When kidneys are no longer a friend: An "out of the box" management for an unexpected evolution of an uncommon disease

Cuando los riñones dejan de ser un amigo: Una gestión "fuera de la caja" de una evolución imprevista de una enfermedad poco común

Dear Editor,

AA amyloidosis (AAA) is one of most severe complications of chronic inflammatory and infectious diseases and may induce nephrotic syndrome.[1] Its association with Crohn's disease has been regularly reported, but amyloidosis complicating ulcerative colitis (UC) has been described only exceptionally.[2]

We report a case of a 58-year-old woman who was admitted with anasarca and nephrotic syndrome (NS). Relevant medical history included UC, gangrenous pyoderma and a tuberculous empyema. In 2002, a NS was identified and a renal biopsy displayed the diagnosis of AAA. In addition to treatment with 5-aminosalicylic-acid, a trial of colchicine was implemented but had to be stopped due to diarrhea. Renal function (RF) was sustainably preserved and the proteinuria spontaneously remitted. Throughout time she had long-lasting, moderate gastrointestinal symptoms with evidence of mild endoscopic inflammation. In 2015 she developed once more disabling proteinuria with normal RF and a diagnostic workup corroborated the clinical impression of recurrence of her amyloidosis (Table 1). An endoscopic review exhibited mild disease and, in addition to messalazine and prednisone, she was started on azathioprine, which had to be suspended due to pancreatitis. Therapy with an angiotensin-converting enzyme inhibitor was initiated but not tolerated; albumin-plus-furosemide infusion led merely to temporary improvement. A decision to deteriorate RF to decrease proteinuria was attempted: indomethacin led to acute renal dysfunction but didn't significantly improved proteinuria. Hemodialysis was started but had to be interrupted due to hemodynamic instability. After a multidisciplinary consultation, she underwent a bilateral nephrectomy. Post-operatively, serum albumin and postural symptoms gradually improved with subsequent better hemodialysis tolerance. Histology revealed extensive amyloid deposits (Fig. 1) and immunohistochemical staining was positive for AA amyloid. Nutritional and functional status gradually improved.

AAA in the setting of UC is a rarity and typically, severe gastrointestinal illness precedes the development of amyloidosis,[3] however this was not the case in our patient, who had a long standing, though mild disease. We speculate that the ongoing activity and the prolonged duration may have had a role; nevertheless, an additional contribution from the tuberculosis cannot be ruled out.

Another peculiar aspect is the spontaneous remission of the patient's NS. Improvement of amyloidosis manifestations is extensively documented in the context of remission of the underlying disease, but spontaneous regression is extremely unlikely.[4]

Patients with large proteinuria due to AAA can experience a life-threatening cachexic state with massive edema, respiratory distress and infectious complications, along with a poor functional status and a reduced quality-of-life. Up to the present, AAA has no specific treatment and despite the development of novel therapies (eprodisate)[5] targeting the formation/stability of fibrils, the current available approach is to treat the underlying condition and thereby reduce the amyloid production. Nevertheless, this goal is not always achieved and the management of proteinuria can be challenging, resorting, in intractable cases like ours, to renal ablation. Medical ablation, with non-steroidal anti-inflammatory drugs[6] has been attempted; bilateral renal artery embolization is an alternative, although frequently complicated by a 'post-infarction syndrome'.[7] Recently, bilateral ureteral ligation[8] has been described, but the experience is limited and can induce persistent loin pain and ascending infections. Surgical nephrectomy is another option: although laparoscopic surgery is a less invasive procedure than an open nephrectomy, it precludes the chance for peritoneal dialysis and, consequently, we elected a bilateral nephrectomy by lombotomy.

The histological examination of the kidneys revealed extensive presence of AA amyloid deposits comprising the glomeruli, the blood vessels and the interstitium, an infrequent finding in the review by Hopfer et al.,[9] who reported interstitium involvement in only 5.9%.

AAA has a major impact in patient's quality of life: Esteve et al.[10] reported that in 1/3 of the patients, dialysis was not

Table 1 – Laboratory tests results.

	Result	Reference range
Hemoglobin (g/dL)	9.7	12–16
Leukocytes ($10^3/\mu L$)	9.3	4–11
Platelets ($10^3/\mu L$)	183	150–400
C-reactive protein (mg/L/sedimentation rate 1st h)	24/127	<5/0–30
Total protein/albumin (g/dL)	4.4/1.2	6.4–8.3/3.5–5.0
AST/ALT/LDH (U/L)[a]	11/18/205	5–34/<55/110–220
Fasting glucose/total bilirubin (mg/dL)	83/0.7	60–110/0.2–1.2
Total/LDL/HDL cholesterol (mg/dL)	270/169/40	<200/<100/≥60
Urea/creatinine (mg/dL)	52/0.7	21–43/0.6–1.1
Urinalysis/24 hours protein (mg/day)	4+ proteinuria/19 538	0+/<300
Serum immunoelectrophoresis/serum kappa-lambda ratio	Absence of monoclonal gammopathy/normal	
Urinary electrophoresis/urinary immunoelectrophoresis	Albumin = 46% and gamma globulin = 14%/no band suggestive of monoclonality	
Tests for hepatitis B and C, HIV[b], and syphilis	Negative	
ANA, anti-dsDNA and ANCA[c] antibodies; C3 and C4 complement levels	Normal	
Serum amyloide A (mg/L)	79.4	<7

[a] AST: aspartate transaminase, ALT: alanine transaminase, LDH: lactate dehydrogenase.
[b] HIV: human immunodeficiency virus.
[c] ANA: antinuclear antibodies, anti-dsDNA: anti-double stranded DNA antibodies, ANCA: antineutrophil cytoplasmic antibodies.

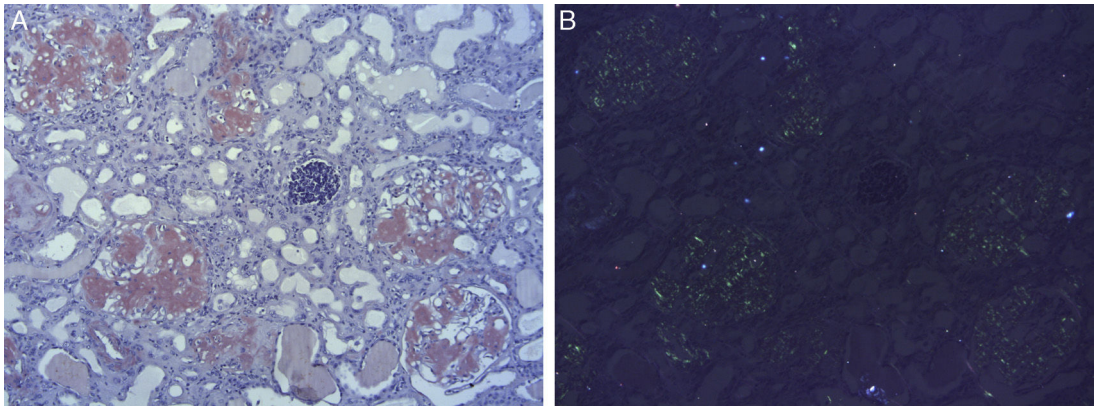

Fig. 1Histological examination of the kidneys. (A) Glomerular nodular deposits of amyloid stained with Congo red. (B) Amyloid showing typical apple-green birefringence under polarized light.

performed due to their poor clinical condition and disturbing quality of life. Bilateral nephrectomy in our patient, led to an improvement in hemodynamic stability allowing hemodialysis to be accomplished. Additionally, her functional and nutritional status enhanced gradually.

Radical bilateral nephrectomy may be considered in seriously ill patients with nephrotic syndrome and disabling complications of proteinuria.

Conflicts of interest

The authors declare that they have no conflict of interest.

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BK virus nephropathy in a renal transplant patient: Potential role of electron microscopy in diagnosis

Nefropatía por virus BK en un paciente con trasplante renal: Papel potencial de la microscopía electrónica en el diagnóstico

Dear Editor,

BK polyomavirus (BKV) causes latent, asymptomatic infection in immunocompetent individuals. In the setting of immunosuppression BKV can reactivate and lead to BK virus nephropathy (BKVN) in renal transplant recipients.[1] BKVN is one of the main causes of allograft failure in renal transplant patients. Acute rejection and different viral infections should be considered in differential diagnosis of renal allograft dysfunction. Electron microscopy (EM) could help to distinguish BKV from other viral factors in allograft tissue.[2] Herein, we described inclusions due to BKV seen by EM in a renal transplant biopsy and we discussed potential role of EM in diagnosis of BKVN.

A 49 years old woman had renal transplantation from non-relative donor 2 years ago. Although she was asymptomatic, her serum creatinine level was increased gradually during last 3–4 months (from 1.2 mg/dl to 1.7 mg/dl). Her primary renal disease was unknown. She had been under the treatment of tacrolimus 2 + 1 mg, prednisolone 5 mg, mycophenolate sodium 3 × 360 mg. Physical examination was normal. Serum creatinine was 1.82 mg/dl, urine microscopy was normal. 154 mg/day proteinuria was obtained. ANA was positive, though ENA was negative. Anti CMV IgM was negative, whereas serum BK/JC PCR was positive. Serum tacrolimus level was 9.5 ng/ml. Transplant renal doppler ultrasonography revealed normal findings. Renal biopsy was performed. Intranuclear inclusions, cytoplasmic and nuclear enlargement in tubular epithelial cells and tubular necrosis were seen on light microscopy. These biopsy findings might suggest viral infection of the renal allograft. Immunohistochemical analysis of the renal biopsy for CMV was negative, but study with SV40 antigen could not be performed as it was not available in our center. Intranuclear spherical viral particles were seen in some tubular epithelial cells on EM (Fig. 1). Viral particles were in paracrystalline structure and about 30 nm in diameter. They were differentiated from inclusions of adenovirus with 80–100 nm in diameter (Fig. 2). Finally, BKVN was diagnosed.

BKVN is one of the well-known reasons of morbidity in renal transplant patients. It occurs with a prevalence of 1–10% in renal transplant patients and graft loss is up to 80%.[3,4] BKVN occurs mostly during the first year after transplantation and it is characterized only by deterioration of renal functions, usually without any symptoms.[1] Early diagnosis is important to prevent allograft dysfunction in kidney transplant patients. Our patient was also declared no symptoms, but only a gradual increase in serum creatinine was observed in the second year of follow up.