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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/m²), 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 $\mu\text{mol/L}$ 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

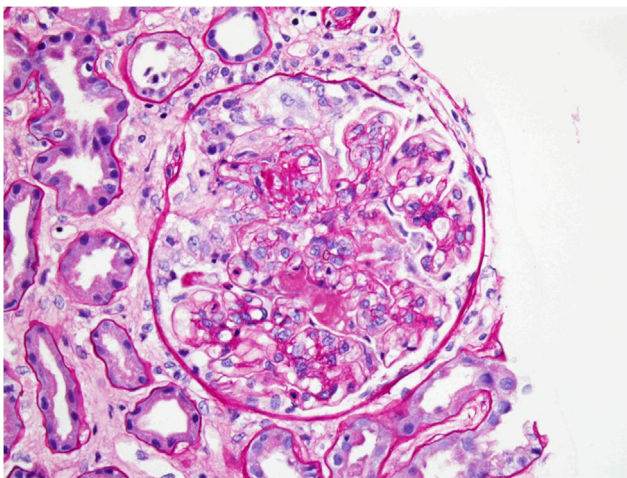


Fig. 1 – Light microscopy: glomerul with necrosis and cellular crescent ($\times 400$, Periodic acid – Schiff stain).

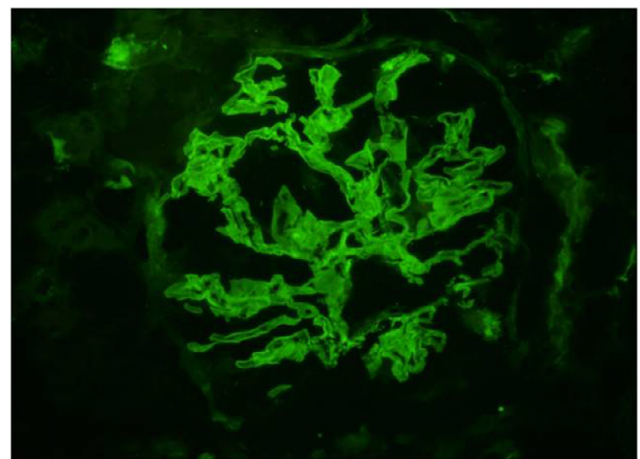


Fig. 2 – Immunofluorescence microscopy: intense linear staining along the glomerular capillary loops for IgA ($\times 400$).

deposits. The findings were consistent with IgA-mediated anti-GBM disease.

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 $\mu\text{mol/L}$ 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 $\alpha 5$ and $\alpha 6$ chains of type IV collagen. That differs from antigens belong to $\alpha 3$ or $\alpha 5$ 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 $\mu\text{mol/L}$) 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 hemorrhage⁶ 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 case¹ 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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BIBLIOGRAFÍA

1. Borza DB, Chedid MF, Colon S, Lager DJ, Leung N, Fervenza FC. Recurrent Goodpasture's disease secondary to a monoclonal IgA1-kappa antibody autoreactive with the alpha1/alpha2 chains of type IV collagen. *Am J Kidney Dis.* 2005;45:397-406. Epub 2005/02/03. PubMed PMID: 15685519.
2. Pedchenko V, Bondar O, Fogo AB, Vanacore R, Voziyan P, Kitching AR, et al. Molecular architecture of the Goodpasture autoantigen in anti-GBM nephritis. *N Engl J Med.* 2010;363:343-54. <http://dx.doi.org/10.1056/NEJMoa0910500>. Epub 2010/07/28. PubMed PMID: 20660402; PubMed Central PMCID: PMC4214144.
3. Moulis G, Huart A, Guitard J, Fortenfant F, Chauveau D. IgA-mediated anti-glomerular basement membrane disease: an uncommon mechanism of Goodpasture's syndrome. *Clin Kidney J.* 2012;5:545-8. <http://dx.doi.org/10.1093/ckj/sfs087>. Epub 2012/12/01. PubMed PMID: 26069798; PubMed Central PMCID: PMC4400543.
4. Wen YK, Wen KI. An unusual case of IgA-mediated anti-glomerular basement membrane disease. *Int Urol Nephrol.* 2013;45:1229-34. <http://dx.doi.org/10.1007/s11255-012-0162-8>. Epub 2012/03/30. PubMed PMID: 22456764.
5. Ghohestani RF, Rotunda SL, Hudson B, Gaughan WJ, Farber JL, Webster G, et al. Crescentic glomerulonephritis and subepidermal blisters with autoantibodies to alpha5 and alpha6 chains of type IV collagen. *Lab Invest.* 2003;83:605-11. Epub 2003/05/15. PubMed PMID: 12746470.
6. Border WA, Baehler RW, Bhatena D, Glassock RJ. IgA antibasement membrane nephritis with pulmonary hemorrhage. *Ann Intern Med.* 1979;91:21-5. Epub 1979/07/01. PubMed PMID: 111592.
7. Maes B, Vanwalleghem J, Kuypers D, Van Damme B, Waer M, Vanrenterghem Y. IgA antiglomerular basement membrane disease associated with bronchial carcinoma and monoclonal gammopathy. *Am J Kidney Dis.* 1999;33:E3. Epub 1999/03/13. PubMed PMID: 10074603.
8. Nakano H, Suzuki A, Tojima H, Watanabe A, Mizuguchi K, Shinozaki T, et al. A case of Goodpasture's syndrome with IgA antibasement membrane antibody. *Nihon Kyobu Shikkan Gakkai Zasshi.* 1990;28:634-8. Epub 1990/04/01. PubMed PMID: 2214406.
9. Levy JB, Turner AN, Rees AJ, Pusey CD. Long-term outcome of anti-glomerular basement membrane antibody disease treated with plasma exchange and immunosuppression. *Ann Intern Med.* 2001;134:1033-42. Epub 2001/06/05. PubMed PMID: 11388816.
10. Shaer AJ, Stewart LR, Cheek DE, Hurray D, Self SE. IgA antiglomerular basement membrane nephritis associated with Crohn's disease: a case report and review of glomerulonephritis in inflammatory bowel disease. *Am J Kidney Dis.* 2003;41:1097-109. Epub 2003/05/02. PubMed PMID: 12722045.

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

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

Sr. Director:

Eikenella corrodens es un bacilo gramnegativo anaerobio colonizador de la flora oral, aparato respiratorio superior y superficies mucosas del aparato digestivo y genitourinario. Las infecciones más frecuentes producidas por este germen son las de cabeza y cuello seguidas de infecciones pulmonares, intraabdominales, cutáneas, óseas, endocarditis y abscesos pélvicos. Suele presentarse como infección polimicrobiana y oportunista en pacientes inmunocomprometidos, siendo más frecuente si tienen morbilidad asociada.

Se trata de un germen de difícil crecimiento en medios no selectivos por lo que su cultivo, aislamiento e identificación son complejos. El tratamiento de elección son las cefalosporinas de tercera generación, carbapenemes y fluoroquinolonas¹. No es productor de betalactamasas y es resistente a cefalosporinas de primera y segunda generación, metronidazol, clindamicina y aminoglucósidos²⁻⁵.

Prevotella oralis es un bacilo gramnegativo anaerobio que forma parte de la mucosa oral, gastrointestinal y vaginal. Provoca principalmente episodios de periodontitis, aunque también puede ser causa de infecciones ginecológicas, urinarias, osteomielitis y de tejidos blandos entre otras⁶. Es sensible a penicilina y cefalosporinas, aunque en los últimos años se ha visto hasta casi un 40% de productoras de beta-lactamasas⁷. Suele presentarse en coinfección con otros gérmenes, sobre todo anaerobios.

Describimos el caso de un varón caucásico de 50 años con enfermedad renal crónica secundaria a enfermedad de Berger que inició diálisis peritoneal a los 41 años. Al año recibió un trasplante renal de donante cadáver con pérdida precoz del injerto por trombosis arterial. El segundo trasplante ocurrió 2 años después con un régimen de inmunosupresión inicial de prednisona, micofenolato y tacrolimus con suspensión de corticoides a los 6 meses por necrosis avascular de ambas caderas. Reinició diálisis

peritoneal tras 6 años de trasplante por disfunción crónica del injerto.

El paciente presentó un episodio de peritonitis, diagnosticado por líquido peritoneal turbio y recuento celular de 124 células/μl con el 88% de polimorfonucleares, por lo que se inicia tratamiento de manera empírica con cefazolina y tobramicina intraperitoneales (IP) según protocolo de infección de peritonitis de nuestro centro. En el cultivo crece *Eikenella corrodens* que en nuestro caso es sensible a aminoglucósidos por lo que se continúa el tratamiento con el mismo, suspendiendo la cefalosporina. El paciente presenta mejoría inicial y recuento celular de líquido peritoneal < 100 células/μl a los 5 días de tratamiento. A la semana del episodio acude de nuevo por líquido turbio y 234 células/μl en líquido peritoneal asociándose vancomicina IP de manera empírica y se realiza una nueva tanda de cultivos en donde crece *Prevotella oralis* resistente a penicilina y *Enterococcus faecalis*. El paciente continúa con mala evolución alcanzando la cifra de 1.962 células/μl por lo que se decide realizar un TAC abdominal objetivándose engrosamiento parietal difuso del colon ascendente y ciego e inflamación de la grasa mesentérica adyacente. Al no presentar mejoría y ante los hallazgos radiológicos se asocia metronidazol al tratamiento de tobramicina y vancomicina además de realizar nuevo cultivo de líquido peritoneal; en este crece en unos días *Escherichia coli* y *Bacteroides merdae*, este último resistente a metronidazol. Se suspende todo el tratamiento antibiótico anterior y se inicia imipenem intraperitoneal con una dosis de carga de 500 mg y posteriormente con 200 mg/intercambio durante 15 días con la completa resolución del cuadro sin necesidad de retirar el catéter.

Eikenella corrodens y *Prevotella oralis* son 2 gérmenes anaerobios de la flora habitual de las mucosas oral y gastrointestinal. Habitualmente presentan infección con otros gérmenes anaerobios⁸, por lo que se recomienda iniciar tratamiento con más de un fármaco de los habitualmente sensibles durante tiempo prolongado, por lo menos 3 semanas.