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Focal segmental glomerulosclerosis associated with polycythaemia vera

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Dear Editor,

Focal segmental glomerulosclerosis (FSGS) is characterised by the presence of nephrotic syndrome, hypertension and progressive deterioration of kidney function. Although in many cases its aetiology is unknown, it has been associated with inherited disorders, viral infections, induced by toxic substances and with hyperfiltration situations.[1]

Polycythaemia vera (PV) is a myeloproliferative disorder of unknown aetiology characterised by excessive production of normal erythrocytes, leukocytes and platelets.[2]

Glomerular involvement in PV is rare. We present a patient diagnosed with PV with nephrotic syndrome secondary to GSF and progressive kidney disease.

An 83 year-old woman, diagnosed with PV 4 years earlier, was admitted for the study of nephrotic syndrome and kidney disease of 2 years evolution.

There was no family history of polycythaemia. Among her background was: left nephrectomy due to hypernephroma at 63 years, bronchiectasis with recurrent bacterial superinfections, hypertension controlled with medication and celiac disease well controlled through diet. Four years earlier she was diagnosed with PV after a bone marrow biopsy, including details of polycythaemia and thrombocytosis, well controlled with hydroxyurea treatment (500mg/day).

In March 2007, she began with nephrotic range proteinuria (4.2g/day) with Crs 1.1mg/dL; antiproteinuric treatment was started with telmisartan 80mg/day and spironolactone 50mg/day. A month later the proteinuria dropped to 1.2g/day with no change in the creatinine. She was admitted to hospital in June 2007 for severe hyponatraemia (107mEq/L), symptomatic, with hyperkalaemia (5.7mEq/L) and metabolic acidosis (pH 7.34) secondary to treatment with spironolactone. Due to the persistence of nephrotic proteinuria and her history of bronchiectasis, a biopsy of rectal and abdominal fat was performed which discarded the existence of amyloidosis. Throughout its evolution, the proteinuria varied between 4-10g/day and started with lower limb oedema, decreased total protein and albumin (5.4/2.7g/dL) and a progressive decline in the glomerular filtration rate (Crs 1.6-1.7mg/dL).

In May 2009 she was admitted to hospital due to a deterioration in her general condition, oedema, Crs 3.6mg/dL and proteinuria 8.4g/day despite treatment with ARB. On admission, her blood pressure was 137/82mmHg; in the physical examination her systolic ejection murmur was heard II/VI in the left sternal border, and she had bilateral pitting oedema up to the root of her thigh. CBC: haemoglobin 16.8g/dL, haematocrit 56%, RBC 6,750,000/µL, 11,690/µl leukocytes with normal formula and platelets 460,000/µl. Crs 4.3, urea 102 (mg/dL). Total protein 5.9, albumin 2.5g/dL, cholesterol 188, triglycerides 260, uric acid 9.8mg/dL. Proteinuria 6.9g/d; 1.4 sediment erythrocytes/field and 5-10 leukocytes/field. Immunology: ANA, anti-DNA, ENA, ANCA and anti-GBM negative. Complement: $C_3$79, $C_4$30mg/dL. CRP 0.37mg/dL. Rheumatoid factor negative. IgG 820, IgA 185, IgM 188mg/dL. Kappa 635, lambda 515mg/dL. Kidney biopsy was performed with 8 glomeruli of which two were completely sclerosed, and the remaining six, one global mesangial expansion with increased mesangial cells could be seen and the other five had segmental proliferative lesions without necrosis accompanied by moderate epithelial proliferation. The interstitium showed moderate fibrosis with tubular atrophy and occasional chronic inflammatory infiltrates. Arterial and arteriolar vessels with hyperplastic lesions with occasional hyaline lesions. These findings were indicative of *cellular variant segmental proliferative glomerulonephritis*.

Treatment was initiated with three shocks of 125mg of 6-methylprednisolone followed by prednisone (1mg/kg/day) and mycophenolate mofetil (360mg/12 hours). No evidence of a decrease in proteinuria was seen and kidney function deteriorated progressively with clinical uraemia. So it was decided to make the right jugular catheter permanent and initiate treatment with periodic haemodialysis. A progressive improvement in the symptoms was seen. Treatment with mycophenolate mofetil was discontinued and prednisone was gradually withdrawn.

The patient developed a nephrotic syndrome secondary to FSGS 4 years after detection of the polycythaemia. It met the WHO criteria for diagnosis of

PV[2] (Hb greater than 16.5g/dL in women, no cases of secondary polycythaemia, decreased EPO levels, splenomegaly, thrombocytosis > 400,000/µl and leukocytosis > 12,000/µL). Despite good control of the PV with hydroxyurea and treatment with high dose steroids and immunosuppressive agents, the nephrotic syndrome did not improve, and was accompanied by a progressive deterioration of kidney function with uremic symptoms and initiation of replacement therapy.

The kidney biopsy showed the existence of a focal segmental glomerulosclerosis cell variant that had a worse prognosis than the other FSGS (perihilar hyalinosis, tip variant and classical variant) and better than collapsing variant.[3]

The joint presence of FSGS and PV is a rare combination. There have only been 6 published cases confirmed histologically in the literature.[4-8] Table 1 summarises the clinical data of the 6 cases reported and of the current one.

From this we can get some interesting data. The average age at the time of kidney biopsy was 60.3 years (range 41-83). FSGS was diagnosed up to 4 years after the detection of polycythaemia in 5 of the 7 cases (71.4%). Four patients (57.1%) developed nephrotic range proteinuria, 3 patients were treated with steroids and immunosuppressive agents, of whom only one had improvement of kidney function. The other two were given haemodialysis due to progressive deterioration of plasma creatinine with onset or worsening of uremic symptoms.

The presence of FSGS in these patients could be directly related to the PV. As noted by Sharma et al,[4] the haemodynamic changes in the PV, as well as kidney vasodilation and increased effective kidney blood flow could trigger kidney glomerulosclerosis. Ferrario et al[9] suggested that the haemodynamic glomerular injury induces the activation of the mesangial cells, leading to overproduction of extracellular matrix. Furthermore, damaged endothelial cells facilitate platelet activation by releasing platelet activating factor, which induces proliferation of endothelial and mesangial cells. These alterations may contribute to the development of glomerular sclerotic changes.

To summarise, we recommend regular testing for the presence of kidney damage in patients with PV. If these patients develop proteinuria, association with FSGS could be considered as a possible complication, although it is rare. The combination of steroids and immunosuppressive drugs administered early in patients with nephrotic range proteinuria may slow the progression of kidney damage.

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Table 1. GSF cases associated with PV

Authors	Age (years)	Sex	Time since PV diagnosis (years)	Proteinuria at kidney biopsy (g/day)	Treatment	Evolution of kidney function	Follow-up period
Sharma et al[4]	41	F	3	1.8	–	Improved	2 years
Au et al[5]	48	M	20	2.5	HU	PD	17 years
Au et al[5]	63	F	22	5.4	HU	PD	4 years
Kosch et al[6]	52	M	4	1.2	Phlebotomies	Improved	18 months
Iyoda et al[7]	66	F	3	9.6	ES, HU	HD	7 years
Okuyama et al[8]	69	F	3	8.3	ES, HU	Improved	4 years
Caso actual	83	F	4	8.2	ES, HU, MF	HD	3 months

HU: hydroxyurea; S: Steroids; M: mycophenolate; PD: peritoneal dialysis; HD: haemodialysis.

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Emhysematous pyelonephritis and polycystic hepatokidney radical nephrectomy

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Dear Editor,

Adult polycystic kidney disease (PCKD) is an inherited disorder characterised by the presence of kidney cysts, which affects approximately one in every 500 to 1,000 people. The most common manifestations are lumbar pain, haematuria and recurrent urinary infections.[1,2] Emphysematous pyelonephritis is a severe infection characterised by the presence of gas in the kidney parenchyma, collecting system or perinephric tissue, and occurs primarily in diabetic patients.[3]

We report the case of a 76 year-old woman with hypertension, diabetes, chronic kidney disease secondary to polycystic hepatokidney disease in a peritoneal dialysis programme since March 2008, when she was admitted for fever, dysuria and haematuria. Laboratory tests showed elevated inflammatory parameters and the presence of *E. coli* from urine and blood culture tests. A CT scan showed a cyst on the upper right kidney complicated with air in the calices and bladder without prior manipulation of the urinary tract (Figure 1). Broad-spectrum antibiotic treatment with meropenem and gentamicin, according to the antibiogram sensitivity, was started and the patient was temporarily transferred to haemodialysis to treat intercurrent septic profile better. Despite this treatment, the patient continued to be febrile and showed a deterioration in her general condition. A new tomographic control was therefore done and a deterioration of the right kidney cyst was seen. Given the poor outcome of the septic profile with a lack of response to treatment, a right radical nephrectomy was performed, which revealed multiple kidney cysts filled with pus (Fig. 2). Further evolution was slow towards the improvement of her general condition, with a practical resolution of fever and progressive normalisation of the inflammatory parameters. Finally, the patient was able to be released after a long period of convalescence in a clinical and haemodynamically stable state, continuing kidney replacement therapy with regular haemodialysis.

In PCKD, recurrent urinary tract infections can cause septic conditions which are difficult to control due to secondary infection of the cysts. The prevalence of cystic infection is high (30-50%), and is more common in women with a history of urinary tract manipulation, nephrolithiasis and/or vesicoureteral reflux. The quinolones, trimethoprim/sulfamethoxazole and chloramphenicol reach good therapeutic concentrations within the cyst. A good response to antibiotic treatment is observed in most cases, and it is rarely necessary to take aggressive interventionist measures such as percutaneous drainage, and much less frequently, nephrectomy.

Emphysematous pyelonephritis is a severe kidney infection, usually caused by gas-producing coliform bacteria, with *E. coli* the most common organism, usually affecting patients with diabetes. It is characterised by its aggressive progression and poor response to treatment. It is associated with a high mortality, so nephrectomy may be advisable in selected cases.

A better understanding of the disease, the vast antimicrobial arsenal available today, with greater synergy and antibiotic potency, the emergence of minimally invasive interventional radiologic techniques and the fact that nephrectomy has a significant rate of morbidity and mortality (12 and 5%, respectively) in high-risk surgical patients, are among the factors to be considered for nephrectomy in patients with terminal kidney disease.[3-5] At present, radical or partial nephrectomy should be considered for patients with a poor response to antibiotic treatment or percutaneous drainage due to its potential complications.

To summarise, the above is an example of a patient with emphysematous pyelonephritis and hepatokidney polycystosis with, firstly, a slow evolution of an unusual and severe kidney infection and, secondly, the need for radical nephrectomy as definitive treatment.

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