

A rare morphologic pattern in a common disease, or two diseases?

Mário Góis^{1,2}, Ana Valada Marques³, Isabel Mesquita¹, Helena Sousa^{1,2}, Fernanda Carvalho^{1,2}, Fernando Nolasco^{1,2}

¹ Department of Nephrology, Centro Hospitalar de Lisboa Central – Hospital Curry Cabral, Lisboa, Portugal.

² Laboratory of Renal Morphology, Centro Hospitalar de Lisboa Central – Hospital Curry Cabral, Lisboa, Portugal.

³ Department of Medicine, Centro Hospitalar do Oeste – Caldas da Rainha, Portugal.

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■ CLINICAL PRESENTATION

An 86-year-old male presented at the emergency room with lower limb oedema, asthenia and a progressive decrease in urine output, with one week of evolution. In the previous 2 weeks he had noticed haematuria without dysuria or other lower tract urinary symptoms, which resolved spontaneously in two days. He did not seek medical attention.

Two months prior to the presentation, his serum creatinine was 0.99 mg/dl, but since 2009 urinalysis had shown microhaematuria.

One month before, after anti-tetanus vaccine, the patient had flu-like syndrome, which resolved in a few days.

There was no history of alopecia, arthritis, oral ulcers, *sicca* syndrome, allergies, diarrhoea, fever, weight loss, nephrolithiasis, recurrent urinary tract infection, taking of NSAIDs, dietary supplements, natural medicines or antibiotics. He also denied animal contact and recent trips.

At presentation, he was oriented and afebrile; his blood pressure was 206/93 mmHg, pulse 52 ppm, and oxygen saturation 100%.

He presented mild inspiratory rales at both lung bases and peripheral oedema (++) . He had two small cutaneous purpuric non-palpable lesions on the back of the right hand and the anterior face of the left leg. The remaining physical examination was unremarkable.

Laboratory test results showed acute renal failure (serum creatinine 4.06 mg/dl, urea 167 mg/dl),

hyperkalaemia (6.3 mmol/l), haemoglobin 12 g/dl, leucocytosis (12700/ μ l), C-reactive protein 22 mg/l and albumin 3.53g/l.

Urinalysis showed haematuria and proteinuria (protein 100mg/dL; red blood 3+cells/HPF), no casts. Urine protein:creatinine ratio 5479,5 mg/g.

Renal and bladder ultrasound showed normal-sized kidneys, small decrease in renal cortical thickness and absence of urinary tract obstruction. No bladder lesions were detected.

His past medical history was significant for hypertension, dyslipidaemia, hyperuricaemia and chronic lymphocytic leukaemia (CLL) diagnosed in 2010, with stable lymphocyte count, without treatment criteria and under annual surveillance in haematology consultation. The patient had undergone a radical prostatectomy in 2011 due to benign prostatic hyperplasia.

His chronic medication was 5mg bisoprolol, 20 mg lisinopril, 5 mg amlodipine, 20mg rosuvastatin and 300 mg allopurinol.

■ COMPLEMENTARY EXAMINATION

Subsequent laboratory study disclosed normal C3 and C4, positive ANA 1:160 with nuclear mitotic apparatus pattern, with anti-dsDNA negative. The remaining laboratory tests, including anti-GBM, ANCA, rheumatoid factor, anti-Jo 1, anti-SSB/La, anti-SSA/Ro, lupus anticoagulant, anti-cardiolipin and anti-beta-2

glycoprotein, HBsAg, anti-HCV, anti-HIV and protein electrophoresis, were negative. Serum immunoglobulin IgA, IgM and IgG were normal and there was no evidence of monoclonal component. The urinary immunofixation was unremarkable. Thyroid function tests were normal. The 24h proteinuria was 3.9g with a urine output of 3000 ml/day. Complementary studies, chest X-rays, ECG and 2D-echocardiogram, did not reveal significant changes.

Dermatological observation excluded skin infiltration of CLL and palpable purpura. Senile purpura was diagnosed.

A kidney biopsy was performed.

HISTOLOGICAL FINDINGS

The paraffin-embedded fragment shows kidney cortical with a total of eleven glomeruli and several small and medium-sized arteries.

Figure 1 shows a section with intense endocapillary hypercellularity (with lymphocytes and monocytes) and podocytes marked hypertrophied. There is also an increased mesangial matrix with PAS (+) deposits.

The activation of podocytes (hypertrophy) is well represented in **Figure 2**. This PAS stain illustrates areas of glomerular capillary loop collapse, with podocyte hypercellularity and with adhesions to Bowman capsule.

In **Figure 3** we can see a glomerulus with podocyte proliferation with prominent and large protein reabsorption droplets.

Finally, we present **Figure 4**. In this methenamine silver stain, intense podocytes and epithelial cells hypercellularity resembling a crescent are seen. A concomitant endocapillary proliferation with increased numbers of mononuclear inflammatory cells in glomerular capillaries, as described in previous figures 1 to 3, is also present.

Immunofluorescence, performed in frozen tissue, shows granular mesangial deposits of IgA (3+) and C3, but less intensive (2+), lambda light chain (1+) and kappa light chain (trace), with extension into the paramesangial capillary walls (see **Figures 5 and 6**).

The diagnosis of collapsing glomerulopathy in a patient with underlying IgA nephropathy was made.

Figure 1

Periodic acid shift (PAS); x400

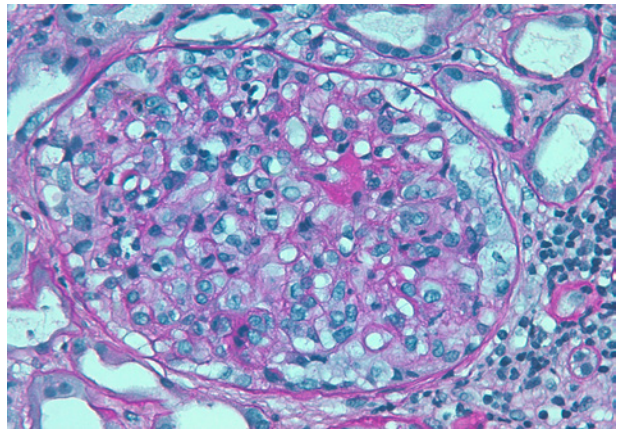


Figure 2

Periodic acid shift (PAS); x400

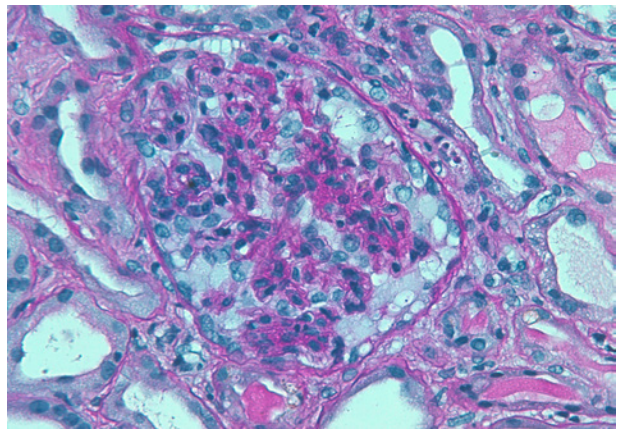


Figure 3

Periodic acid shift (PAS); x400

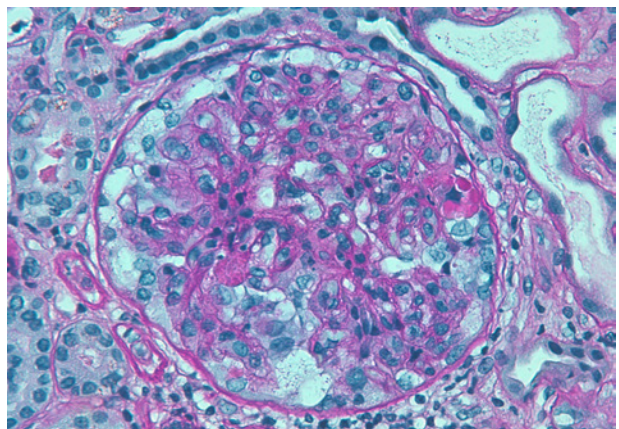
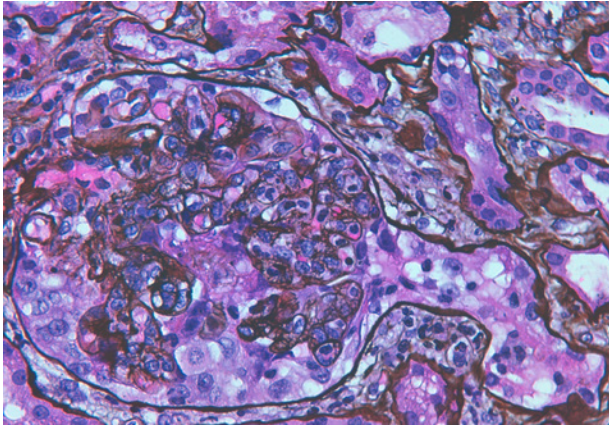
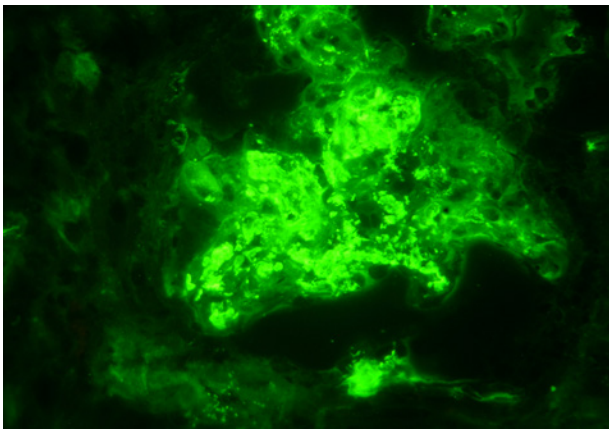


Figure 4

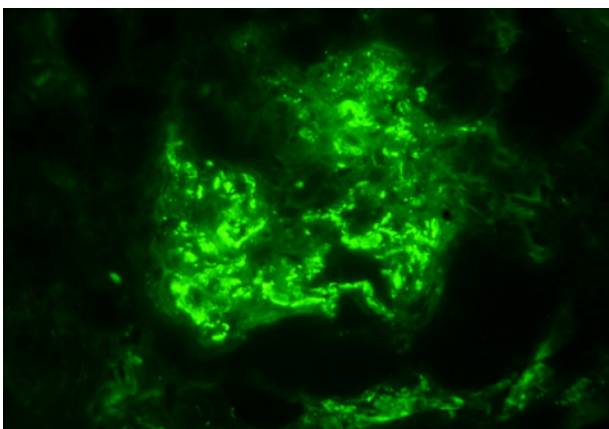
Methenamine silver; x400

**Figure 5**

Immunofluorescence; IgA; x400

**Figure 6**

Immunofluorescence; C3; x400



According with Oxford-MEST classification, this kidney biopsy has a MOE1S1T2 score.

■ TREATMENT AND EVOLUTION

The patient was treated with 1000 mg IV of methylprednisolone on 3 consecutive days followed by 0.7 mg/kg/day (40 mg/day) of prednisolone. Unfortunately, progressive renal dysfunction was observed despite preserved urine output. The patient started haemodialysis and as of the present date has not recovered kidney function.

■ DISCUSSION

IgA nephropathy is the most common glomerulonephritis, with a heterogeneous clinical course¹. This entity has a wide spectrum of morphological patterns, which vary from a mild mesangial proliferation to crescentic and collapsing variants².

This case described a patient, probably with a long-duration IgA nephropathy (corroborated by the presence of microhaematuria in his past medical history), with an indolent clinical course. Prior to this episode the patient had a flu-like syndrome, which can act as trigger for the worsening of kidney function, with the development of a collapsing variant. So, if we consider this hypothesis, the patient has only one disease – IgA nephropathy – with secondary lesions of segmental and focal glomerulosclerosis, in this case a collapsing variant. The negative impact on prognosis of the lesions of FSGS in patient with IgA nephropathy is well recognized, with the collapsing variant carrying the worse prognosis³. Another important aspect is the fact that elderly patients with new-onset IgA patients have a more severe renal involvement and worse renal and vital prognosis⁴.

On the other hand, as the clinical and laboratorial data revealed, the patient had a severe glomerular involvement. So, we can formulate the hypothesis that the patient has, in fact, IgA nephropathy, but has a superimposed collapsing glomerulopathy, without any evident cause in this case, in spite of the extensive clinical and laboratory investigations performed. The patient has LLC, well-controlled, and to best of our knowledge, there is no clear association with LLC and collapsing glomerulopathy. In our case,

the lymphocyte infiltrate in kidney parenchyma is scanty and located mainly in a subcapsular area and around few glomeruli. It is also important to clarify that the renal prognosis is poor, as is demonstrated by significant interstitial fibrosis and tubular atrophy (>50% of renal parenchyma).

This case emphasizes the central role of renal biopsy, with an unexpected diagnosis, in an elderly patient with multiple co-morbidities, acute renal failure and nephrotic proteinuria

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References

1. Levy M, Berger J. Worldwide perspective of IgA nephropathy. *Am J Kidney Dis.* 1988 Nov;12:340-347.
2. Ferrario F, Rastaldi MP, Napodano P. Morphologic features in IgA nephropathy. *Ann Med Interne.* 1999; 150:108-116.
3. Karoui KE, Hill GS, Karras A, et al. Focal segmental glomerulosclerosis plays a major role in the progression of IgA nephropathy. II. Light microscopy and clinical studies. *Kidney Int.* 2011; 79: 643-654.
4. Wen YK, Chen ML. Differences in new-onset IgA nephropathy between young adults and the elderly. *Ren Fail.* 2010; 32:343-348.

Correspondence to:

Mário Góis

Department of Nephrology, Centro Hospitalar de Lisboa Central – Hospital Curry Cabral, Lisboa, Portugal

Laboratory of Renal Morphology, Centro Hospitalar de Lisboa Central – Hospital Curry Cabral, Lisboa, Portugal

E-mail: mariovgois@gmail.com