

Case Report

Primary Prostatic High-Grade B-Cell Lymphoma with MYC and BCL2 and/or BCL6 Rearrangements: A Case Report and Literature Review

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Prostatic lymphoma (mostly secondary involvement) is rare, accounting for 0.09% of all prostate tumors and 0.1% of non-Hodgkin lymphoma. Primary prostate lymphoma is extremely rare, by far only limited number of cases have been reported in English literature. Here we report a case of primary prostatic high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements (HGBCL-MBBR) in an 81-year-old Caucasian male who presented with urinary outlet obstruction as sole symptom. He was diagnosed as benign prostate hyperplasia, followed with transurethral resection of prostate. Incidentally, a lymphoma was identified on H&E stains. Microscopic finding, Immunohistochemistry, and FISH study all support a diagnosis of HGBCL-MBBR. To our knowledge, this is the first case of HGBCL-MBBR reported so far.

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INTRODUCTION

Prostatic lymphoma is rare, accounting for 0.09% of all prostate tumors and 0.1% of non-Hodgkin lymphoma (NHL).^{1,2} NHL of the prostate is classified into primary or secondary, based on whether the lymphoma cells are localized to the prostate gland or not. In addition, to diagnosing primary prostate lymphoma, the following 2 conditions must also be satisfied: 1) the presence of an enlarged prostate at the beginning of the disease, and 2) the absence of involvement of any other tissue or lymph node within 1 month of diagnosis.³ By these criteria, the majority of prostatic lymphomas are secondary, with involvement by diffuse large B-cell lymphoma (DLBCL) as most common, followed by involvement by chronic lymphocytic leukemia.^{3,4}

High-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements (HGBCL-MBBR) is the modified entity in WHO Classification 2016 (Revised 4th edition), arising from the previous "B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and Burkitt lymphoma" in WHO Classification 2008.⁵ HGBCL-MBBR is defined as an aggressive mature B-cell lymphoma that harbors a MYC rearrangement at chromosome 8q24 and a rearrangement in BCL2 at chromosome 18q21 and/or in BCL6 at chromosome 3q27. This entity mostly present in

elderly patients, with slight male predominance. Microscopically, about half of the cases have the morphology of DLBCL, NOS, the others show a morphology mimicking that of Burkitt lymphoma (BL), or has features intermediate between DLBCL and BL, or have a blastoid cytomorphology. Immunophenotypically, the lymphoma cells are generally positive for CD19, CD20, CD79a, PAX5, CD10, Bcl2, Bcl6, MYC, with a variable Ki-67 proliferative index (30-95%).⁵

Primary prostatic lymphoma is extremely rare, and most of them are diffuse large B-cell lymphoma.^{6,7} Here for the first time, we report a case of primary prostatic HGBCL-MBBR in a patient complaining urinary outlet obstruction.

CASE REPORT

The patient is an 81-year-old Caucasian male who presented with urinary outlet obstruction. He was diagnosed as benign prostate hyperplasia and urinary tract infection. He had no lymphadenopathy or splenomegaly. His CBC was within normal limits. His previous medical history was unremarkable. A transurethral resection of prostate (TURP) was performed. Post-surgery care was without event.

The prostate chips were processed in histology lab. On H&E sections, the prostate gland is completely replaced by a population of atypical lymphoid cells. Some tissue fragments are lined with urothelial epithelial cells, which are positive for GATA-3 on immunostaining (**Figure 1. A, B, C, and E**). There are no prostatic acinar glands or ducts identified in the specimen. There is diffuse infiltration of the atypical

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lymphoid cells, which are medium in size for majority, with vesicular chromatin and prominent nucleoli. A “starry sky” pattern is also observed, although a few of the atypical lymphocytes were larger than typical Burkitt lymphoma cells (**Figure 1. A**). Immunohistochemistry studies reveal that the atypical lymphocytes are positive for CD20, PAX5, and BCL2, but negative for CD10 and BCL6, with a Ki-67

proliferative index around 75% (**Figure 1. D, F, G, H, and I**). FISH study shows that the tumor cells harbor chromosomal rearrangements involving BCL6 and MYC, but not BCL2 (results from Integrate Oncology, Manhattan, NY. not shown). Taken together, a primary prostatic HGBCL-MBBR was rendered. To our knowledge, this is the first case of HGBCL-MBBR reported so far.

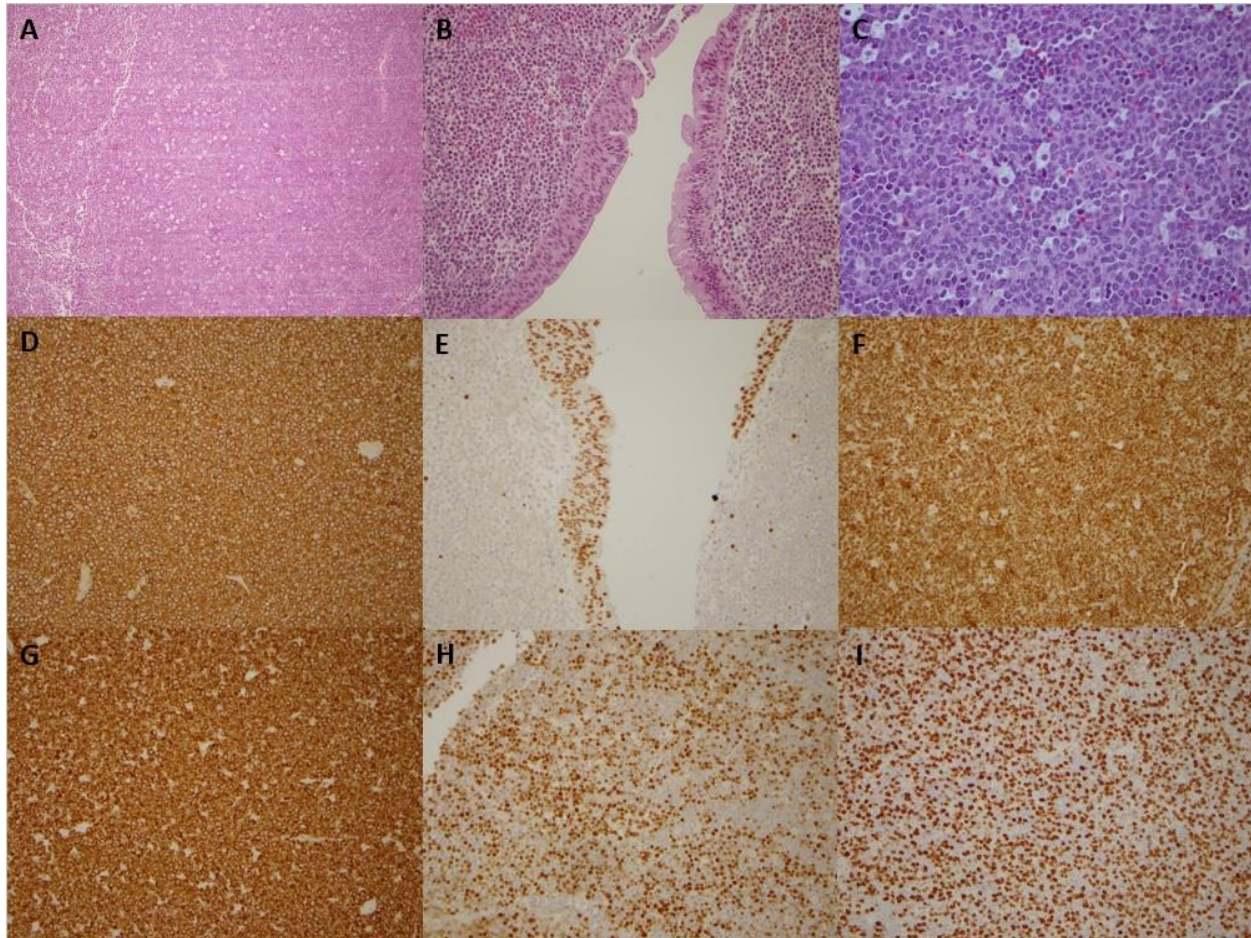


Figure 1. Prostatic primary HGBCL-MBBR. **A.** H&E section, showing “starry sky” pattern, 100X. **B.** H&E section, with lining urothelium, 200X. **C.** H&E section, 400X. **D.** Immunostaining for CD20. **E.** Immunostaining for Gata 3, positive for urothelial cells. **F.** Immunostaining for Pax5. **G.** Immunostaining for Bcl-2. **H.** Immunostaining for Bcl-6. **I.** Immunostaining for Ki-67.

DISCUSSION

Lymphoma involving prostate only accounts for 0.09% of prostatic malignancy and 0.1% of all NHL. Among them, the majority cases are secondary in nature, representing tumor extension into prostate from advanced nodal lymphoma or CLL.^{1,2} Primary prostatic lymphoma is extremely rare, representing about 0.2-0.8% of extranodal lymphomas. Based on literature, the reported cases of primary prostatic lymphoma are mostly of diffuse large B-cell lymphoma.^{6,7} Our case report would be the first case of HGBCL-MBBR.

The distinction between primary or secondary prostatic lymphoma is sometimes challenging, especially for those non-CLL cases. Bostwick and Mann proposed 3 criteria for

determination of primary prostatic lymphoma: 1) symptoms attributable to prostate enlargement; 2) the prostate as the predominant site of involvement; and 3) the absence of involvement of liver, spleen, or lymph nodes within 1 month of diagnosis. After thorough clinical and radiological examination, our case abides by all the 3 criteria and consequently the establishment of the diagnosis. The largest study on primary prostatic lymphomas so far included only 22 cases pooled from 3 tertiary referral centers. The study showed that most of the cases were DLBCL, with rare cases of small lymphocytic lymphoma, follicular lymphoma, and Burkitt lymphoma.

Primary prostatic lymphoma usually occurs in senior patients and is manifested as urinary outflow obstruction as the sole symptom, which, is commonly seen in benign prostate hyperplasia (BPH).⁸⁻¹⁰ As the matter of fact, due to its rarity, most of the primary prostatic lymphoma was mis-diagnosed as BPH or urinary tract infection and treated accordingly. Unfortunately, imaging modalities such as CT and MRI are often non-specific, although PET might be helpful in detecting the increased metabolic activity.

The newest WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues (2016) proposed a narrow definition of HGBCL-MBBR: an aggressive mature B-cell lymphoma that harbors a MYC rearrangement at 8q24 and a rearrangement in BCL2 (at 18q21) and/or in BCL6 (at 3q27).⁵ This is a significant clarification of the previous vague entity in WHO classification 2008, “B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and Burkitt lymphoma”, which is largely based on morphologic features, although “double-hit”/“triple-hit” lymphomas are also mentioned in this category. The current HGBCL-MBBR classification strictly requires the presence of MYC translocation, together with BCL2 and/or BCL6 translocation, which, must be detected by a cytogenetic/molecular method such as FISH. The presence of only copy-number increase/amplification or somatic mutations, without an underlying rearrangement, is insufficient to qualify a case for this category. Instead, these lymphoma cases should be classified into “high-grade B-cell lymphoma, NOS” in the current WHO classification (2016). Of note, there are two exceptions for HGBCL-MBBR classification: one is a proven follicular lymphoma (positive for BCL2 rearrangement) with MYC translocation, which should still be classified as follicular lymphoma; the other is B-lymphoblastic leukemia/lymphoma, NOS, regardless of MYC, BCL2, or BCL6 translocation status, should be still classified as ALL.⁵

CONCLUSIONS

Here we report the first case of primary prostatic HGBCL-MBBR, a high grade B-cell lymphoma recently re-classified in the newest WHO lymphoma classification 2016. The clinical history, tumor morphology, immunohistochemistry and FISH studies of this case all supports a diagnosis of this entity. Up to date, the patient shows no lymphadenopathy or bone marrow involvement. He is received chemotherapy and doing fine.

CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

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