vascular asociado de forma significativa a la enfermedad renal crónica[8-10].

La concordancia encontrada entre ambas ecuaciones (C-G y MDRD-4) mejora cuanto mayor es el grado de afectación del FG, siendo muy buena en pacientes que se encuentra en el estadio 3.

En conclusión, los datos nos muestran la incidencia cada vez mayor de personas con enfermedad renal en las consultas de Atención Primaria, probablemente debido al envejecimiento poblacional, a enfermedades concomitantes, así como al aumento en el consumo de fármacos en general, y principalmente los que pueden afectar a la función renal. Se aprecia, además, el alto porcentaje de personas con FG disminuido a pesar de mantener cifras de creatinina plasmática normales y que habitualmente pasan desapercibidas de no estimarse de un modo más fiable el FG.

Conflictos de interés

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

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Necrotizing crescentic glomerulonephritis in a patient with positive serologies for lupus and antineutrophil cytoplasmic antibodies

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Dear Editor,

Patients with acute renal failure due to pauci-immune necrotizing and crescentic glomerulonephritis with antinuclear antibody (ANCA) seropositivity can present with positive lupus serologies.[1] On the other hand, patients with lupus nephritis present with ANCA seroconversion in 20% of cases. The fact that systemic lupus erythematosus (SLE) and positive myeloperoxidase (MPO) ANCA titers with kidney involvement can present with scant subendothelial deposits in the kidney biopsy, may suggest a forme fruste of lupus nephritis or a concomitant renal vasculitis with neutrophil priming.

A 77-year-old man with chronic kidney disease due to hypertension, presented with hematuria, nausea, and vomiting and red discoloration of urine. Laboratory data Table 1, serology tests Table 2. Renal ultrasonography unremarkable. Patient developed hemoptysis. Chest radiograph revealed bilateral diffuse airspace opacities. Intravenous methylprednisolone was administered. The patient received hemodialysis. Renal biopsy showed mesangial hypercellularity (Figure 1), crescents (Figure 2), segmental necrosis (Figure 1). There was moderate tubular atrophy an occasional eosinophil. Immunofluorescence microscopy demonstrated granular IgG (1+), C3 (2+), and C1q (1+) deposition in the mesangial areas and glomerular basement membranes (Figure 3). EM showed numerous electron-dense deposits in the mesangial areas and few subepithelial and subendothelial electron-dense deposits (Figure 4). Focal effacement of podocyte foot processes was

noted. Histological diagnosis: immune complex-mediated necrotizing and crescentic glomerulonephritis.

Patient received pulse Rituximab and cyclophosphamide. The hospital course was complicated by hypoxic respiratory failure. Folow up computed tomography of the chest showed a right lower lobe pulmonary embolism. Anticoagulation with heparin was initiated. Serological tests were repeated (Table 2) and showed normalization of p-ANCA (<1:20) and anti-double-stranded DNA antibodies. Anti-MPO antibodies were reduced at 9.8U/mL after induction therapy. The patient expired.

Pauci-immune necrotizing and crescentic glomerulonephritis (GN) due to the activation of neutrophils by ANCA, differs from lupus nephritis in that glomerular necrosis and crescent formation occurs in the absence of cellular proliferation and in the presence of scant immune-complex deposition. ANCA are implicated in the pathogenesis targeting cytokine-primed leukocytes that expressed MPO or proteinase 3 (PR 3) instead the white blood cell surface.[2]

Lupus nephritis is an immune complex-mediated renal disease were the formation of glomerular immune deposits results in complement activation, leukocyte infiltration, cytokine release, cellular proliferation, crescent formation, and necrosis under certain circumstances. The final result is glomerular scarring.[1] There are cases of lupus nephritis in which focal or diffuse glomerular necrosis and crescents occur without substantial subendothelial deposits.[3] Patients with lupus nephritis IV-S (2003 International Society of Nephrology/Renal Pathology Society classification/(endocapillary or extracapillary GN involving >50% of glomeruli with segmental lesions) had extensive fibrinoid necrosis and less immune-complex deposition findings resembling a pauci-immune GN at times.[4] Approximately 20% of patients with SLE have ANCA positivity by immunofluorescence microscopy (IF), mainly with a perinuclear (p-ANCA) pattern.[5] Antinuclear antibody seropositivity by enzyme-linked immune-sorbent assay (ELISA) is less frequent, and target antigens are most commonly lactoferrin (LF), cathepsin G, and MPO.[5] Galeazzi *et al*. evaluated 566 patients with SLE and found ANCA positivity by immunofluorescence microscopy in 16.4% of them including 15.4% p-ANCA and 1% c-ANCA pattern. By ELISA, 9.3% had MPO-ANCA positivity and 1.7% had PR3-ANCA positivity.[6] There is difficulty in distinguishing p-ANCA from ANA by immunofluorescence microscopy.[7] There are also conflicting reports on biological significance of ANCA in patients with SLE. Antinuclear antibody positivity has been associated with the presence of nephritis, particularly diffuse proliferative lupus nephritis, as well as anti-dsDNA antibodies.[8] While other reports have failed to show a correlation between ANCA and organ involvement.[9]

Table 1. Laboratory data

Analyte	Reference range	On admission
Sodium (mmol/L)	135-145	142
Potassium (mmol/L)	3.4-4.8	4.2
Chloride (mmol/L)	99-109	106
Carbon dioxide (mmol/L)	21-30	20
Urea nitrogen (mg/dL)	7-22	**107**
Creatinine (mg/dL)	0.5-1.4	**8.1**
Glucose (mg/dL)	65-200	101
Calcium (mg/dL)	8.4-10.2	8.2
Protein (g/dL)	5.5-8.7	7.6
Albumin (g/dL)	3.5-5.0	3.0
Lipase	-	-
Amylase (IU/L)	-	-
Aspartate transaminase (IU/Liter)	17-59	16
Alanine transaminase (IU/L)	21-72	11
Alkaline phosphatase (IU/L)	35-104	45
Leukocytes (x10³/mm³)	4.8-10.8	5.2
Hematocrit (%)	35.0-47.0	25.5
Platelets (x10³/mm³)	130-400	186

Analyte	Reference range	On admission
Urinalysis		Day 1
Color	Yellow	Yellow
Turbidity	Clear	Cloudy
pH	4.6-7.8	6.0
Specific gravity	1.001–1.035	1.014
Glucose	Negative	Negative
Ketones	Negative	Negative
Bilirubin	Negative	Negative
Blood	Negative	**Large**
Protein (mg/dL)	Negative	**≥300**
Nitrites	Negative	Negative
Leukocyte esterase	Negative	Negative
White blood cells/hpf	0-2	**5-10**
Red blood cells/hpf	0-2	**Too numerous**
Urine protein (mg/dL)	5-25	**577.5**
Urine creatinine (mg/dL)	20-370	79
Urine protein/creatinine	0.02-0.13	7.0

Values out of the reference range are in bold.

Table 2. Serologic tests

Analyte	Reference Range	Day 3	Day 19
Antinuclear Ab	Negative	1:80	
p-ANCA	0.0-3.5	**>1:640**	<1:20
c-ANCA	<1:20	<1:20	<1:20
Anti-myeloperoxidase Ab	0.0-9.0	**33.7**	**10.9**
Anti-proteinase-3 Ab	0.0-3.5	<3.5	<3.5
Anti-ds DNA Ab (IU/mL)	<4.9	**Positive**	Negative
Anti-SSA/Ro	Negative	Negative	-
Anti-SSB/La	Negative	Negative	-
Anti-smooth muscle	Negative	Negative	-
Complement C3 (mg/dL)	85-193	85	67.5
Complement C4 (mg/dL)	12-36	25.5	25.4

Values out of the reference range are in bold.

Nasr *et al*. evaluated a cohort of ten patients with SLE, ANCA positivity and renal biopsy findings of lupus nephritis and ANCA-associated GN. All biopsies exhibited necrosis and crescents with no or rare subendothelial deposits.[7] Nine patients had p-ANCA positivity by IF. The high incidence of MPO-ANCA seropositivity in patients with SLE, raises the possibility that the findings are not coincidental occurrence of two unrelated diseases. One condition might trigger the other one or vice versa. Systemic lupus erythematous may facilitate MPO autoantibody formation by promoting neutrophil degranulation and priming neutrophils to increase surface expression of MPO.[7] On the other hand, the association of autoantibodies to MPO in drug-induced SLE has been reported independently.[10] There are conflicting reports on the correlation between the presence of ANCA in SLE and clinical features. Some reports show no correlation between organ involvement and the presence of ANCA, whilst others report a link. In the largest population of patients studied, Galeazzi *et al*. reported significant positive correlations between IF ANCA and venous thrombosis as well as serositis.[6] In this case, our patient presented with an episode of pulmonary embolism, which is consistent this hypothesis. Here, we presented a patient with systemic vasculitis with rapid progressive glomerulonephritis and necrotizing and crescentic changes. Lupus serologies probably represented an autoimmune response to the antinuclear antibody activity. The fact that he had few sub endothelial deposits and lack of hypocomplementemia goes against activation of immune complexes due to SLE. In the other hand, the possibility of a simultaneous ANCA/lupus nephritis involvement represents an interesting hypothesis.

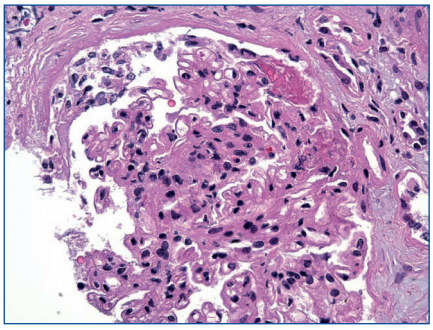

Figure 1. H&E: mesangial hyeprcellularity and necrotizing crescentic glomerulonephritis.

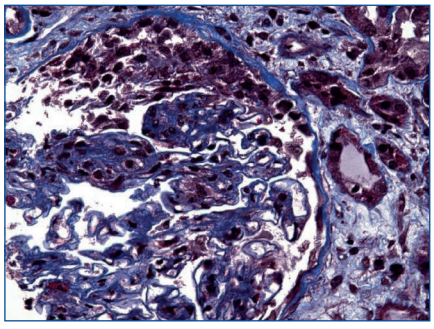

Figure 2. Tricrome: shows cellular crescent (stained red) extending from 11 to 2 o'clock postion.

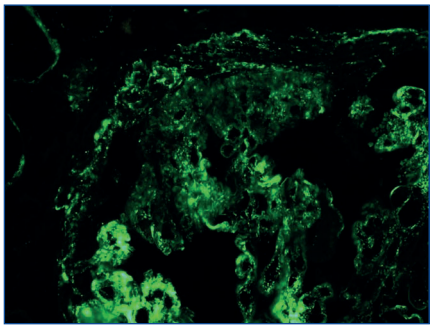

Figure 3. IF for C3: granular predominantly mesangial deposits.

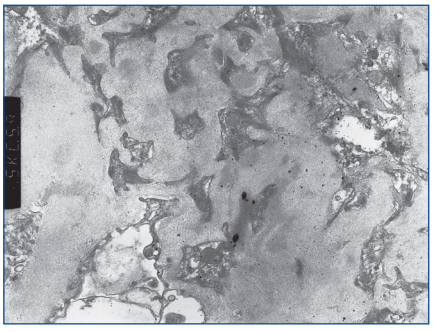

Figure 4. EM: electron dense immune complex deposits in glomerular mesangium (high power).

Conflict of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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C) CASOS CLÍNICOS BREVES

Rápida progresión de poliquistosis renal durante el tratamiento con anticuerpos neutralizantes antifactor de necrosis tumoral

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Sr. Director:

La poliquistosis renal autosómica dominante (PQRAD) es una enfermedad hereditaria producida por mutaciones en los genes pkd1 y pkd2 que codifican las poliquistinas 1 y 2[1]. La enfermedad suele progresar más rápidamente en los pacientes con afectación del pkd1, aunque existe gran variabilidad interindividual, incluso dentro de una misma familia. Es más, la progresión en un mismo paciente no es lineal y en ocasiones puede acelerarse. Entre las explicaciones para esta variabilidad fenotípica se contempla la existencia de mutaciones de diversa gravedad, la carga genética del individuo, la necesidad de un segundo *hit* genético y el impacto de factores ambientales o tercer *hit*[2]. De la hipótesis del segundo *hit* se deduce que la enfermedad poliquística es fenotípicamente dominante pero molecularmente recesiva, de tal manera que, para que una célula tubular origine un quiste, es precisa una segunda mutación somática en el segundo gen pkd1 o pkd2, además de la mutación genética heredada. Con respecto al tercer *hit*, existe evidencia en modelos animales de que la inflamación puede contribuir a la progresión de la cistogénesis. El factor de necrosis tumoral (TNF), la citoquina proinflamatoria por excelencia, disminuye la expresión de poliquistina 2 en ratones[3,4]. Comunicamos la evolución de la función y del volumen renal en un paciente con PQRAD tratado durante más de un año con anticuerpos neutralizantes anti-TNF por otra enfermedad.

CASO CLÍNICO

Varón de 35 años diagnosticado de espondilitis anquilosante HLA B27 positiva en 2011. Una ecografía abdominal mostró múltiples quistes hepáticos y renales. Riñón derecho de 18 cm e izquierdo de 19 cm. Ante ausencia de historia familiar de enfermedades quísticas, se diagnostica de enfermedad poliquística por mutación *de novo*.

En marzo de 2011 inicia tratamiento con adalimumab (Humira®) 40 mg cada 15 días. En ese momento presenta: hemoglobina (Hb) 12,4 g/dl, creatinina (Cr) 2,3 mg/dl, filtrado glomerular estimado (FGe) MDRD (Modification of Diet in Renal Disease) 34 ml/min/1,73 m^2, proteinuria de 10 mg/dl. En septiembre de 2011 muestra: Cr 3,24 mg/dl, FGe MDRD 23 ml/min/1,73 m^2, proteinuria 1,78 g/24 h (figura 1). Se suspende el tratamiento en enero de 2012 por el desarrollo de polineuropatía y púrpura. En febrero de 2012 una resonancia magnética nuclear (RMN) demuestra riñón derecho de 18 cm (volumen de 2450 ml) y riñón izquierdo de 18 cm (2250 ml).