—Case Reports—

A Case of Primary Malignant Lymphoma of the Prostate Gland Presenting as Right Lower Back Pain and Dysuria

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A 73-year-old man presented with right lower back pain and dysuria. Right hydronephrosis and a large pelvic large mass were seen on computed tomography (CT). Although his prostate-specific antigen (PSA) was 0.5 ng/mL, an irregularly enlarged, stony, hard prostate was palpable on digital rectal examination. A prostate tumor was suspected, and a transrectal prostate biopsy and right transurethral ureteral stent placement were performed. Histological and immunohistochemical studies revealed diffuse large B-cell lymphoma. Positron emission tomography-computed tomography showed abnormal uptake in the stomach, cecum, right obturator lymph nodes, para-aortic lymph nodes, and dorsal left kidney. No abnormal findings were seen on bone marrow histology. Clinical stage IVA was confirmed according to Ann Arbor criteria. The patient achieved a complete response after 8 cycles of combination chemotherapy with rituximab, pirarubicin, cyclophosphamide, vincristine, and prednisolone.
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Key words: malignant lymphoma, prostate, dysuria, hydronephrosis, International Prognostic Index (IPI)

Introduction

Primary malignant lymphoma of the prostate gland is rare, accounting for 0.09% of all prostatic malignancies. The prostate gland is the site of 0.1% of non-Hodgkin lymphoma (NHL), 0.9% of extranodal lymphoma and 0.1% of newly diagnosed lymphoma[1]. Despite the accumulation of case reports of this pathology in Japan, prostatic lymphoma still appears widely overlooked in clinical practice. Here, we report a case of primary malignant lymphoma of the prostate gland in a patient presenting with right lower back pain and dysuria, and achieving complete remission using rituximab-containing chemotherapy.

Case Report

A 73-year-old man presented with right lower back pain and dysuria. At the time of his visit, his Eastern Cooperative Oncology Group Performance Status (ECOG PS) score was 0 and his International Prostate Symptom Score (IPSS) was 26. Digital rectal examination detected an irregularly enlarged, stony, hard prostate. Initial laboratory findings revealed: white blood cell count, 8,300/μL without atypical cells; hemoglobin, 12.9 g/dL; platelet count, 24.7 × 10^4/μL; and serum prostate-specific antigen, 0.5 ng/mL. Computed tomography (CT) showed right hydronephrosis and a large pelvic mass measuring 85 mm in diameter. Magnetic resonance imaging (MRI) revealed hyperintensity of the right lobe of the prostate gland on diffusion-weighted imaging (**Fig. 1**). Transrectal ultrasound-guided prostate needle biopsy and right transurethral ureteral stenting were performed. At the time of the procedure, transrectal ultrasonography showed a hypoechoic area of the right lobe of the prostate gland with rich blood flow, and cystoscopy revealed

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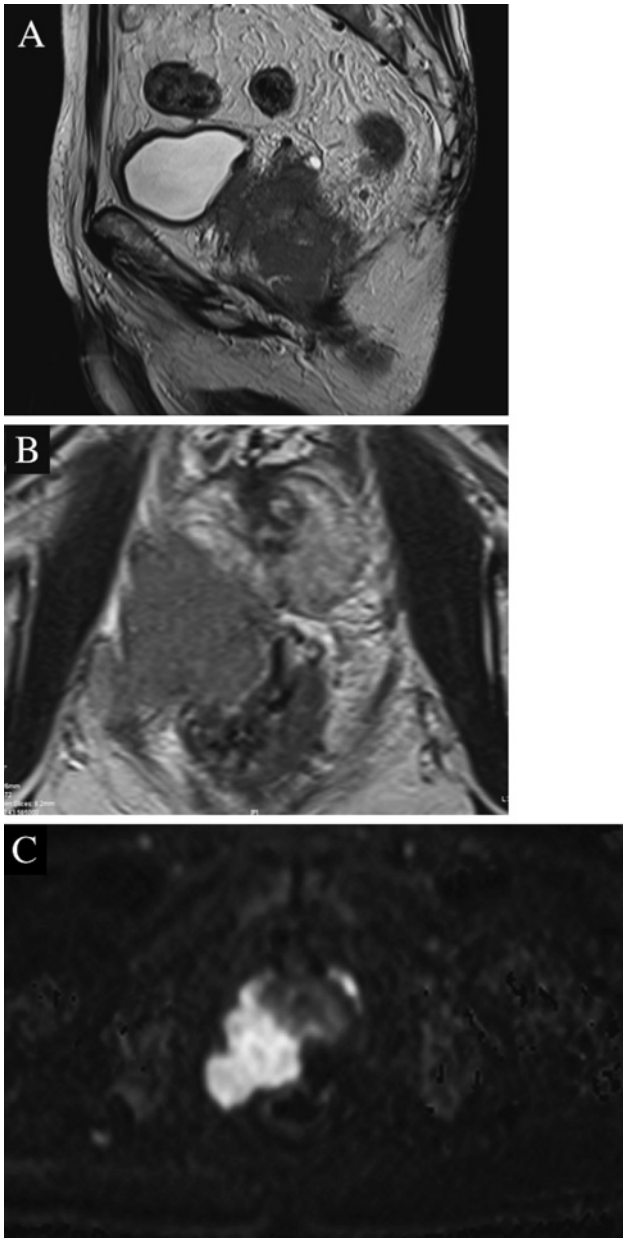

Fig. 1
A, B) Signal-hypointense tumor with a long diameter of 85 mm in contact with the bladder and rectum is evident in the right lobe of the prostate gland on pelvic T2-weighted magnetic resonance imaging (MRI).
C) Massive tumor with diffuse signal hyperintensity on diffusion-weighted imaging.

no neoplastic lesions in the bladder.

Histopathological findings revealed that normal prostatic tissue had been almost entirely replaced by atypical cells with large, circular nuclei. Almost all tumor cells proved positive for CD20 and MUM1, and negative for CD3 and CD10 on immunohistochemical examination. The Ki67 proliferation index accounted for approximately 80–90% of tumor cells (**Fig. 2**). The definitive diagnosis was non-germ cell-type primary diffuse large B-cell lymphoma (DLBCL) of the prostate gland. Subsequent positron emission tomography (PET) showed abnormal 18F-Fluorodeoxyglucose (FDG) uptake in the stomach, cecum, right obturator lymph nodes, para-aortic lymph nodes and dorsal left kidney. Subsequent esophagogastroduodenoscopy revealed irregular mucosa in the stomach, accompanied by ulcers and abnormal blood vessels, and biopsy results indicated lymphoma of the prostate gland. Further colonoscopy showed a tumor near Bauhin's valve in the cecum that was determined by biopsy to also be lymphoma. No abnormal findings were seen from bone marrow histology. The disease was therefore confirmed as clinical stage IVA according to the Ann Arbor criteria and classified as high-risk based on the International Prognostic Index score (4 points).

During the above inspections, exacerbation of symptoms such as dysuria, dyschezia, and general malaise were observed. Thus, on day 40 after diagnosis, he was emergently hospitalized to the hematology department because of severe general fatigue and received chemotherapy with rituximab, pirarubicin, cyclophosphamide, vincristine, and prednisolone (R-CHOP). After 1 course of R-CHOP, a repeat CT scan showed a significant reduction in the size of the prostatic lesion and clinical symptoms were also improved, so the second and subsequent courses were provided as ambulatory chemotherapy. In the eighth course, he developed febrile neutropenia and received in-hospital treatment, but it was only classified as a grade 3–4 side effect. After finishing 8 courses of chemotherapy, because PET imaging revealed complete remission, the right urethral stent was removed (**Fig. 3**). Moreover, IPSS scores before and after treatment changed from 26 to 6 and his dyschezia also improved.

Discussion

Primary malignant lymphoma of the prostate gland is rare, but Bostwick et al. reported 62 cases in 1998[2]. In Japan, Kishimoto et al. reported 41 cases in 2010[3]. As far as we could investigate, another 11 cases have been seen since 2011, and the present case appears to represent the 53rd described in Japan (**Table 1**).

The diagnostic criteria for primary malignant lymphoma of the prostate gland, proposed by Bostwick et al[2]. to clarify whether malignant lymphoma of the prostate gland is primary or secondary, are widely used. According to the criteria, there are three conditions in which lymphoma in the prostate is determined to be primary: 1) presentation with symptoms attributable to prostatic enlargement, 2) involvement of the prostate

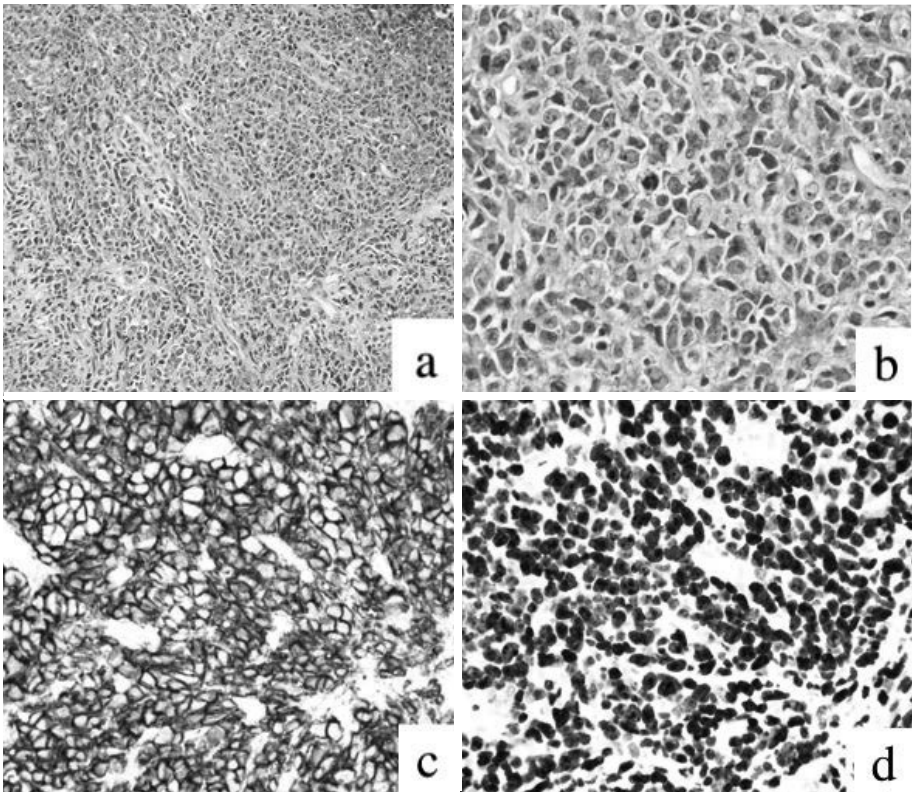

Fig. 2
a, b) Atypical cells with large similar circlular nuclei are diffusely increased (a: HE, ×40 b: HE, ×400).
c, d) Almost all tumor cells were positive for CD20 (c). Ki67 proliferation index accounted for approximately 80–90% of tumor cells (d).

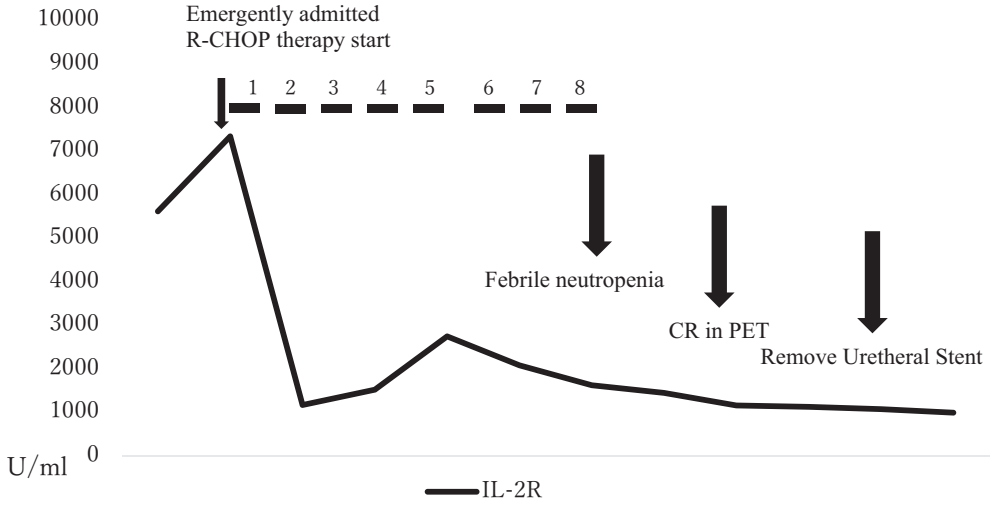

Fig. 3
Complete response (CR) was achieved after 8 courses of R-CHOP therapy.

gland predominantly, with or without involvement of adjacent tissue, 3) absence of involvement of the liver, spleen, lymph nodes or peripheral blood within 1 month of diagnosis of prostatic involvement. In this case a PET-CT scan was performed more than one month after diagnosis, so that our case satisfied these criteria and was thus considered to have arisen in the prostate gland.

As a background to diagnosis, malignant lymphoma of

Table 1 Reports of primary malignant lymphoma of the prostate gland in Japan after 2011

	Author	Year	Age (y)	PSA (ng/mL)	Symptoms	DRE	Diagnostic opportunity	Pathological findings	Stage	Treatment	Outcome
1	Toyoda	2011	78	3.99	Urinary retention	-	TUR	DLBCL	III	CT	PR
2	Monzen	2011	85	-	Dysuria・Hydronephrosis	-	NB	DLBCL	II	Obs	-
3	Manabe	2012	66	1.99	Urinary retention・Dyschezia	Enlarged Irregular	NB	DLBCL	I	CT	CR
4	Nishida	2012	87	Normal	Dysuria	-	NB	DLBCL	III	CT	Dead
5	Hori	2013	77	4.65	Lower back pain・Hydronephrosis	Hen egg size Irregular Stony hard	TUR	DLBCL	IV	CT	CR
6	Matsuura	2014	68	1.47	Hematuria	Enlarged hard	-	DLBCL	I	CT	-
7	Tachibana	2014	63	-	Dysuria	-	TUR	Follicular	IV	CT	CR
8	Nagata	2015	57	-	Dysuria・Frequent urination	Enlarged Irregular Elastic hard	NB	DLBCL	IV	CT	CR
9	Uemura	2015	71	-	Dysuria	-	TUR	MALT	I	Obs	Stable
10	Kinjyo	2016	65	Normal	MRI abnormality	-	NB	MALT	I	CT RT	-
11	Hayashi	2016	51	0.905	Urinary retention・Hydronephrosis	Hen egg size Irregular Elastic hard	NB	DLBCL	II	CT	-
12	Our case	2017	73	0.5	Lower back pain・Hydronephrosis・Dyschezia	Enlarged Irregular Stony hard	NB	DLBCL	IV	CT	CR

TUR, transurethral resection; NB, needle biopsy; CT, chemotherapy; Obs, observation; RT, radiotherapy; DRE, digital rectal examination; PSA, prostate specific antigen; MALT, mucosa assisted lymphoid tissue; DLBCL, diffuse large B-cell lymphoma; CR, complete response; PR, partial response; MRI, magnetic resonance imaging

the prostate gland is often found as a result of a prostate needle biopsy or transurethral prostatectomy following symptoms such as urinary retention, hematuria and frequent urination[3]. Symptoms and diagnoses for 53 cases in Japan were dysuria and frequent urination in 29 cases, hematuria in 6 cases, urinary retention in 8 cases, perineal pain, anal pain and dyschezia in 6 cases, hydronephrosis in 4 cases, MRI abnormality in 1 case, other in 5 cases (lower abdominal pain and ejaculation difficulty), and no description in 11 cases. In particular, cases after 2011 may be triggered by hydronephrosis or MRI abnormality. Even in asymptomatic patients, cases are sometimes found incidentally as imaging for various reasons has become more widespread. One case involved a patient who complained of defecation difficulties and needed a temporary colostomy[4]. At the time of diagnosis, serum PSA level was only slightly elevated in 27 of the 53 cases, and was within normal range in 17 cases; the maximum reported value was 13.8 ng/mL.

Rectal examination revealed prostate gland enlargement in most cases. Hardness varied from soft to stony hard, but 27 of 35 cases for which this was described were elastic hard to stony hard. In addition, all 6 cases reported after 2011 had findings of surface irregularities. Malignant lymphoma of the prostate gland should be considered as a differential diagnosis when a hard and irregular prostate gland is palpated and PSA level is low.

Regarding treatment, surgical therapy and radiotherapy were performed before the 1990s, but multi-drug combination chemotherapies such as R-CHOP therapy became common after treatment for malignant lymphoma was established[1]. Responses to treatment in the 53 Japanese cases were good, with 29 cases of complete response (CR), 5 cases of partial response (PR), 5 cases of death, 2 cases of follow-up with no treatment, and 12 cases without a description of treatment[3].

Prognostic factors such as the international prognostic index (IPI) are also used for aggressive lymphoma[5]. This index includes: 1) stage; 2) age; 3) serum lactate dehydrogenase (LDH) value; 4) performance status (PS); and 5) extranodal lesion number, classifying the presence of 3 items as high-intermediate risk, and ≥4 items as high risk. We examined 7 cases of DLBCL with stage III or more out of 53 cases in which IPI was described or estimated (**Table 2**). For convenience, outpatient visit cases were set to PS 0 or 1. In the 4 cases categorized as high-intermediate risk, 2 cases achieved CR and 2 cases achieved PR. In 3 cases categorized as high risk showed CR in 1 case and 2 deaths (gastrointestinal bleeding due to gastric metastasis of lymphoma, pneumonia). In general, high-intermediate risk shows a CR rate ≥50%, compared to <50% for high risk[6]. In the case of DLBCL of primary malignant lymphoma of the prostate gland, IPI may be useful as a prognostic predictor for other malig-

Table 2 Seven patients for whom the International Prognostic Index (IPI) was determined※

	Author	Year	Age	Ann Arbor	LDH	ENL	Outcome	IPI
1	Ninomiya	2000	66	IV	-	−	PR	≤3
2	Toyoda	2011	78	III	-	−	PR	≤3
3	Hori	2013	77	IV	Normal	+	CR	≤3
4	Nagata	2015	57	IV	-	+	CR	3
5	Kiuchi	2010	84	IV	-	+	Dead	5※※
6	Nishida	2012	87	III	-	+	Dead	≤4
7	Our case	2017	73	IV	423 U/mL	+	CR	4

ENL, extranodal lesion; PR, partial response; CR, complete response; LDH, lactate dehydrogenase
※Described in the literature as satisfying all IPI criteria.
※※Performance Status is assumed to be ≤1, except for reports by Kiuchi et al.

nant lymphomas. Meanwhile, observation without treatment was performed in two cases of DLBCL and mucosa assisted lymphoid tissue (MALT) type, both of which are under stage II[7]. In particular, MALT type is known to be of low grade and a good prognosis may be obtained by accurate histopathological diagnosis and staging. Molecular pathological diagnosis using flow cytometric surface marker tests and fluorescence *in situ* hybridization is becoming more frequently used for definitive diagnosis of malignant lymphoma. When primary malignant lymphoma of the prostate gland is suspected, fresh tissue not fixed in formalin needs to be collected at biopsy for these tests[8]. In our case, malignant lymphoma was not assumed to be present before biopsy, so fresh tissue was not obtained. Differential diagnoses for tumor masses in the area of the prostate gland along with low serum PSA levels include hematological diseases as in this case, small cell neuroendocrine carcinoma, ductal cell-type prostate cancer, prostatic stromal sarcoma, prostatic stromal proliferation of uncertain malignant potential, and urothelial carcinoma[9]. Even if the patient's PSA level is relatively low, when digital rectal examination reveals stony hardness, urinary disorder and dyschezia are present with poor improvement following treatment, we should further investigate via imaging and tumor marker examination considering with the possibility of malignant lymphoma of the prostate gland. Primary malignant lymphoma of the prostate gland has shown good clinical outcomes in recent years, but prognosis remains poor in subsets such as elderly patients and patients with advanced-stage disease. Early detection and intervention are required.

Conflict of Interest: The authors declare that they have no competing interests.

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