

Case Report

Primary diffuse large B-cell lymphoma of the urinary bladder: a case report and review of literature

Yi Wang^{1*}, Shaofeng Chen^{1*}, Qingfei Xing¹, Zhanjun Guo¹, Changying Li², Binshuai Wang¹, Guang Sun¹, Xiaoqiang Liu¹

¹Department of Urology, ²Tianjin Key Laboratory of Urology, Tianjin Institute of Urology, Second Hospital of Tianjin Medical University, Tianjin 300211, China. *Co-first authors.

Received November 17, 2015; Accepted March 20, 2016; Epub June 1, 2016; Published June 15, 2016

Abstract: The urinary bladder is involved in less than 0.2% of lymphomas, and most of these are mucosa-associated lymphoid tissue (MALT); fewer than 20% of lymphomas of the urinary bladder are diffuse large B-cell lymphoma (DLBCL). Herein, we report a case of DLBCL in a 62-year-old man treated by 6 cycles of R-CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone plus the monoclonal antibody rituximab) chemotherapy, without local or distant recurrences after 16-month's follow-up. A literature review is included.

Keywords: Bladder cancer, chemotherapy, lymphoma, prognosis

Introduction

From 25% to 40% of all lymphomas are primary extranodal, the most common sites being the stomach, connective tissue, and skin. Primary lymphomas of the urinary bladder are very rarely, or about 0.2% of all extranodal lymphoma cases. The first described case of primary lymphoma of the urinary bladder was reportedly by Eve and Chaffey in 1885 [1]. The majority of primary bladder lymphomas have been extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma) that are low-grade tumors with a good prognosis. About 20% are high-grade diffuse large B-cell lymphoma (DLBCL) [2].

Case report

A 62-year-old man suffered from intermittent painless gross hematuria and clot for 2 weeks. He had a history of frequency, urgency, and painful urination, which had been treated with oral medicines for 2 months. There was no history of urinary trauma or infection, or hypertension or diabetes.

Laboratory examinations such as blood count and serum biochemistry were in the normal

range. Urine cytology tests were negative. Pelvic computed tomography (CT) scan revealed a 4.7×3.0 cm soft-tissue shadow of nodular density on both sides of the bladder without a clear boundary, between the left seminal vesicle and prostate. Enhancement CT scan showed filling defects within the range of the bladder (**Figure 1A**).

For further tests, ¹⁸F-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET)/CT was performed, which showed: (1) intense uptake within the range of the bladder; (2) a mean SUVmax ratio of the primary tumor of 6.7 (range: 1.8-17.1) in the bladder-PET/CT; (3) no thick swollen lymph nodes or radioactive anomalies in the abdomen or retroperitoneum. The liver, gallbladder, pancreas, spleen, stomach, and duodenum had normal radioactive uptake. Bilateral kidneys, ureters and prostate were normally radioactive. No unusual elevation in radioactivity was observed in the FDG/PET CT scan of the lung and brain.

Transurethral specimens of the bladder were obtained for pathological evaluation. Microscopically, the tumors consisted of nests of small blue cells, with scant cytoplasm, embedded in a densely fibrotic stroma and focal tubule

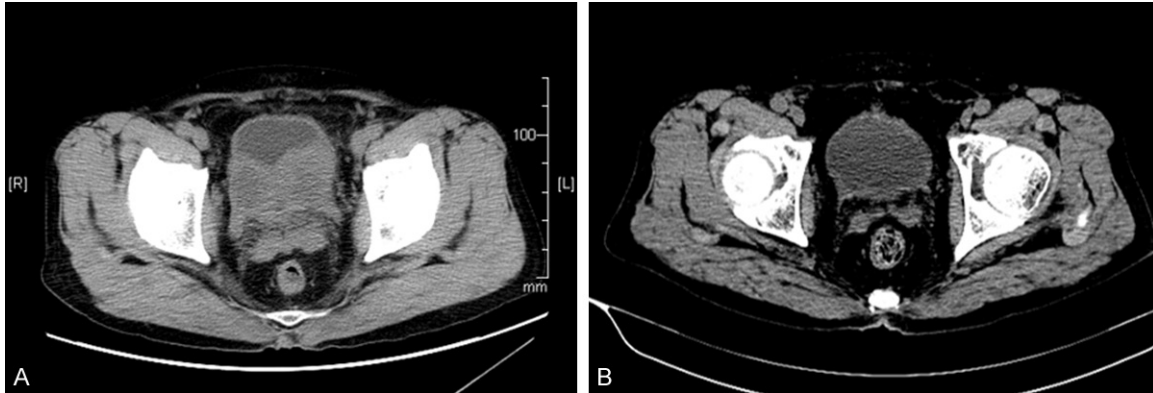


Figure 1. Abdominal CT images (A) before and (B) after 4 cycles of chemotherapy treatment. (A) Before treatment, diffuse thickening of the bladder wall with suspected involvement of the prostate and bilateral seminal vesicles. (B) Primary bladder lymphoma after 4 cycles of R-CHOP. The thickening of the bladder wall recovered after treatment.

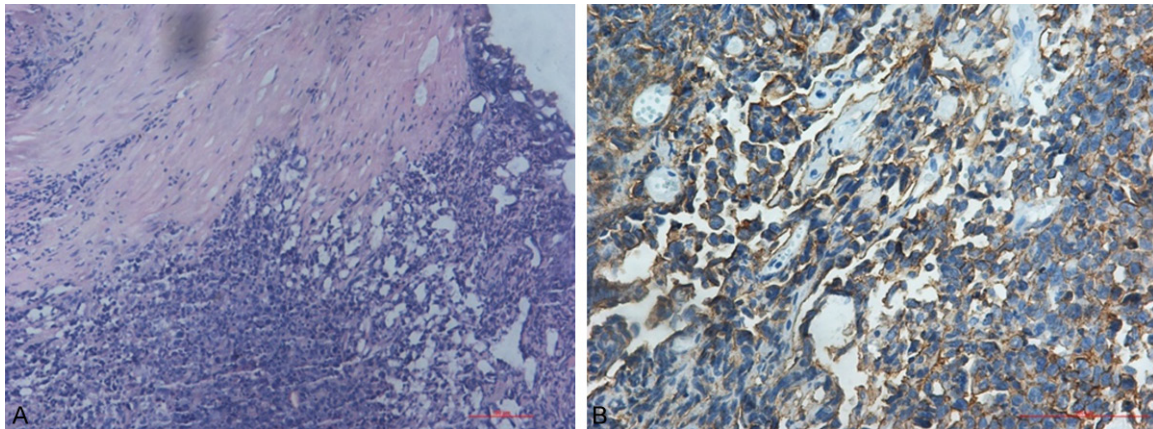


Figure 2. Pathological staining of bladder specimens. A. Atypical large cells showed a diffuse infiltration accompanied by follicles of small lymphoid cells (hematoxylin and eosin staining; 100 \times). B. The atypical cells in the bladder were positive for the B-cell marker CD20 (200 \times).

formation. The bladder lesions were aggressively invaded by atypical large cells accompanied by follicles of small lymphoid cells (**Figure 2A**).

Immunohistochemical stains were positive for cluster of differentiation (CD)79 alpha (CD79A), B-cell lymphoma 2 (BCL2) and CD20 (**Figure 2B**), but negative for CD3. The Ki-67 proliferation index was 60%. These findings were interpreted as diffuse large B-cell lymphoma with high-grade features.

The patient received 6 cycles of R-CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone plus the monoclonal antibody rituximab). Cycles were repeated every 21 days. There was no local or distant recurrence found

within the 16 months of follow-up, based on 18F-FDG PET/CT and CT scan findings (**Figure 1B**).

Discussion

The diagnosis of primary lymphoma originating in the urinary bladder is exceedingly rare. Including the present case, 16 cases of primary DLBCL of the urinary bladder were reviewed [3-9], shown in **Table 1**.

DLBCL of the bladder has been found twice as often in women as in men. Patients had a mean age of 68 years (35-89 y). Hematuria is the most common presenting symptom of DLBCL of the bladder, which is similar to primary bladder lymphomas. Of the 16 cases in the present

DLBCL of bladder

Table 1. Epidemiology, therapy and outcomes of the DLBCL cases reviewed from the literature

First author	Year	Country	Presenting symptoms	Age, y	Gender	Treatment	Survival Δ
Current	2015	China	Hematuria, frequency	62	Male	R-CHOP \times 6	Alive, 16 mo; CR
Bates*	2000	UK	Hematuria	67	Male	Radiation + chemo	Alive, 16 y
Bates*	2000	UK	Hematuria	84	Female	NA	Deceased
Bates*	2000	UK	Hematuria	80	Female	Radiation	Alive, 3 y; CR
Evans*	2007	UK	Hematuria, weight loss	64	Female	R-CHOP	Treatment ongoing
Hayashi	2009	Japanese	Inguinal lymph node swelled	75	Female	R-half CHOP \times 3	Treatment ongoing
Horasanli*	2008	Turkey	Hematuria, dysuria, frequency	65	Female	Radiation + CHOP \times 4	Alive, 1 y; CR
Hughes*	2005	UK	Hematuria	70	Female	Surgery + CHOP \times 6	Alive, 4 y; CR
Hughes*	2005	UK	Hematuria	75	Female	ICHIP	Deceased
Khaitan	2004	India	Hematuria	55	Male	CHOP \times 4	18 mo, died

*Nine cases reviewed by Simpson. Δ Time from diagnosis. Chemo: chemotherapy.

review, 68.8% (11 cases) presented with hematuria. Other presenting symptoms of primary DLBCL are urinary frequency, dysuria, nocturia, and recurrent urinary tract infections (UTIs). A history of chronic cystitis may be a potential instigating cause of DLBCL of the bladder [7]. In the present reviewed cases, 3 had a history of chronic cystitis. Our patient had no history of chronic cystitis or systemic hematological malignancy.

Immunohistochemical stain is important to diagnosis of primary lymphoma of the urinary bladder. Immunohistochemical staining for B-cell type lymphomas routinely test positive for CD20, CD79A and BCL2, while low-grade lymphomas test positive for CD20, CD21, and CD43 [9]. Specimens from the present patient stained positive for CD79A, BCL2, and CD20, but negative for CD3.

Surgery, radiation therapy, and chemotherapy, either alone or in combination, are used as therapeutic modalities for urinary bladder lymphoma. However, chemotherapy is most often the first choice, and R-CHOP, CHOP, and ChIVP (chlorambucil, vincristine, and prednisolone) have been reported successful. R-CHOP is the regime used most frequently according to the available literature; it is an improved form of CHOP with the addition of rituximab that has increased the rate of complete responses in DLBCL patients. Systemic chemotherapy was used in the 16 cases reviewed from the literature, that is, with the CHOP regimen (3 cases), R-CHOP (5 cases) and ChIVP (1 case).

Radiotherapy can be applied separately especially in low-grade tumors or as an adjuvant after resection, but cannot constitute a stan-

dard treatment [10]. For urothelial bladder cancer that has yet to invade the muscularis propria (stage Ta, Tis, and T1), transurethral resection of the bladder tumor (TURBT) has proven effective. However, no recommendations on lesion size have been published for TURBT.

Follow-up evaluations in most cases should take place every 3 or 6 months for the first 2 years and yearly thereafter, as is the case for transitional cell carcinoma, and must include at least ultrasound examination and cystoscopy.

Conclusion

Primary DLBCL of the bladder is quite rare. Chemotherapy is recommended as the first-line treatment, especially in high-grade or locally advanced tumors, and seems to give good results.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Xiaoqiang Liu, Department of Urology, Second Hospital of Tianjin Medical University, Tianjin Institute of Urology, 23 Pingjiang Road, Tianjin 300211, China. E-mail: fall-river@sina.com

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