

Letters

Preventing end-stage kidney disease: a personal opinion from the Third World

Sir,

I read with great interest the editorial, by Schieppati, Perico and Remuzzi, which was recently published in *NDT* [1]. I also enjoyed the special note, written by the editors in chief of both *NDT* and *Kidney International*, about the importance of the prior scientific paper [2].

As a Latin American nephrologist, I know the socio-economic and sanitary status of this region. In recent years, an increase in the prevalence and incidence of end-stage kidney disease (ESKD) has been observed in Latin America and around the world. At the same time, we have witnessed the arrival of more expensive new technologies for renal replacement treatment. In consequence, I have become aware of the necessity for a social projection of nephrology [3]. To achieve this it is vital to establish health programmes to prevent or at least lessen the impact of ESKD in our communities, by screening the general population for renal diseases and risk factors for renal function (principally, diabetes and hypertension) [3,4].

It is, indeed, very satisfying to confirm that we are neither alone nor forgotten in this world and that colleagues of regions with elevated standards of development and better sanitary structures than ours, have perceived the magnitude of the problem and have proposed possible solutions. One of the most relevant ideas expressed in the paper was that 'the magic bullet that is indispensable to cure most of the problem is money' [1].

I firmly support the creation of a global fund to fight renal diseases. But, as was stated in July 2002 in the *Lancet* [5], 'without supporting biomedical and health-sciences research on the problems facing the world's poor, the long-term value of these global funds will be severely compromised.' The approach is not easy, it will be large and with a lot of stumbling blocks. However, with determination and tenacity, working together and aiming at the same objective, we can succeed.

I offer my gratitude as a physician, a nephrologist and a researcher in renal epidemiology to the authors of the editorial for their noble purpose. I also thank them as a Latin American and a human being.

Conflict of interest statement. None declared.

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DOI: 10.1093/ndt/gfg422

Systemic AA amyloidosis and nephrotic syndrome associated with small cell carcinoma of the bladder

Sir,

Amyloidosis is a well-known cause of nephrotic syndrome and renal failure, which is usually associated with chronic inflammatory disease (e.g. rheumatoid arthritis), chronic infections (e.g. tuberculosis and bronchiectasis) or familial Mediterranean fever (FMF). All of these conditions are associated with elevated circulating levels of serum amyloid A (SAA). SAA is one of the acute phase proteins in inflammation and is a precursor of AA amyloid. AA amyloidosis has also been described in association with some tumours [1–3]. We report here the first case of small cell carcinoma (SCC) of the bladder complicated with nephrotic syndrome and renal failure due to systemic AA amyloidosis.

Case. A 57-year-old male was referred to our hospital because of generalized oedema and intermittent macroscopic haematuria of 2 months duration. He had no history of fever, recurrent infections or chronic inflammatory disease. He had neither a family history nor a clinical presentation compatible with FMF or familial amyloidosis. Systemic physical examination was found to be normal except for marked, pitting oedema on both legs.

The haemoglobin level was 11 g/dl (normochromic normocytic anaemia), the white blood cell count was 6120/mm³ and the platelet count was 254 000/mm³. The erythrocyte sedimentation rate (ESR) (120 mm/h) and C-reactive protein (CRP) (6.93 mg/dl) were elevated, but no source of infection was found. Blood chemistry was as follows: urea 90 mg/dl, creatinine 6 mg/dl, total serum protein 4.2 g/dl, albumin 1.4 g/dl, triglycerides 355 mg/dl, total cholesterol 300 mg/dl, glucose 85 mg/dl, AST 20 U/l and ALT 25 U/l, with normal serum electrolyte levels. Serum protein and immunoelectrophoresis revealed hypoalbuminaemia with no monoclonal gammopathy.

Serum IgA was 349 mg/dl (normal 93.2–445), IgG 1177 mg/dl (normal 802–1760), IgM 125 mg/dl (normal 65–280), C3 89.1 mg/dl (normal 52.6–120) and C4 37.9 mg/dl (normal 20.5–49). The urine was 4+ for protein and 10–15 red blood cells were observed per high power field. Twenty-four hour urinary protein excretion was 12 g; Bence-Jones proteinuria was not present. Serological tests for ANA, HBsAg, anti-HBsAg, anti-HCV, anti-HIV, VDRL, p-ANCA, c-ANCA, cryoglobulins, rheumatoid factor as well as tuberculin skin test were all negative.

A computerized tomography (CT) of the abdomen and pelvis showed a 4 × 3 cm solid mass on the left lateral bladder wall with no evidence of lymphadenopathy or metastasis. Cystoscopy revealed a solitary friable tumour. Transurethral resection was performed. The histopathological examination

of the transurethral specimens revealed SCC of the bladder invading muscularis propria. CT of the chest, MRI of the brain and bone scan showed no evidence of metastasis. The tumour was staged as T2N0M0 and the patient underwent pelvic radiotherapy.

Proteinuria, hypoalbumin and other laboratory data suggested that our patient had nephrotic syndrome. Because of the suspicion of systemic amyloidosis, a rectal biopsy was performed, which revealed AA-type amyloid deposition. Renal biopsy also demonstrated glomerular amyloid deposition of AA type.

After transurethral resection of the tumour and pelvic irradiation (6600 cGy), urinary protein excretion decreased to 4 g/24 h, serum albumin concentration increased to 2.5 g/dl and generalized oedema partially regressed. ESR decreased to 40 mm/h and serum CRP level to 1.26 mg/dl. The patient was then treated with a combination chemotherapy regimen including cyclophosphamide, adriamycin and vincristin. Cyclophosphamide dosage was adjusted according to creatinine clearance. A total of four cycles of chemotherapy were administered. Laboratory parameters of renal function and proteinuria remained stable during chemotherapy.

Six months after the last cycle of chemotherapy, haemodialysis was started because of end-stage renal disease. The patient died without evidence of local recurrence or distant metastasis 13 months after the diagnosis of SCC of the bladder.

Comment. AA amyloidosis may occur as a complication of neoplastic disorders [1–3]. Secondary amyloidosis in malignancies should be diagnosed after exclusion of other formerly mentioned disorders. Several studies have reported increased SAA levels in malignancy. In cancer patients, SAA concentrations are increased due to several pro-inflammatory mediators, particularly tumour necrosis factor alpha and interleukin-6. Secondary amyloidosis in malignancies may be caused by the overproduction of SAA. Although certain tumours, such as lung and renal cell carcinoma, produce very high SAA titres [4], progression to amyloidosis occurs rarely, suggesting the role of other unknown mechanisms in the development of AA amyloidosis in malignancy.

SCC of the bladder is a rare tumour and represents <1% of all bladder neoplasms [5]. The biological behaviour and prognosis of bladder SCC is similar to that of lung SCC. The overall 5 year survival rate for all reported cases has been estimated as 8.3% [5]. To the best of our knowledge, the association of AA amyloidosis and SCC of the bladder have not been described previously. Our patient had systemic amyloid deposition proven by rectal and renal biopsies. We could not measure the serum SAA level in this patient. Although rare, the absence of any sign of a chronic inflammatory, infectious or autoimmune disease in our patient that could lead to secondary amyloidosis led us to postulate a direct correlation of secondary amyloidosis with bladder SCC.

Based on this observation and literature reports, we speculate that the prognosis of AA amyloidosis secondary to malignancy depends on the development of end-stage renal disease. If the underlying condition is cured or controlled, deposition of AA fibrils may be halted and perhaps even reversed. Thus, surgical removal of the tumour bulk may result in a marked decline in proteinuria and prevent the development of renal failure [1,3,6].

In conclusion, we presume that the concurrent presence of systemic amyloidosis, as in our case, may adversely affect survival. We suggest that SCCB be included in the list of neoplastic diseases predisposing to AA amyloidosis.

Conflict of interest statement. None declared.

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DOI: 10.1093/ndt/gfg391

Paralysis due to renal potassium wasting: an unusual presentation of leptospirosis

Sir,

Case. A 43-year-old male was admitted to hospital 16 h after onset of myalgia, progressive quadriparesis, respiratory muscle weakness and dysphagia. He was conscious, with a pulse of 120/min, BP 120/70 mmHg and tachypnoeic, and had conjunctival suffusion, flaccid hyporeflexic weakness and flexor plantar responses. Sensations were normal and meningeal signs absent. He had abdominal distension with absent bowel sounds.

Arterial blood showed mixed respiratory and metabolic acidosis with a pH of 7.20, pO₂ 60 mmHg, pCO₂ 46 mmHg, oxygen saturation 92% and bicarbonate 17.6 mmol/l. The serum sodium was 140 mmol/l, potassium 2.6 mmol/l, chloride 116 mmol/l and blood urea nitrogen (BUN) 12 mg/dl. He was endotracheally intubated and mechanically ventilated. Following i.v. correction of hypokalaemia, serum potassium improved to 3.6 mmol/l and the patient was weaned off the ventilator and extubated within 12 h.

Investigations revealed BUN 25 mg%, serum creatinine 1.2 mg% and normal liver function, total leukocyte count (TLC) and platelet counts. The urine pH was 5.22, urine potassium 27.9 mmol/l, sodium 23.2 mmol/l, chloride 54.8 mmol/l, urine osmolality 351 mOsm/kg, plasma osmolality 294 mOsm/kg and total urine volume 4500 ml. The arterial pH