Interesting Case

Acute renal failure due to a malignant lymphoma infiltration uncovered by renal biopsy

Lorenz Sellin¹, Cornelia Friedl², Guido Klein², Rüdiger Waldherr³, L. Christian Rump¹ and Stefan M. Weiner¹

¹Department of Nephrology, Marienhospital Herne, Hospital of the University of Bochum, Herne, ²Division of Hematology and Oncology, Department of Medicine I, Marienhospital Herne, Hospital of the University of Bochum, Herne and ³Clinical Pathology, Heidelberg, Germany

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Introduction

Renal involvement by large B-cell lymphoma represents an exceptional manifestation of non-Hodgkin lymphoma. Acute renal failure (ARF) by a lymphoma infiltration of the kidney is extremely rare (so far 11 cases have been reported in the literature). We report a patient who was hospitalized for upper GI bleeding. Clinical examination revealed a tumour of the os sacrum. A CT-guided needle biopsy led to the diagnosis of a sarcoma. At this time, progressive renal failure was observed. Ultrasound showed enlarged kidneys with normal arterial and venous perfusion conditions. No urinary tract obstruction was detected. The cause of ARF was diagnosed by renal biopsy to be a diffuse infiltration of a large B-cell non-Hodgkin lymphoma. The re-evaluation of the primary histology of the os sacrum confirmed the renal biopsy diagnosis of the B-cell lymphoma. Subsequent staging showed an additional lymphoma infiltration of the lung and liver, but no bone marrow infiltration. Adequate dose-adjusted chemotherapy (CHOP) led to recovery of renal function in the follow-up. This report shows the importance of a renal biopsy in the work-up of ARF even in patients with known malignant diseases.

Case

A 73-year-old female was admitted to the Department of Surgery with acute upper GI bleeding. During this hospitalization a tumour of the os sacrum was discovered. A CT-guided needle biopsy led to the histological diagnosis of a neoplasm, probably sarcoma (positive immunohistology for vimentin and negative results for cytokeratins, smooth muscle actin, desmin and protein S100).

During the hypotensive period of the upper GI bleeding, elevated serum creatinine (160 µmol/l) was observed. However, 2 months previously the serum creatinine was within normal limits. Further follow-up revealed progressive renal failure (serum creatinine 391 µmol/l) within 2 weeks. Laboratory tests showed pathologic results for BUN 114 mg/dl, LDH 315 U/l, CRP 6.7 mg/dl and creatinine clearance 10 ml/min. In the urine sediment a high leukocyte count with leukocyte casts, moderate erythrocyte count, sporadic bacteria and uric acid crystals were detected. The adipose patient (BMI 28.6 kg/m²) complained about nausea and loss of appetite. Physically she presented with no peripheral lymphoma, heart, lungs and abdomen without pathological findings, prominent peripheral oedema. A palpable tumour of approximately fist size adjacent to the ilium was still present. The ultrasound showed massively enlarged kidneys (right kidney 16 cm, left kidney 14 cm), with no signs of urinary obstruction. The parenchyma was hypeoechogenic (Fig. 1A and B). Colour-coded duplex sonography revealed increased intrarenal resistive indices (RI 0.9) at both sides, no signs of renal vein thrombosis, but reduced parenchymal perfusion. Due to a markedly elevated uric acid (14.4 mg/dl) a conservative pharmacological therapy was started to treat an assumed uric acid nephropathy. However, in uric acid nephropathy the typical ultrasound finding is a hyperechogenic but

Correspondence and offprint requests to: L. Christian Rump, Department of Nephrology, Medicine I, Marienhospital Herne, Hospital of the University of Bochum, Hölkeskampring 40, D-44625 Herne, Germany.
Email: Christian.Rump@ruhr-uni-bochum.de
not hypoechoic renal parenchyma, suggesting another cause of renal failure.

Since the urine alkalization did not result in a major improvement of renal function, a diagnostic renal biopsy was performed. Histology showed a highly malignant large B-cell non-Hodgkin lymphoma with diffuse infiltration (Fig. 2A), positive for vimentin, CD45, CD19 and CD20 on immunohistology (Fig. 2B). The reassessment of the previous tumor biopsy of the sacrum region revised the initial diagnosis of a sarcoma and confirmed the highly malignant large B-cell lymphoma.

A restaging was performed. The cranial CT scan showed no tumor infiltration, the thorax CT scan presented round shaped intrapulmonary tumors and a mediastinal lymph node of 18 mm diameter. An abdominal CT scan documented an extended tumor infiltration of the left-sided pelvic soft parts, fracture of the ilium and arrosion of the sacrum. The left-sided pelvic lymph nodes were pathologically enlarged and thereby shift the pelvic vessels to medio-ventral. There was a solitary tumor of 22 mm diameter in the left lobe of the liver (segment 7). Both kidneys were enlarged. These findings correspond to a clinical stage IV A (according to the Ann Arbor classification).

Despite the risk of an additional renal challenge by tumor lysis during chemotherapy, a dose-adjusted systemic chemotherapy according to the CHOP protocol was applied. Forced diuresis and urine alkalization were taken as renoprotective measurements during the systemic chemotherapy. Fortunately the renal function improved remarkably with a serum creatinine of 123 µmol/l under continued therapy (Fig. 3). Renal ultrasound, performed immediately after the first cycle of chemotherapy, showed a normalization of the renal size (right kidney 12.2 cm, left kidney 11.2 cm) and intrarenal resistance indices (RI 0.78) (Fig. 1C and D). A follow-up abdominal CT scan was performed 5 weeks after the first application of systemic chemotherapy showing an overall tumor regress in the region of the pelvic soft parts (M. gluteus medius et minimus, M. ileopsoas) and disappearance of the tumor in the liver and pelvic lymph nodes. The adequate dose-adjusted chemotherapy led to a recovery of the renal function with a serum creatinine of 94.6 µmol/l. The systemic chemotherapy according to the CHOP protocol will be continued.

Discussion

ARF, as a consequence of renal lymphoma infiltration, is an exceptional clinical entity, although neoplastic infiltration has been documented in about one-third of all lymphoma patients who underwent a post-mortem
autopsy without signs of prior ARF during their lifetime [1].

After excluding causes of ARF such as volume depletion, sepsis, uric acid nephropathy in association with tumour lysis syndrome, post-renal obstruction and, renal vein thrombosis, the presence of leukocyte casts in the urine sediment demanded a renal biopsy to confirm or rule out a glomerulonephritis. In this case the ultrasound showed enlarged hypoechochogenic kidneys with no sign of post-renal obstruction or pelvic dilatation. Colour-duplex sonography proved a homogenous central renal perfusion without signs of arterial stenosis or renal vein thrombosis. However, the parenchymal perfusion was severely reduced and the intraparenchymal resistance indices were markedly increased, suggesting intraparenchymatous oedema.

Common causes of intrinsic ARF in association with a malignant disease such as sarcoma are mainly toxic effects due to overdosed chemotherapy or microbial treatment (e.g. methotrexate [2], ifosfamide [3,4] and cisplatin [5]), post-renal obstruction due to progressive tumour growth [4], paraneoplastic thrombosis of the vena cava and renal veins [6], and most frequently, tumour lysis syndrome leading to acute urate crystalluria [7]. The urine sediment with leukocytes, erythrocytes and sporadic uric acid crystals suggested a uric acid nephropathy: not unlikely in association with a sarcoma, but the morphological findings of the kidney in the ultrasound did not support this diagnosis. As expected, conservative renal therapy with hydration and urine alkalization did not result in an improvement of renal function. Definite diagnosis was obtained by renal biopsy, which revealed diffuse infiltration by a large B-cell non-Hodgkin lymphoma. The subsequent reassessment of the previous biopsy specimen from the pelvic tumour by immunohistology confirmed the diagnosis of a large B-cell non-Hodgkin lymphoma. The tumour cells showed a high proliferative activity (~70% positive for Ki67), consistent with a highly malignant large B-cell lymphoma. Unlike some previous reports [8], in this case a renal biopsy was performed to elucidate the cause of renal failure, to substantiate the diagnosis and to select the appropriate renal therapy. Here the patient and the renal function recovered under therapy; however, the prognosis in general is rather poor. The median survival in a group of eight patients with primary renal lymphoma reached 6 months; with systemic chemotherapy the median survival improved to 8.6 months [9]. However, recent multicentre trials in patients with aggressive non-Hodgkin lymphoma showed that rituximab, a monoclonal anti-CD20 antibody, in addition to CHOP is associated with superior survival rates [10].

In summary, we report a patient with ARF due to diffuse kidney infiltration by a large B-cell non-Hodgkin lymphoma. This case underlines the importance of renal biopsy to obtain a correct diagnosis and to select an appropriate therapy. Subsequent chemotherapy led to an impressive improvement of renal function within a few weeks, so that even intercurrent renal replacement therapy was unnecessary.

Fig. 2. Kidney biopsy. (A) Light microscopy showing diffuse infiltration of the renal parenchyma by atypical lymphoid cells. Masson trichrome stain, ×200. (B) Lymphoma cells strongly express CD20 (B-cells). Immunocytochemistry (biotin-streptavidin method), ×400.

Fig. 3. The graph shows the rapid increase of the serum creatinine during the development of ARF. The first administration of chemotherapy (CHOP) led within days to an overall decline and near normalization of the serum creatinine.
Conflict of interest statement. None declared.

References


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