CASE REPORT

Primary follicular lymphoma of the prostate

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ABSTRACT

Only 5 cases of follicular lymphoma (FL) have been reported in the prostate. A 68-year-old man presented with dysuria. Laboratory data did not indicate malignancy in the prostate with serums PSA of 4.6 ng/ml. Imaging techniques identified no tumors and lympho-adenopathy other than the prostatic enlargement. The patient was clinically diagnosed as prostatic hyperplasia, and trans-urethral resection of prostate (TURP) (65 g) was done. Histologically, the TURP-specimens showed severe nodular proliferation of atypical small lymphocytes consisting of small centrocytic lymphocytes and large centroblastic lymphocytes, the number of the latter being 2/HPF. Immunohistochemically, the tumor cells and nodular areas were positive for CD45, CD20, CD79a, bcl-2, bcl-6, and CD10. They were negative for pan-cytokeratin (AE1/3, CAM5.2), CD3, CD45RO, CD56, PSA, chromogranin-A, synaptophysin, NSE, CD138, CD15, CD30 and cyclin D1. No significant number of plasma cells were seen by immunohistochemistry for light chains and CD138. A pathological diagnosis of primary FL (grade 1) of the prostate was made. No tumors were identified by various imaging techniques, and the prostatic FL was diagnosed as primary. The patient underwent low-dose R-CHOP chemotherapy and focal radiation, probably resulting in complete remission. No recurrence has been found 5 months after the diagnosis.

Key Words: Prostate, Follicular lymphoma, Histopathology

1. INTRODUCTION

Malignant lymphoma of the prostate is very rare.[1–3] A group of B-cell lymphomas composed of small lymphocytes are characterized by relatively indolent clinical course.[4–7] These biologically indolent B-cell lymphomas includes the following five categories: small lymphocytic lymphoma/CLL (SLL/CLL), lympho-plasmacytic lymphoma (LPL), marginal zone B-cell lymphoma (MZBL) (aka MALT lymphoma), follicular lymphoma (FL), and mantle cell lymphoma (MCL). FL is thought to originate from germinal center B-cells, and is characterized by follicular or nodular structures, partially or totally, with a bcl-2 aberrant immuno-expression. It is subclassified into Grade 1, 2 and 3, depending on the amount of centroblastic cells. To date, only 5 cases of primary prostatic FL has been reported, with 2 being case reports[8,9] and the remaining 3 being case series,[1] to the best of the author's knowledge.

2. CASE REPORT

A 68-year-old man presented with dysuria, and consulted to urologists. The digital rectal examination revealed an enlarged prostate. Blood laboratory data showed no significant changes except for slightly elevated serum prostate-specific antigen (PSA) (4.6 ng/ml). He was diagnosed as having prostatic hyperplasia and underwent trans-urethral prostatic resection (TURP). Imaging techniques including X-ray, ultrasound, computed tomography (whole body), and magnetic resonance showed no abnormal findings except for the pro-

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static enlargement.

Microscopically, heavy infiltrates of small atypical lymphocytes were recognized in numerous sections of the TURP specimens which weighed totally 65 g (see Figure 1A-B). They occasionally formed follicular structures (see Figure 1C), while a minority formed compact architectures. The follicular structures were composed of small atypical lymphocytes (centrocytes) and large lymphocytes with nucleoli and vesicular nuclei (centroblasts); the number of the latter was found to be 2/HPF (FL, Grade 1). Neither polarity nor tingible body macrophages were noted in the follicular areas. The aggregates of the lymphoid cells were adequate to be called as lymphoma, and the atypia of them corresponded to low-grade lymphoma (see Figure 1A-F). The tumor cells showed hyperchromasia and mild to moderate atypical nuclear features (see Figure 1). Some atypical lymphocytes had clear cytoplasm. Mitotic figures were scattered (see Figure 1B); the mitotic index was 3/10HPF. No necrotic areas were seen. No areas of diffuse large lymphoma were recognized. No features of Hodgkin's disease including Hodgkin and Reed-Sternberg cells were found.

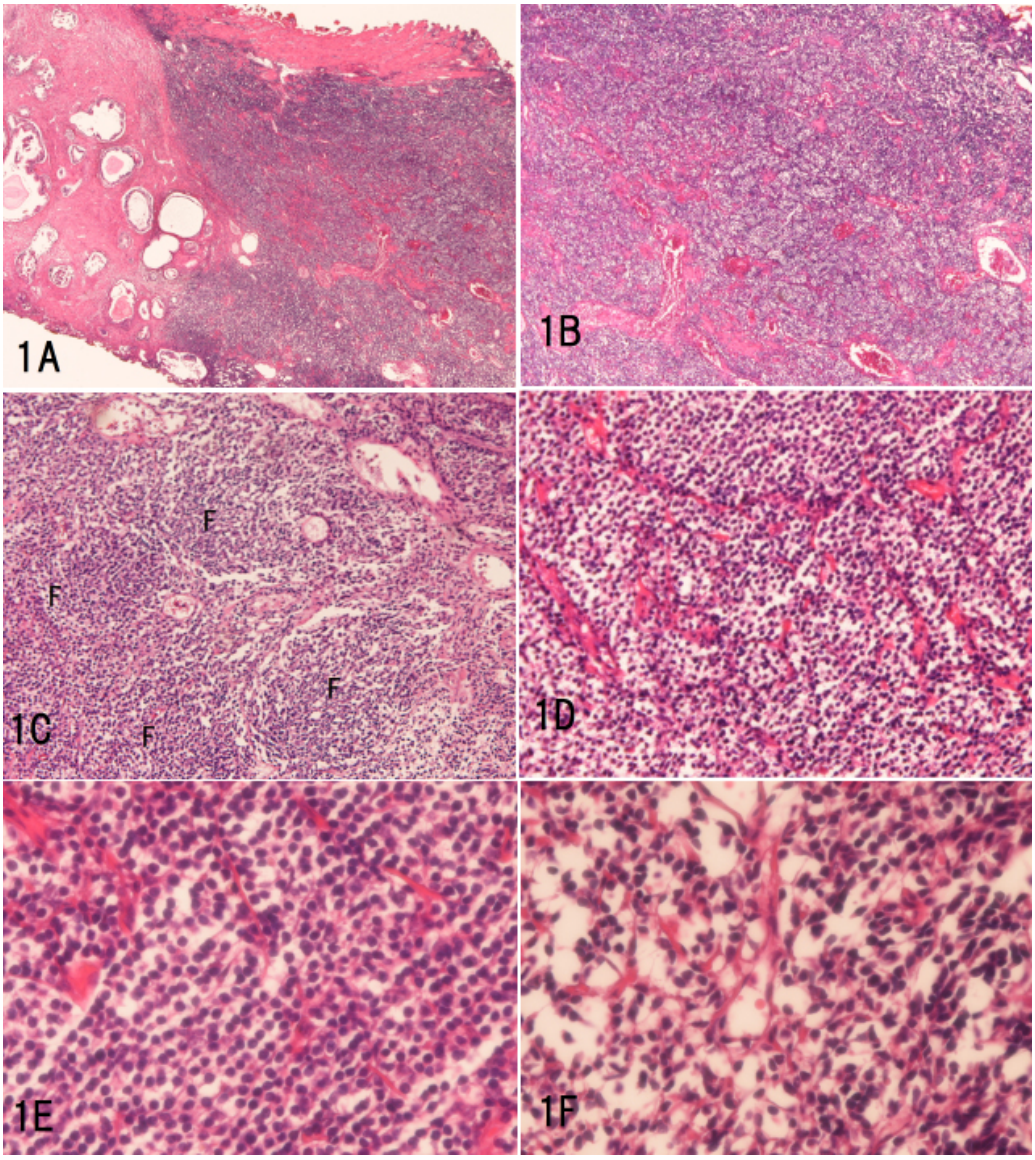

Figure 1. Histological features of prostate follicular lymphoma

A: Low power view of shows intense tumorous lymphoid infiltrates with focal follicular patterns in prostatic TURP specimens. HE, ×20. B: Medium-power view shows tumorous, monomorphic proliferation of atypical small lymphocytes. HE, ×100. C: Medium-power view shows a follicular pattern of small atypical lymphocytes. HE: ×100. D: High-power view shows atypical small lymphocytes with scattered mitosis. HE, ×200. E, F: Highest power view shows atypical small lymphocytes. Centroblasts are a few in number. The atypia of small lymphocytes (centrocytes) is evident. HE, ×250.

An immunohistochemical study was performed by Dako Envision method.[10,11] The tumor cells were positive for vimentin, CD45, CD20 (see Figure 2A), CD79a (see Figure 2B), bcl-2 (see Figure 2C), bcl-6, CD10 (see Figure 2D), Ki-67 (labeling index = 12%) (see Figure 2E), and p53 (focal; see Figure 2F). The areas of follicular structures were positive for bcl-2 (see Figure 2C), bcl-6 and CD10 (see Figure 2D). They were negative for pan-cytokeratin (CK) AE1/3, CAM5.2, CD3, CD45RO, CD56, chromogranin-A, synaptophysin, NSE, CD138, CD15, CD30, cyclin D1, and PSA. No significant number of plasma cells were seen by immunohistochemistry for light chains and CD138. A pathological diagnosis of primary FL (grade 1) of the prostate was made.

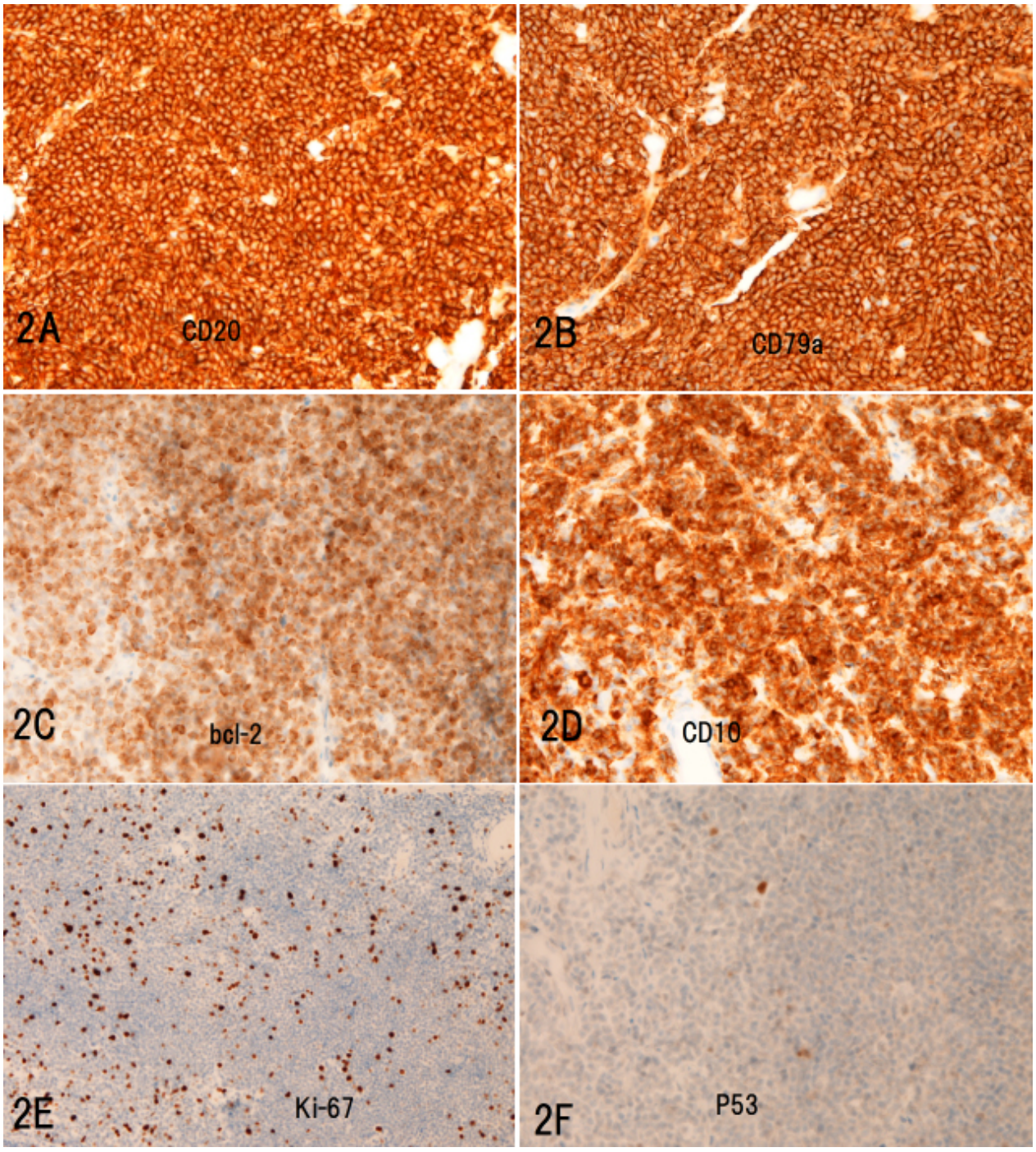

Figure 2. Immunohistochemical findings

The atypical small lymphocytes are positive for CD20 (A), CD79a (B), bcl-2 (C), CD10 (D), Ki-67 (labeling index = 12%) (E), and p53 (F: only focal). A-F: ×200.

Although no biopsy or smear of bone marrow was performed, the patient was diagnosed to be in Ann Arber stage 1. The staging was largely based on pathological findings and findings of imaging techniques. The patient underwent low-dose R-CHOP (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine, and prednisone) chemotherapy and local radiation (40 gray). Serum PSA decreased (2.3 ng/ml). Now, the prostate reduced in size (probable in complete remission), and no recurrence is fount 5 months after the diagnosis.

3. DISCUSSION

Since primary FL of the prostate is extremely rare, many differential diagnoses should be made. The present tumor should be differentiated from inflammatory infiltrates of lymphocytes in chronic prostatitis. The present case microscopically showed an obvious tumor formation and the lymphocytes showed significant atypia though the lymphocytes were small in size. In addition, the infiltrates were dense, heavy and compact, and the lymphoid proliferations were so marked that the TURP samples weighed as much as 65 g. Therefore, the present lymphocytic proliferation should be regarded as a neoplasm, and it is concluded that the lymphoid proliferations are not those seen in chronic prostatitis. The Ki-67 labeling index of 12% is above the cut-off value (10%) and implies a high proliferative fraction of tumor. The focal p53 immunoreaction seems not to indicate mutant p53 but to show wild-type p53. Because few plasma cells were noted, the light chain restriction was obscure. No molecular techniques such as IgH rearrangements were done in the present study.

It is very likely that the present tumor is primary in the prostate, because no other tumor formations were seen in various imaging techniques. No lympho-adenopathy was also seen. The present tumor is definitely FL in histological and Immunohistochemical appearances, and obviously belongs to B-cell lymphomas composed of small B lymphocytes. Among the five types of them, the present tumor is thought to be FL because of the presence of characteristic follicular structures and positive bcl-2 immunoreactivity. Although strict criteria of B-cell lymphomas composed of small lymphocytes are not performed in the present tumor, the present tumor is not SLL/CLL because of the present of follicular structure. The present tumor is not LPL because of negative plasma cells. The present tumor is not MZBL because of the lack of lympho-epithelial lesions, centrocyte-like cells, monocytoid B cells, and plasma cells. The present case is not MCL because of different histological features as well as of negative cyclin D1 protein.

The present prostatic FL should be differentiated from other types of lymphomas reported to be common in prostate,[1] such as diffuse large B-cell lymphoma (DLBCL), SLL/CLL, FL, and Burkitt lymphoma (Converted to Updated WHO classification from revised REAL classification[1]). The present case is apparently different from DLBCL which shows tumor lymphocytes having much more large, atypical features and not showing follicular formations. The present case is not SLL/CLL which belongs to lymphoma composed of small tumor cells like FL but never shows follicular structures. The present case was not Burkitt lymphoma which show monotonous proliferation of large tumor lymphocytes with scattered macrophages featuring "starry-sky appearance". The present case is of course not Hodgkin's lymphoma.

Malignant lymphoma of the prostate is extremely rare and represents only 0.09% of all prostatic neoplasms.[1–3] Most of prostatic lymphomas are secondary involvements of primary nodal and extra-nodal non-prostatic lymphoma. Bostwick[1] showed a clinic-pathological analysis of 62 cases of lymphoma of prostate which consisted of 30 secondary lymphomas, 22 primary prostatic lymphomas, and 10 cases that were unclassifiable as primary or secondary lymphomas. The 22 primary prostatic lymphomas included small lymphocytic lymphoma (n = 4); follicular center cell lymphoma, diffuse, small cell (n = 2); follicular center cell lymphoma, grade 1 (n = 1); small cleaved lymphoma (n = 1); grade 2 (mixed) lymphoma (n = 1); diffuse large B-cell lymphoma (n = 12); and high grade B-cell lymphoma, Burkitt-like (n = 2): the classification was according to the revised REAL classification.[1] They were most often seen in middle aged man with mean of 62 years and main clinical manifestation was signs and symptoms related to lower urinary tract obstruction.[1] Bouet et al.[8] reported an asymptomatic case of primary FL of prostate, which was discovered by digital rectal examination. Görgel et al.[9] reported a case of primary FL of prostate presenting with lower urinary tract symptoms. As mentioned above, Bostwick et al.[1] reported 62 cases of malignant lymphoma of the prostate, which included 3 cases of primary prostatic FL. They did not describe detailed clinical and pathological features of the 3 cases. Thus only 5 cases of primary prostatic FL have been reported in the English literature; so the present case is the sixth case. Therefore, the clinical and pathological features of prostatic FL are not known. Accumulation of cases is mandatory.

4. CONCLUSION

Herein reported is an extremely rare case of definitive primary prostatic FL. To the best of the author's knowledge, the present case is the sixth of primary FL in prostate in the English literature.

CONFLICTS OF INTEREST DISCLOSURE

The author declares no conflicts of interest.

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