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Case Report

# Bilateral renal cell lymphoma: Case report and review of literature

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ABSTRACT

Primary renal cell lymphoma is a rare type of non-Hodgkin's lymphoma, with B-cell lymphoma being the most common subtype. Imaging and preoperative biopsy are fruitful ways to diagnose renal cell lymphoma. We report a rare case of primary renal cell lymphoma with bilateral renal involvement in a 52-year-old woman based on imaging findings, histopathology, and immunohistochemical markers. The patient is being treated with Rituximab, cyclophosphamide, adriamycin, vincristine, prednisolone, and intrathecal methotrexate. Furthermore, the present study also reviewed 22 cases of bilateral PRL that have been reported in this century to date. With this case report, we focus the spotlight on the fact that, though rare, the diagnosis of primary renal cell lymphoma still needs to be in the differential diagnosis of renal masses.



## 1. Introduction

Non-Hodgkin's lymphoma is the most common hematological malignancy worldwide constituting approximately 3% of cancer diagnoses and death.[1] In lymphomas, extranodal involvement is commonly seen in 25 – 40% of cases. The most frequent sites of extranodal lymphoma are the gastrointestinal system, waldeyer's ring, lung, liver, and bone. Among the genitourinary system, kidneys are a common site of predilection for non-Hodgkin's lymphoma.[2]

Renal cell lymphoma is categorized as primary renal lymphoma (PRL) and secondary renal lymphoma depending on the presence or absence of widespread nodal or extranodal lymphoma in the presence of renal involvement. PRL, a rare entity, is described as lymphoma primarily involving the kidneys alone without any lymphatic involvement outside the kidneys.[3] Conversely, secondary renal lymphoma is the presence of widespread nodal or extranodal lymphoma in addition to renal involvement.

The exact cause of renal lymphoma is still unknown. Various case reports have raised queries regarding its origin since kidney is an extranodal organ, lacking lymphoid tissue.[3,4] PRL commonly presents as flank or abdominal pain, fever, weight loss, night sweats, hematuria, palpable abdominal mass, or acute renal failure[3]. The symptoms of PRL may imitate renal cell carcinoma. Typical imaging findings suggestive of PRL includes hypoechoic masses usually multiple, enlarged kidneys bilaterally, soft-tissue masses involving the sinus or hilum, and direct renal involvement from the retroperitoneal tumors.[5] It is of utmost importance to make an accurate diagnosis

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because PRL is best managed with the R-CHOP regimen (Rituximab, cyclophosphamide, adriamycin, vincristine, and prednisolone) while renal cell carcinoma is best managed by upfront surgery and systemic therapy.[6] Renal biopsy is the gold standard to differentiate between PRL and renal cell carcinoma.

This case represents a rare entity with under 100 cases reported to date. This case report is aimed at describing PRL occurring bilaterally with emphasis on the fact that clinicians should be vigilant while evaluating renal masses to make an accurate diagnosis and to ensure appropriate management of these cases.

A search of the terms "Bilateral renal lymphoma", "primary bilateral renal lymphoma" was conducted using PubMed. Only English literature published from 2000 to 2022 was included. Data on gender, age, tumor pathology, clinical presentation, type of treatment, and follow-up time were compiled from the original case reports published (Table 1).

## 2. Case Description

A 52 years old female patient presented with chief complaints of gross, painless hematuria and left flank pain for 2 months. The pain was moderate in intensity, non-radiating without any relieving or aggravating factors. The patient was taking over-the-counter analgesic medications without much relief. There was a history of low-grade fever with night sweats, and weight loss (lost 4 kg in 2 months). Clinical examination revealed a mass palpable in the left upper quadrant of the abdomen with no palpable lymph nodes. She underwent ultrasonography of the abdomen that indicated hypoechoic area with heterogenous echotexture noted at the right inferior pole of kidney measuring 55.3 x 44.7 mm? mass. Left kidney showed poorly marginated hypoechoic area near its superior pole measuring 34.1 x 37.4 mm with hypoechoic altered texture ?focal nephritis. She was advised contrast-enhanced computed tomography of abdomen to establish the nature of the mass. This revealed hypo-enhancing masses of approximate size 47 x 59 x 38 mm and 23 x 26 x 20 mm in the lower and mid-poles of the right kidney respectively. Left kidney was noticed to be enlarged and hypodense as compared to right kidney. Another hypo-enhancing mass lesion was seen in the upper pole of left kidney measuring 46 x 49 x 27 mm. The hematological investigations results showed following values: hemoglobin level of 8.7 gm/dl, total leucocyte count of 36,800 / cumm, and platelet count of 2.48 lakh/cumm. Differential count reported was neutrophils 45.4%, lymphocytes 46.8%, monocytes 7%, eosinophil 0.2% and basophils 3%. Renal function tests were within normal range.

In the present case, whole body fluorine-18-fluorodeoxyglucose positron emission tomography with computed tomographyFigure 1 (FDG-PET/CT) scan demonstrated FDG-avid large, well-defined heterogeneously enhancing hypodense mass lesion arising from the upper and mid-pole of the left kidney, measuring approximately 3.2 x 4.8 x 4.5 cm in size (SUV=15.39 gm/ml), another hypodense lesion arising from the lower pole of the right kidney, measuring approximately 4.1 x 5.3 x 4.1 cm in size (SUV=20.85 gm/ml), and another FDG-avid heterogeneously enhancing hypodense lesion arising from the upper pole of the right kidney, measuring 2.2 x 1.8 x 2.8 cm in size (SUV=9.76 gm/ml) consistent with the features of multifocal renal lymphoma. This lesion is indenting the right inferior border of the liver and the gall bladder fossa. These hypodense lesions are seen to abut the medial surfaces of the bilateral psoas muscles. No other metabolically active lesion or lymphadenopathy is demonstrated elsewhere in the body. Plain CT scan showed multiple parenchymal renal masses. The lymphomatous masses had less enhancement than the normal renal tissue with lower attenuation than that of the surrounding cortex. Based on PET-CT findings, a diagnosis of primary renal lymphoma was made (Figure 1).

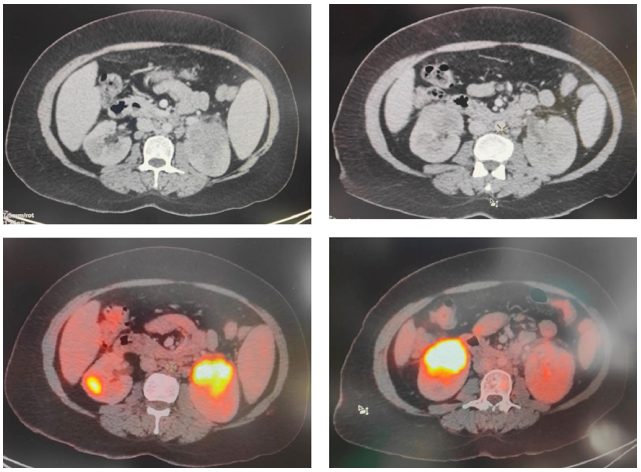

**Fig. 1:** PET-CT scan images revealing metabolically active large well-defined heterogeneously enhancing hypodense mass lesions, arising from the upper and mid pole of the left kidney and upper and lower pole of the right kidney – consistent with the features of primary renal lymphoma involving both kidneys.

CT-guided trucut biopsy from the right renal mass was subsequently performed and revealed lymphoid cells in a diffuse pattern with nuclear streaking. The possibility of renal lymphoma was considered. The tissue was subjected to immunohistochemistry which showed the tumor cells to be positive for CD20, CD10, BCL-6, and Ki-67 immunoreactive in 60 – 70% of lesional cells while CD3, CD68, CK, MUM-1, CD138, CD43, and Cyclin-D1 were non-immunoreactive. The morphological and immunohistochemical features were compatible with the diagnosis of B-cell non-Hodgkin's lymphoma, possibly Diffuse large B-cell lymphoma –

Germinal center type.Figure 2

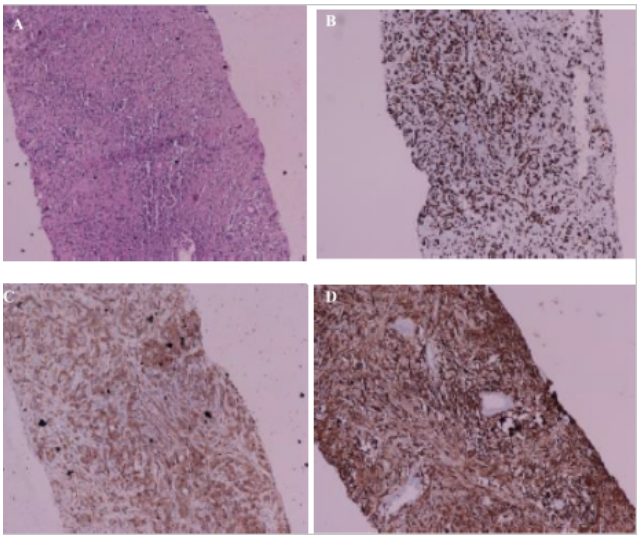


**Fig. 2:** Immunohistochemical staining showing thepositive staining of HE (**A**), CD10 (**B**), CD20 (**C**), as well as Ki-67(**D**) immunoreactive in 60-70% of lesional cells

For staging purposes, the patient was subjected to bone marrow biopsy and aspiration. Bone marrow aspiration revealed 1 – 2 NRBC / 100 WBC with raised total leucocyte count and increased lymphocytes. The bone marrow biopsy showed an increase in lymphoid cells with 5 – 6 packed marrow spaces showing 90 – 95% cellularity. There was patchy involvement of marrow by lymphoid cell collection. Erythropoiesis, myelopoiesis, and megakaryopoiesis appeared normal. In view of the absence of any nodal disease elsewhere in the body, a final diagnosis of PRL was made. The patient has been started on systemic chemotherapy with the R-CHOP regimen and intrathecal methotrexate therapy.

## 3. Discussion

To the best of our knowledge, we could identify 23 reported cases of bilateral PRL after thoroughly searching PubMed. PRL is a rare entity defined as non-Hodgkin's lymphoma arising in the renal parenchyma. PRL is responsible for 0.7% of all extranodal lymphomas and comprises <1% of all diagnoses for renal masses.[7] For the establishment of PRL where there is no lymphatic tissue, several hypotheses could be identified as that PRL might be originating from the renal capsule and infiltrating the renal parenchyma, chronic renal inflammation inducing infiltration of lymphoid cells in the kidney eventually resulting in lymphoma, or hematogenous spread involving the kidneys[8] (Table 1).

PRL usually occurs in elderly males with male to female ratio of 1.6:1.[3] A population-based analysis of the Surveillance, Epidemiology and End-Result database (1973-2015) has reported the median age of PRL as 72 years, and more than three-fourths being above 62.5 years with a male predominance.[28] The literature has varied reports from pediatric age group as early as three-year-old boy to elderly 79-year-old male (range 3-79 years) and mainly affecting the male gender.[13,29] Taking into consideration the data published so far, we found that this disease when occurs bilaterally has a predilection for those younger than 50 years of age.[4,8,13]

Clinical presentation for PRL may be varied from abdominal pain, mainly in the flank region, gross hematuria, proteinuria, or nephrotic syndrome, and may result in end-stage renal failure, especially when both kidneys are involved. Renal failure is among the most common complications of PRL. Silverman et al.[29] have described the case of an asymptomatic patient who presented with acute kidney injury and was found to have B-cell lymphoma of follicular center cell origin. However, our patient inspite of having bilateral renal masses had normal renal function with no signs of nodal or extranodal involvement. The possible explanation for PRL with bilateral renal involvement is assumed to be spread via hematogenous dissemination. Various studies have reported that patients with bilateral renal involvement have poorer survival (mean, 21 months) as compared to unilateral renal involvement (mean, 68 months).[3,7] The criteria for diagnosing PRL include 1. Multiple renal masses without any obstructive features. 2. No evidence of lymphomatous involvement outside the kidneys either in other organs or lymph nodes. 3. Diagnosed on renal biopsy.[30]

Since PRL is a rare disease and there is a dearth of literature regarding its existence and etiology, it is often neglected in the differential diagnosis of renal masses such as renal cell carcinoma, metastasis, or renal cysts. Kidney biopsy is the only way to unveil the correct diagnosis of PRL. In addition, biopsy helps to differentiate it from the more common diagnosis of renal cell carcinoma. Although, imaging findings do give a clue to the diagnosis of PRL as in this case PET-CT scan was suggestive of multifocal PRL. However, PRL has a tendency to mimic renal cell carcinoma.[31] FDG-PET/CT scan is the main imaging modality employed for the establishment of the correct diagnosis. The standardized uptake value of PRL (SUVmean, 6.37±2.28) is reported to be higher than renal cell carcinoma ($SUV_{mean}$, 2.58±0.62). Chen et al.[3] recommended that PET/CT scan indicates the diagnosis of PRL even prior to biopsy results. Similar to this, we were directed to the PRL diagnosis based on PET/CT scan findings.

Diffuse large B-cell lymphoma is the most common histology reported in PRL. Other histologies reported are follicular lymphoma, mucosa-associated lymphoid tissue, mantle B-cell NHL, and Burkitt's lymphoma among others.[28,32] There has been an earlier report by Cupisti A et al,[12] where bilateral PRL with left kidney showing

**Table 1:** List of bilateral PRLs reported in the literature in the $21^{st}$ century

| Author (year) | Age (yrs) | Sex | Tumor pathology | Presentation | Treatment | Follow up (mths) |
|---|---|---|---|---|---|---|
| Al-Mokhtar N et al[9] (2001) | 46 | F | PRL | Vomiting, abdominal pain | Chemotherapy | 36 |
| Levendoglu-Tugal et al[10] (2002) | 15 | M | PRL | Hypercalcaemia, acute renal failure | - | - |
| O'Sullivan AW et al[11] (2003) | 57 | F | PRL | Left flank pain, fever | Chemotherapy | - |
| Cupisti A et al[12] (2004) | 46 | M | DLBCL | Chronic renal failure | Surgery followed by chemotherapy | 67 |
| Jindal B et al[13] (2009) | 3 | M | PRL B-cell type | Abdominal distension, pain | Chemotherapy | - |
| Dash S et al[8] (2011) | 7 | F | MALToma | Abdominal pain, headache | Chemotherapy | - |
| Akici FF et al[14] (2014) | 14 | M | B-cell lymphoblastic lymphoma | Acute renal failure | Chemotherapy | 60 |
| Dhull VS et al[15] (2015) | 8 | - | B-cell NHL | B/L renal masses | Chemotherapy | - |
| Aggarwal S et al[16] (2015) | 4 | M | B-cell NHL | Abdominal pain, fever | Chemotherapy | - |
| Mitome T et al[17] (2016) | 64 | M | DLBCL | Gross hematuria, hypertension, acute renal failure | Chemotherapy | - |
| Chen X et al[3] (2016) | 70 | F | DLBCL | USG detected mass in right kidney | Chemotherapy | 2 |
| Erdogmus S et al[18] (2016) | 19 | M | DLBCL | Hematuria, acute kidney injury | Chemotherapy | - |
| Butani L et al[4](2017) | 12 | M | PRL | Progressive worsening fatigue | Chemotherapy | - |
| Kara PO et al[19] (2017) | 27 | F | DLBCL | Mediastinal mass | - | - |
| Thakur K et al[20] (2020) | 3 | F | NHL | Fever, pedal edema | - | - |
| Arriola ML et al[21] (2020) | 18 | M | NHL | Polydipsia, polyuria | - | - |
| Bruce G et al[22](2020) | 12 | M | PRL | Headache, fatigue, hypertension | Chemotherapy | - |
| Bokhari SRA et al[23] (2020) | 21 | M | B-cell lymphoblastic NHL | Left shoulder pain, fever, weight loss | Chemotherapy | - |
| Wei L et al[24] (2020) | 13 | M | T-lymphoblastic lymphoma | Renal enlargement, acute nephritis | Chemotherapy | - |
| Benameur Y et al[25] (2021) | 17 | F | DLBCL | Diplopia, nasal obstruction, fever | Chemotherapy | - |
| Ninh et al[26] (2021) | 4 | M | Burkitt's lymphoma | Abdominal pain, anorexia, vomiting | Chemotherapy | - |
| Rossini B et al[27] (2021) | 44 | F | DLBCL, NOS | Flank pain | Chemotherapy | - |

only microscopic involvement limited to the upper pole was managed successfully by conservative surgical resection followed by systemic therapy. This patient had 67-month survival, which was beyond mentioned in the literature.[12] Over time, systemic therapy has taken its place as the most common form of treatment for PRL. This treatment consists of 6-8 cycles of R-CHOP resulting in reported 5-year survival of only 40-50%.[33]

Rituximab is a monoclonal anti-CD20 antibody found on the surface of normal and malignant B lymphocytes. It has a distinct mechanism of action that includes cell cycle arrest, apoptosis induction, complement-mediated cytotoxicity, antibody-dependent cellular cytotoxicity, and sensitization toward chemotherapeutic drugs.[34] The patient under discussion is being treated with R-CHOP regimen with intrathecal methotrexate. Shimada et al. have reported higher 2-year survival rates for patients being treated with chemotherapy and rituximab versus patients receiving only chemotherapy (OS 66% vs. 46%).[35] The use of central nervous system prophylaxis is recommended in PRL, specifically in cases of high-risk central nervous system international prognostic index. However, the optimal route of its administration whether systemic vs. intrathecal still remains unclear.[31]

## 4. Conclusion

The patient in the present study presented with bilateral renal masses. The imaging findings were suggestive of PRL which was confirmed with renal biopsy. Modern imaging techniques and biopsies play an important role in the confirmation of diagnoses. The main learning point is although it could be rare, we should have a high index of suspicion of PRL when evaluating renal masses for establishing an accurate diagnosis and guiding further management.

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## 6. Conflicts of interest

There are no conflicts of interest.

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