Nephrotic syndrome in a 60-year-old man

Miguel Garcia Pardo ,[1] Inmaculada Aparicio,[1] Marta Arregui,[1] Rosa Melero,[2] Francisco Díaz,[3] Rosa Álvarez,[1] Antonio Calles,[1] Miguel Martin[1]

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[1]Medical Oncology, Hospital General Universitario Gregorio Maranon, Madrid, Spain
[2]Nephrology, Hospital General Universitario Gregorio Maranon, Madrid, Spain
[3]Pathology, Hospital General Universitario Gregorio Maranon, Madrid, Spain

Correspondence to
Dr Miguel Garcia Pardo, Hospital General Universitario Gregorio Maranon, Madrid 28007, Spain; miguelgarcia.pds@gmail.com

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CLINICAL QUESTION

A man in his 60s presented with increased oedema in the lower limbs and dyspnoea. Chest X-ray showed right pleural effusion and a body CT scan revealed a severe right pleural effusion as well as presence of solid nodules and pleural plaques. It was decided then to obtain a CT-guided pleural biopsy. Pathology of this biopsy showed an epithelioid mesothelioma. Blood test showed hypoproteinaemia (4.2 g/dL) with hypoalbuminaemia (2.2 g/dL), proteinuria of 1.4 g /24 hours and non-oliguric acute renal failure with serum creatinine of 3.28 mg/dL. A renal biopsy was performed (online supplementary appendix 1).

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WHAT IS YOUR DIAGNOSIS?

A. A (secondary) amyloidosis
B. Collapsing variant of focal segmental glomerulosclerosis
C. Diabetic nephropathy
D. Membranous nephropathy
E. Minimal change disease.

The correct answer is after the Discussion.

DISCUSSION

A clinical suspicion of secondary membranous nephropathy (MN) was made due to the increase in the parietal thickness of the glomerular capillaries, with no evidence of areas of mesangial proliferation or increase in the matrix and areas of moderate fibrosis with tubular atrophy observed in the interstice (online supplementary appendix 1A).

Serology to PLAR2 and PLA2R staining on kidney biopsy was both negative (online supplementary appendix 1B).

Membranous glomerulonephritis (MGN) is associated with different types of malignant neoplasms.[1] Moreover, MGN is the most frequent renal paraneoplastic syndrome in patients with solid tumours, appearing in approximately 75% of patients with nephrotic syndrome and non-haematological cancer.[1] The total incidence of cancer among patients with MGN is 7.9% 2, reaching up to 22% in elderly patients.[2] Since in most cases the nephrotic syndrome precedes about 6 months or appears parallel to the diagnosis of malignant pleural mesothelioma (MPM),[3] it is important to perform an active search for occult neoplasia in adult patients with new-onset nephrotic syndrome, after ruling out a primary origin. The diagnosis of paraneoplastic nephrotic syndrome can be considered if the following criteria are present: (1) no evidence of other aetiology, (2) nephrotic syndrome appears 6 months before or after diagnosis of cancer, (3) cancer treatment is associated with a decrease of proteinuria and (4) tumour relapse is associated with an increase in proteinuria.[1 3] However, in very few cases, all these criteria are met.

Glomerular damage in MGN occurs by two mechanisms: either by subepithelial deposition of circulating immune complexes containing tumour antigens or by deposition of antibodies against tumour antigens that have been attached to the outer surface of the basement membrane.[4] Immunofluorescence microscopy reveals a diffuse granular pattern of immunoglobulin G (IgG) and C3 staining along the glomerular basement membrane. MGN can be staged according to the extent to which the subepithelial immune deposits are surrounded by the glomerular basement membrane. However, this staging has no necessary relationship to the severity of the proteinuria or responsiveness to treatment. Variations in the degree of proteinuria can be useful as a marker of response, since treatment of the primary tumour, by decreasing tumour burden and producing tumour antigens, improves proteinuria in most cases. Likewise, an increase in proteinuria is frequently associated with tumour recurrence or progression.[1]

The association of MGN with pleural mesothelioma is very rare. In the review published by Yildiz H *et al*,[3] only 11 cases have been reported in the literature.

Severe hypoalbuminaemia and nephrotic range proteinuria are typically seen in primary MN but are also described in secondary forms of MN.

Answer: D

Key messages

- Membranous glomerulonephritis is frequently associated with different malignant neoplasms.
- In the presence of a PLA2R-negative membranous nephropathy, it is essential to rule out the presence of a hidden solid tumour[5] .

Correction notice This article has been corrected since it was published Online First. Aperio slide links have been corrected.

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ORCID iD
Miguel Garcia Pardo http://orcid.org/0000-0001-6339-8501

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