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N. Haghi

Zucker School of Medicine at Hofstra/Northwell, nhaghi12@northwell.edu

X. Zhang

J. Kreshover

Zucker School of Medicine at Hofstra/Northwell, jkreshover@northwell.edu

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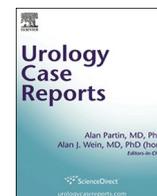


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Oncology

Primary follicular lymphoma of the bladder mimicking inflammatory condition: Case report and review of the literature

Nina Haghi^{a,*}, Xinmin Zhang^a, Jessica Kreshover^b

^a Department of Pathology and Laboratory Medicine, Hofstra Northwell School of Medicine, 6 Ohio Drive, Suite 202, New Hyde Park, NY, 11042, USA

^b Department of Urology, Northwell Health, New Hyde Park, NY, 11042, USA



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ABSTRACT

Primary lymphoma of the bladder is rare and may present with nonspecific symptoms and infection. Primary follicular lymphoma of the bladder is extremely rare with only a dozen reported cases. We present one case clinically mimicking an inflammatory process. A 79 year-old woman presents with recurrent urinary tract infections, urinary incontinence and frequency. Cystoscopic examination demonstrated a raised but flat lesion, suspicious for inflammatory lesion. Biopsy revealed a diagnosis of follicular lymphoma, grade 1–2. The presentation of primary follicular lymphoma of the bladder may be nonspecific, therefore it is important to consider this diagnosis in patients with unremitting symptoms.

Introduction

Primary lymphoma of the bladder (PLB) is very rare and may present with non-specific symptoms and infection. PLB has a female predominance. The most common subtype of PLB is mucosa associated lymphoid tissue (MALT) lymphoma followed by diffuse large B cell lymphoma (DLBCL). Primary follicular lymphoma of the bladder is extremely rare with only a dozen reported cases in the literature. Given the low frequency of primary follicular lymphoma of the bladder, its clinical and biological behaviors are not well-studied and standard therapeutic guidelines are not established. Here, we present one case of primary follicular lymphoma of the bladder clinically mimicking inflammatory process.

Case presentation

A 79 year-old woman presents with recurrent urinary tract infections with symptoms of urinary incontinence and frequency. Past medical history is significant for gastroesophageal reflux disease, hyperlipidemia, macular degeneration and nephrolithiasis. Most recent urinalysis was positive for leukocyte esterase with elevated white blood cell (WBC) of $10 \times 10^9/L$, and negative for glucose, bilirubin, ketones, protein, urobilinogen, nitrites, blood and bacteria. Ultrasound of the kidney and bladder showed small bilateral renal cysts and sub-centimeter non-obstructing renal calculi measuring up to 0.5 cm in the lower pole of the

right kidney and 0.6 cm in the upper pole of the left kidney. Mild right-sided pelvic fullness was noted on post-void bladder imaging. Cystoscopic examination reveals a slightly raised but flat lesion which appeared somewhat different in color from the surrounding mucosa, suspicious for an inflammatory lesion. It was completely resected transurethraly. Retrograde pyelograms revealed no filling defects.

Grossly the specimen measured $0.2 \text{ cm} \times 0.3 \text{ cm}$ in maximum dimension. Histological examination demonstrated a fragment of urothelial mucosa with nodular lymphoid proliferation which is confined to the submucosa. The neoplastic follicles show attenuation of the mantle zones and are composed of predominantly small lymphocytes with irregular/cleaved nuclear contours (centrocytes) and occasional centroblasts (less than 5 per high power field) (Fig. 1). Immunohistochemical stains revealed that the neoplastic cells were positive for CD20, Pax-5, CD10, Bcl-6, Bcl-2, CD23 and negative for CD5, CD43, cyclin D1, Mum-1 (Fig. 2). Ki-67 proliferation index was approximately 10% overall (Fig. 2). B-cell gene rearrangement studies were positive for both immunoglobulin heavy chain (IgH) and immunoglobulin kappa light chain (IgK) genes. Fluorescence in situ hybridization (FISH) analysis was positive for *BCL2-IGH* [translocation t(14;18)] rearrangement in 75% of cells. Based on these findings, a diagnosis of follicular lymphoma, grade 1–2 involving the bladder was rendered.

The patient showed no other signs of disease on whole body positron emission tomography (PET) scan. Complete blood count showed WBC count of $6.29 \times 10^9/L$, hemoglobin on 13.1g/dL, platelet count of

* Corresponding author., Department of Pathology and Laboratory Medicine, 6 Ohio Drive, Suite 202, New Hyde Park, NY, 11042, USA.

E-mail address: Nhaghi12@northwell.edu (N. Haghi).

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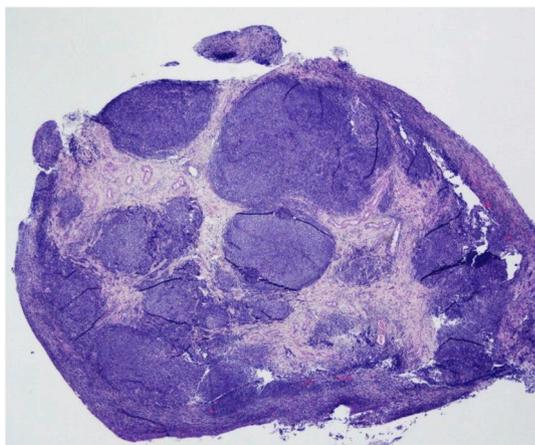


Fig. 1. Hematoxylin & eosin, 2x magnification.

$348 \times 10^9/L$. Automated differential was unremarkable. A bone marrow biopsy was not performed. Given the low clinical stage (stage 1E) and complete resection of the lesion, the patient did not receive additional therapies. Follow-up was not available.

Discussion

Lymphoma of the bladder may be seen in the setting of systemic disease, and is more commonly seen in middle-aged females.¹ PLB, however, is very rare with less than 150 cases reported in the literature

and comprise 0.2% of all extranodal non-Hodgkin lymphomas. As hematopoietic and lymphoid tissue are lacking in the urinary tract and bladder, it has been theorized that recurrent infections may play a role in the pathogenesis of these lymphomas. Radiologic imaging usually shows a solitary submucosal mass, while multiple masses and diffuse bladder thickening are less common.

The most common subtype of PLB is MALT lymphoma,¹ which has an excellent prognosis and may be treated conservatively. MALT lymphoma is commonly associated with chronic cystitis. Other reported subtypes include DLBCL, other subtypes of B-cell lymphoma, and T-cell lymphomas. A recent case series of men with primary lymphoma of the urinary tract and male genital organs shows that DLBCL was the most common type seen in the bladder, while no MALT lymphoma cases were reported. This is suggestive of a possible female predominance of MALT lymphoma bladder cases. Treatment for primary bladder lymphoma may include antibiotics for MALT lymphoma), surgery, chemotherapy and/or radiation.

Primary follicular lymphoma can arise in extranodal sites with the most common being gastrointestinal tract (often with mesenteric lymph node involvement) and less frequently soft tissue, breast and ocular adnexa. Such cases tend to be grade 3 and may lack BCL2 positivity as well as BCL2 translocation. Our case, however, was positive for IGH/BCL2 translocation by FISH. Primary follicular lymphoma of the bladder is extremely rare, and perhaps underdiagnosed. No standard treatment guidelines have been established. Three other cases of definitive primary follicular lymphoma of the bladder have been reported in the literature to our knowledge (Table 1).²⁻⁴ One case is an 80 year-old male who presented with symptoms of urinary tract infection, found to have follicular lymphoma in the bladder. Follow-up was not available. The

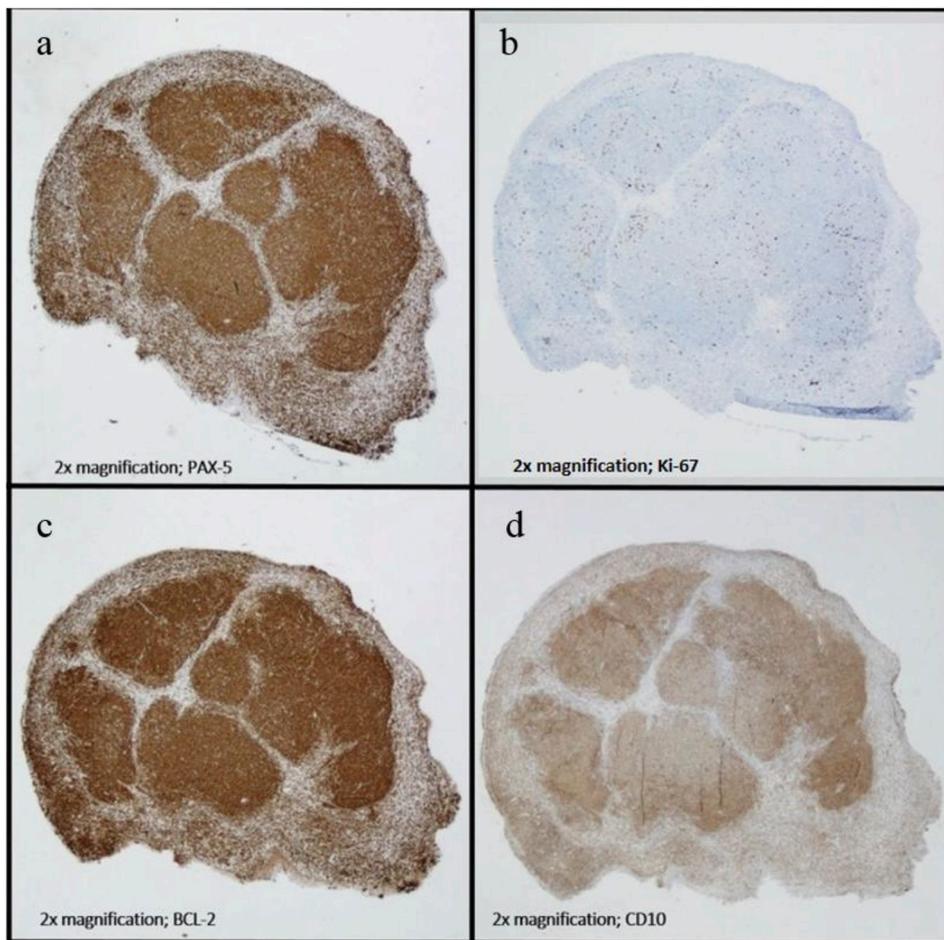


Fig. 2. 2x magnification of immunohistochemical stains for a) Pax-5, b) Ki-67, c) BCL-2 and d) CD10.

Table 1
Reported cases of follicular lymphoma of the bladder.

Paper	Sex	Age	Clinical history	Procedure	Radiologic/Gross findings	Diagnosis	Primary?	Treatment	Follow up
Current case, 2018	Female	79	Incontinence, frequency and recurrent urinary tract infections	Cystoscopy	0.2 cm × 0.3 cm raised flat lesion	FL, grade 1-2	Yes	Unknown	No follow-up
Roberts, 2013	Female	42	Hematuria, dysuria	Cystoscopy with failed loop resection	Radiologic CT showed 12 × 8.5 × 9 cm solid mass	FL, grade 2	Yes	R-CHOP	3 months, no evidence of disease
Schniederjan, 2009	Male	80	Not available	Not available	Not available	FL, grade not specified	Yes	Unknown	No follow-up
Pontius, 1963	Female	69	Gross hematuria, nocturia	Partial cystectomy	8.5 × 7 × 3.5 cm mass	FL, grade not specified	Yes	RT	19 months, no evidence of disease

RT = radiotherapy; TUB = transurethral biopsy; FL = follicular lymphoma; R-CHOP = rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate.

other case was a 42 year-old female with hematuria and dysuria who was treated with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP regimen) and achieved complete remission (disease-free at 2-year follow-up). The third case is a 69 year-old female with large gross hematuria found to have an 8.5 cm mass in the bladder wall with no evidence of systemic disease. Patient was treated with radiotherapy with no recurrence.

A population-based cohort analysis identified 195 cases of PLB from 18 Surveillance, Epidemiology, and End (Results (SEER) registries between 1998 and 2010.⁵ Ten of these cases were reported to be follicular lymphoma. However, this study did not provide any clinical and pathological findings for these cases. This study showed that PLB of low-grade B cell subtype had better outcomes compared with high-grade PLB.

Conclusion

The presentation of primary follicular lymphoma of the bladder may be nonspecific and mimic inflammatory processes. It is therefore important to consider this diagnosis in patients with unremitting

symptoms.

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Declarations of interest

None.

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