Original Research Paper

Volume - 10 | Issue - 12 | December - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Pathology

EXTRANODAL DIFFUSE LARGE B-CELL LYMPHOMA OF THE PROSTATE: A UNIQUE QUAGMIRE

Dr. Rachna Garg* MD/Pathology, Junior Consultant, Department Of Pathology, Jawaharlal Nehru Cancer Hospital And Research Centre, Bhopal, Madhya Pradesh, India. *Corresponding Author

Dr. Deepak Nayak M MD/Pathology, Associate Professor, Department Of Pathology, KMC, Manipal Academy Of Higher Education, Manipal, Karnatka, India.

ABSTRACT Non Hodgkin Lymphoma (NHL) of extranodal nature are not infrequent in occurrence. Involvement of sites such as prostate is rare and merely accounts for 0.09% of prostate cancers and0.1% of all NHL, as per the current WHO data. We report a case of diffuse large B-cell (DLBCL) non-Hodgkin lymphoma in a 69-year-old male patient with a past history of chronic renal failure who presented to the urology OPD with complaints of urinary obstruction, dysuria, and grade 3 prostatomegaly on transrectal ultrasonography. A trucut biopsy and immunohistochemistry helped to establish the diagnosis. As the symptoms at the time of presentation are similar to other benign prostatic diseases, lymphomas are seldom considered in the differential diagnosis of prostatic carcinomas and their diagnosis remains a challenge. Histopathological analysis with Immunohistochemical techniques and molecular studies are mandatory to reach final diagnosis. We herein present one such rare occurrence with an emphasis on diagnostic mimics and therapeutic challenge.

KEYWORDS : Prostate, Lymphoma, Extranodal NHL, Histopathology, Immunohistochemistry.

INTRODUCTION

Non Hodgkin Lymphoma (NHL) of extranodal nature have been reported in the literature. Involvement of sites such as prostate is rare and merely accounts for 0.09% of prostate cancers and 0.1% of all NHL, as per the current WHO data.[1]

Diffuse Large B Cell Lymphoma (DLBCL) is an aggressive, fatal and rapidly growing neoplasm composed of lymphoid cells with nuclei comparable in size or larger than those of reactive histiocytes. It's occurrence in prostate represents a disseminated version of an advanced nodal disease. However, a primary (extranodal) DLBCL of the prostate accounts for 0.2-0.8% of extranodal NHL.[2] As the presenting symptoms mimic benign prostatic diseases, they are often missed in the differential diagnosis. Although rare, this entity should be kept in mind to avoid unnecessary surgery.

The objective of this study was to highlight the clinicopathological features of extranodal DLBCL of the prostate and review of the available literature.

CASE REPORT

A 69-year-old male patient with a past history of chronic renal failure presented to the urology out-patient department with complaints of urinary obstruction and dysuria. The physical examination was normal. An initial laboratory test showed hemoglobin of 10.4gm% (normal 13.5–17.5), a total leucocyte count of $7.5x10^3$/ cu.mm, and a platelet count of $120 x10^3$/ cu.mm. He had no family history of prostate cancer and serum prostate-specific antigen (PSA) level was 3.2ng/mL (normal 0-4ng/mL). Transrectal ultrasonography showed a grade III prostatomegaly with nodularity in the peripheral zone, thus raising a suspicion of prostatic carcinoma.

Cystoscopy showed mild thickening of the posterior wall of urinary bladder- suggestive of inflammation or a suspicion for malignancy. No evidence of bladder malignancy was reported in urine cytology.

The prostatic trucut core biopsy was sent for histopathological evaluation and immunohistochemical analysis. All 4 linear cores submitted showed diffuse aggregates of large abnormal lymphoid cells with a dispersed chromatin and prominent nucleoli, and smudge artifacts. Few mitotic figures were seen (>10/10hpf) (Image 1). A provisional histopathologic diagnosis of a non-Hodgkin lymphoma or a poorly differentiated carcinoma was made and a search for a primary nodal disease was requested.

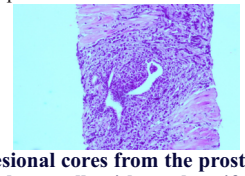

Image 1: Trucut lesional cores from the prostate showing diffuse sheets of malignant large cells with crush artifacts (H&E; x100)

CT scan showed no significant lymphadenopathy. Staging bone marrow aspiration was performed that showed a normocellular to hypocellular marrow. There were no abnormalities of granulocytes or monocytes, and blasts were not increased. An ensuing bone marrow core biopsy showed normocellular marrow with adequate multilineage hematopoiesis, and was reported as no evidence of lymphoma or metastatic malignancy, and adequate iron storage. The cerebrospinal fluid (CSF) cytology showed no evidence of lymphoma.

On immunohistochemistry, [Image 2], tumor cells were strongly positive for CD45, CD20, Bcl-6 , Bcl-2, MUM-1 and CD10 and were negative for markers such as CD3, Cyclin D1, Cytokeratin, Synaptophysin and Desmin.

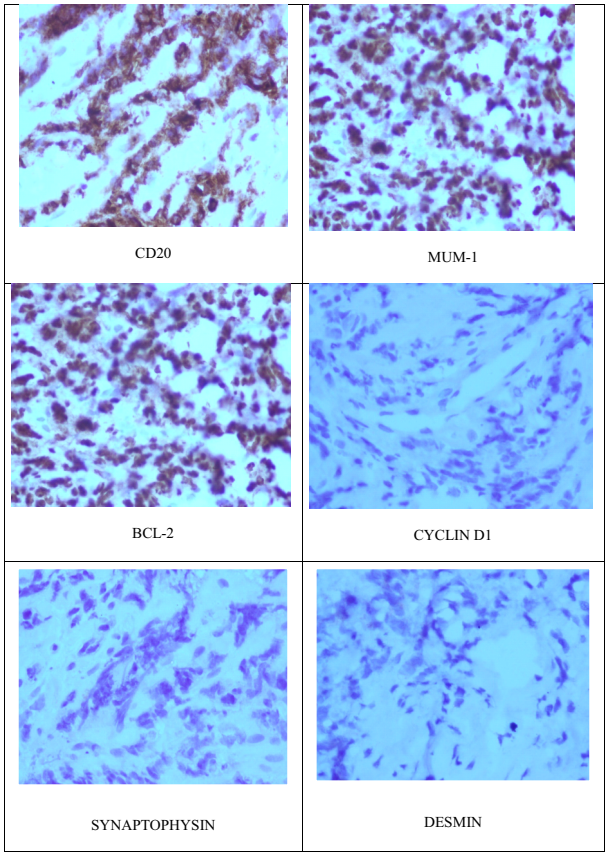

Image 2: IHC staining profile of the tumour cells (Monoclonal Ab; x400)

The proliferation index (Ki67) was approximately 98%. A differential diagnosis of either DLBCL or Burkitt Lymphoma was suggested. Molecular studies for MYC mutation and EBER were negative. A final diagnosis of DLBCL was then rendered. The patient was placed on R-CHOP chemotherapy regimen and was referred to a higher center for further continuation of treatment.

DISCUSSION

Non-Hodgkin lymphoma involving prostate gland is a well-known late manifestation of advanced nodal disease. Various subtypes of NHL of the prostate have been reported, including follicular lymphomas, Burkitt lymphomas, mantle cell lymphomas, and mucosa-associated lymphoid tissue lymphomas. A primary prostatic NHL is rare, and when reported, is usually of a low-grade type, predominated by small lymphocytic lymphoma/chronic lymphocytic leukemia.[3] DLBCL is both, rare and aggressive[3].

Non-Hodgkin lymphoma (NHL) of the prostate is classified into primary or secondary based on whether the cancer is localized to the prostate gland. One of the largest study of case series of prostatic lymphomas conducted till date, used the following criteria to identify primary prostatic lymphomas: (i) Presenting symptoms attributable to prostatic enlargement; (ii) involvement of prostate predominantly, with or without involvement of adjacent tissue; and (iii) absence of involvement of liver, spleen, or lymph nodes within 1 month of diagnosis of prostatic involvement[4]. Based on the literature, primary extranodal lymphoma of the prostate is extremely rare, representing about 0.2–0.8% of extranodal lymphomas[3].

Prostatic lymphoma usually occurs in elderly men (mean age: 60–63 years). In our case patient was 69 yrs old. The clinical presentation of the patient is variable. Most patients present with lower urinary tract obstruction, such as urinary frequency, urgency, hematuria, or acute retention, sometimes leading to renal failure[4]. A finding concordant with our case. The patients of benign prostatic neoplasm or carcinoma also present with similar clinical symptoms causing a delay in diagnosis and treatment. Systemic symptoms such as fever and weight loss are usually absent, while serum PSA levels are normal[4]. In our case also, normal levels of PSA helped to rule out carcinoma.

Primary prostate lymphoma can be diagnosed by histopathology, employing ancillary studies, such as immunophenotyping and molecular techniques. Histopathologically, the morphologic mimickers of an NHL include, prostatic carcinoma (Gleason score 5), urothelial carcinoma (poorly differentiated), small cell carcinoma and high-grade sarcoma. IHC remains the only useful ancillary tool in differentiating these neoplastic mimics (table 1)

An array of immunohistochemical markers to differentiate between a primary non Hodgkin lymphoma of prostate and other epithelial tumors of the prostate and also between the other lymphomas of the gland with a large cell morphology is mandatory. Prostatic carcinomas are AMACR+, while urothelial carcinomas were GATA-3+. Burkitt lymphomas are Bcl-2 negative while mantle cell lymphoma are strongly positive for cyclin-D1. Tdt positivity points towards a T-lymphoblastic lymphoma. Hodgkin lymphoma show MUM-1 reactivity. This case was inconclusive for all the other markers discussed above. (table 1 and 2)

Table 1: Comparison of IHC markers in different neoplasms of the prostate

IHC Markers	Cd45	Cytokeratin	Synaptophysin	Desmin	Others
NHL	+	-	-	-	CD20+ Bcl-6+ Bcl-2+
Prostatic carcinoma	-	+	-	-	AMACR+ PSA+
Urothelial Carcinoma	-	+	-	-	GATA-3+ p63+
Small cell carcinoma	-	+/-	+	-	Chromogranin +
Sarcoma	-	-	-	+	Vimentin+ Myo-D1+

Table 2 : Comparison of IHC markers in lymphomas with large cell morphology

Marker	CD 45	CD 20	CD 3	CD 5	Bcl-2	Bcl-6	CyclinD1	EBER	Others
DLBCL	+	+	-	-	+	+	-	-	CD10+ MUM -1+
Burkitt lymphoma	+	+	-	-	-	+	-	++	CD10+ Ki67 100%
Mantle cell lymphoma (blastoid variant)	+	+	-	+	-	-	++	-	CD10-
B-Lymphoblastic lymphoma	dim +/-	+	-	-	-	-	-	-	CD10+ Tdt +
Hodgkin lymphoma	+/-	+/-	-	-	-	-	-	-/+	MUM -1+
Peripheral T cell lymphoma	+	-	++	+/-	-	-	-	-	

Other investigative tools like Computed Tomography and Magnetic Resonance Imaging are often non-specific for diagnosis of DLBCL of the prostate. PET scan is helpful in determining the metabolic 18F-fluorodeoxyglucose activity in suspicious lesions and is useful in disease monitoring prior to and after treatments[3].

Currently, there is no consensus on therapeutic modalities for treatment of primary DLBCL of the prostate. Preceding the development of adequate chemotherapy and radiotherapy for lymphoma, a retrospective study showed a 33% five-year survival rate.[4]

Radical surgery is not indicated since local disease is well controlled with chemotherapy or radiation therapy. Although the prognosis of these tumors is classically considered poor, some articles suggest that prolonged survival could be expected with chemotherapy or radiotherapy [5]. While some excellent outcomes are seen with Anthracycline-based chemo- and radiotherapy, others have shown equally good outcomes with R-CHOP with or without radiotherapy.[5]

The impressive efficiency seen with R-CHOP has been attributed to the synergistic effect of Rituximab (anti-CD20) with CHOP, which enhances the chemo-sensitivity of the lymphoma cells. Our patient was treated with an R-CHOP regimen followed by 36 Gy of fractionated radiotherapy to the prostate and entire seminal vesicles[6]. He had a partial response and requested a transfer to a higher centre for continuation of treatment.

CONCLUSION

A prostatic primary DLBCL is an infrequent neoplasm. The diagnostic challenges aside, the significance of labeling it as primary or secondary has profound implications with reference to the staging of the neoplasm and therapy-alike. IHC remains an indispensable tool in identifying this elusive entity. It is hoped that further studies on this rare entity will shed light on prognostic implications.

REFERENCES

1. Paquaalucci L, Dalla-Favera R. The genetic landscape of diffuse large B cell lymphoma . Semin Hematol 2015;52(2):67-76.
2. Terris MK, Hausdorff J, Freiha FS. Hematolymphoid malignancies diagnosed at the time of radical prostatectomy. J Urol. 1997;158(4):1457–1459.
3. Ezekwudoa DE, Ogunleyea F, Gbadamosia B, Blankenshipa LM,Kinoyanb M, Kraussc D et al. Case Rep Oncol 2017;10:199–204.
4. Kakkar A,RajeshwariM, Bhethanabhotla S, Kaur K, Jain D,Gogia A, et al. Primary diffuse large B-cell lymphoma of the prostate: A report of two cases with diagnostic considerations. Journal of Cancer Research and Therapeutics - October-December 2015 - Volume 11(4): 977-79.
5. Alvarez CA, Rodriguez BA, Perez IA.Primary Diffuse Large B-Cell Lymphoma of the Prostate in a Young Patient. International Braz J Urol 2006; 32 (1): 64-5.
6. 5. Diffuse large B-cell non-Hodgkin lymphoma of the prostate presenting with urinary outlet obstruction: A case report. Rao RN ,Bansal M, Raghuvanshi S, Ansari MS, Zafar Neyaz Z. Urol Ann. 2015 Jan-Mar; 7(1): 100-3.