The concordance found between the two equations (C-G and 4-variable MDRD) improves as the degree of GFR involvement increases, being very good in patients in stage 3.

In conclusion, the data show the ever increasing incidence of individuals with kidney disease in Primary Care clinics, probably due to an ageing population, concomitant diseases and the increase in medication use in general, and mainly medications that can affect renal function. We also noted the high percentage of individuals who had a decreased GFR despite maintaining normal plasma creatinine and who usually are undetected since their GFR is not estimated using a more reliable method.

Conflicts of interest

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

1. Otero A, Gayoso P, García F, de Francisco AL. Epidemiology of chronic renal disease in the Galician population: results of the pilot Spanish EPIRCE study. Kidney Int Suppl 2005;(99):S16-9.
2. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16:31-41.
3. Alcázar R, de Francisco ALM. Acción estratégica de la SEN frente a la enfermedad renal crónica. Nefrologia 2006;26:1-5.
4. Rodrigo MP, Andrés MR. Detección de insuficiencia renal oculta en consulta de atención primaria mediante la aplicación de la ecuación MDRD-abreviada: Análisis de 1000 pacientes. Nefrologia 2006;26:339-43.
5. Labrador PJ, Mengotti T, Jiménez M, Macías M, Vicente F, Labrador J, et al. Insuficiencia renal oculta en Atención Primaria. ¿Un problema exclusivo de mujeres? Nefrologia 2007;27:716-20.
6. Otero A, Abelleira A, Camba MJ, Pérez C, Armada E, Esteban J, et al. Prevalencia de insuficiencia renal oculta en la provincia de Ourense. Nefrologia 2003;23(Suppl 6):26.
7. de Francisco ALM, De la Cruz JJ, Cases A, de la Figuera M, Egocheaga MI, Górriz JI, et al. Prevalencia e insuficiencia renal en centros de atención primaria de España. Estudio EROCAP. Nefrologia 2007;27(3):300-12.
8. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004;351:1296-305.
9. Brosius FC III, Hostetter TH, Kelepouris E, Mitsnefes MM, Moe SM, Moore MA, et al. Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease: a science advisory from the American Heart Association Kidney and Cardiovascular Disease Council; the Councils on High Blood Pressure Research, Cardiovascular Disease in the Young, and Epidemiology and Prevention; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: Developed in Collaboration With the National Kidney Foundation. Circulation 2006;114:1083-7.
10. Keith DS, Nichols GA, Gullion CM, Brown JB, Smith DH. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. Arch Intern Med 2004;164:659-63.

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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) at 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) can have of 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.

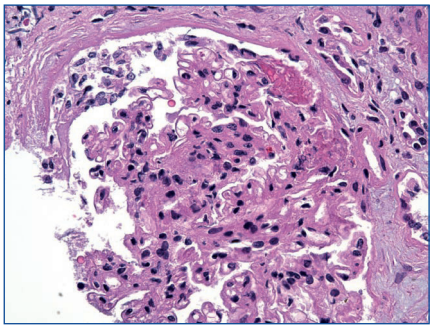

Figure 1. H&E: mesangial hyeprcellularity and necrotizing crescentic glomerulonephritis.

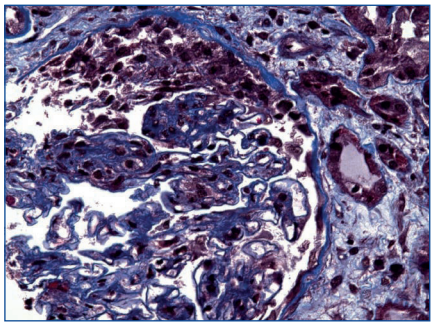

Figure 2. Tricrome: shows cellular crescent (stained red) extending from 11 to 2 o'clock postion.

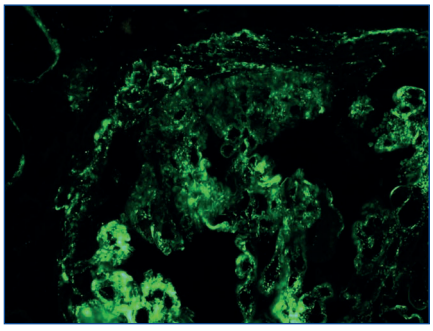

Figure 3. IF for C3: granular predominantly mesangial deposits.

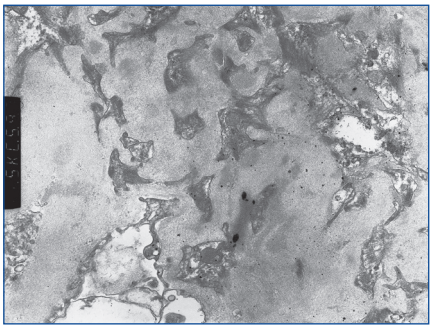

Figure 4. EM: electron dense immune complex deposits in glomerular mesangium (high power).

Conflict of interest

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

1. Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, Appel GB, et al. The classification of glomerulonephritis in systemic lupus erythematosus revisited. Kidney Int 2004;65:521-30.
2. Jeannette JC, Xiao H, Falk RJ. Pathogenesis of vascular inflammation by anti-neutrophil cytoplasmic antibodies. J Am Soc Nephrol 2006;17:1235-42.
3. Schwartz MM, Roberts JL, Lewis EJ. Necrotizing glomerulitis of systemic lupus erythematosus. Hum Pathol 1983;14:158-67.
4. Najafi CC, Korbet SM, Lewis EJ, Schwartz

MM, Reichlin M, Evans J; Lupus Nephritis Collaborative Study Group. Significance of histologic patterns of glomerular injury upon long-term prognosis in severe lupus glomerulonephritis. Kidney Int 2001;59:2156-63.
5. Sen D, Isenberg DA. Antineutrophil cytoplasmic autoantibodies in systemic lupus erythematosus. Lupus 2003;12:651-8.
6. Galeazzi M, Morozzi G, Sebastiani GD, Bellisai F, Marcolongo R, Cervera R, et al. Anti-neutrophil cytoplasmic antibodies in 566 European patients with systemic lupus erythematosus: prevalence, clinical associations and correlation with other autoantibodies. European Concerted Action on the Immunogenetics of SLE. Clin Exp Rheumatol 1998;16(5):541-6.
7. Nasr SH, D'Agati VD, Park H-R, Sterman PL, Goyzueta JD, Dressler RM, et al. Necrotizing and crescentic lupus nephritis with antineutrophil cytoplasmic antibody seropositivity. Clin J Am Soc Nephrol 2008;3:682-90.
8. Chin HJ, Ahn C, Lim CS, Chung HK, Lee JG, Song YW, et al. Clinical implications of antineutrophil cytoplasmic antibody test in lupus nephritis. Am J Nephrol 2000;20:57-63.
9. Nishiya K, Chikazawa H, Nishimura S, Hisakawa N, Hashimoto K. Anti-neutrophil cytoplasmic antibody in patients with systemic lupus erythematosus is unrelated to clinical features. Clin Rheumatol 1997;16:70-5.
10. Cambridge G, Wallace H, Bernstein RM, Weaker B. Autoantibodies to myeloperoxidase in idiopathic and drug-induced systemic lupus erythematosus and vasculitis. Br J Rheumatol 1994;33:109-14.

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C) BRIEF CASE REPORT

Rapid progression of polycystic kidney disease during treatment with tumour necrosis factor-neutralising antibodies

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To the Editor,

Autosomal dominant polycystic kidney disease (ADPKD) is a hereditary disease caused by mutations in genes PKD1 and PKD2, which codify polycystins 1 and 2[1]. The disease usually progresses more quickly in patients with PKD1 involvement, although there is wide interindividual variability, even within the same family. Furthermore, the progression of a given patient is not linear and may occasionally accelerate. Explanations for this phenotypic variability include the existence of mutations of varying severity, the individual's genetic load, the need for a second genetic hit and the impact of environmental factors or a third hit[2]. From the second hit hypothesis, it is deduced that polycystic kidney disease is phenotypically dominant but molecularly recessive, such that, for a tubular cell to create a cyst, a second somatic mutation in the second pkd1 or pkd2 gene would be necessary, as well as the inherited genetic mutation. With respect to the third hit, there is evidence in animal models that inflammation may contribute to the progression of cystogenesis. Tumour necrosis factor (TNF), the quintessential proinflammatory cytokine, decreases the expression of polycystin 2 in mice[3,4]. We reported the evolution of kidney function and volume in a patient with ADPKD treated for more than one year with TNF-neutralising antibodies due to another disease.

CASE REPORT

A 35-year-old male diagnosed with HLA B27-positive ankylosing spondylitis in 2011. An abdominal ultrasound displayed multiple hepatic and renal cysts. The right kidney was 18cm and the left kidney was 19cm. Given the lack of a family history of cystic diseases, he was diagnosed with polycystic kidney disease due to *de novo mutation*.

In March 2011, he began treatment with 40mg adalimumab (Humira®) every 15 days. At that time he had: haemoglobin (Hb) 12.4g/dl, creatinine (Cr) 2.3mg/dl, estimated glomerular filtration rate (eGFR) (according to Modification of Diet in Renal Disease) 34ml/min/1.73m^2, proteinuria 10mg/dl. In September 2011 he had: Cr 3.24mg/dl, eGFR MDRD 23ml/min/1.73m^2, proteinuria 1.78g/24h (Figure 1). Treatment was discontinued in January 2012 because the patient developed polyneuropathy and purpura. In February 2012 a nuclear magnetic