Do not Forget Burkitt's Lymphoma! Unusual Case of Primary Malignant Lymphoma of the Prostate in a Young Patient

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Primary Burkitt's lymphoma (BL) of the prostate is rare in the adolescent population. The etiology remains poorly understood. There has been some proposed associations to Epstein-Barr virus and HIV. Clinical and histopathologic data of a 17-year-old patient who underwent transurethral resection of the prostate was obtained. We report the first case of primary malignant BL of the prostate in a 17-year-old Caucasian male who presented with hematuria, lower urinary tract symptoms. Differential diagnosis of a prostatic mass in adolescent patients must be primary or secondary lymphoma of the prostate, including BL as described for the first time in this article. UROLOGY 138: 152–155, 2020. © 2019 Elsevier Inc.

The 2017 World Health Organization classification of hematopoietic and lymphoid neoplasms, classifies Burkitt's lymphoma (BL) as a mature B-cell neoplasm.[1,2] It is a rare and highly aggressive B-cell lymphoma and the most frequent in pediatric patients.[2,3] Three epidemiologic variants are recognized. The endemic variant which has an association with Epstein-Barr virus (EBV) in 95% of cases, the immunodeficiency-associated BL, that occurs in association with human immunodeficiency virus (HIV) and the sporadic variant which is the most common in the western world and usually not associated with EBV or HIV.[2,4] Prostate lymphoma accounts for less than 1% of the surgical pathology specimens and BL for less than 0.1% of lymphomas comprising the genitourinary tract.[2,5]

CASE REPORT

Seventeen-year-old male, presented to the emergency department with a 3-day history of macroscopic hematuria, lumbar and pelvic pain, dysuria, bladder stone passage, and urinary retention 2 months prior to this consultation. Patient denied weight loss, nocturnal sweats, or fever. Past medical history was noncontributory. At physical examination vitals were normal, the abdomen was soft with no palpable masses. Digital rectal examination showed a painful diffusely enlarged prostate with obliteration of the median furrow. Routine laboratory tests were normal, including a prostate-specific antigen of 0.43 ng/mL. HIV, EBV, hepatitis B and C serologies all negative.

Contrast enhanced computerized tomography of the abdomen and pelvis showed a 49 × 63 × 68 mm, irregular, heterogenous mass arising from the prostate, protruding into the bladder's lumen, with soft tissue density and calcifications. No adenopathy was visible and there was no upper-tract filling defects present (Fig. 1). Computerized tomography of the chest, neck, and brain MRI ruled out distant metastasis.

Differential diagnosis was prostate or bladder rhabdomyosarcoma. We opted for cystourethroscopy under general anesthesia as a diagnostic test which revealed an obstructive prostate occupied by a protruding lesion extending into the bladder's lumen. The mass was arising from the left lateral lobe of the prostate. (Fig. 2). Given the ease to obtain a transurethral tissue biopsy, we carried on and sent it for pathologic analysis.

Tissue biopsy revealed prostatic tissue infiltrated with large lymphoid cells against a background of scattered macrophages with "starry-sky" pattern characteristic of Burkitt's lymphoma associated with monomorphic cells with high mitotic activity with a Ki-67 proliferation index 100%. Immunohistochemical stains showed positivity for MUM-1, CD10, CD20, BCL-6, and C-MYC >80%. CD3 and BCL-2 stains were negative confirming BL diagnosis and excluding diffuse large B-cell lymphoma (DLBCL) and B-cell lymphoma, unclassifiable. Negative CD34 and terminal deoxynucleotidyl transferase confirmed that the BL was a primary tumor of the prostate (Fig. 3).

The postoperative course was uneventful, induction therapy with dose adjusted etoposide, prednisone, vincristine,

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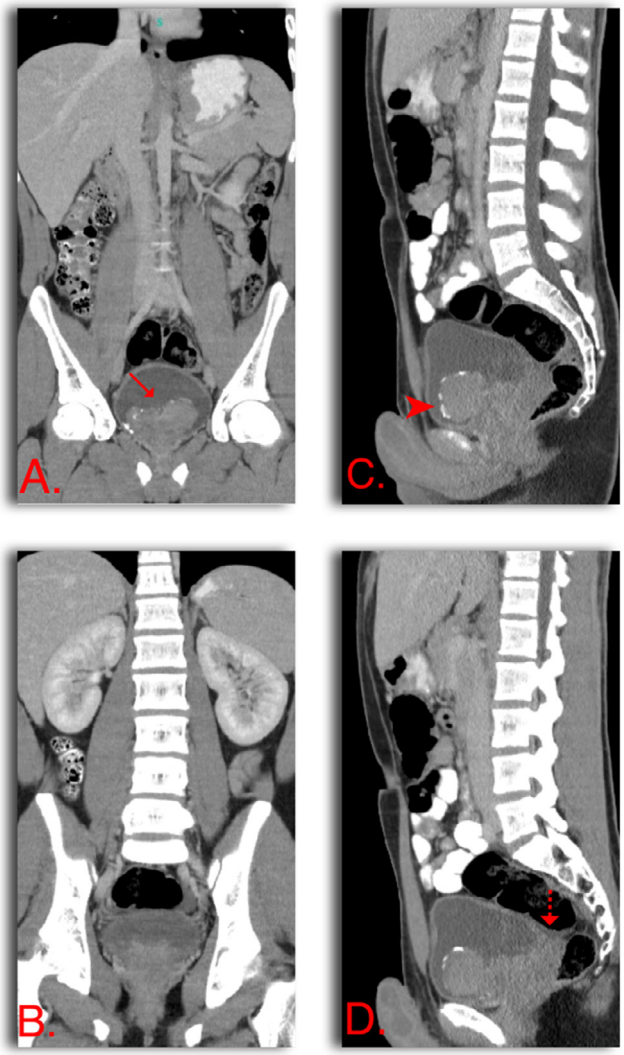

Figure 1. Contrast enhanced CT (**A**) and (**B**) coronal section showing a 49 × 63 × 68 mm, irregular, heterogenous mass arising from the prostate, protruding through the bladder lumen, with soft tissue density, lobulated (arrow.) (**C**) and (**D**) Sagittal section shows a prostatic space-occupying lesion with calcifications (arrow head) and unclear rectal boundaries (dotted arrow). (Color version available online.)

cyclophosphamide, and doxorubicin + rituximab (DA-EPOCH) regimen with intrathecal methotrexate was indicated. At 6-month follow-up the patient had completed 6 chemotherapy cycles and 4 intrathecal cycles. Follow-up images showed a partial response (90% reduction in product of perpendicular diameters) according to the Lugano Criteria for response evaluation.[6]

DISCUSSION

Prostate cancer is the second most frequently diagnosed cancer among males worldwide, being the fifth most common cause of death by cancer among males.[7,8] BL is the most frequent lymphoma in pediatric patients but still represents less than 0.1% of lymphomas compromising the urinary tract.[2,5]

Primary extranodal lymphoma of the prostate although rare, tends to occur in patients around the fifth and sixth decades of life. Most cases of lymphoma arising from the prostate are non-Hodgkin lymphoma (NHL) and the most common subtype is the DLBCL accounting for 52% of cases.[1,3,9] More unusual than primary lymphoma of the prostate is BL of the prostate, only 1 case has been previously reported in a 24 years old.[10]

Most cases have a deregulation of MYC gene, caused by a translocation (8q24). Almost all cases have a MYC mutation.[2,11] Between 40% and 70% of patients would have mutations in *TCF3* gene which encodes a protein that plays a critical role in B and T lymphopoiesis. Thirty eight percent of sporadic variants and 67% in the immunodeficiency-associated variant have mutations in *CCND3* gene which is activated by *TCF3* and encodes cyclin D3, which promotes cell cycle progression.[2,11]

NHL of the prostate is difficult to distinguish from other prostatic diseases as prostatitis, benign prostatic enlargement.[3,4,9,10] It usually manifests with lower urinary tract symptoms and in some cases hematuria. B-symptoms (weight loss, fever, and night sweats) are rare.[3,9,12]

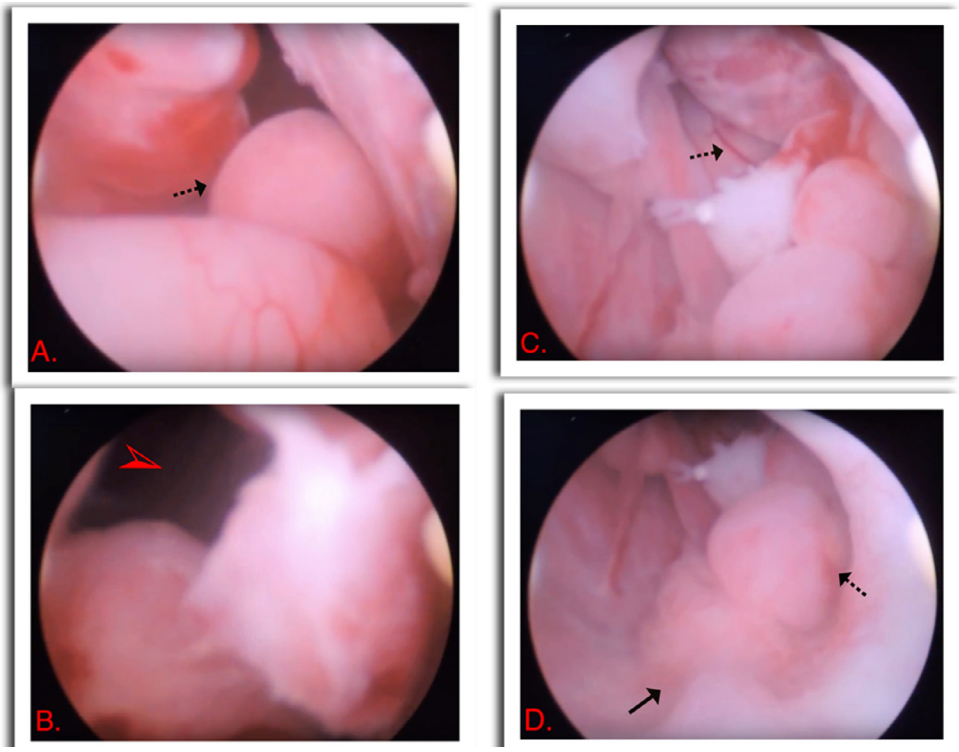

Figure 2. Cystoscopy (**A**) and (**B**) obstructive prostate occupying lesion (dotted arrow) protruding to the bladder lumen (arrow head) dependent of the left lateral lobe of the prostate. (**C**) and (**D**) Lobulated, irregular mass protruding from the left lobe of the prostate (dotted arrow), proximal to the verumontanum (arrow). (Color version available online.)

The histologic pattern of BL is defined by a monomorphic cell proliferation with a cohesive pattern and the presence of pleomorphism or prominent nucleoli and a characteristic pattern of a starry sky in the H&E stain. BL being derived from a germinal center B cell, have a immunophenotype defined by high expression of CD10, BCL6, CD20, and negativity for terminal deoxynucleotidyl transferase as well as BCL2 because the early germinal center B-cell, lacks BCL-2.[2,11] When the diagnosis of BL is made, EBV, HIV, and Hepatitis B testing must be performed.[1]

Given the rarity of BL and the paucity of clinical trials, the optimal therapeutic approach is controversial. National comprehensive Cancer Network published its last clinical practice guideline on B-cell lymphoma in July 2019 but there is not a specific approach for primary or secondary BL of the prostate.[1] The cornerstone for the management of BL is chemotherapy.[1,2,4] For treatment strategies it is recommended to classify patients with BL in low risk (Normal LDH or Stage I and completely resected abdominal lesion or single extra-abdominal mass <10 cm) or high risk (Stage I and abdominal mass or extra-abdominal mass >10 cm or Stage II-IV).[1] For low-risk patients actual recommendation is CODOX-M (cyclophoshamide, doxorubicin, vincristine cytarabine followed by high-dose systemic methotrexate) ± rituximab, a DA-EPOCH/rituximab or a HyperCVAD/rituximab (cyclophosphamide, vincristine, doxorubicin and dexamethasone alternating with high-dose methotrexate and cytarabine + rituximab) regimen.[1] All regimens include intrathecal methotrexate. cyclophosphamide, doxorubicin, vincristine, prednisone is not an adequate therapy anymore.[1]

There is scarce literature regarding lymphoid neoplasms of the prostate. The most common type of NHL of the prostate is DLBCL.[3,9,13] Tong-Fang reported 29 cases with primary lymphoma of the prostate, 52% being DLCBL, extraprostatic involvement became evident in 65% of patients and 34% died with a median overall survival of 23 months.[13] Bostwick reported 62 cases of NHL involving the prostate and Schniederjan on 8 cases.[3,9] Only 3 cases of BL of the prostate have been reported, 2 secondary and 1 primary, but none in an adolescent patient. (Table 1—electronic supplementary material).[3,4,10]

Limitations of our study are that is a single case report, given the rarity of the disease. Good initial clinical response to chemotherapy, but lacking information in terms of long-term follow-up, prognosis, and cancer-specific survival data.

CONCLUSION

Primary BL of the prostate is a rare and highly aggressive disease. Differential diagnosis in pediatric or young adult patients with lower urinary tract symptoms, hematuria, urinary retention, should raise suspicion about a lymphoid tumor of the prostate, there is still lacking of information regarding long-term follow-up in patients with primary BL

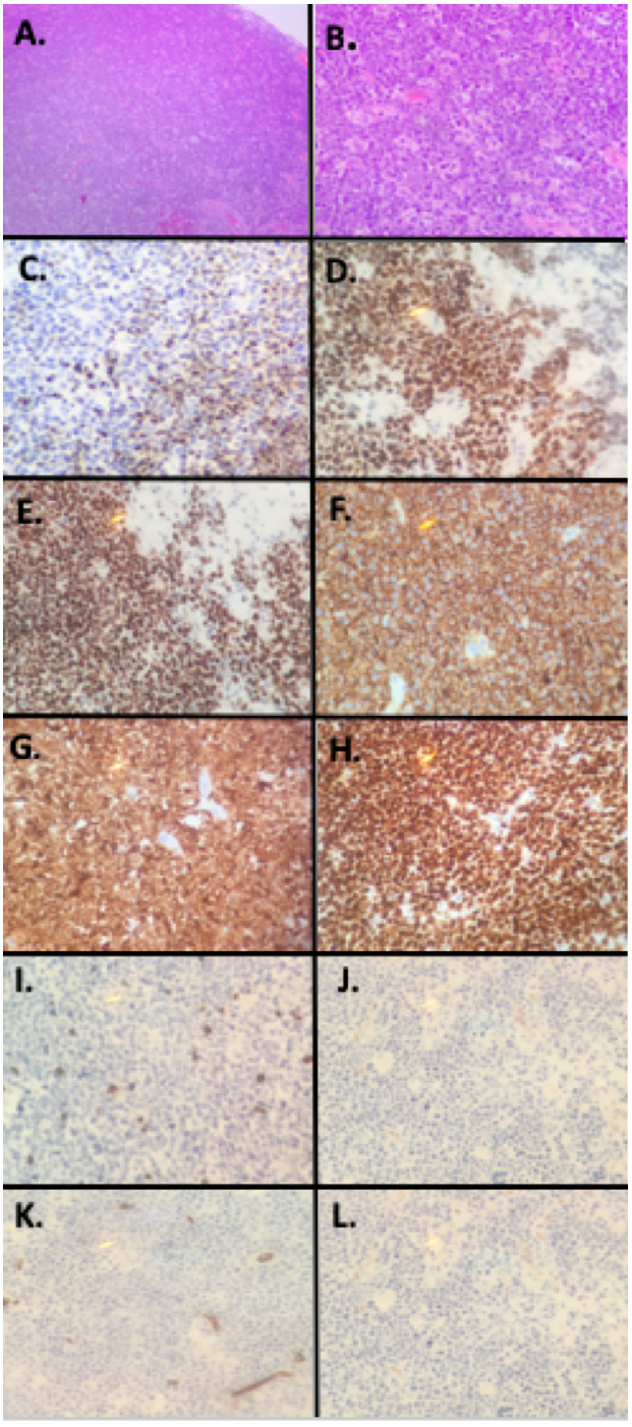

Figure 3. (**A**) 10× H&E stain. Prostatic tissue infiltrated with large lymphoid cells against a background of scattered macrophages with "starry-sky" pattern characteristic of Burkitt's lymphoma. (**B**) 40× H&E stain. Monomorphic cells with high mitotic activity. Inmunohistochemical stains showed positivity for MUM-1 (**C**), CD10 (**D**), CD20 (**E**), BCL-6 (**F**), and C-MYC >80% (**G**), Ki-67 Proliferation index 100% (**H**). CD3 (**I**) and BCL-2 (**J**) stains were negative confirming BL diagnosis and excluding. Diffuse large B-cell lymphoma and B-cell lymphoma, unclassifiable. Negative CD34 (**K**) and terminal deoxynucleotidyl transferase (TdT) (**L**) confirmed that the BL was a primary tumor of the prostate. (Color version available online.)

of the prostate and most cytotoxic regimens are derived from central nervous system clinical trials data or extraprostatic BL. Urologists, Oncologists, and Pediatricians must be aware of this unusual disease to improve oncological and functional outcomes in this patients.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.12.011.

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