Arch. Esp. Urol. 2009; 62 (6): 461-465

# *PRIMARY RENAL LYMPHOMA: REPORT OF THREE NEW CASES AND LITERATURE REVIEW*

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**Summary.-** *OBJECTIVES: We report the cases of three patients with primary renal lymphoma. Diagnosis and subsequent treatment are discussed.*

*METHODS: The literature on the origin, epidemiology, clinical presentation, diagnosis, treatment and prognosis of primary renal lymphoma was reviewed.*

*RESULTS: The first patient was diagnosed after radical nephrectomy and subsequently was given six cycles of CVP (cyclophosphamide, vincristine, prednisone). The diagnosis of the second patient was established by renal biopsy, and the patient received six cycles of CHOP (cyclophosphamide, adriamycin, vincristine and prednisone). The last patient had a lymphoma, secondary to immunosuppression, in a transplanted kidney. In this case transplant nephrectomy sufficed to cure the patient's lymphoma. All patients had B-cell non-Hodgkin lymphoma (an extrarenal origin was ruled out by bone marrow biopsy), and were disease-free 15 months, 7 months, and 6.5 years after diagnosis, respectively.*

*CONCLUSIONS: Primary renal lymphoma is rare. Diagnosis is established by renal biopsy, although it often presents as a mass simulating renal cell cancer and diagnosis is obtained after radical nephrectomy. Treatment consists of chemotherapy (CHOP) associated with rituximab.*

**Keywords:** *Renal neoplasia. Lymphoma. Chemotherapy.*

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Accepted for publication: May 30th, 2008.

**Resumen.-** *OBJETIVOS: Se presentan tres casos clínicos de pacientes con linfoma renal primario, su diagnóstico y posterior tratamiento.*

*MÉTODOS: Se realiza una revisión bibliográfica del origen, epidemiología, características clínicas, diagnóstico, tratamiento y pronóstico de esta enfermedad.*

*RESULTADOS: En nuestro primer caso la paciente es diagnosticada tras una nefrectomía radical y tratada posteriormente con seis ciclos de CVP (ciclofosfamida, vincristina, prednisona). En el segundo paciente el diagnóstico se llevó a cabo mediante biopsia renal, administrándose seis ciclos de CHOP (ciclofosfamida, adriamicina, vincristina y prednisona). El último caso se trata de un linfoma secundario a la inmunosupresión en*

*un riñón trasplantado en la que la realización de una trasplantectomía fue suficiente. Todos los casos fueron linfomas no-Hodgkin de células B descartándose el origen extrarrenal con biopsia de médula ósea, estando libres de enfermedad tras 15, 7 meses y 6.5 años del diagnóstico respectivamente.*

*CONCLUSIONES: El linfoma renal primario es muy raro. El diagnóstico se realiza mediante biopsia renal aunque con frecuencia se presenta como una masa simulando un cáncer renal y es diagnosticado tras nefrectomía radical. El tratamiento consiste en quimioterapia (CHOP) asociada a rituximab.*

**Palabras clave:** *Neoplasia renal. Linfoma. Quimioterapia.*

## INTRODUCTION

Lymphomas are malignant tumors characterized by the proliferation of lymphoid tissue cells. Lymphomatous involvement of the genitourinary organs occurs in 3% of the cases, most frequently in the testicles. Primary renal lymphoma is exceptional. Most cases of renal lymphoma are due to a secondary invasion and post mortem studies reveal that approximately 50% of the patients who die of non-Hodgkin lymphoma have renal involvement. Primary renal lymphoma occurs in less than 1% of renal lesions (1). In the Okuno series of 176 cases of renal lymphoma, only 5 were primary (2).

## CLINICAL CASES

### *Clinical Case 1*

A 77-year-old woman with a history of high blood pressure and ischemic heart disease (effort angina) consulted for anorexia, astenia, and malaise of two months duration. Creatinine was 1.61 and urea 64 in blood tests. Ultrasonography revealed a solid mass that deformed the left renal contour; an enlarged left renal vein and a conglomerate of enlarged lymph nodes. MRI demonstrated a solid multilobulated mass measuring 9.6 x 8.1 x 8.8 cm that occupied the lower two thirds of the kidney and invaded the renal vein, as well as multiple left para-aortic retroperitoneal lymph nodes but no vena cava involvement.

Suspecting a renal adenocarcinoma, left radical nephrectomy was performed. Histopathological study demonstrated diffuse large B-cell lymphoma (CD 20+, BCL 2+, CD 10+/-, BCL 6-, CD30-, p53-, high Ki-67 proliferation index: 90%) (Figures 1 to 3) with areas of necrosis, extensive infiltration of the renal parenchyma, and spread into the perirenal fat and perihilar lymph nodes. Bone marrow biopsy of the iliac crest confirmed the absence of neoplastic infiltration. Scattered micronodules consistent with metastasis were present in the parenchyma of both lungs on CT scan. The patient tolerated six cycles of CVP well and had an excellent response. Follow-up PET and CT scans 15 months after diagnosis were clean. The patient is presently receiving adjuvant treatment with rituximab.

### *Clinical Case 2*

A 46-year-old male with no relevant past history presented weight loss, evening fever and upper abdominal pain of six months duration. CT scan (Figure 4) revealed an 11-cm tumor with irregular margins in the right kidney with areas of low uptake suggestive of necrosis and retrocaval lymph node enlargement. Percutaneous biopsy of the renal mass yielded a diagnosis of diffuse large B-cell lymphoma (CD 45+, CD 20+, BCL +, BCL 6+/-, CD 10-, ALK-, CD 30-, p53+ in 30% of cells, Ki-67 proliferation index: 75-80%). In view of these findings, the tumor extension was studied. Thoracic CT and bone marrow biopsy showed no abnormalities, but PET revealed multiple hypermetabolic foci compatible with tumor activity in the stomach, spleen, both adrenal glands, liver, retroperitoneal lymph nodes, right testicle, and penile base. Treatment with CHOP and rituximab was well tolerated. After six cycles, follow-up PET and CT images demonstrated complete disappearance of the hypermetabolic foci 7 months after diagnosis.

### *Clinical Case 3*

A 47-year-old man with a history of high blood pressure, hepatitis C virus positivity, colostomy since childhood for imperforate anus, left renal agenesis, chronic renal failure due to coraliform lithiasis with chronic pyelonephritis, and hemodialysis for 17 years. He had a kidney transplantated in the right iliac fossa.

Three years after the renal transplantation the patient developed a chronic graft dysfunction. CT scan and MRI images revealed a poorly delimited heterogeneous tumor measuring 5 x 4 cm in the renal graft. After graft resection, histopathology confirmed the presence of high-grade B-cell CD 30+ lymphoma associated with Epstein-Barr virus (LMP 1+). The bone marrow biopsy was normal and the study of exten-

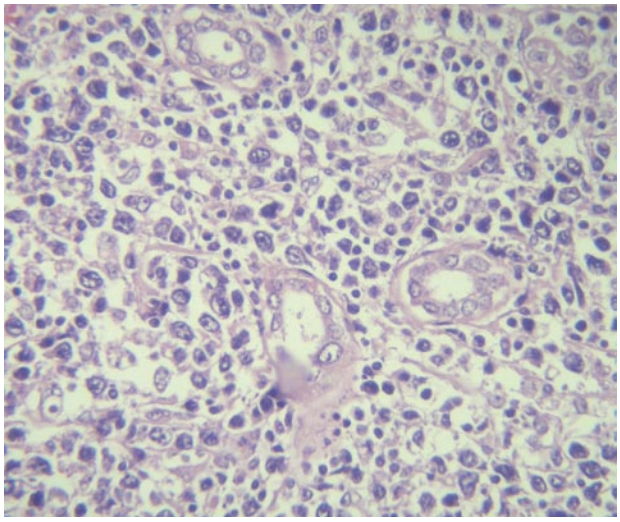

FIGURE 1.

sion was negative. As the lymphoma was Epstein-Barr virus-associated and transplant immunosuppression-related, immunosuppression was discontinued and no chemotherapy was required. Follow-up results were satisfactory 6.5 years after graft resection. Presently, the patient is on hemodialysis.

## DISCUSSION

Primary renal lymphoma is a rare and disputed condition, because the renal parenchyma does not contain lymphatic tissue. There is no agreement as to whether it is a primary disease or an initial manifestation of rapidly progressing systemic disease. Many published cases are questioned because the study of extrarenal disease is incomplete or post-mortem studies are lacking (3,4). The etiology is unknown, although primary renal lymphoma has been linked with factors like chronic inflammatory processes and chronic pyelonephritis, Sjogren's syndrome, systemic lupus erythemathosus (5) and Epstein-Barr virus (6). Several hypotheses have been postulated about the histogenesis of the neoplasm. It has been suggested that primary renal lymphoma may originate in the lymph nodes of the renal sinus or in the lymphatic network of the renal capsule, and form cords of cells that penetrate the renal parenchyma (7). Duanay postulated that pre-existing inflammatory processes lead to the recruitment of lymphoid cells by the renal parenchyma (8).

Primary renal lymphoma usually affects adults with a mean age 60 years, more often men. However, it has also been described in children (9). The tumors are frequently unilateral and rarely bilateral (10).

The clinical manifestations are similar to those of other renal tumors, pain being the most frequent symptom. Primary renal lymphoma may appear with proteinuria, nephrotic syndrome or progressive renal failure with oliguria or anuria when both kidneys are involved (3,6). Primary renal lymphoma should be considered in the presence of atypical renal masses or inexplicable renal symptoms (11-14).

It is highly aggressive, with rapid systemic dissemination.

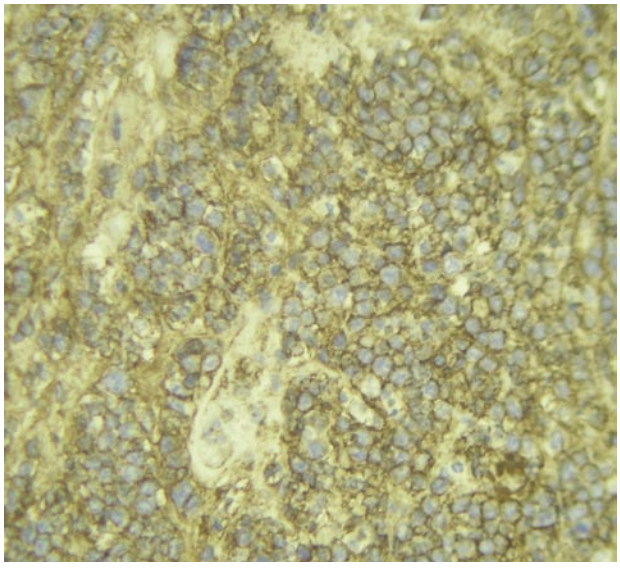

FIGURE 2.

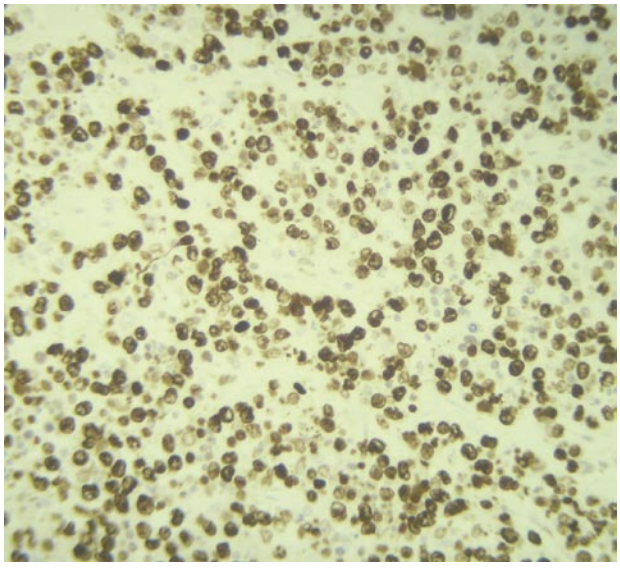

FIGURE 3.

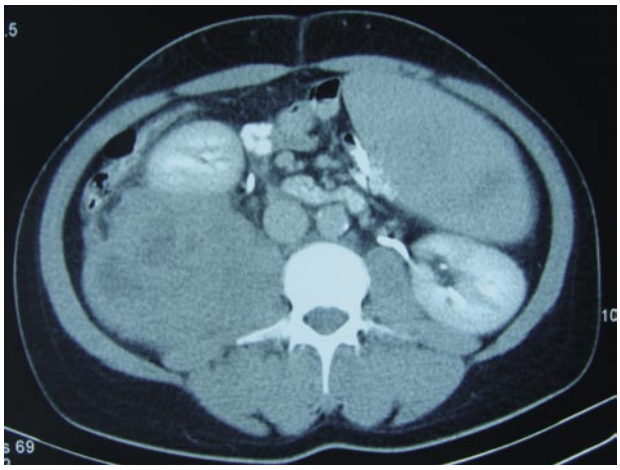

FIGURE 4.

Imaging studies can suggest the diagnosis. Ultrasonography shows homogeneous, hypoechoic masses, although the imaging study of choice in primary renal lymphoma is CT, where the typical image is hypovascular masses with minimal contrast enhancement and homogeneous attenuation, unlike the heterogeneneity of renal cell carcinoma (15). In some cases, MRI has been used to characterize complex renal masses. Histopathology is diagnostic. Fine-needle aspiration biopsy should be performed, although the diagnosis is established in most cases after studying the nephrectomy specimen, because this lymphoma often presents as a renal mass with an appearance similar to renal cell carcinoma (10). Most primary renal lymphomas are B-cell non-Hodgkin lymphomas, although other types of lymphomas have been described (4,16). Bone scintigraphy and bone marrow biopsy complete the study.

Systemic chemotherapy is the treatment of choice. For some authors, the CHOP regimen is the treatment of choice (7), as occurs in B-cell non-Hodgkin lymphoma (17-19), but no standard therapy has been established due to the low number of cases. Adriamycin should be avoided in patients with heart disease, which was why CHOP was not given to patient 1. Rituximab is a murine/human monoclonal antibody that specifically targets the membrane antigen CD20, which is expressed by more than 95% of B-cell non-Hodgkin lymphomas. It acts by restoring immune effector functions, which mediates B-cells lysis through different mechanisms, including induction of cellular apoptosis (20). Evidence supports the efficacy of the combined CHOP + rituximab regimen with respect to CHOP alone in the treatment of diffuse large B-cell lymphoma. The combined regimen increases the complete response rates and prolongs the disease-free period and survival without significantly increasing the rate of side-effects. The most frequent side-effects are leukopenia, fever, and chills (21,22). These findings suggest that adding rituximab to the combined regimen can be useful (23). In view of this background and the good results obtained in our series, we recommend CHOP + rituximab for the treatment of primary renal lymphoma. Adjuvant radiotherapy may be useful (7), but it was not used in our series. The prognosis of primary renal lymphoma is poor, with a one-year mortality rate of 75% (1), though this was not the case in our patients. The prognosis might be improved by early diagnosis and treatment with systemic chemotherapy combined with rituximab. In primary renal lymphoma due to Epstein-Barr virus infection of the renal graft, graft resection is a treatment option and the prognosis is favorable.

## CONCLUSIONS

Primary renal lymphoma is rare. Diagnosis is established by renal biopsy, although it often presents as a mass simulating renal cell cancer and is diagnosed after radical nephrectomy. Treatment consists of chemotherapy (CHOP) associated with rituximab.

## REFERENCES AND RECOMENDED READINGS (*of special interest, **of outstanding interest)

1. Barreto F, Dall`oglio MF, Srougi M. Renal lymphoma. Atypical presentation of a renal tumor. Int Braz J Urol. 2006 Mar-Apr; 32.
**2. Okuno SH, Hoyer JD, Ristow K, et al. Primary renal non-Hodgkin's lymphoma. An unusual extranodal site. Cancer. 1995 May 1; 75 (9): 2258-61.
3. Tefekli A, Baykal M, Binbay M, et al. Lymphoma of the kidney: Primary or initial manifestation of rapidly progressive systemic disease?. Int Urol Nephrol. 2006; 38 (3-4): 775-8.
4. Venizelos ID, Rombis V, Tulupidis S, et al. Primary anaplastic large cell lymphoma of the kidney. Leuk. Lymphoma. 2003 Feb; 44 (2): 353-5.
5. Brouland JP, Meeus F, Rossert J, et al. Primary bilateral B-cell renal lymphoma: A case report and review of the Literature. Am J Kidney Dis, 1994; 24:586-589.
6. Stallone G, Infante B, Manno C, et al. Primary renal lymphoma does exist: Case report and review of the literature. J Nephrol, 2000; 13:367-372.
*7. Torrecilla Garcia-Ripoll JR, Pascual Samaniego M, Martin Blanco S, et al. Primary renal lymphoma. Actas Urol Esp. 2003 Jul-Aug; 27 (7): 555-8.

8. Duanay PN. Linfosarcoma y linfosarcomatosis de los riñones: part II. Rev Med Trop Parasitol Bacterial Clin Lab, 1940; 6: 213.
9. Porcaro AB, Dámico A, Novella G, et al. Primary lymphoma of the kidney. Report of a case and update of the literature. Arch Ital Urol Androl. 2002 Mar; 74 (1): 44-7.
*10. Ahmad AH, Maclennan GT, Listinsky C. Primary renal lymphoma: a rare neoplasm that may present as a primary renal mass. J Urol. 2005 Jan; 173 (1): 239.
*11. Sebastian Montal L, Batalla Cadira JL, Delas Amat J. Primary renal lymphoma. Apropos of a case. Arch Esp Urol. 1998 Mar; 51(2): 180-2.
12. Gellrich J, Hakenberg OW, Naumann R, et al. Primary renal non-Hodgkin's lymphoma - a difficult differential diagnosis. Onkologie. 2002 Jun; 25 (3): 273-7.
13. Choi JH, Choi GB, Shim KN, et al. Bilateral primary renal non-Hodgkin's lymphoma presenting with acute renal failure: successful treatment with systemic chemotherapy. Acta Haematol. 1997; 97(4): 231-5.
14. Zahner J, Gerharz CD, Bach D, et al. Association of primary renal non-Hodgkin's lymphoma with mesangioproliferative glomerulonephritis. Am J Hematol. 1996 Oct; 53(2): 126-32.
**15. Urban Bruce A, Fishman Elliot K. Renal lymphoma: CT patterns with emphasis on helical CT". RadioGraphics 2000; 20:197-212.
16. Sharma SK, Hemal AK, Goswami AK, et al. Primary renal Hodgkin's lymphoma: case report. Urol. Int. 1989; 44 (5): 313-5.
17. Hallack Neto AE, Pereira J, Beitler, E, et al. Results of CHOP chemotherapy for diffuse large B-cell lymphoma. Braz J Med Biol Res. 2006 Oct; 39(10): 1315-22.
18. Khaled HM, Zekri ZK, Mokhtar N, et al. A randomized EPOCH vs. CHOP front-line therapy for aggressive non-Hodgkin's lymphoma patients: long-term results. Ann Oncol. 1999 Dec; 10(12): 1489-92.
19. Tirelli U, Errante D, Van Glabbeke M, et al. CHOP is the standard regimen in patients > or = 70 years of age with intermediate-grade and high grade non Hodgkin's lymphoma: results of a randomized study of the European Organization of Research and Treatment of Cancer Lymphoma Cooperative Study Group. J Clin Oncol. 1998 Jan; 16(1): 27-34.
*20. Tokar M, Rogachev B, Levi I, et al. Rituximab in a patient with acute renal failure due to B-cell lymphomatous infiltration of the kidneys. Leuk Lymphoma. 2004 Apr; 45(4):819-20.
21. Lin TY, Zhang HY, Huang H, et al. Comparison between R-CHOP regimen and CHOP regimen in treating naive diffuse large B-cell lymphoma in China: a multi-center randomized trail. Zheng. 2005 Dec; 24(12):1421-6.
22. Coiffier B, Lepage E, Briere J, et al. CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large B-cell lymphoma. N Engl J Med. 2002 Jan 24; 346(4): 235-42.
**23. Diskin CJ, Stokes TJ, Dansby LM, et al. Acute renal failure due to a primary renal B-cell lymphoma. Am J Kidney Dis 2007 Nov; 50(5):885-9.