal necrotizing crescentic glomerulonephritis with cellular and fibrous crescents (Fig. 1). 40% of glomeruli were globally sclerotic. Immunofluorescence microscopy demonstrated linear (2+) staining along the glomerular capillary loops for IgA (Fig. 2) along with weak linear staining for IgG, anti-kappa and anti-lambda antibodies. Interstitial fibrosis and tubular atrophy occupied 40% of renal parenchyma. By electron microscopy there were no immune complex-type deposits. The findings were consistent with IgA-mediated anti-GBM disease.

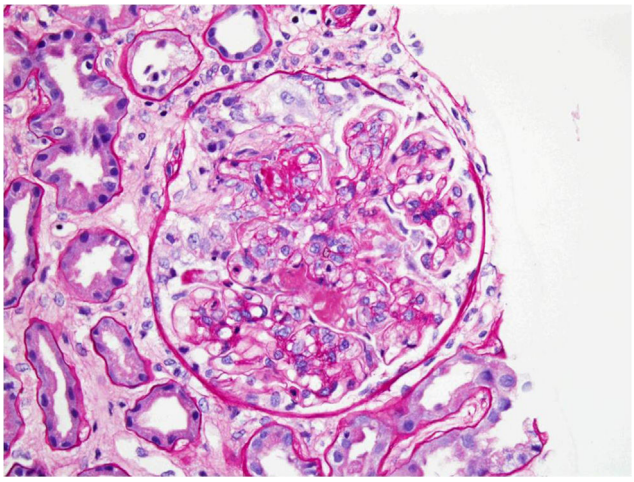

Fig. 1 – Light microscopy: glomerul with necrosis and cellular crescent (×400, Periodic acid – Schiff stain).

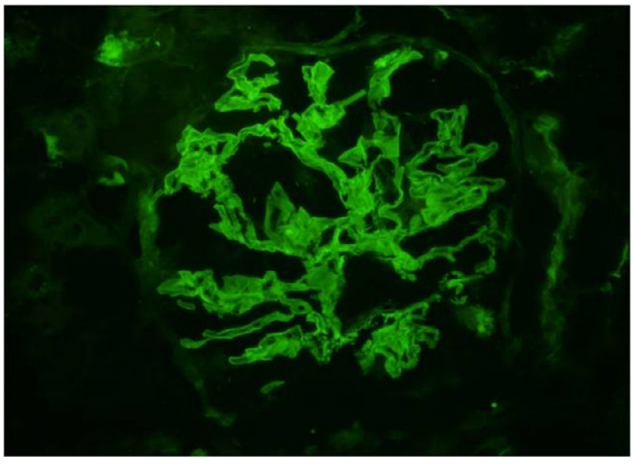

Fig. 2 – Immunofluorescence microscopy: intense linear staining along the glomerular capillary loops for IgA (×400).

The patient had 12 plasma exchanges during a 1 month time, along with albumin substitution. He was given intravenous cyclophosphamide (CYC) (1 g the first day) and steroids (methylprednisolone, 1 g/day) during 3 days, and continued with oral prednisone 60 mg/day.

Two months after the diagnosis of IgA-mediated anti-GBM disease the patient had serum creatinine level 258 μmol/L and proteinuria of 4.6 g/day. He continued albumin substitution and oral prednisone (60 mg/day) therapy. He was given another cycle of CYC, but the therapy was stopped because of sepsis. He started chronic hemodialysis 3 months after the onset of the disease.

As our case demonstrated, standard assays used for detecting circulating IgG anti-GBM antibodies can perceive only IgG and they will fail to detect IgA anti-GBM antibodies. Thus the recognition of the disease depends on linear staining of IgA on glomerular basement membranes detected using immunofluorescence microscopy on the kidney biopsy.[3,4]

In IgA-mediated anti-GBM disease antigens belong to α5 and α6 chains of type IV collagen. That differs from antingens belong to α3 or α5 chains of type IV collagen found in IgG-mediated anti-GBM disease.[5]

The patient we presented did not had signs of alveolar hemorrhage. In previously described cases of IgA-mediated anti-GBM disease pulmonary involvement was found in 5 cases.[1,4,6–8]

Major predictors of piteous renal outcome in anti-GBM disease are high serum creatinine level (≥5.7 mg/dL, 503.9 μmol/L) and many circumferential crescents.[9] Comparing to the IgG-mediated anti-GBM disease, prognosis of IgA-mediated anti-GBM disease is poor.[3,4] Renal function usually does never improve and in most cases the disease leads to the end-stage renal failure.[1,3,4] Also, 2 patients described in previous reports died because of uncontrolled alveolar hemorrhage[6] and pneumonia.[10]

Classically, IgA-mediated anti-GBM disease is treated in the same way as its IgG counterpart, with the triple regimen of plasmapheresis, steroids and oral CYC.[1,3,4] Whether this intensive treatment is the best option in IgA-mediated anti-GBM disease is unknown as this approach was used in only few cases and in all described cases the patients developed ESRD.[1,3–5]

Kidney transplantation is the treatment of choice for patients who develop ESRD caused by anti-GBM disease. In 2 previously described cases of IgA-mediated anti-GBM disease the patients underwent renal transplantation. In the report by Moulis et al.[3] there was no recurrence of the disease 5 months after transplantation. In other case[1] the disease was secondary to a plasma cell dyscrasia. The disease recurred and caused the loss of the allograft 2 years after the transplantation.

In order to make the right diagnosis, performing the renal biopsy is essential in cases of rapidly progressive glomerulonephritis. Early diagnosis of IgA-mediated anti-GBM disease can ensure the treatment in earlier stages of the disease and ESRD can possibly be prevented or at least delayed. As current treatment regimens result in poor prognosis, the disease might require more specific treatment strategy, distinct from the therapy for IgG anti-GBM disease.

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Eikenella corrodens and *Prevotella oralis* peritonitis in patients on peritoneal dialysis☆

Peritonitis por *Eikenella corrodens* y *Prevotella oralis* en pacientes en diálisis peritoneal

Dear Editor,

Eikenella corrodens is an anaerobic Gram-negative bacillus which colonises the flora of the oral cavity, upper respiratory tract and mucosal surfaces of the digestive and genitourinary tract. The most common infections caused by this bacterium are head and neck infections followed by pulmonary, intra-abdominal, skin and bone infections, endocarditis and pelvic abscesses. It tends to present as a polymicrobial and opportunistic infection in immunocompromised patients and is more common if patients have associated morbidity.

It is a difficult bacterium to grow in non-selective media. Its culture, isolation and identification are therefore complex. Third-generation cephalosporins, carbapenems and fluoroquinolones are the treatment of choice.[1] It does not produce beta-lactamases and it is resistant to first- and second-generation cephalosporins, metronidazole, clindamycin and aminoglycosides.[2–5]

Prevotella oralis is an anaerobic Gram-negative bacillus which forms part of the oral, gastrointestinal and vaginal mucosa. It mainly causes episodes of periodontitis, although it can also be the cause of gynaecological and urinary infections, osteomyelitis and soft tissue infections, among others.[6] It is sensitive to penicillin and cephalosporins, although in recent years up to almost 40% of beta-lactamase-producing bacteria have been observed.[7] It tends to present as a co-infection with other bacteria, especially those which are anaerobes.

We describe the case of a 50-year-old Caucasian male with chronic kidney disease secondary to Berger's disease who started peritoneal dialysis at the age of 41. After one year, he received a kidney transplant from a deceased donor with early loss of the graft due to arterial thrombosis. The second transplant took place two years later with an initial immunosuppression regimen of prednisone, mycophenolate and tacrolimus, with withdrawal of corticosteroids after six months due to avascular necrosis of both hips. He re-started peritoneal dialysis six years after the transplant due to chronic graft failure.

The patient presented with an episode of peritonitis, diagnosed by cloudy peritoneal fluid and a cell count of 124 cells/μl with 88% of polymorphonuclear cells. Empirical treatment was therefore started with cefazolin and intraperitoneal (IP) tobramycin, in accordance with the peritonitis infection protocol at our site. *E. corrodens* grew in the culture, which, in our case, was susceptible to aminoglycosides. Treatment was therefore continued with aminoglycosides, and cephalosporin was withdrawn. The patient presented initial improvement and a peritoneal fluid cell count <100 cells/μl after five days of treatment. A week after the episode he came again due to cloudy fluid and 234 cells/μl in peritoneal fluid associated empirically with IP vancomycin. A new batch of cultures was performed, in which *P. oralis* resistant to penicillin and *Enterococcus faecalis* grew. The patient continued to do poorly make poor progress, reaching values of 1962 cells/μl. It was

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