

and 10%) are gastrointestinal problems, headache and abnormalities in laboratory tests such as pancytopenia and lactic acidosis. Central nervous system disorders and bacterial or fungal superinfection appear less frequently.

We present the case of a 79-year-old man with a history of with drug-controlled hypertension, benign prostatic hyperplasia and chronic kidney disease stage 4 in outpatient nephrology follow-up for 8 months. He underwent surgery for a prosthetic left knee in a local hospital on 18<sup>th</sup> March 2010, and needed subsequent surgical cleaning for prosthetic infection on April 26<sup>th</sup>, when antibiotic treatment with linezolid and levofloxacin was started. He was discharged on 28<sup>th</sup> May. The patient maintained treatment with linezolid for 7 weeks. The germ causing the prosthetic infection was unknown.

On June 10 the patient visited the emergency department of our hospital for malaise, asthenia, anorexia, vomiting and weight loss. Upon arrival, the patient was in good general condition, without signs of poor peripheral perfusion. Blood pressure was 118/52mm Hg, temperature of 36.5°C and the heart rate was 72 beats/min. There was a slight increase in local temperature of the left knee, with minimal effusion. Laboratory tests included the following: urea 184mg/dl, creatinine 2.6mg/dl, potassium 5.7mmol/l, leukocytes 4000/ $\mu$ l, with 61.3% neutrophils, haemoglobin 9g/dl, platelets 45000/ $\mu$ l, lactic acid 3.11mmol/l, pH 7.25 and bicarbonate 18.5mmol/l. The patient was admitted to orthopedic surgery.

Given these laboratory findings and the absence of signs of systemic infection justifying lactic acidosis or pancytopenia, they were considered as side effects of linezolid. This was therefore withdrawn without any antibiotic alternative.

Progressive improvement of the pancytopenia and renal function after hydration of the patient were reported in subsequent days, so the patient was transferred to the hospital where underwent surgery. Upon discharge, the following results were found: creatinine 1.51mg/dl, total leukocyte count 5300/ $\mu$ l, haemoglobin 9g/dl and platelets 59 000/ $\mu$ l.

Although linezolid is a very effective antibiotic in cases refractory to conventional antibiotics, its possible side effects must always be taken into account. In this case it caused pancytopenia and lactic acidosis, which improved after withdrawal of the drug.

1. Uptodate.
2. [https://sinaem4.agedmed.es/consaem/fichas\\_Tecnicas.do?metodo=buscar](https://sinaem4.agedmed.es/consaem/fichas_Tecnicas.do?metodo=buscar)
3. Nefrologia 2008;Supl 6:119-24.

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### Another patient with a natural history of diabetic nephropathy: current situation and means of prevention

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#### To the Editor,

Diabetic nephropathy (DN) is the leading cause of chronic kidney disease (CKD) in developed countries,<sup>1</sup> with an increasing incidence and prevalence. We describe the effects of diabetes mellitus (DM) on the kidney after

years of natural development (without prior renoprotective treatment and poor metabolic control).

#### CASE REPORT

A 60-year old man with a previous history of type 2 DM for more than 20 years, treated with antidiabetic agents initially and insulin for the last 5 years, and with poor metabolic control. Non-proliferative diabetic retinopathy. Ex-smoker of 30 cigarettes per day until 5 years ago.

The patient visited the emergency department complaining of generalised oedema of one month duration, dyspnoea, and 2-3 times nocturia. On physical examination, the patient was in good general condition, was conscious and oriented. Blood pressure was 160/110mm Hg, heart rate 80 beats/min. Jugular venous distension. Cardiac auscultation was rhythmic. Pulmonary auscultation showed minimum crackles in the bases. Pitting oedema to knee. The rest of the examination was normal.

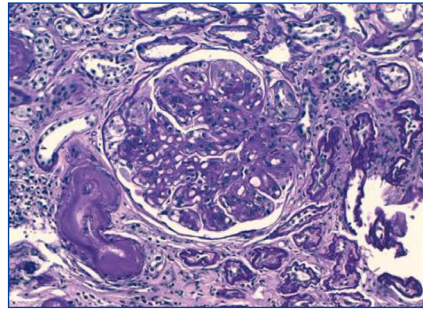
Blood analysis revealed glucose 200mg/dl, urea 52mg/dl, creatinine 1.2mg/dl, uric acid 5.3mg/dl, cholesterol 313mg/dl, triglycerides 144mg/dl, albumin 1.9g/dl, total protein 4.4g/dl, calcium 7.6mg/dl, phosphorus 3.2mg/dl, iron 41  $\mu$ g/dl, and ferritin 155ng/ml. The haemoglobin was 11.6g/dl, haematocrit 34.3%, and the rest of the blood count and coagulation tests were normal. The thyroid hormones, antibodies, viruses (HIV, hepatitis B and C) and PSA were normal. Haemoglobin A<sub>1c</sub> was 8.3%. The immunological test, including immunoglobulin, complement, rheumatoid factor, ASO, ANA, anti-DNA, ANCA and C-reactive protein were also normal.

The urinalysis revealed protein +++, blood + glucose ++ and negative nitrite. Proteinuria in 24-hour urine

collection was 10g. In urine electrophoresis, proteinuria was non-selective, with the Bence-Jones proteinuria negative.

The chest x-ray revealed cardiomegaly and signs of venocapillary stage II hypertension. The abdominal ultrasound found the right kidney to be 12cm, of normal morphology, and the left kidney was 15cm, with dilatation of the excretory system.

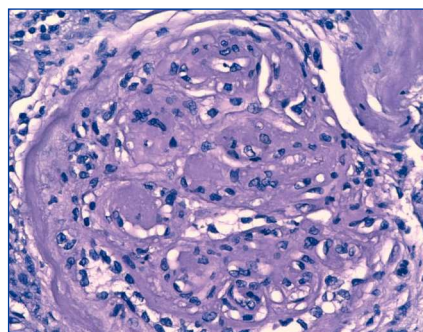
Depletive treatment was initiated with diuretics, angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs), statins, low molecular weight heparin, and improvement of glycaemic control was recommended. Given the left kidney hydronephrosis caused by ureteropelvic junction syndrome, pyeloplasty was performed and a percutaneous nephrostomy tube was placed in the left kidney. Despite these measures, the patient required further hospital admissions for acute nephrotic syndrome, with plasma creatinine increasing to 2.5-3mg/dl and persistent nephrotic proteinuria, which is why it was decided to initiate haemodialysis. Although DN was initially suspected, as poor volume control persisted during haemodialysis, with biochemical activity of the nephrotic syndrome, we decided on a renal biopsy to rule out associated glomerulopathy. The biopsy findings were: 12 glomeruli per section, five of them completely sclerosed. All the glomeruli studied showed mesangial expansion with acellular nodules (Kimmelstiel-Wilson). Immunofluorescence was negative. In the interstitium, there was moderate fibrosis with associated focal tubular atrophy. The vascular tissue showed a striking hyalinosis of the wall, being the final pathological diagnosis consistent with a diffuse (Figure 1) and nodular (Figure 2) glomerulosclerosis, with a morphological substrate of diabetic disease.



**Figure 1.** PAS technique (x20): diffuse glomerulosclerosis with hyalinosis of the efferent arteriole and intense hyalinosis of the medium-calibre vessels.

### Discussion

Metabolic and haemodynamic factors have been implicated in the pathogenesis of DN,<sup>2</sup> Angiotensin II plays a main role in the pathogenesis and progression of DN, and its inhibition confers renoprotection in patients with diabetes.<sup>3</sup> A delay in starting treatment with ACE inhibitors or ARBs in patients with type 2 diabetes, proteinuria and renal failure, makes them less effective, hence the importance of early treatment.<sup>3</sup> In the case presented, despite starting therapy during the first admission with renin-angiotensin-aldosterone system (RAAS) inhibitors, the nephrotic syndrome remained uncontrolled and the patient had to be readmitted for hypoxic decompensation. This lack



**Figure 2.** Haematoxylin-eosin technique (x40): typical nodular glomerulosclerosis

of response to treatment may be explained, firstly, by the long history of diabetes, with poor metabolic control; secondly, by the presence of severe proteinuria when the patient was first examined and the absence of prior therapy with antiproteinuric drugs; and thirdly, by the histological findings of the renal biopsy.

With current treatment, the progression of DN to CKD remains, so the RAAS inhibition may not be enough. Recently, new therapeutic agents have been described that may have a role in slowing the progression of DN.<sup>4</sup> Hormone receptors that play a protective role in cardiovascular, inflammatory and metabolic diseases have been seen. Thus, its modulation may provide new “targets” for treatment. In the case of DM, the most studied receptors are oestrogen, PPAR-gamma and vitamin D.<sup>5</sup>

Chronic hyperglycaemia promotes the generation of advanced glycation end products, AGEs.<sup>2</sup> Thus, AGE inhibitors (aminoguanidine, ALT-946, pyridoxamine, thiamine) and AGE receptor (RAGE) antagonists<sup>4</sup> have been described.

Another potential agent (due to its rheological and anti-inflammatory properties) is pentoxifylline,<sup>6</sup> which has been shown to have renoprotective and antiproteinuric effects in animal studies.<sup>7</sup> In addition, a recent meta-analysis of randomised controlled trials reported that pentoxifylline has an antiproteinuric effect in patients with diabetic kidney disease.<sup>8</sup>

There is also evidence that activation of protein kinase C (PKC) causes renal failure (hyperfiltration, basement membrane damage and glomerulosclerosis). Among the PKC inhibitors, ruboxistaurin has demonstrated a promising effect in the prevention of diabetic vascular complications.<sup>4</sup>

Lastly, several growth factors are expressed in the normal kidney and have been implicated in the pathogenesis of DN, and TGF- $\beta$ , CTGF and VEGF inhibitors are potential therapeutic agents.<sup>9</sup>

In short, in the RAAS inhibition era, it is still possible to detect patients with a natural course of DN. The delay in the start of treatment makes the subsequent response discrete. In the coming years, new therapeutic agents will be assessed for their utility in preventing the onset of DN and/or delaying the progression to CKD.

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004;27:1047-53.
2. Cooper ME. Interaction of metabolic and

haemodynamic factors in mediating experimental diabetic nephropathy. *Diabetologia* 2001;44:1957-72.

3. Ruggenti P, Cravedi P, Remuzzi G. The RAAS in the pathogenesis and treatment of diabetic nephropathy. *Nat Rev Nephrol* 2010;6:319-30.
4. Turgut F, Bolton WK. Potential New Therapeutic Agents for Diabetic Kidney Disease. *Am J Kidney Dis* 2010;55:928-40.
5. Wang XX, Jiang T, Levi M. Nuclear hormone receptors in diabetic nephropathy. *Nat Rev Nephrol* 2010;6:342-51.
6. Navarro JF, Mora C, Rivero A, Gallego E, Chahin J, Macia M, et al. Urinary protein excretion and serum tumor necrosis factor in diabetic patients with advanced renal failure: effects of pentoxifylline administration. *Am J Kidney Dis* 1999;33(3):458-63.
7. Lin SL, Chen YM, Chien CT, Chiang WC, Tsai CC, Tsai TJ. Pentoxifylline attenuated the renal disease progression in rats with

remnant kidney. *J Am Soc Nephrol* 2002;13(12):2919-29.

8. Mc Cormick BB, Sydor A, Akbari A, Fergusson D, Doucette S, Knoll G. The effect of pentoxifylline on proteinuria in diabetic kidney disease: a meta-analysis. *Am J Kidney Dis* 2008;52(3):454-63.
9. Declèves AE, Sharma K. New pharmacological treatments for improving renal outcomes in diabetes. *Nat Rev Nephrol* 2010;6(6):371-80.

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## C) BRIEF CASE REPORTS

### Hydrothorax in peritoneal dialysis: a rare complication

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#### To the Editor,

Hydrothorax is an uncommon complication in patients on peritoneal dialysis (PD), and is estimated at 1.6%-10%. It usually involves the abandonment of the treatment.

We present 2 cases of PD patients with this disease.

#### Case 1

A 47-year-old woman with a history of glycogen storage disease type V (McArdle's disease), chiari malformation, chronic renal failure of

unknown aetiology, retinal atrophy and hypertension.

A peritoneal catheter was implanted on 19/05/2000 in other hospital, and dialysis started with a 2-litre infusion 15 days later. From the start, the patient suffered abdominal discomfort, pleuritic pain in the right chest and dyspnoea. A chest x-ray identified hydrothorax (Figure 1), so PD was suspended and she was referred to our hospital.

In our centre, the pleural effusion was drained (transudate) and the chest x-ray performed was normal. PD was tried again with less infusion volume and the pleural effusion reappeared soon after. Subsequently, we tried an arteriovenous fistula (AVF) puncture, which was complicated by leakage and by myositis.

The patient refused haemodialysis or any other treatment option to solve the



**Figure 1.** Hydrothorax. Case 1.