Case Report

Nephrotic syndrome and renal failure as an unusual presentation of solid tumour

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Abstract

Glomerular diseases may occur as primary manifestation of cancer, especially in patients older than 60 years. Among glomerulopathies, membranous nephropathy is preferentially associated with respiratory and gastrointestinal tract adenocarcinomas, whereas minimal change disease is most often seen in haematological malignancies. Though breast cancer is one of the most frequent malignancies in women, paraneoplastic glomerular disease is rarely observed. We describe the case of a 79-year-old female patient who presented with nephrotic syndrome and renal failure. Breast cancer was found. Pathological studies of kidney and breast biopsy revealed a minimal change disease and an infiltrating ductal carcinoma, respectively.

Keywords: acute kidney injury; minimal change disease; nephrotic syndrome; paraneoplastic glomerulopathy; solid tumour

Introduction

Nephrotic syndrome may occur in a wide variety of clinical settings such as diabetes mellitus, amyloidosis, systemic lupus erythematosus, membranous nephropathy, focal glomerulosclerosis, as well as minimal change disease (MCD). It is generally recognized that MCD accounts for up to 15% of all cases of adult nephrotic syndrome and is most often of idiopathic origin [1]. However, drugs, infections, atopy and neoplasms may be associated with MCS. The paraneoplastic minimal change nephrotic syndrome, generally defined by a close time relationship between the glomerular disease and the malignancy, is mainly secondary to haematological malignancies [2]. Occasionally, solid tumours are associated with MCD and therefore should be searched, especially in older patients [3,4]. We report on a case of a woman who presented with acute kidney injury and nephrotic syndrome secondary to MCD as the inaugural manifestation of a breast cancer. The patient came off dialysis after a 4-week course of steroids combined with enalapril, and surgical removal of the breast tumour.

Case report

A 79-year-old woman was referred by her family doctor for dyspnoea, ascites and lower limb oedema that appeared a few weeks previously and rapidly worsened. Her past medical history consisted in essential hypertension well controlled by barnidipine and bumetanide, and osteoporotic fractures treated by alendronate. She had no personal or familial history of kidney disease. A recent determination of serum creatinine was within the normal range. She had no known atopy.

Upon admission, the physical examination revealed widespread oedema and wet rales on auscultation of the chest. Blood and urine tests demonstrated a functional acute kidney injury (serum creatinine: 256.4 μmol/l; blood urea: 34.9 mmol/l, fractional excretions of sodium: 0.14% and of urea: 4.6%) with hypoalbuminaemia (24 g/l) and hypercholesterolaemia (6.9 mmol/l). Nephrotic syndrome was further confirmed on a 24-h urine collection with a protein/creatinine ratio at 1338 mg/mmol. Neither haematuria nor casts were found in voided urine sample. Serological studies for antinuclear antibodies, antineutrophil cytoplasmic antibodies, rheumatoid factors, antistreptolysin-O, HBC, HCV, HIV and complement levels were all negative. Blood and urine protein electrophoreses were unremarkable. No pulmonary opacities were observed on the chest x-ray. A transthoracic echocardiography revealed a normal cardiac anatomy and function. The renal Doppler ultrasonography displayed normal-sized kidneys without any sign of obstruction or renal veins thrombosis. A renal biopsy was performed. Histopathological examination demonstrated optically normal glomeruli, mild tubular atrophy and the absence of complement or immunoglobulin deposits by immunofluorescence microscopy, consistent with a diagnosis of MCD (Figure 1A and B). Drugs, infection, atopy and haematological malignancies were reasonably ruled out as possible causal factors of MCD on the basis of biological and clinical findings.

During the first days, the patient’s outcome was marked by a pulmonary oedema uncontrolled by high doses of diuretics, and requiring haemodialysis. A few days later, the
Fig. 1. (A) Representative photomicrographs of renal biopsy showing glomerulus of the normal size and no segmental lesions. Mild tubular atrophy is found, probably as a result of ischaemic and protein overload processes (silver stain, 400×). (B) At higher magnification, the glomerular basement membrane is thin without any spikes (silver stain, 1000×). Fourteen glomeruli were observed on the renal biopsy specimen.

Fig. 2. Time course evolution of renal functional parameters (serum creatinine and proteinuria) along with major clinical events.
patient received prednisolone (1 mg/kg per day, orally) and the angiotensin-converting enzyme inhibitor enalapril. A progressive reduction of proteinuria was observed and renal function parameters improved, allowing us to taper the steroid dosage (Figure 2).

Careful physical examination revealed a suspect mass (20 × 15 mm) in the inner quadrant of her right breast that was further confirmed by mammography and ultrasonography. Histopathological examination of a breast biopsy tissue sample demonstrated a moderately differentiated infiltrating ductal carcinoma (grade II) expressing oestrogen and progesterone hormones receptors but not the erb-2 protein. The supraclavicular and axillary areas were free of enlarged lymph nodes and no distant metastasis was found. Serum markers CA 15-3 and CEA were at 27 U/ml (<25 U/ml) and 6.2 ng/ml (<4.5 ng/ml), respectively.

One month later, the patient was dialysis free and the surgical removal of the breast cancer was performed (final staging pT1cN1cM0 according to the WHO classification). The immediate postoperative period resulted in the nearly complete remission of the renal disease with a serum creatinine level at 114.9 μmol/l (Figure 2). Unfortunately, the patient developed a fulminant septic shock due to *Staphylococcus aureus* and died 48 h later.

### Discussion

The present case draws the physician’s attention to the possible presentation of MCD nephrotic syndrome and acute kidney injury as inaugural manifestations of solid tumour. Cancer-related MCD is preferentially linked to haematological malignancies whereas membranous nephropathy is mostly associated with solid tumours such as respiratory and gastrointestinal tract adenocarcinomas [4,5]. The association between MCD and solid tumours is extremely rare, especially those associated with breast cancer [3,6,7].

In this case, the simultaneous presentation of the nephrotic syndrome and the breast cancer is in favour of an association between those two entities. Moreover, alternative causes of MCD such as non-steroidal anti-inflammatory agents or antibiotics were excluded. Rare cases of biphosphonate-induced nephrotic syndrome have been reported in the literature; most of them were collapsing focal glomerulosclerosis due to pamidronate and exceptionally to alendronate [8,9]. On the other hand, Barry *et al.* observed two cases of biphosphonate-related MCD but both after i.v. administration of pamidronate [10].

The term paraneoplastic glomerulopathy generally refers to a glomerular disease without specific aetiology and which develops in parallel with cancer evolution phases (improvement, remission, recurrence) [4]. In about half of cases, the diagnosis of nephrotic syndrome precedes those of cancer while the simultaneous presentation of both diseases occurs in ~30% [4]. Renal improvement is mainly observed after complete clinical remission of the cancer. However, the two conditions can independently evolve [4]. Taking together, the firm causal link is often missing as in many similar cases, which makes the formal diagnosis of paraneoplastic glomerulopathies uneasy.

Finally, the beneficial effect of steroid therapy observed in our patient cannot distinguish idiopathic form from cancer-associated MCD since pathophysiology of paraneoplastic glomerulopathies involves numerous immunological processes (cytokines, growth factors or tumour antigens) susceptible to be efficiently reduced by immunosuppressive treatment [4]. In conclusion, the diagnosis of idiopathic MCD may be firmly assessed only after exclusion of all possible causes such as drugs, infections, allergies and neoplasms, among others solid tumours. Our case highlights the fact that a cancer as common as a breast malignancy may have an uncommon inaugural manifestation such as a MCD nephrotic syndrome.

Conflict of interest statement. None declared.

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