



Bilateral Renal Infiltration by Burkitt Lymphoma: Case Report

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Abstract

Non-Hodgkin lymphomas represent the third leading cause of cancer in the pediatric age group. Primary renal lymphoma is an uncommon presentation. We describe the diagnosis and treatment of a 6-year-old boy who presented with bilateral renal involvement, abdominal pain, vomiting, and weight loss. Initial investigations were consistent with presumed non-oliguric end-stage renal disease and anemia. Subsequent imaging demonstrated enlarged kidneys bilaterally. Histology revealed a Burkitt lymphoma that was highly responsive to chemotherapy, including the anti-CD20 monoclonal agent rituximab. Specific treatment was introduced with corticosteroids, vincristine, cyclophosphamide, and rituximab, resulting in the resolution of acute renal failure within 72 hours and complete response at the second induction with ANHL 1131 protocol.

Keywords

Non-Hodgkin Lymphomas, Burkitt Lymphoma, Primary Renal Lymphoma, Anti-CD20 Monoclonal Agent, Rituximab

Introduction

Lymphomas are a diverse group of malignant neoplasms that originate in lymphoid tissues. Based on their histology, cytogenetics, and immunophenotype, they are divided into Hodgkin's lymphomas (HL) and non-Hodgkin's lymphomas (NHL), which have distinct clinical, pathological, demographic, and epidemiological characteristics. In childhood, Non-Hodgkin's lymphomas account for 6% of all malignant neoplasms [1]. These lymphomas differ from adult NHLs due to their predominant extranodal involvement, high-grade nature, different staging system, and favorable response to treatment with intensive chemotherapy regimens.

Primary renal lymphomas are rare entities that

constitute 0.7% of extranodal lymphomas [2]. Although first described by Gibson in 1948 [3], the first confirmed case was reported by Coggins in 1980 [4]. They are considered NHLs that occur exclusively in the kidney without causing obstruction, and they lead to acute renal failure that resolves with the initiation of chemotherapy. Primary renal lymphomas can be mistaken for other childhood malignant diseases, particularly Wilms tumor, renal cell carcinoma, and neuroblastoma [5]. The etiology of this entity is not well determined, but there are theories that suggest its origin is in the renal capsule with parenchymal infiltration or renal infiltration with lymphoid cells in response to chronic inflammation [6,7].

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The diagnostic criteria for primary renal lymphoma include the presence of a unilateral or bilateral renal mass without infiltration of other organs or lymph nodes, histological confirmation, no renal disease attributable to another cause, and improvement of renal function after treatment [8,9].

Case Presentation

A 6-year-old boy presented to the emergency department with complaints of a diffuse lump in the left flank, which was incidentally noticed by his mother, as well as abdominal pain, sporadic nausea with vomiting, anorexia, weight loss, and night fever. There was no family history of renal disease or other physical illness.

Clinical Examination Findings:

Upon examination, a pale and slim boy with edema

in both hands and the lower third of both lower extremities was observed. An abdominal tumor was palpated at the level of the left hypochondrium, with no ill-defined border, which exceeded the abdominal midline.

Evaluation of Laboratory Tests:

Initial investigations revealed moderate anaemia with a normal leukogram and thrombocytosis, elevated creatinine at 130mg/dl, and LDH at 1024 U/L. Hepatitis B surface antigen and anti-hepatitis C were negative.

Imaging Evaluation:

Abdominal ultrasound revealed a right kidney with an isoechogenic image in the upper pole and irregular borders, measuring 39 x 24 mm. The left kidney showed an isoechogenic image in the upper and lower

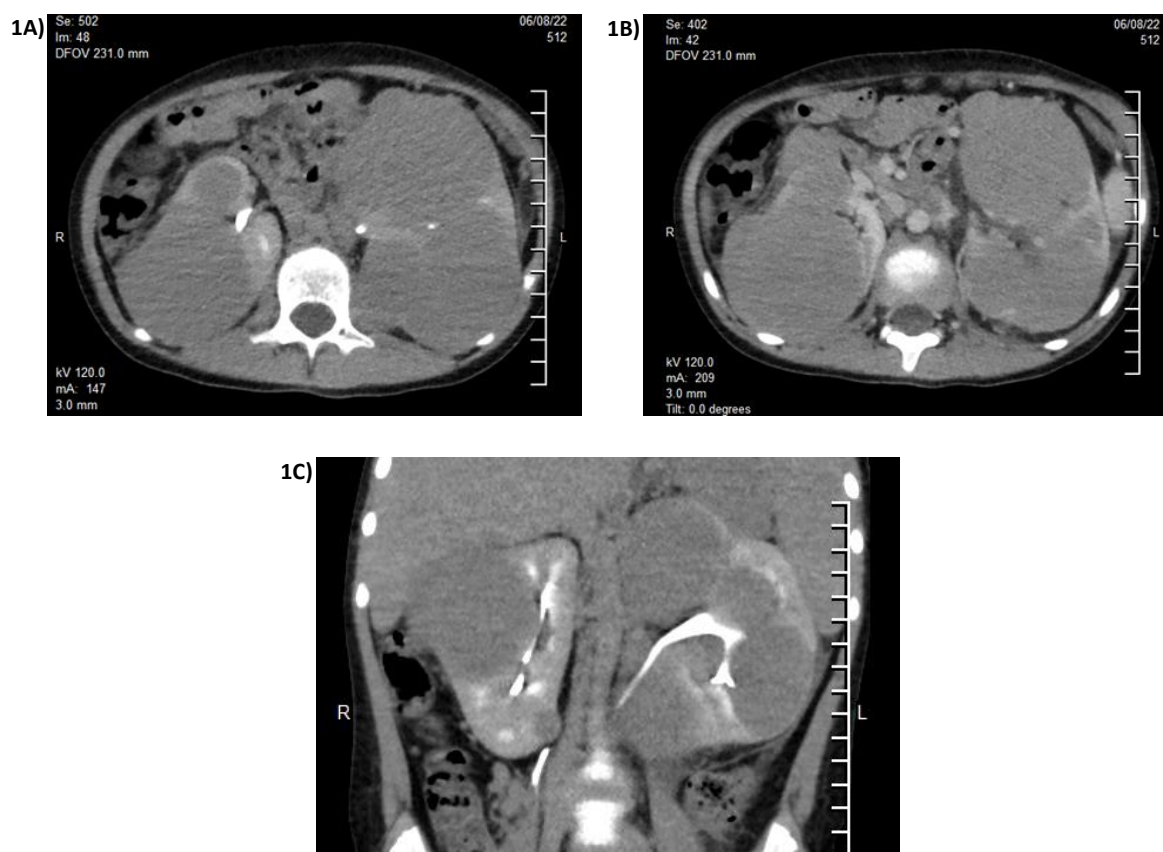


Fig-1:

Computed axial tomography with intravenous contrast, axial sections and MPR reconstructions, showing, A) presence of multiple images in the form of mass, hypodense, bilateral, with little contrast enhancement with respect to the renal parenchyma, growing towards the pararenal spaces and contacting the peritoneal line bilaterally. B) In the renal excretory phase, compression, displacement and deformity of the excretory system are observed without destruction of these and with adequate excretion of the contrast. C) Coronal MPR reconstruction showing compression and displacement of the caliceal groups and pelvis.

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pole of nodular aspect occupying most of the organ and measuring 104 x 57 mm with peripheral and central vascularization. Both renal images had a nodular aspect. CT of the skull, neck, thorax, abdomen, and pelvis with contrast showed both kidneys with multiple nodular images with poor contrast enhancement. The largest image in the left kidney was 56 mm and contacted the peritoneal line, and no retroperitoneal adenopathies were detected (**Fig-1A**, **Fig-1B**, and **Fig-1C**).

A biopsy was performed, which reported Non-Hodgkin's lymphoma with an IHC panel of CD20+, CD19+, CD22+, BCL2-, and BCL6+. The Ki-67 was 98%. Bone marrow biopsy and cerebrospinal fluid cytology were negative. The diagnosis was Burkitt non-Hodgkin lymphoma (B-NHL) with bilateral renal involvement, showing elements of a primary renal lymphoma, a rare entity with very few cases reported in the literature. The patient was diagnosed as B-NHL Stage III A, Group B of high risk and started on chemotherapy with the ANHL 1131 protocol.

Treatment:

In view of the significant lymphoma burden, tumour lysis syndrome was considered a real risk, particularly in the context of severe renal dysfunction. Therefore, prophylactic hydration plus oral Allopurinol was commenced shortly before the administration of the first dose of chemotherapy. A reduction of more than 20% of lesions in both kidneys was achieved with a dose of the pre-phase of cyclophosphamide, vincristine, and prednisone (COP) associated with intrathecal chemotherapy with methotrexate and



Fig-2:

Computed axial tomography with intravenous contrast showing hypodense areas, unchanged by contrast administration, in both kidneys, with good definition of the renal sinus, no infiltration of the perirenal fat.

hydrocortisone, with normalization of creatinine and LDH levels (**Fig-2**). At the end of the 2nd induction cycle with R-COPADM3 (rituximab, cyclophosphamide, prednisone, adriamycin, methotrexate plus intrathecal therapy), he was in complete remission. He continued with consolidation treatment with R-CYM (rituximab, cytarabine, and methotrexate) according to protocol. The final evaluation showed complete remission of his disease.

Discussion

Burkitt's NHLs constitute 40% of pediatric NHLs, and their extranodal location is mainly common at the abdominal level [10,11]. This is an unusual case, with a mostly renal presentation that was initially approached as a bilateral Wilms tumor, but the biopsy showed it to be a Burkitt's NHL.

The most common causes of benign enlargement of the kidneys are hydronephrosis, polycystic kidney disease, mesoblastic nephroma, multilocular cystic nephroma, multicystic dysplastic kidneys, renal abscess, mesoblastic nephroma, and medullary cystic disease complex. The common malignant kidney tumors are Wilms tumor, clear cell sarcoma, rhabdoid tumor, renal cell carcinoma, and neuroblastoma.

A primary renal lymphoma is an NHL that originates directly in the renal parenchyma without systemic extension. In this case, it was not considered as such because it did not meet one of the main criteria proposed by authors such as Malbrain [6] and Stallone [12], as extrarenal disease was found.

The Malbrain criteria are:

- Histologic confirmation
- Renal volume increase without obstruction
- No presence of nodal or extranodal lymphoma
- Renal involvement not attributable to another cause
- Improvement of renal function after treatment

The Stallone criteria are:

- Lymphomatous renal inflammation
- Increase of renal volume without obstruction
- Non-presence of extrarenal lymphoma

The presentation of primary renal lymphomas is generally unilateral, although a population analysis in the USA shows that in children under 18 years of age, the proportion of bilateral involvement is higher than in adults [13] (39.1% vs. 6.9%, $p < 0.001$) with greater tumor volume in the left kidney, which is similar to what was observed in this patient. Additionally, this study shows that the majority are NHL (93.2%) and the predominant histological subtype was diffuse large B-cell non-Hodgkin's lymphoma (56.3%), followed by follicular lymphomas (9.0%) and marginal zone lymphoma (7.8%); Burkitt's NHL only 1.5%. The age-adjusted incidence was 0.053x100000 persons with a predominance of males (0.078x100000 inhabitants), who compared to females had higher mortality (0.059x 10000 in males vs. 0.020 x 10000 in female patients).

It was observed that the overall survival of patients reported with this entity improved since 2000, which is due, in some measure, to the introduction of immunotherapy with Rituximab associated with chemotherapy [8,14,15].

This case exhibits elements that are similar to primary renal lymphomas, such as (a) bilateral renal location with a high tumor burden, (b) incipient renal function involvement with a decreased glomerular filtration rate, and edema in upper and lower limbs with preserved diuresis, but it differs in that there was an extension of the disease at the maxillary level.

The first-line treatment schemes in Burkitt's lymphoma depend on the risk stratification proposed by the French Society of Pediatric Oncology and the BFM (Berlin-FranKfurt-Münster), using the staging system according to Murphy's criteria (known as St. Jude criteria). In stage I and II, the suggestion to use the treatment of the POG 9219 [16] protocol or the FAB/LMB 96 [17] group A regimen is maintained. In the case of stages III and IV, the protocol of choice would be COG ANHL1131 (based on FAB/LMB96) regimen B and C [18]. This treatment protocol is considered with a level of evidence 1, due to a significant improvement in progression-free survival at 3 years (93% vs. 83%, HR: 0.40) compared to the chemotherapy scheme of the LMB 96 protocol and better overall survival at 3 years

(95% vs. 87%, HR: 0.36).

Among the unfavorable prognostic factors, LDH elevation is mentioned in many investigations. In this patient, it was elevated, but the prognosis was favorable. Intensive treatment with the combination of cyclophosphamide, vincristine, prednisone, adriamycin, methotrexate, cytarabine, etoposide, and rituximab was used with an excellent response.

Conclusions

Pediatric Burkitt's NHL is characterized by predominant extranodal involvement. A rare case is shown with bilateral renal involvement and a good response to treatment using chemotherapy based on the ANHL 1131 protocol, which includes the use of immunotherapy with Rituximab.

Consent to publish the case report was not obtained. However, this report does not contain any personal information that could lead to the identification of the patient.

Conflict of Interest

The authors have read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

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