Acute kidney injury associated with lymphangitic carcinomatosis

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ABSTRACT

Acute kidney injury (AKI) is a major complication in patients with cancer, associated with significant morbidity and mortality. Only two cases of kidney lymphangitic carcinomatosis associated with AKI have been reported, in gastric and colorectal adenocarcinoma. Here, we report on a 53-year-old man with pancreatic adenocarcinoma who developed AKI as a result of kidney lymphangitic carcinomatosis. The patient rapidly became anuric and required haemodialysis. Kidney lymphangitic carcinomatosis should be considered as a cause of AKI in patients with cancer and may become a more frequent clinical finding as patients with metastatic carcinoma survive for longer.

Keywords: acute kidney injury, cancer, immunohistochemistry, kidney biopsy, lymphangitic carcinomatosis

BACKGROUND

Acute kidney injury (AKI) is common in patients with cancer and is associated with significant morbidity and mortality. In addition to the common causes of AKI, this condition can be triggered by factors that are more prevalent in (or indeed specific to) a cancer setting. In patients with solid cancers, the main causes of AKI are the nephrotoxic effects of cancer drugs, metabolic disturbances, sepsis, tumour infiltration, vascular compression and ureteral obstruction. Only two biopsy-proven cases of AKI associated with kidney lymphangitic carcinomatosis have been reported to date, in gastric and colorectal adenocarcinoma [1, 2].

Here, we report on a patient with pancreatic adenocarcinoma in whom AKI subsequently developed as a result of biopsy-documented lymphangitic carcinomatosis of the kidney.

CASE REPORT

A 53-year-old male patient was admitted with fatigue and anorexia. He had been diagnosed with pancreatic adenocarcinoma and secondary liver lesions 6 months earlier and had received the last of 10 cycles of FOLFIRINOX chemotherapy (5fluorouracil, oxaliplatin and irinotecan) 1 month before his admission. His blood pressure was 110/70 mmHg. A clinical
examination revealed ascites, jaundice and oliguria. In the month before admission, the patient’s serum creatinine level had increased from 106 to 398 µmol/L with proteinuria value of 1.5 g/day. Urine electrophoresis evidenced tubular proteinuria consisting of albumin (70%) and low-molecular weight proteins (30%). Microscopic haematuria was present (173 300 red blood cells/mL; n < 25 000), whereas leucocyturia was absent (3500/mL; n < 20 000). Renal ultrasound showed a known pyelic dilatation associated with a horseshoe kidney. Laboratory tests revealed a cholestatic background with elevated total bilirubin (25 mg/dL), alkaline phosphatase (172 IU/L) and γ-glutamyltranspeptidase (154 IU/L) levels. The patient also had elevated aspartate (92 IU/L) and alanine aminotransferase (110 IU/L) levels. The C-reactive protein level was elevated (50 mg/L), and the serum Ca19-9 level had decreased from 1578 to 571 U/mL over the course of chemotherapy. Anti-neutrophil cytoplasmic antibodies (ANCAs) were negative, and complement levels were normal. Despite the presence of portal hypertension, hepatorenal syndrome was ruled out by the maintenance of natriuresis (sodium excretion: 110 mmol/L).

A kidney biopsy was performed to determine the cause of the AKI. Eight glomeruli were observed, and none was abnormal. The lymphatic vessels were seen to be dilated by clusters of atypical cells (predominantly in the medulla and along the corticomedullary junction) with a high nucleus/cytoplasm ratio and prominent nuclei (Figure 1A). Interstitial oedema and scattered mononuclear inflammatory cells were also observed. Focal lesions of acute tubular injury were identified. There were no bile casts. Immunohistochemical staining for podoplanin confirmed the lymphatic nature of the tumour cell-filled vessels (Figure 1B). The tumour cells stained strongly for cytokeratin 7, an epithelial marker, and for mucin SAC, a marker for pancreatic origin (Figure 1B). In summary, the kidney biopsy revealed kidney lymphangitic carcinomatosis caused by pancreatic adenocarcinoma.

Shortly after the kidney biopsy, the patient became anuric and required haemodialysis therapy. Treatment with corticosteroids was initiated (prednisolone 1 mg/kg/day). Unfortunately, the patient died 2 weeks later.

**DISCUSSION**

AKI is common in patients with cancer and is associated with substantial morbidity and mortality. In the largest yet study of AKI among patients with incident cancer, the 1-year risk of AKI was 17.5% [3]. Patients with cancer and AKI have a poor prognosis with in-hospital mortality rate ranging from 49% to 87% [4]. AKI also accentuates the toxicity of cancer drugs, and thereby restricts patients’ treatment options.

Lymphangitic kidney carcinomatosis constitutes a very rare cause of AKI in patients with a documented history of cancer [1, 2]. With the advent of more sensitive non-invasive imaging modalities and prolonged survival of patients with cancer, renal metastases are increasingly likely to be detected during the patient’s lifetime. According to the literature data, the majority of patients with symptomatic secondary carcinoma of the kidney presented with macroscopic haematuria, flank pain or a mass, while kidney failure was infrequent [5]. In our case, dilation of the kidney's lymphatic vessels by clusters of tumour cells led to interstitial oedema containing scattered mononuclear inflammatory cells, together with focal lesions of acute tubular injury. In the largest review yet of cases of AKI caused by solid tumour renal metastases, the injury was usually due to extensive tissue replacement and destruction; only one case resulted from lymphatic metastases [5]. The pathophysiological mechanism for oliguric AKI was assumed to be similar to that postulated for post-transplantation lymphocele [1]. Impaired lymph circulation influences the drainage of interstitial fluid and results in lymphostasis; the lymphatic vessels fail to drain fluid from the interstitial space and thus cannot return it to the blood. The injured tubular cells release cytokines and growth factors that promote interstitial inflammation, extracellular matrix accumulation and, ultimately, fibrosis.

In the present case, laboratory tests revealed a cholestatic background and elevated transaminases. In the setting of liver disease, AKI is most frequently caused by a hepatorenal syndrome. Severe jaundice may also contribute to AKI via direct bile acid injury to renal tubular cells and obstruction by bile casts. Given that natriuresis was maintained and a kidney biopsy did not show any intratubular bile casts, we were able to rule out these diagnoses.

To the best of our knowledge, this is the first report of lymphangitic carcinomatosis of pancreatic origin spreading into the kidney. Hence, lymphangitic carcinomatosis should be considered as a potential cause of AKI in patients with a history of cancer. As patients with metastatic carcinoma survive for longer, complications such as AKI might become more frequent clinical findings.
CONFLICT OF INTEREST STATEMENT
None declared.

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