

## Case Reports

# Acute kidney injury secondary to lymphomatous infiltration and the role of kidney biopsy

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### ABSTRACT

هذه حالة مريض ذكر يبلغ من العمر 47 سنة حيث كان يعاني من فشل كلوي حاد و لوحظ عليه تضخم كبير في حجم الكليتين. عدا عن بعض التضخم في الغدد اللمفاوية داخل البطن لم يكن هناك أي تضخم في الغدد اللمفاوية الأخرى أو الأعضاء الأخرى خزعة الكلية أدت إلى تشخيص لمفوم لا هودجكني. كانت الاستجابة للمعالجة الكيميائية جيدة. هذه الحالة تثبت أن الكلية يمكن أن تكون العضو الرئيسي للإصابة باللمفوم اللا هودجكني. إضافة إلى ذلك فقد أثبتنا أن خزعة الكلية كافية لتشخيص اللمفوم بدون الحاجة إلى إجراءات أكثر تعقيداً.

We report a 47-year-old male patient who developed acute kidney injury requiring hemodialysis, associated with massive enlargement of both kidneys. A part from intra-abdominal lymphadenopathy, there was no other organ or lymph node involvement. A kidney biopsy established the diagnosis of non-Hodgkin's lymphoma. The patient received chemotherapy with good response. This case demonstrates that the kidney could be the primary organ involved in non-Hodgkin's lymphoma. In addition, we have shown that renal biopsy is adequate to make a diagnosis of lymphoma without the need to do more invasive testing.

*Saudi Med J 2008; Vol. 29 (12): 1808-1810*

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*Received 7th July 2008. Accepted 2nd November 2008.*

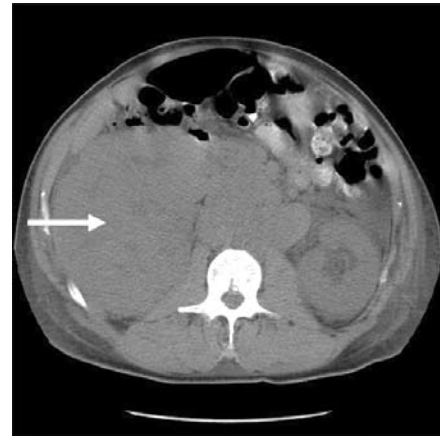
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Primary renal lymphoma is a rare entity with only a few reports in the literature. It has been long debated whether renal lymphoma is truly a primary lesion, or whether the kidney gets invaded by lymphoma arising from extra renal tissues. This report demonstrates that the kidney could be the primary organ involved in non-Hodgkin's lymphoma. In addition, the role of renal biopsy will be highlighted.

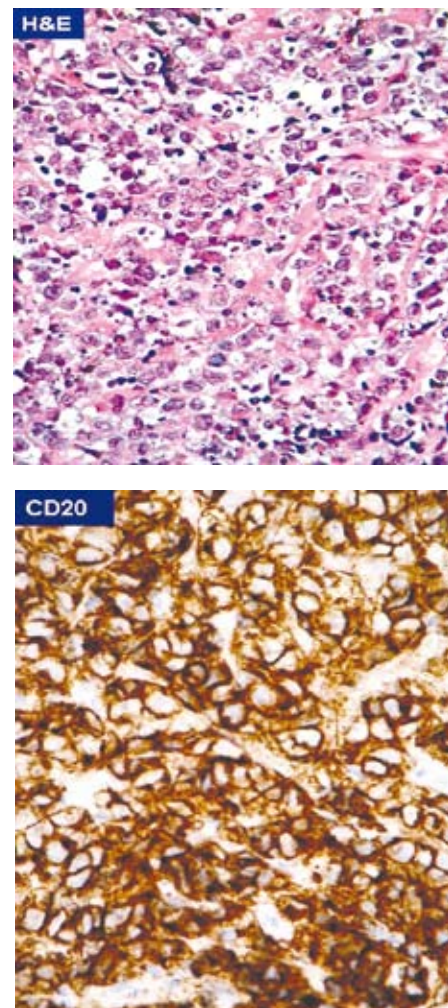
**Case Report.** A 47-year-old male patient (African-American) who had no significant past medical history presented with a 2-month history of back pain for which he was treated with diclofenac. Three days prior to his admission, he noticed a significant decrease of his urine output associated with nausea and vomiting. In addition, he had a significant weight loss of 10 kg over 3 months without fever or sweats. His grandfather died of end stage renal disease (ESRD) of unknown etiology at age 90 years. Detailed examination revealed no cervical, axillary or inguinal lymphadenopathy. The abdomen was soft with mild generalized tenderness. There was a palpable large lobulated mass extending from the right upper quadrant to the right groin. He was anuric. The initial tests revealed urea 93 mg/dl (79-22 mg/dl) and creatinine of 16.1 mg/dl (0.9-1.4 mg/dl). Sodium was 134 mEq/L (137-145 meq/L), potassium 6.5 mEq/L (3.3-5.3 mEq/L), chloride 97 mEq/L (98-107 mEq/L), and carbon dioxide was 22 mEq/L (21-28 mEq/L). The lactate dehydrogenase was elevated at 1,668 iu/L (321-597iu/L), but the other liver enzymes were within normal values. The hemoglobin was 12.8 gm/dl (13.5-17.5 gm/dl), white blood cells were 5700/mm<sup>3</sup> (4000-10000/mm<sup>3</sup>) with 53% neutrophils, 18% lymphocytes, 10% monocytes and 19% eosinophils. The platelet count was 200,000/mm<sup>3</sup> (150,000-450,000/mm<sup>3</sup>). The uric acid (UA) was 16.1 mg/dL (2.8-7.7 mg/dL). On ultrasound, the right kidney was hypoechoic with a lobulated cortical surface and measured 22 x 13 cm. The left kidney measured 13.5 cm in the longest diameter and appeared diffusely echogenic. There was no dilation of the collecting systems, and both renal veins were patent. Computer tomography showed a massive enlargement

of the right kidney with widespread lymphadenopathy in the abdomen, pelvis and retroperitoneum, **Figure 1**. A mercapto acetyl tri glycine (MAG3) renal scan showed no uptake or function on the right side. There was good blood flow and uptake on the left side, however, the drainage was poor. A core biopsy was performed from the right kidney. The light microscopy showed diffuse involvement by malignant neoplasm composed of large lymphoid cells with irregular and prominent nucleoli. Marked apoptosis was noted. The small amount of renal medullary tissue was infiltrated by lymphocytes and large lymphoid cells. No cortical tissue or glomeruli were seen, **Figure 2a**. Immunohistochemistry showed large lymphoid cells, which were diffusely positive for CD20, CD79, CD10, and kappa light chain, **Figure 2b**. The majority of the neoplastic cells were positive for Ki67 (proliferation index approximately 90%). These cells were negative for CD3, CD43, CD5, CD30 and Bcl2. The multiparametric flow cytometric analysis showed only rare CD19 positive cells that were inconclusive for clonality. The histologic features and the immunohistochemical profile were consistent with diffuse large B-cell lymphoma. The patient was started on hemodialysis through an internal jugular Permacath with rapid resolution of the uremic symptoms. Chemotherapy was started by using a combination of rituximab, vincristine, doxorubicin, prednisone and cyclophosphamide (R-CHOP). One week later he started producing urine and the kidney function rapidly recovered to a creatinine of 1.2 mg/dl (0.9-1.4 mg/dl). A repeat CT scan of the abdomen after 2 cycles of chemotherapy revealed a significant decrease in the size of the kidneys and the intra-abdominal lymph nodes. A repeat MAG3 renal scan showed normal flow, uptake and drainage on the left side, but no uptake in the right kidney. Positron emission tomography after 6 cycles of chemotherapy showed no active uptake leading us to suspect that despite persistent residual enlargement of the right kidney, it contained no viable tumor cells. A repeat right kidney biopsy after 6 cycles of treatment demonstrated extensive fibrosis associated with chronic inflammation composed of small and reactive lymphocytes with focal collections of histiocytes. No residual tubules were seen. The glomeruli were globally sclerotic. Immunohistochemical stains demonstrated that nearly all of the inflammatory cells were CD3-positive (T-cells) and CD20-negative (B-cell). After completion of chemotherapy, he received consolidation external beam radiation to the right kidney that resulted in a significant size reduction. The patient was alive and well 20 months following the initial diagnosis.

**Discussion.** The patient developed acute kidney injury (AKI) and presented with uremic symptoms.



**Figure 1** - Unenhanced CT axial image of the abdomen showing diffuse severe enlargement of the right kidney (arrow) with significant retroperitoneal lymphadenopathy.



**Figure 2** - A core biopsy showing a) diffuse proliferation of malignant large lymphocytes (40 x Hematoxylin & eosin). b) The cells are diffusely and strongly positive for CD20 (B-cell marker).

He was found to have large kidneys bilaterally, more pronounced on the right side. The diagnosis of non-Hodgkin's lymphoma was established by percutaneous kidney biopsy. In this case, the renal biopsy tissue was adequate to perform the required tests including flow cytometry and immunohistochemistry studies, without the need for lymph node biopsy. The right kidney was extensively infiltrated by lymphomatous cells that caused irreversible destruction of the renal architecture. The left kidney was also enlarged, most likely due to the same process; however, a tissue to confirm this suspicion was not obtained. The changes in the renal size by CT and ultrasound following treatment with chemotherapy indicates that both kidneys were affected by the same process. Furthermore, the rapid improvement of renal function following initiation of chemotherapy supports the notion that lymphomatous infiltration of the kidneys was the main cause of renal failure. Other causes of AKI such as hyperuricemia and exposure to nonsteroidal anti-inflammatory drugs may have played a role as well. Renal failure related to lymphoma could be the result of many factors such as sepsis, volume depletion, uric acid nephropathy in association with tumor lysis syndrome, obstructive uropathy, nephrotoxic drugs, renal vein thrombosis and glomerulonephritis. Acute kidney injury related to lymphomatous invasion of the kidneys has been a rare finding with only a few reports in the literature.<sup>1-6</sup> The question whether renal lymphoma was a primary lesion was debated.<sup>7</sup> In autopsy studies, invasion of the kidneys by lymphoma has been estimated at 6-60%.<sup>6, 8-10</sup> The majority of the cases were asymptomatic and the clinical evidence of renal failure was found only in 0.5% of cases.<sup>6,10</sup> In most reported cases, the diagnosis of lymphoma was established by conventional means such as lymph node biopsy, and only in rare cases was the diagnosis made by renal biopsy. The first report of lymphoma diagnosed by renal biopsy was reported by Coggins in 1980.<sup>8</sup> Since then, a total of 57 cases, including ours have been reported in the English literature.<sup>1,3</sup> The majority of cases presented with AKI and bilateral kidney enlargement (87%), while nephrotic range proteinuria was present in only 9%.<sup>3</sup> As in our case, the majority of cases were CD20 positive large B-cell lymphoma. In most cases, the kidney function recovered within one to 2 weeks after initiation of chemotherapy. The mechanism of AKI related to lymphomatous infiltration is not very clear. Increased intrarenal pressure with compression of the renal tubules and interruption of the blood supply for a prolonged period of time may lead to a permanent destruction of the renal tubules as seen in our case.<sup>12</sup> The rapid recovery of renal function within days after initiation of chemotherapy gives an indirect hint of the role of increased intrarenal pressure in the

pathogenesis of renal failure. In our case, the recovery of renal function was attributed to normalization of the function of the left kidney that was apparently affected to a much lesser degree than the right kidney.

In summary, our case demonstrates that lymphomatous infiltration of the kidneys can directly cause renal failure. Prompt diagnosis and treatment is essential to preserve the renal function. In addition, we have shown that renal biopsy is a useful tool to establish the diagnosis of lymphoma without the need to perform other tests such as lymph node biopsy.

**Acknowledgment.** *The authors would like to acknowledge the Saudi Aramco Medical Services Organization (SAMSO) facilities for research data used in this article. Opinions expressed in this article are those of the authors and not necessarily of SAMSO.*

## References

- Sellin L, Friedl C, Klein G, Waldherr R, Rump LC, Weiner SM. Acute renal failure due to a malignant lymphoma infiltration uncovered by renal biopsy. *Nephrol Dial Transplant* 2004; 19: 2657-2660.
- Simsek S, Oen AL, Comans EF, Hoeven JJ, Zijlstra J. Acute renal failure due to non-Hodgkin lymphoma infiltration of the kidneys detected by ultrasonography and confirmed by positron emission tomography. *Clin Nephrol* 2003; 59: 383-387.
- Törnroth T, Heiro M, Marcussen N, Fransilla K. Lymphomas diagnosed by percutaneous kidney biopsy. *Am J Kidney Dis* 2003; 42: 960-971.
- Obrador GT, Price B, O'Meara Y, Salant DJ. Acute renal failure due to lymphomatous infiltration of the kidneys. *J Am Soc Nephrol* 1997; 8: 1348-1354.
- Ellman L, Davis J, Lichtenstein NS. Uremia due to occult lymphomatous infiltration of the kidneys. *Cancer* 1974; 33: 203-205.
- Humphreys BD, Soiffer RJ, Magee CC. Renal failure associated with cancer and its treatment: an update. *J Am Soc Nephrol* 2005; 16: 151-161.
- Kandel LB, McCullough DL, Harrison LH, Woodruff RD, Ahl ET Jr, Munitz HA. Primary renal lymphoma. Does it exist? *Cancer* 1987; 60: 386-391.
- Coggins CH. Renal failure in lymphoma. *Kidney Int* 1980; 17: 847-855.
- Xiao JC, Walz-Mattmüller R, Ruck P, Horny HP, Kaiserling E. Renal involvement in myeloproliferative and lymphoproliferative disorders. A study of autopsy cases. *Gen Diagn Pathol* 1997; 142: 147-153.
- Richmond J, Sherman RS, Diamond HD, Craver LF. Renal lesions associated with malignant lymphomas. *Am J Med* 1962; 32: 184-207.
- Cossu A, Deiana A, Lissia A, Satta A, Cossu M, Dedola MF, et al. Nephrotic syndrome and angiotropic lymphoma report of a case. *Tumori* 2004; 90: 510-513.
- Glicklich D, Sung MW, Frey M. Renal failure due to lymphomatous infiltration of the kidneys. Report of three new cases and review of the literature. *Cancer* 1986; 58: 748-753.