Inicia tratamiento conservador con IECA y ARAII. Al cuarto mes del diagnóstico, por ausencia de respuesta, se inicia CsA sin éxito. Al sexto mes, se cambia el tratamiento a clorambucil y prednisona manteniéndose durante ocho meses sin obtener respuesta y suspendiéndose por leucopenia. Al año y medio posbiopsia se objetiva remisión parcial (proteinuria: 5 g/día) con tratamiento conservador. A los dos años aparece un nódulo en el lóbulo pulmonar inferior izquierdo (figura 1). La fibrobroncoscopia confirma carcinoma epidermoide en estadio IV. El estudio de extensión muestra numerosos nódulos compatibles con metástasis pleurales, óseas y hepáticas.

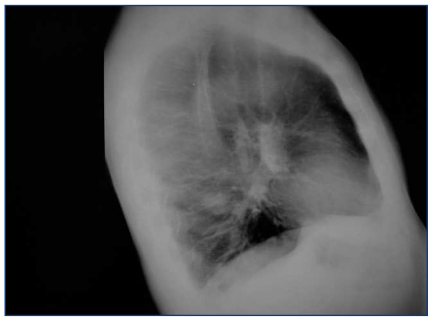

Figura 1. Radiografía lateral de tórax. Caso 2. Nódulo pulmonar en lóbulo inferior izquierdo.

DISCUSIÓN

En el estudio etiológico de la GNM, ¿con quién debemos ser «agresivos» en el *screening* de malignidad y hasta qué punto? En el caso 1, la aparición de GNM y tumor sólido son simultáneos, sin una presentación clínica evidente de neoplasia. En el caso 2, el tumor aparece 2 años después del diagnóstico de GNM coincidiendo con remisión parcial, lo que cuestiona su relación causal, ya que resulta más plausible una activación tumoral latente por la inmunosupresión.

Un 10% de las GNM son paraneoplásicas secundarias a tumores de pulmón, próstata y gastrointestinales[1]. El cáncer de pulmón es el tumor más frecuente en varones adultos[2], fumadores y mayores de 65 años. Muchos autores defienden un *screening* agresivo en pacientes con GNM. La relación entre neoplasia y GNM puede ser causa o consecuencia del tratamiento inmunosupresor, o también simple coincidencia. Se ha descrito la aparición de tumores hasta 5 años después del diagnóstico de GNM[3].

En los últimos años parece despejarse esta controversia entre idiopática y secundaria. El antígeno tipo M del receptor de la fosfolipasa A_2 se asocia con GNM idiopática[4], así como la anti aldosa reductasa y el anti manganeso superóxido dismutasa, mientras que la ausencia de depósitos glomerulares de IgG4 sugeriría un proceso neoplásico[5]. Pero se trata de técnicas aún no disponibles en muchos hospitales.

Nuestros casos describen dos patrones distintos de asociación entre GNM y tumores. Consideramos que desde el diagnóstico y durante el seguimiento debemos mantener una actitud vigilante para detectar neoplasias que condicionen el pronóstico.

Conflictos de interés

Los autores declaran que no tienen conflictos de interés potenciales relacionados con los contenidos de este artículo.

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M. Teresa Mora-Mora, Gema Rangel-Hidalgo, M. Sandra Gallego-Domínguez, Clarencio J. Cebrián-Andrada, Silvia González-Sanchidrián, Pedro J. Labrador-Gómez , Vanesa García-Bernalt, Jesús P. Marín-Álvarez, Inés Castellano, Ricardo Novillo-Santana, Javier Deira, Juan R. Gómez-Martino Arroyo
Sección de Nefrología.
Hospital San Pedro de Alcántara. Cáceres.
Correspondencia: M. Teresa Mora Mora
Sección de Nefrología.
Hospital San Pedro de Alcántara. Cáceres.
maytemorabis@hotmail.com

Membranous glomerulonephritis associated with myeloperoxidase anti-neutrophil cytoplasmic antibody-associated glomerulonephritis

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Dear Editor,

Membranous glomerulonephritis (MGN) is a common cause of nephrotic syndrome in adults which is characterized by formation of subepithelial immune complex deposits with resultant changes to glomerular basement membrane (GBM), most notably GBM spike formation. The onset of this disorder is slow and the clinical course is often benign. Anti-neutrophil cytoplasmic antibody (ANCA)-associated glomerulonephritis is the most frequent cause of rapidly progressive glomerulonephritis and is usually classified as a pauci-immune type characterized by glomerular *necrosis* and *crescent formation*. MGN complicated by ANCA-associated glomerulonephritis is an unusual concurrence and only rare cases have been reported previously;[1-6] however, none of them was presented in Chinese population and most of the cas-

es reported were related to some backgrounds. Here we first report an elderly Chinese male patient with MGN and myeloperoxidase (MPO)-positive ANCA-associated glomerulonephritis without any detectable backgrounds.

A 64-year-old man presented with arthralgia, shortness of breath, nausea, oliguria, and edema without previous history of disease. Laboratory examinations showed the following results: serum creatinine concentration 350.8μmol/L, serum albumin level 21.3g/L, serum total cholesterol 7.1mmol/L and a 24-hr protein excretion of 5.4g/d. The urinalysis showed 3+ urine protein, 2+ urine blood and RBC casts. MPO-ANCA was detected in serum screening test by indirect immunofluorescence and the serum concentration of MPO-ANCA was subsequently determined by enzyme-linked immunosorbent assay (ELISA) to be 145U/mL (reference range, 0-10U/mL). Other immunological tests showed the decrease of serum complement 3 concentration to 0.571g/L and other autoantibodies including anti-nuclear antibodies (ANAs), anti-Sm antibody, anti-dsDNA antibody, anti-cyclic citrullinated peptide (CCP) antibody, anti-proteinase-3 (PR3)-ANCA and anti-glomerular basement membrane (GBM) antibody were negative. There was no evidence of systemic lupus erythematosus (SLE), infection, malignancy, or drugs. Percutaneous renal biopsy was subsequently performed to determine the diagnosis.

Upon light microscopy, renal biopsy revealed thickening of glomerular capillary wall and 2 out of 19 glomeruli were sclerosed. Four glomeruli showed cellular crescents, 5 showed fibrocellular crescents formation and 2 showed fibrinoid necrosis (Figure 1 A). Immunofluorescence examination displayed granular deposition of IgG and C3 along the glomerular capillary walls (Figure 1 B). Electron microscopy showed thickened glomerular basement membranes with diffuse subepithelial deposits and foot process effacement which was consistent with the stage II of MGN (Figure 1 C). Therefore renal histology and laboratory examinations supported the diagnosis of MGN and MPO-positive ANCA-associated glomerulonephritis.

The patient was treated initially with pulse methylprednisolone 500mg/d for 3 days followed by prednisone (40mg/d) and antihypertensives, anticoagulant were also administrated. Because of no sign of improvement shown a week later, steroid pulse therapy was performed again followed by prednisone (40mg/d) and intravenous cyclophosphamide 0.4g once a week. On review after 1 month of treatment, proteinuria and renal function had improved significantly with urine protein down to 1.9g/d and creatinine down to 182.7μmol/L. MPO-ANCA testing was repeated and showed seronegative. The patient remained stable at a follow-up of 1 year.

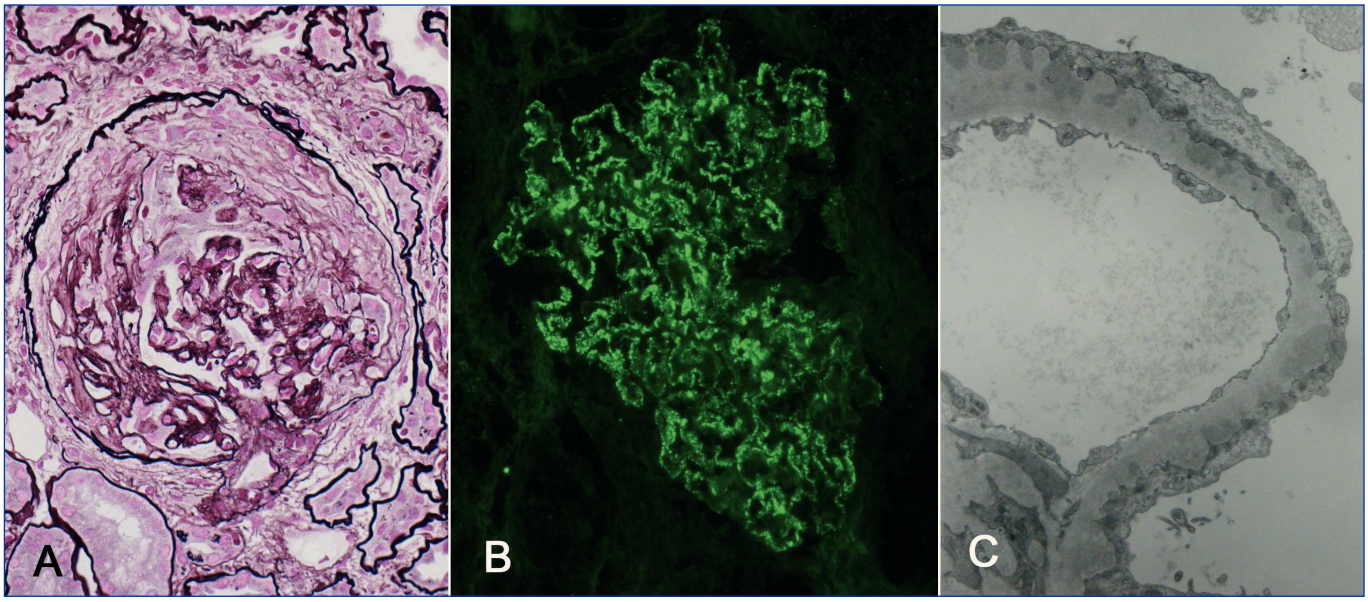

Figure 1. Renal biopsy findings in membranous glomerulonephritis associated with anti-neutrophil cytoplasmic antibody-associated glomerulonephritis.
(A) Light microscopy showing thickened glomerular capillary walls and a fibrocellular crescent (PAM stain, x400).
(B) Immunofluorescence staining revealing deposition of IgG along glomerular capillary walls (x200). (C) Electron micrograph showing thickened glomerular basement membrane with diffuse subepithelial deposits and foot process effacement (x6500).

As we know, crescent formation and fibrinoid necrosis are rarely encountered in membranous glomerulonephritis. Although MGN associated with ANCA-associated glomerulonephritis has been described previously in white adults and Japanese population, most of the cases reported were related to some rheumatic diseases such as SLE,[7] anti-GBM disease,[8,9] malignancy such as esophageal carcinoma,[10] or drugs.[11] The coexistent MGN and ANCA-associated glomerulonephritis without the above backgrounds is a rare occurrence with less case reported. Here we first show the Chinese patient with MGN complicated by ANCA-associated glomerulonephritis without the evidence of underlying backgrounds. Tse WY reported 10 patients with MGN and ANCA-associated glomerulonephritis including 9 males and 1 female and the median age was 63.5 years.[2] Cases described by Nasr SH involved 8 males and 6 females and the median age was 58.7 years.[5] Added with the case of 64-year-old man we present here, MGN associated with ANCA-associated glomerulonephritis may mainly occur in the elderly patients and the incidence in male seemed to be higher than in female. The clinical course is more aggressive than MGN alone and is characterized by nephrotic syndrome, hematuria and acute renal failure with or without systemic vasculitis involving extrarenal organs. Renal pathology involves both the membranous changes and crescent formation with fibrinoid necrosis. As for the prognosis, Tse WY and Nasr SH reported a similar outcome that 50% of patients reaching endpoints of ESRD or death whether or not treated with immunosuppressive agents;[5] however, our patient showed well response to immunosuppressive treatment.

The mechanism of MGN associated with ANCA-associated glomerulonephritis is unknown. Some case reports have noted an association with the presence of anti-GBM antibodies that may play a role in the pathogenesis because the development of glomerular crescents requires disruption of the GBM integrity sufficient to allow the efflux of cells and macromolecules into Bowman's space.[8,9] The autoantibodies in lupus nephritis type III and V or type IV and V may also contribute to the combination of crescentic and membranous glomerulonephritis that is not uncommon in patients with SLE.[7] But in case of MGN associated with ANCA-associated glomerulonephritis without anti-GBM nephritis, SLE and other related diseases, the mechanism is difficult to elucidate because of the fact that the pathogenesis of MGN and ANCA-associated glomerulonephritis is distinct from each other. Whether ANCA is associated with the pathogenesis or not remains unclear and whether MPO-ANCA-associated glomerulonephritis is superimposed on idiopathic membranous nephropathy (MN) or MPO-ANCA-associated glomerulonephritis induce a secondary MGN is still unknown. Suwabe and Watanabe examined IgG subclass deposition and found that the cases with MGN and ANCA-associated glomerulonephritis showed both IgG1 and IgG4 deposited on the glomerular capillary walls, which suggested secondary MGN;[4,6] however, no disease or drug was found to induce secondary MGN. The fact only a few MPO-positive cells in the glomeruli and MPO stains on the glomerular capillary walls near the MPO-positive cells may suggest that the patient had MPO-ANCA-associated glomerulonephritis superimposed on idiopathic MN.[6] But Nasr SH was inclined to regard the co-existence of MGN and ANCA-associated glomerulonephritis as a coincidence.[5] Further research is required to clarify the pathogenesis of the rare occurrence.

In summary, MGN with ANCA-associated glomerulonephritis is a rare dual glomerulopathy seen in patients with heavy proteinuria and acute renal failure. In case of nephrotic syndrome with seropositive MPO-ANCA and progressive renal failure even though without evidence of SLE or anti-GBM nephritis, we should consider the coexistence of MGN and ANCA-associated glomerulonephritis. Although prognosis is variable, remission was observed after administration of steroids and cyclophosphamide in this dual glomerulopathy.

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Conflict of interest

The author declares that there is no conflict of interest associated with this manuscript.

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Guang-Yu Zhou
Department of Nephrology.
China-Japan Union Hospital of Jilin University.
Changchun, Jilin Province (China)
Correspondence: Guang-Yu Zhou
Department of Nephrology.
China-Japan Union Hospital of Jilin University,
No.126, Xiantai Street, 130033 Changchun.
Jilin Province, China.
guangyu8@yahoo.com.cn
zhougy@jlu.edu.cn

Comunicación pleuroperitoneal en paciente en diálisis peritoneal

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Sr. Director:

La diálisis peritoneal (DP) es una opción terapéutica cada vez más frecuente como tratamiento de la enfermedad renal crónica avanzada. No obstante, dicha técnica no está exenta de complicaciones, siendo la más habitual la peritonitis, aunque también se pueden presentar otras, como infecciones del orificio de salida del catéter peritoneal, infección del túnel subcutáneo, hernias, dolor abdominal o lumbar, hemoperitoneo, quilotórax, o la comunicación pleuroperitoneal o hidrotórax.

La infusión del líquido en la cavidad peritoneal produce un aumento de la presión intraabdominal; dicho aumento de presión puede dar lugar a paso de líquido peritoneal hacia el tórax, produciendo una comunicación pleuroperitoneal. También se han descrito casos de comunicación pleuroperitoneal secundaria a peritonitis[1,2].

Presentamos el caso de un varón de 77 años con enfermedad renal crónica, secundaria probablemente a nefroangioesclerosis, en DP continua ambulatoria desde hace 15 días. A los 8 días presenta un episodio de peritonitis causada por *Streptococcus* grupo *viridans* tratado según protocolo, con vancomicina y ciprofloxacino. Acude a Urgencias por presentar un cuadro de disnea, fiebre y tos de 24 horas de evolución, junto con un déficit de ultrafiltración en los últimos días.

En la exploración destaca un regular estado general acompañado de taquipnea e hipoventilación bilateral, más acentuada en campo pulmonar derecho.

La radiografía de tórax muestra un derrame pleural derecho moderado e izquierdo leve.

Se inicia tratamiento con antibioterapia empírica para infección respiratoria, cediendo el síndrome febril pero continuando el cuadro de disnea.

Se realiza una toracocentesis dignóstica y terapéutica, con características de transudado, presentando una glucosa en líquido pleural mayor que en plasma, con mejoría de la disnea. El

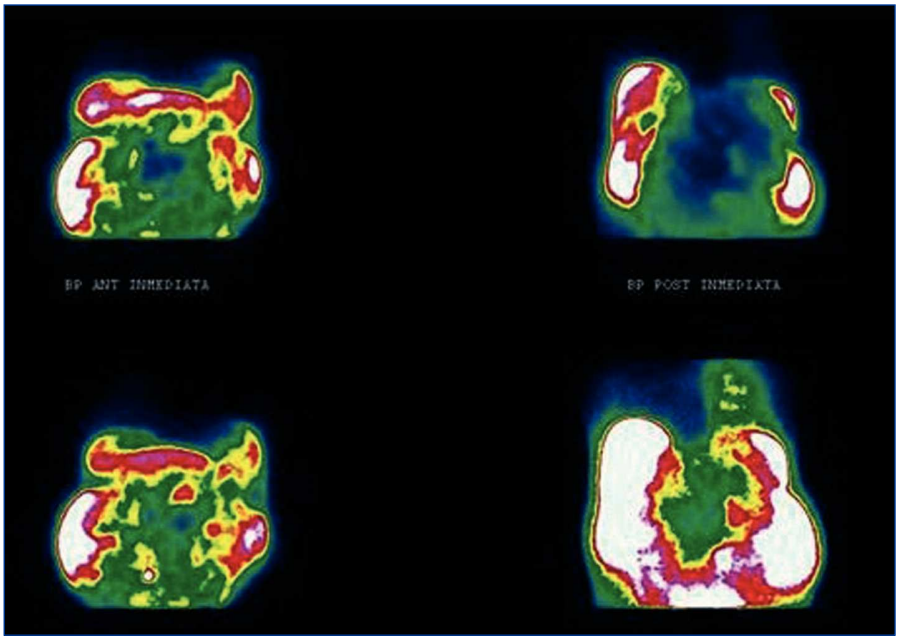

Figura 1. Gammagrafía peritoneal con 99mTc-MAA.
Proyecciones anterior y posterior en decúbito supino en las que se observa el paso del trazador a hemitórax derecho.