Hypokalaemia is not a common side effect. Studies have compared it to amphotericin B, the prevalence of hypokalaemia is 18.8% and only 2.4% have potassium levels below 2.5mmol/l.[3,5]

Many new drugs are increasingly being reported to be involved in various electrolyte disturbances (Table 1). Therefore, the medication that all patients with hypokalaemia receive should be examined, including both drugs traditionally associated with hypokalaemia, such as diuretic agents, beta-adrenergic agonists and amphotericin B, and new antibiotic, antiretroviral and immunosuppressant drugs.

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Extracapillary glomerulonephritis type I with the coexistence of positive anti-GBM and p-ANCA antibodies

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To the Editor,

Extracapillary glomerulonephritis (EGN) is characterised by the presence of potentially pathogenic antibodies or immune complexes in the plasma. These include the antiglomerular basement membrane antibodies (anti-GBM Ab), characteristic of type I EGN, and anti-neutrophil cytoplasmic antibodies (ANCAs), which are usually present in type III EGN.[1,2]

A substantial proportion of patients with EGN are double positive for anti-GBM and ANCA. We report a patient with type I EGN with plasma coexistence of anti-GBM Ab and p-ANCA and severe renal impairment. The patient did not respond to triple therapy with plasmapheresis, corticosteroids and cyclophosphamide.

Case report

A 62-year old man was referred from the emergency department to the nephrology department for general discomfort associated with bilious vomiting and evening fever. He was taking azithromycin. The patient reported a reduction in diuresis in the previous days, without lower urinary tract symptoms. He was not taking NSAIDs or any other nephrotoxic drugs. The medical history showed chronic obstructive pulmonary disease, obstructive sleep apnoea syndrome, chronic otitis media monitored by an otolaryngologist and botulism, which required ICU admission in 2007. No history of hypertension, diabetes mellitus, dyslipidaemia or any known heart disease. The physical examination revealed a normal general state, he was eupneic at rest, conscious, oriented, collaborative, with normal perfusion and hydration. BP was 143/95mm Hg, HR was 75 beats/min, temperature 36.5°C, and oxygen saturation 97%. There were no lesions on the skin or in the mucous membranes.

Cardiopulmonary auscultation: rhythmic without audible murmurs. Vesicular murmur without superimposed noise was found. Abdomen: soft and palpable. No signs of peritoneal irritation. No masses or organomegaly on palpation. The lower extremities showed pitting oedema to the root of the limbs, without signs of deep vein thrombosis (DVT) or chronic venous insufficiency, with positive pulses. The neurological examination found isochoric and normally reactive pupils, normal cranial nerves, and segmentally conserved strength and sensitivity. There were no signs of meningeal irritation.

The analytical results on admission showed: haemoglobin 11g/dl, haematocrit 34.7%, MCV 92fl, WBC 9000 (85% neutrophils, 9.1% lymphocytes), platelets 213 000, glucose 102mg/dl, urea 265mg/dl, creatinine 12.2mg/dl, sodium 137mEq/l, potassium 7mEq/l, chloride 107mEq/l, procalcitonin 0.92mg/dl, protein 7g/l, calcium 9.6mg/dl, corrected calcium 9.8mg/dl, CRP 272.8, total bilirubin 0.6mg/dl, AST 19U/l, ALT 39U/l, GGT 28U/l, ALP 61U/L, amylase 84. Urinalysis: protein 100mg/dl, 300 red cells, negative nitrites, no leukocyte. Chest x-ray showed no signs of condensation or leakage, and normal mediastinum. The plain abdominal x-ray showed non-specific meteorism.

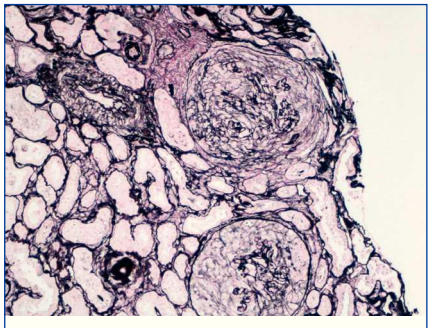
Venous blood gases: metabolic acidosis with pH 7.28, total CO_2 20mmol/l, HCO_3^- 18.8mmol/l, BE -7.5. ECG: sinus rhythm at 75 beats/min, normal PR, narrow QRS, no acute repolarisation changes. Abdominal ultrasound: liver and spleen without ultrasound abnormalities. Enlarged right kidney (15cm), with loss of cortico-medullary

differentiation, no observed dilation of the excretory tract. Hypoplastic left kidney (described in previous studies). ^{99m}Tc-MAG3 renal scan: non-functioning left kidney. Severe parenchymal nephropathy in the right kidney. Immunology: IgG 795mg/dl, IgA 123mg/dl, IgM 25.1mg/dl, C3 133mg/dl, normal C4, kappa chains 161mg/dl, normal lambda.

Autoimmunity: ANA, anti-DNA Ab and c-ANCA negative, p-ANCA 41U/ml and anti-GBM Ab 287U/ml. Normal serum protein. Serology for HBV and HCV negative.

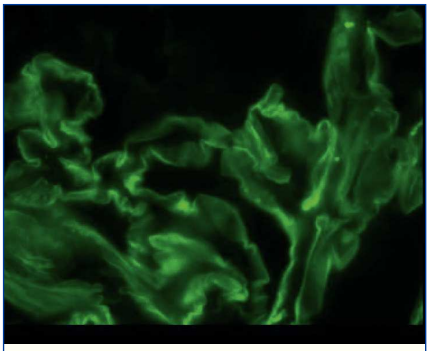
Given these clinical and analytical findings, a renal biopsy was performed via open lumbotomy, as the patient had a single functional kidney.

The anatomical pathology described a total of 49 glomeruli, three of them sclerosed and the structure of the others was extensively affected. Fibrinoid necrosis and extracapillary cell and circumferential proliferation were found in 100% of the glomeruli. The small vessels also had necrotising vasculitis. The direct IF study provided a linear and diffuse positive in the glomerular basement membrane, with IgG positive and the rest of the antibodies negative. In summary, extracapillary glomerulonephritis was detected with intense involvement of 100% of the glomeruli of the sample and IF typical of anti-GBM Ab-mediated extracapillary glomerulonephritis (type I), see Figures 1 and 2.



Fibrinoid necrosis and extracapillary proliferation

Figure 1. Silver technique.



The direct IF study provided a linear and diffuse positive in the glomerular basement membrane, with IgG positive and the rest of the antibodies negative.

Figure 2. Immunofluorescence.

From admission, the patient required renal replacement therapy. He was treated with intravenous cyclophosphamide at a dose of 1.5mg/kg/day, methylprednisolone 500mg/24h for 3 days and plasmapheresis (7 sessions). The cyclophosphamide was discontinued due to thrombocytopaenia. There was no pulmonary involvement at any time during evolution.

Currently, the patient is on haemodialysis with arteriovenous fistula as the vascular access.

Discussion

The percentage of serum coexistence of p-ANCA and anti-GBM Ab was quantified in different series at around 25%.[1,3-5] Currently, the clinical profile, the prognosis and the pathophysiological role of each antibody in the serum of patients with p-ANCA and anti-GBM Ab coexistence is still under investigation. It is not clear whether the ANCA-associated GN predisposes the development of the anti-GBM Ab-mediated disease or if the ANCA becomes positive in the course of the anti-GBM Ab-mediated GN.

However, one of the most relevant factors is that IF studies are not routinely described in the literature. Therefore, we are not sure if "double positive" cases are type III or type I EGN.

In type III ANCA+ EGN, the existence of anti-GBM Ab has been described in up to 5% of cases. Due to the greater frequency of this disease, most reported cases are included in this group. Some studies suggest that ANCA GN appears first, followed by anti-GBM Ab disease.[1,3] In these cases, it has been suggested that there is an exposure of the glomerular basement membrane antigens and the development of anti-GBM Ab.

In type I EGN, it has been reported that up to 30% of cases may be associated with the existence of ANCA. Due to the lower frequency of this disease, fewer cases have been reported.[4,5] The pathogenesis of this condition is not clear and it seems that altered immune regulation results in the development of both, p-ANCA and anti-GBM Ab.

In addition, it has been suggested that patients with ANCA and anti-GBM Ab, paradoxically, have a better prognosis.[6] However, this has not been confirmed, and it has even been stated that renal survival in patients with dual positive is no better than those with only anti-GBM Ab.[1,3,8] In a study by Lindic et al.,[10] patients with anti-GBM Ab, ANCA and a creatinine of higher than 5.6mg/dl on admission did not recover renal function, despite treatment with prednisolone, cyclophosphamide and plasma exchange.

We reported a case of type I EGN with positive linear IF and serum coexistence of anti-GBM Ab and p-ANCA. The poor prognosis of renal function in these cases was seen in our patient, who was dependent on haemodialysis despite aggressive treatment.

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Late venous thrombosis of renal allograft: two cases with different treatment and outcome

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To the Editor,

Renal transplant (RT) patients have a higher incidence of thrombotic events and an increased risk of recurrence after the withdrawal of anticoagulation. Thrombosis of the allograft vein is a well-described complication of renal transplantation. It can occur early after transplant, related to surgical technical complications or many years post-transplant associated to multiple inciting factors. The treatment includes surgery, thrombolytics and anticoagulation.

We present two cases of late renal allograft venous thrombosis with different treatments and outcome: conventional hipocoagulation led to renal failure but surgical thrombectomy allowed patient improvement and renal function recovery. Based on the cases, a review of the literature about pathophysiology, clinical presentation, diagnosis and treatment options of late venous thrombosis of the renal allograft was made.

RT patients have a higher incidence (ranging 0.6-25%) of thrombotic events.[1,2] Thrombosis of the allograft vein is a well-described early complication,[3] usually associated with acute rejection or surgical complications.[4] The typical presentation is that of a sudden painful and swollen allograft, haematuria and oliguria with deterioration of graft function.[4,5] Partial vein thrombosis presents as a late event, with chronic oedema and progressive deterioration of renal function.[6]

Diagnosis can be made by Doppler ultrasound, computed tomography (CT) or magnetic resonance venogram[7] and the treatment includes surgery, thrombolytics and anticoagulants.[7] The authors present two cases of late allograft venous thrombosis with different treatments and outcome.

CLINICAL CASES

Case1

A 63-year-old man, with chronic renal failure (CRF) secondary to adult polycystic kidney disease (APKD), was submitted to RT in 1988 and treated with cyclosporine (CsA), azathioprine (AZA) and prednisolone (P). Nineteen years after RT, serum creatinine (Cr) increased to 2.5mg/dl and nephrotic proteinuria was documented. In 2007, chronic allograft nephropathy (CAN) was confirmed. One year latter, a rectal adenoma was diagnosed and after four months (on March 2009), he had acute diverticulitis complicated by peritonitis and needed surgery.

On July 2009, he was admitted with painful oedema of the right leg with one week of evolution. Doppler revealed femoral vein thrombosis and partial thrombosis of allograft vein, iliac and inferior vena cava (IVC). Renal function had declined (Cr: 5.84 mg/dl) and serum albumin was reduced (2.68g/dL). Pulmonary embolism was excluded and anticoagulation with low molecular weight heparin (LMWH) was started, followed by accenocumarol. Renal function deteriorated and one week latter he started haemodialysis. The study for other neoplasms was negative. Three months latter, he is asymptomatic but remains on haemodialysis.

Case 2

A 58-year-old man, with CRF secondary to APKD, was submitted to RT in 1993. He was treated with CsA, AZA and P and renal function stabilized on Cr: 1.8mg/dl, without proteinuria. Posttransplant erytrocytosis was documented in 1996 and treated with phlebotomies.

On May 2009, he was admitted with thrombosis of right popliteal vein. He had erytrocytosis (Hb: 18.3g/dL) and