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Original article

C3 deposits worsens the prognosis in type III extracapillary glomerulonephritis☆

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ABSTRACT

Introduction: Type III extracapillary glomerulonephritis (PEGN) is a common cause of rapidly progressive glomerulonephritis and it is usually associated with circulating anti-neutrophil cytoplasmic antibodies (ANCAs). Recent evidence points to complement activation as an important factor in the pathogenesis of PEGN.

The aim of the present study was to assess the value of C3 deposits in the prognosis of PEGN.

Methods: All patients diagnosed of PEGN from 1995 to 2015 ($n = 72$) were included in this study. Progression of renal disease in patients with positive staining for C3 by immunofluorescence was compared with those with negative staining. Mean follow up was 73 months. Progression to end-stage renal disease in relation to clinical and histological variables was analyzed.

Results: Positive staining for C3 was observed in 22 out of the 72 patients (30.5%).

At the time of diagnosis, patients with C3 deposits had higher serum creatinine concentration than those without C3 staining (5.00 vs. 3.85 mg/dl, $p = 0.050$). Renal survival at 10 years was 36.9% in patients with positive C3 staining vs. 64.4% in patients with negative staining ($p = 0.005$). Mortality at 10 years was higher in patients with C3 deposits than in patients without deposits (77 vs. 49.3%).

Conclusions: Thus, our study shows that PEGN with deposits of C3 is associated with worse renal prognosis and greater mortality. These results would support the hypothesis that activation of the alternative pathway complement may play an important role in the generation of renal injury associated with PEGN.

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El depósito de C3 en la glomerulonefritis extracapilar de tipo III condiciona un mal pronóstico

Palabras clave:
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Semilunas

RESUMEN

Introducción: La glomerulonefritis extracapilar (GNEC) pauciinmune o de tipo III es una de las causas más comunes de glomerulonefritis rápidamente progresiva y suele estar asociada con la presencia de anticuerpos antineutrófilos citoplasmáticos (ANCA). Están reportándose evidencias sobre la importancia de la activación del complemento en la patogénesis de la GNEC.

El objetivo de nuestro estudio fue evaluar el papel pronóstico del depósito de C3 en las GNEC de tipo III.

Métodos: Se estudió a pacientes diagnosticados de GNEC de tipo III entre 1995 y 2015 (n = 72). Comparamos a pacientes con tinción positiva para C3 en el estudio de inmunofluorescencia con aquellos con tinción negativa. Se analizaron variables clínicas e histológicas y se relacionaron con progresión a enfermedad renal terminal.

Resultados: Se encontró tinción positiva para C3 en 22 pacientes de un total de 72 (30,5%). Basalmente los pacientes con depósitos de C3 tenían peor función renal que aquellos sin depósitos (creatinina sérica 5 vs. 3,85 mg/dl; p = 0,050). La supervivencia renal a los 10 años fue del 36,9% en los pacientes con tinción positiva para C3 frente al 64,4% en los pacientes con tinción negativa (p = 0,005). La supervivencia a los 10 años fue peor en los pacientes con depósitos de C3 (77 vs. 49,3%).

Conclusiones: Nuestro estudio revela que la presencia de depósito de C3 en la GNEC de tipo III se asocia a un peor pronóstico renal y de la supervivencia del paciente. Estos resultados son compatibles con la hipótesis de que la activación de la vía alternativa del complemento contribuye al daño renal asociado a la GNEC de tipo III.

Introduction

Extracapillary glomerulonephritis (ECGN) type III is a severe glomerular disease that is associated with a progressive deterioration of renal function. The term extracapillary glomerulonephritis is generally used in glomerulonephritis with crescents in more than 50% of the glomeruli. It is not a specific disease but rather a manifestation of severe glomerular damage caused by many etiological factors.[1,2]

Classically, it has been associated with the presence of antineutrophil cytoplasmic antibodies (ANCA). The ANCA are mainly directed to 2 antigens, myeloperoxidase and proteinase.[3]

Some aspects of the pathogenesis of this disease are not clear. In the past, it was assumed that the role of complement was minimal.[4] Presently, with the recent advances, it is postulated that the activation of the alternative pathway of the complement could contribute to the pathogenesis of this disease. Experimental models have demonstrated the importance of alternative pathway of complement activation in this entity.[5]

Only few studies have analyzed the presence of complement in kidney samples. Chen et al.[6] observed C3c deposits in 33% of patients with type III ECGN. The presence of C3c deposits was associated with more severe renal insufficiency and increased proteinuria at the onset of type III ECGN. Xing et al.[7] detected the presence of C3d in glomeruli and small blood vessels in renal samples from patients with type III ECGN. Hilrost et al.[8] found complement factors in renal biopsies of patients with type III ECGN and the presence of C3d and properdin was associated with a greater proportion of crescents and greater proteinuria. Recently, Villacorta et al.[9] showed demonstrated that the presence of C3d is an independent risk factor for survival in type III ECGN.

The aim of our study was to evaluate the short and long term prognostic value of C3 deposits in patients with type III ECGN.

Methods

Patients

This is a retrospective observational study including 72 patients with the histological diagnosis of type III ECGN during the years 1995–2015 at the Reina Sofía University Hospital (Córdoba). Demographic, clinical and analytical variables were collected at the time of the biopsy and the analytical and clinical course was observed during the years of follow-up.

In each patient, the reference point was established at the time of biopsy. The follow-up time was established as the interval between the renal biopsy and the last follow-up visit, death or the need for renal replacement therapy (dialysis or renal transplant). The main objective of the study was to analyze whether in type III ECGN the prognosis is modified by the presence of C3 deposits detected by immunofluorescence.