CASE REPORT

Acute kidney injury as first presentation of lymphoma: the role of renal biopsy

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SUMMARY

A 65-year-old man with an insidious history of being generally unwell with weight loss, a poor appetite and night sweats was transferred to a tertiary nephrology unit after being found to be in acute kidney injury (AKI). A renal biopsy was performed on the same day which revealed lymphomatous infiltration of the renal parenchyma. He required temporary haemodialysis as he was oliguric and was started on chemotherapy. His renal function improved to baseline 3 weeks after treatment. This case illustrates the uncommon presentation of direct lymphomatous infiltration as a cause of AKI and the integral role of renal biopsy in ascertaining the diagnosis.

BACKGROUND

Patients with symptoms such as weight loss, fever, night sweats and lymphadenopathy should alert physicians to the possibility of a haematological malignancy. Although renal involvement is common in such malignancies, acute kidney injury (AKI) is rarely the presenting feature and has only been reported sporadically in the literature. In this report, we describe the rapid diagnosis of high-grade lymphoma on a renal biopsy and successful resolution of the AKI on the start of chemotherapy. This illustrates that timely renal biopsies allow appropriate treatment and management of these patients.

CASE PRESENTATION

A 65-year-old man had attended his local hospital with a 5-week history of progressive symptoms of lethargy, fatigue, decreased appetite, night sweats and weight loss. He was found to be in AKI on admission and was transferred to our tertiary nephrology unit for further management.

He was a normally fit and healthy man who never smoked and had a background of hypertension and osteoarthritis. His medications were lisinopril and naproxen (which were initially suspected as a cause of his AKI but which he had in fact stopped 3 weeks prior to presentation), tramadol and pregabalin. There was no significant medical or family history.

INVESTIGATIONS

Laboratory investigations revealed haemoglobin of 11.3 g/dL, white cell count $11.0 \times 10^9/L$, platelet count $56 \times 10^9/L$, serum urea 41.2 mmol/L and creatinine 797 $\mu\text{mol/L}$. Antinuclear antibodies, anti-neutrophil cytoplasmic antibodies and antiglomerular basement membrane antibodies

were not detected. A renal biopsy was performed on the same day of admission. This revealed interstitial infiltrate of the renal parenchyma with atypical lymphocytes which were diffusely positive for CD20 staining (figures 1 and 2).

Further biochemical analysis revealed serum lactate dehydrogenase of 12 000 IU/L and urate in excess of 15 000 $\mu\text{mol/L}$; indicative of severe tumour lysis syndrome. Bone marrow aspirate found a population of large vacuolated blast cells which were CD10 and CD38. Fluorescence in situ hybridisation determined this to be a high-grade lymphoma with features intermediate between diffuse large B-cell lymphoma and Burkitt's lymphoma.

TREATMENT

The patient's abnormal serum biochemistry and oliguria necessitated renal replacement therapy via a femoral line which was started a day after presentation. Following the results of the bone marrow aspirate on the fifth day of admission, he was started on rituximab, cyclophosphamide, doxorubicin, vincristine, methotrexate etoposide, ifosfamide (the RCODOX-M/IVAC chemotherapeutic regime for the management of high-grade Burkitt's lymphoma—with cytarabine excluded from the regime initially). Rasburicase was also administered for his tumour lysis syndrome. Intrathecal cytarabine was added 7 days after the chemotherapy regime was started.

OUTCOME AND FOLLOW-UP

Haemodialysis continued for 2 weeks, with renal function returning to baseline values 3 weeks after admission (figure 3).

Figure 1 H&E stain ($\times 20$)—renal cortex showing diffuse infiltration of interstitium by lymphoid cells.

To cite: On W, Udberg M. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-202196

Figure 2 CD20 staining (x40) showing atypical lymphoid cells which are diffusely positive for the B-cell marker CD20.

Cerebrospinal fluid analysis in preparation for intrathecal cytarabine revealed central nervous system involvement of high-grade lymphoma. Despite a positive initial response to chemotherapy, he developed sudden visual loss in his right eye with widespread vascular occlusion and chorioretinal atrophy and subsequently developed spastic paraparesis. Further chemotherapy with wide-beam craniospinal irradiation was given.

Owing to the advanced nature of the disease, the patient decided against further treatment and was referred for palliative care. He died 6 months after presentation.

DISCUSSION

The causes of AKI are commonly categorised into prerenal, intrinsic and postrenal. Prerenal AKI is caused by hypoperfusion of the kidneys secondary to circulatory volume depletion such as gastrointestinal tract losses or inadequate perfusion pressures such as in cardiac failure and sepsis. Urine biochemistry analysis typically reveals low sodium levels, low fractional excretion of sodium and urea and increased urine osmolality. However, urinary sodium may be affected by diuretic use and biochemical analysis should be interpreted in conjunction with the clinical scenario.

Intrinsic AKI can be caused by prolonged prerenal insult, nephrotoxic medications, glomerulonephritis or iatrogenic endovascular intervention. Investigations include but are not limited to urinalysis and urine microscopy, an autoimmune screen, erythrocyte sedimentation rate, complement levels, cryoglobulins, hepatitis screen and a blood film. A renal biopsy may be warranted if an intrinsic cause of AKI is suspected.¹

Postrenal AKI is due to obstruction of the urinary tract due to kidney stones, tumours, bladder neck outflow obstruction or retroperitoneal fibrosis. Ultrasonography may reveal hydronephrosis or hydroureter and further imaging such as CT may be required to reveal the cause of obstruction. Urgent intervention such as bladder catheterisation or nephrostomy insertion may be indicated.

Involvement of the kidneys in lymphoma is common and in a series of 322 autopsies of patients who had died of malignant lymphoma, the kidneys were involved in 121 (37.6%) of them.² Impairment of kidney function in patients with lymphoma is usually the consequences of prerenal, intrinsic and postrenal factors such as sepsis, renal vein thrombosis, precipitation of light chains causing tubular obstruction, glomerulonephritis, obstructive uropathy and the side effects of treatment.³

AKI as a primary presenting feature of lymphomas remains a rare clinical entity and are only sparsely reported in the literature.⁴ Most renal lymphomas are due to infiltration from a secondary origin as was the case in our patient. However, primary renal lymphomas are becoming increasingly recognised and both types have been reported to be a cause of AKI. Regardless of the origin of the lymphoid malignancy, improvement of renal function has been observed on initiating early treatment.³⁻⁸

The pathophysiology of AKI caused by lymphoma in the absence of the aforementioned causes remains uncertain. It has been postulated that the infiltrative lymphoid cells compress the renal tubules and vasculature resulting in obstruction and ischaemia. Cytokines secreted by the lymphoma cells may also play a role in causing cellular reaction and interstitial fibrosis.^{3,9} The improvement of renal function after the start of chemotherapy, as is the case in our patient, highly suggests that his kidney impairment was a result of direct infiltration of the lymphomatous cells although concurrent treatment for tumour lysis syndrome was likely to have contributed to the improvement. In the case reported by Sellin *et al*⁷ a normalisation of the size of the kidneys and improvement of the biochemical indices of kidney function tests were observed after the first cycle of chemotherapy. Patients with oliguria such as the case reported by Jorge *et al*⁵ and our patient may require intermittent haemodialysis if there is recurrence of AKI or the underlying disease is refractory to treatment.

The importance of early renal biopsy to establish the cause of AKI and to initiate appropriate treatment is echoed in many other literature reports where lymphomatous infiltration of the kidneys has been established by biopsy. Our report adds weight to the importance of this investigation and hopefully is a reminder of its usefulness when investigating AKI of unknown causes with systemic symptoms.^{4,10-12}

Figure 3 Graph showing serum creatinine against time.

Learning points

- Causes of acute kidney injury (AKI) are categorised into prerenal, intrinsic and postrenal.
- AKI as a presenting feature of lymphomas is a rare but recognised clinical entity.
- Determining the cause of AKI is essential for guiding optimal management.
- Renal biopsy should be considered when an urgent diagnosis is needed.
- Rapid recovery of kidney function may be achieved with timely treatment.

Acknowledgements The authors would like to acknowledge Dr Rema Saxena, consultant nephrologist, Royal Liverpool University Hospital NHS trust; Dr Arti Bakshi, consultant histopathologist, Royal Liverpool University Hospital NHS trust and Dr Arvind Arumainathan, consultant haematologist, Royal Liverpool University Hospital NHS trust.

Contributors WO and MU were involved in the care of the patient. MU collected data and wrote up the presentation of the patient. WO reviewed the literature and revised the manuscript for intellectual content.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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