Pediatr Nephrol (2004) 19:912–914
DOI 10.1007/s00467-004-1521-1

BRIEF REPORT

Fatih Ozaltin · Bilgehan Yalçın · Diclehan Orhan · Neriman Sari · Melda Caglar · Nesrin Besbas · Aysin Bakkaloglu

An unusual cause of acute renal failure: renal lymphoma

Received: 21 January 2004 / Revised: 12 April 2004 / Accepted: 13 April 2004 / Published online: 16 June 2004

Abstract Renal involvement is a common finding in non-Hodgkin's lymphoma (NHL). Acute renal failure at initial presentation due to lymphomatous infiltration of the kidneys has been described infrequently. We report a 17-year-old male who presented with acute renal failure due to massive lymphomatous infiltration of the kidneys, which necessitated hemodialysis. The diagnosis of B-cell NHL was established by tru-cut biopsy of the kidneys and the patient had an excellent response to high-dose chemotherapy with no major complication. The presence of extrarenal involvement in the testes and the retroperitoneal lymph nodes made the diagnosis of primary renal lymphoma debatable. However, considering the delay in diagnosis and the high proliferative rate of B-cell NHL, we might postulate that the disease had originated primarily in the kidneys. We recommend that in NHL cases with severe renal involvement, full-dose chemotherapy should be instituted with meticulous clinical and laboratory follow-up in order to improve clinical and renal failure status rapidly and to avoid further dissemination of NHL.

F. Ozaltin · N. Besbas · A. Bakkaloglu
Nephrology Unit, Department of Pediatrics, Faculty of Medicine, Hacettepe University, Ankara, Turkey

B. Yalçın · N. Sari
Oncology Unit, Department of Pediatrics, Faculty of Medicine, Hacettepe University, Ankara, Turkey

D. Orhan · M. Caglar
Pathology Unit, Department of Pediatrics, Faculty of Medicine, Hacettepe University, Ankara, Turkey

F. Ozaltin (✉)
Department of Pediatric Nephrology, Faculty of Medicine, Hacettepe University, 06100 Sihhiye Ankara, Turkey
e-mail: fozaltin@hacettepe.edu.tr
Tel.: +90-312-3051246
Fax: +90-312-3094232

Keywords Acute renal failure · Non-Hodgkin's lymphoma · Renal lymphoma

Introduction

Renal involvement is a common finding in non-Hodgkin's lymphomas (NHL) and is reported in up to 50% of patients [1]. However, primary renal lymphoma (PRL) presenting with acute renal failure is extremely rare, especially in children. Acute renal failure as the only presenting symptom due to lymphomatous infiltration of the kidneys has been described infrequently in adults [2, 3]. We present an adolescent boy with acute renal failure due to bilateral massive lymphomatous infiltration of the kidneys.

Case report

A 17-year-old male patient was referred to the Department of Pediatric Nephrology, Hacettepe University Faculty of Medicine in October 2003, due to renal failure. He was first evaluated at another center for pallor, malaise, and weight loss, which had lasted for 1 month. There was knee and ankle pain as well as a high fever for 15 days. He had complained of right flank pain for the last 3 days. There was no history of upper respiratory infection or oliguria. His past history was unremarkable. His older brother had been treated for steroid-sensitive nephrotic syndrome (focal segmental mesangial proliferation), which had been diagnosed at the age of 4 years.

Physical examination of the patient showed hypertension (160/90 mmHg), pallor, bilateral palpable flank masses, and bilateral enlarged and firm testes. No peripheral lymphadenopathy was found and other systemic findings were normal. Laboratory findings included hemoglobin 7.9 g/dl, hematocrit 23.4%, white blood cell count 6,800/mm^3 with a differential of 55% neutrophils, 28% monocytes, 16% lymphocytes, and 1% myelocytes and platelets 160,000/mm^3. The erythrocyte sedimentation rate was 40 mm/h. Urinalysis was normal except for hyposthenuria (specific gravity 1,008). Blood urea nitrogen was 73 mg/dl (normal 10–20 mg/dl), creatinine 5.3 mg/dl (normal 0.9–2 mg/dl), uric acid 9.2 mg/dl (normal 2–6 mg/dl), sodium 138 mEq/l, potassium 5.8 mEq/l, chloride 108 mEq/l, bicarbonate 16.9 mmol/l with a blood pH of 7.36, total protein 5.7 g/dl, albumin 3.5 g/dl, aspartate aminotransferase 46 U/l (normal <50 U/l), alanine aminotransferase 65 U/l (normal <40 U/l), and lactate dehydrogenase (LDH) 696 U/l

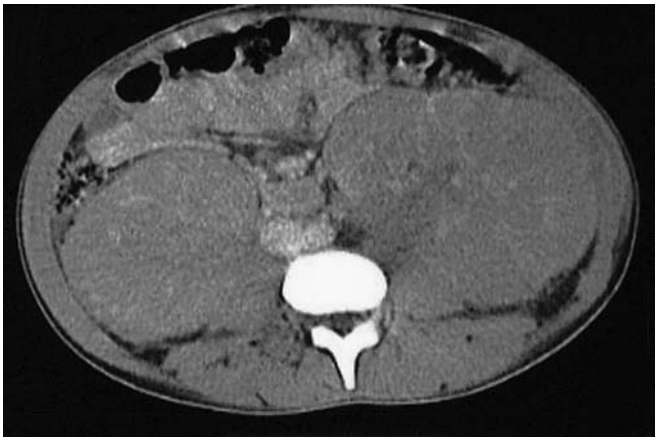

Fig. 1 Contrast-enhanced computed tomography of the abdomen. Bilateral enlarged kidneys with multiple hypodense areas and para-aortic multiple enlarged lymph nodes were noted

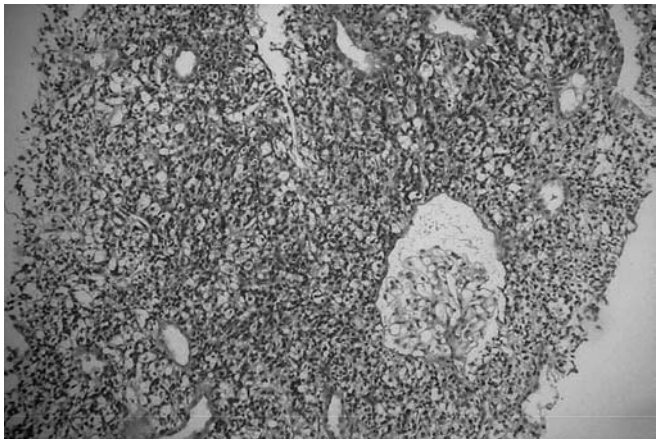

Fig. 2 Diffuse infiltration of the tubulointerstitium with atypical lymphoid cells and macrophages. Glomeruli and tubuli were spared (hematoxylin and eosin, ×50)

(normal 150–400 U/l). Creatinine clearance was 20 ml/min per 1.73 m^2. Serum iron and iron binding capacity were normal but the ferritin level was high (2,020 ng/ml, normal 5–148 ng/ml). Vitamin B_{12} and folic acid levels were also within normal limits. C3 and C4 as well as quantitative immunoglobulin levels were all within normal limits, with negative antinuclear antibody and anti-double stranded DNA tests. Viral serology showed hepatitis B infection with positivity for HBsAg, HBeAg, and HBc IgG, as well as a high HBV DNA titer (3,333 pg/ml, normal 0–5 pg/ml), but with no anti-HBs, anti-HBe, and anti-HBc IgM. Serology for acute Epstein-Barr virus and cytomegalovirus was negative. Chest X-ray was normal. Abdominal ultrasonography showed bilateral enlarged kidneys with increased echogenicity, splenomegaly (168 mm), and minimal fluid in the pelvis. The right and left kidneys measured 198 mm and 207 mm, respectively. Parenchymal thickness was 23 mm for both. Bilateral testicular involvement was demonstrated by scrotal ultrasonography. Computed tomography (CT) of the abdomen confirmed the presence of bilateral enlarged kidneys with multiple hypodense areas and para-aortic multiple enlarged lymph nodes (largest <2 cm in size). Both the liver and spleen were slightly enlarged with normal parenchyme (Fig. 1). Chest CT showed bilateral minimal pleural effusion without parenchymal lesions. Bone marrow aspiration showed reactive hemophagocytosis without malignant infiltration. A percutaneous tru-cut biopsy of the kidney was performed and histopathological examination revealed NHL with mature B-cells (Fig. 2). With the diagnosis of "stage III NHL", the cytoreductive COP (cyclophosphamide, vincristine, prednisolone) chemotherapy of the modified LMB-89 regimen was started [4]. During the first 3 days he underwent daily hemodialysis. By the end of the cytoreductive chemotherapy, creatinine clearance had increased to 65 ml/min per 1.73 m^2 concomitant with increased urinary output. The requirement for dialysis ceased and the patient was considered in partial remission by clinical and ultrasonographic findings. We continued with further chemotherapy and completed the second course of COPADM (cyclophosphamide, vincristine, prednisolone, adriamycin, methotrexate) therapy with high-dose methotrexate uneventfully. During each chemotherapy course, serum methotrexate levels were slightly elevated in the following days and he received calcium folinate for a total of 10 days. He exhibited no signs of chemotherapy toxicity other than neutropenia and fever, which was managed by empirical antibiotic therapy. The patient is now in complete remission following the completion of the whole chemotherapy regimen. His most recent serum creatinine value was 1 mg/dl and creatinine clearance was 85 ml/min per 1.73 m^2.

Discussion

In our hospital, among 1,365 children followed with NHL, 7.6% had uni- or bilateral renal involvement at initial presentation. Such involvement is almost invariably secondary and primary renal NHL is extremely rare [5]. Some criteria have been suggested for the diagnosis of primary renal lymphoma. These include (1) renal failure as the initial presentation, (2) enlargement of the kidneys without obstruction, and without other organ or nodal involvement, (3) diagnosis only made by renal biopsy, (4) absence of other causes of renal failure, and (5) rapid improvement of renal function after radiotherapy or systemic chemotherapy [6]. Our patient, with no other causes of renal failure, mostly fulfills these criteria. The patient had massive infiltration of the kidneys accompanied by bilateral testicular infiltration and some enlarged retroperitoneal lymph nodes, which made the diagnosis of PRL debatable. Childhood B-cell NHL is characterized by a high proliferation rate and rapid dissemination [4]. Saito [7] reported that most PRLs disseminate rapidly from their renal origin. Considering the delay in the diagnosis of NHL in our patient and the severe involvement of the kidneys, we postulate that the disease had originated primarily in the kidneys and other sites were involved secondarily. Rapid improvement of renal function following chemotherapy was also remarkable, which is one of the criteria suggested for the diagnosis of PRL [6].

PRL is extremely rare. It usually affects adults and is usually Burkitt type or less frequently lymphoblastic lymphoma [8, 9]. It accounts for 0.7% of all extranodal lymphomas in adults in North America [5]. Its occurrence in childhood is much more rare than in adults. To date, 11 pediatric cases with PRL have been reported and 3 of them have had extrarenal involvement [10, 11, 12, 13, 14, 15, 16, 17, 18, 19]. Many reported cases have been described as PRL according to absence of extrarenal disease. However, a systematic review of the literature by Stallone et al. [2] showed that only 28 of 60 cases that

had been reported as PRL [3] could fulfill all of the criteria.

Our patient presented with non-oliguric acute renal failure. The mechanism of renal failure has not been clearly established. Some investigators suggested that renal failure was the result of diffuse infiltration [12], while others postulated that dense tumor infiltration of the renal parenchyme might cause compressive alteration of tubules and impairment of the renal vasculature [13]. This might explain several specific characteristics of renal lymphoma, as observed in our patient, including the absence of significant proteinuria and the absence of tumor cells in the urine, markedly elevated serum creatinine, and a rapid recovery of renal function after chemotherapy.

In our patient, the elevated LDH in conjunction with the radiological findings suggested the diagnosis of NHL. Mills et al. [20] proposed that acute renal failure associated with an elevated LDH or lymphopenia should suggest diffuse renal infiltration by lymphoma.

CT scan and nuclear magnetic resonance imaging, as well as nuclear scan, have improved the accuracy of staging in renal lymphomas [18, 21, 22]. However, the gold standard in the diagnosis is histopathological examination. In our patient, following CT scan of the abdomen, which showed bilateral renal enlargement suggesting NHL, the diagnosis was established by histopathological examination of the renal biopsy. Once diagnosed, systemic chemotherapy was started immediately. Despite significant renal dysfunction, we administered full-dose chemotherapy. The occurrence of tumor lysis syndrome was a high probability considering the bulky nature of the disease, which would have further worsened the renal dysfunction. Rapid clinical and biochemical improvement were observed concomitant with decreased dialysis requirement. Initial 1-week cytoreductive chemotherapy was followed by high-dose COPADM treatment with 3 g/m^2 methotrexate, which carried the potential risk of delayed renal clearance and significant systemic toxicity. The whole chemotherapy protocol was very well tolerated and completed. The patient is under regular follow-up with mild loss of renal function but no evidence of primary disease.

In conclusion, renal lymphoma should seriously be considered in the differential diagnosis of acute renal failure associated with infiltrative renal disease. Renal biopsy is essential for the diagnosis. NHLs are highly chemosensitive tumors of childhood. Full-dose chemotherapy should be instituted with meticulous clinical and laboratory follow-up as soon as possible in order to improve clinical and renal failure status rapidly and to avoid further dissemination of the primary disease.

References

1. Richmond J, Sherman RS, Diamond HD, Craver LF (1962) Renal lesions associated with malignant lymphomas. Am J Med 32:184–207
2. Stallone G, Infante B, Manno C, Campobasso N, Pannarale G, Schena FP (2000) Primary renal lymphoma does exist: case report and review of the literature. J Nephrol 13:367–372
3. Fernandez-Acenero MJ, Galindo M, Bengoechea O, Borrega P, Reina JJ, Carapeto R (1998) Primary malignant lymphoma of the kidney: case report and literature review. Gen Diagn Pathol 143:317–320
4. Kutluk T, Varan A, Akyüz C, Büyükpamukçu M (2002) Clinical characteristics and treatment results of LMB/LMT regimen in children with non-Hodgkin's lymphoma. Cancer Invest 20:626–633
5. Freeman C, Berg JW, Cutler SJ (1972) Occurrence and prognosis of extrarenal lymphomas. Cancer 29:252–260
6. Malbrain ML, Lambrecht GL, Daelemans R, Lins RL, Hermans P, Zachee P (1994) Acute renal failure due to bilateral lymphomatous infiltrates. Primary extranodal non-Hodgkin's lymphoma (p-EN-NHL) of the kidneys: does it really exist? Clin Nephrol 42:163–169
7. Saito S (1996) Primary renal lymphoma. Case report and review of the literature. Urol Int 56:192–195
8. Okuno SH, Hoyer JD, Ristow K, Witzig TE (1995) Primary renal non-Hodgkin's lymphoma. An unusual extranodal site. Cancer 75:2258–2261
9. Ferry JA, Harris NL, Papanicolaou N, Young RH (1995) Lymphoma of the kidney. A report of 11 cases. Am J Surg Pathol 19:134–144
10. Camitta BM, Casper JT, Kun LE (1986) Isolated bilateral T-cell renal lymphoblastic lymphoma. Am J Pediatr Hematol Oncol 8:8-12
11. Kutluk MT, Büyükpamukçu M, Göğüş S, Sarıalioğlu F, Akhan O, Beşbaş N (1989) Renal lymphoma. An unusual presentation in a child. Turk J Pediatr 31:71–77
12. Dobkin SF, Brem AS, Caldamone AA (1991) Primary renal lymphoma. J Urol 146:1588–1590
13. Arranz Arija JA, Carrion JR, Garcia FR, Tejedor A, Perez-Manga G, Tardio J, Menarguez FJ (1994) Primary renal lymphoma: report of 3 cases and review of the literature. Am J Nephrol 14:148–153
14. Vujanic GM, Webb D, Kelsey A (1995) B-cell non-Hodgkin's lymphoma presenting as a primary renal tumour in a child. Med Pediatr Oncol 25:423–426
15. Sieniawska M, Bialaszk D, Jedrzejowski A, Sopylo B, Maldyk J (1997) Bilateral renal Burkitt lymphoma in a child presenting with acute renal failure. Nephrol Dial Transplant 12:1490–1492
16. Karadeniz C, Oguz A, Ataoglu Ö, Çitak Ç, Buyan N, Pinarli G, Özkaya O, Kapucu Ö (2002) Primary renal lymphoma and xanthogranulomatous pyelonephritis in childhood. J Nephrol 15:597–600
17. Levendoglu-Tugal O, Kroop S, Rozenblit GN, Weiss R (2002) Primary renal lymphoma and hypercalcemia in a child. Leuk Lymphoma 43:1141–1146
18. Moon LD, Brenner C, Ancliff P, McHugh K, DeBruyn R (2004) Non-Hodgkin's lymphoma presenting with uterine and renal enlargement in a young girl. Pediatr Radiol 34:277–279
19. Kemper MJ, Bergsträsser E, Pawlik H, Gaspert A, Neuhaus TJ (2003) An 8-year-old boy with recurrent macroscopic hematuria, weight loss, and kidney failure. J Pediatr 142:342–345
20. Mills NE, Goldenberg AS, Liu D, Feiner HD, Gallo G, Gray C, Lustbader I (1992) B-cell lymphoma presenting as infiltrative renal disease. Am J Kidney Dis 19:181–184
21. Chepuri NB, Strouse PJ, Yanik GA (2003) CT of renal lymphoma in children. AJR Am J Roentgenol 180:429–431
22. Yen TC, Tzen KY, Lin KJ (1999) The role of Ga-67 whole-body and Tc-99m DMSA renal scan in primary bilateral B-cell renal non-Hodgkin's lymphoma. Clin Nucl Med 24:193–194