CASE REPORT

Primary prostatic lymphoma with components of both diffuse large B-cell lymphoma (DLBCL) and MALT lymphoma.

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Abstract
Although lymphomas involving the prostate gland are rare, they should always be considered in the differential diagnosis. We report a case of primary prostatic NHL in a 70-year-old man presented with hematuria and urinary obstructive symptoms. Routine laboratory tests were within normal limits and prostate-specific antigen (PSA) was 0,01 ng/ml. The patient underwent radical prostatectomy. Histologically, two different coexisting patterns of non-Hodgkin lymphoma, infiltrating the prostatic tissue, were identified. The diagnosis of diffuse large B-cell lymphoma (DLBCL) presenting with an associated low-grade lymphoma of MALT-type was confirmed by immunohistochemistry. The patient received chemotherapy without any complication and has been followed-up for 2 years since surgical resection with no recurrence. The clinicopathologic characteristics of prostatic lymphomas are discussed, while reviewing the current English-language literature. Hippokratia. 2012; 16 (1): 86-89

Key words: diffuse large B-cell lymphoma, MALT lymphoma, NHL, prostate gland, primary prostatic lymphoma

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In the United States 20% of new cancer cases among the male patients involve the prostate, while 10% of the cancer related deaths is due to prostate carcinoma. The majority of these cases are adenocarcinomas[1] whereas other less common subtypes may occur. On the other hand, prostate lymphomas are very rare with few reported cases in the literature[2-4]. Primary Non Hodgkin lymphomas (NHLs) of the prostate account for 0.09% of prostatic neoplasias and 0.1% of all NHLs[2,5]. The classification of primary NHL of the prostate according to specific criteria has been suggested by Bostwick et al[6]. According to these criteria, a prostate tumor is classified as a primary NHL when i) there is no lymph node, liver, spleen or bone marrow involvement, ii) the major presenting symptoms involve the prostate and adjacent structures, iii) there is at least one month progression free interval from diagnosis.

All types of lymphomas have been described in prostate gland, with DLBCL (Diffuse large B-cell lymphoma) being one of the commonest and MALT (Mucosa associated lymphoid tissue) lymphoma one of the rarest[6]. The majority of MALT lymphomas occur in the gastrointestinal tract (50%) with stomach being the most common location (85%). Nevertheless, they have been detected at a variety of other sites[7-9], including the prostate. They usually have an indolent clinical course but some cases may progress to DLBCL. To the best of our knowledge, only 8 cases of primary prostatic MALT lymphomas have been previously reported without any coexistence with DLBCL[2,10-15]. Herein, we report an interesting case of primary prostatic DLBCL colocalised with a MALT lymphoma and discuss it in the light of the published data.

Case report

A 70-year-old patient was referred to Medical Oncology department after a radical prostatectomy performed two months earlier. He had haematuria and symptoms of obstructive uropathy during last year. Five months prior to his referral to the department of Medical Oncology, he underwent two transurethral interventions to relieve symptoms and a biopsy, which was non-diagnostic. Physical examination did not demonstrate any lymphadenopathy or splenomegaly. Routine laboratory tests were within normal limits and prostatic specific antigen (PSA) was found 0.01 ng/ml. The rest of the workup examination including a computerized tomography (CT) of the thorax, the abdomen and pelvis did not show extraprostate disease. A bone scan was also performed which did not show any osseous involvement.

Paraffin embedded tissue of radical prostatectomy specimen was sent for consultation to the Pathology department (Medical School, Aristotle University of Thessaloniki). Microscopic examination revealed prostatic tissue infiltration by neoplastic lymphoid cells. Most of the cells were large in size with centroblastic and immunoblastic characteristics (Figure 1A), whereas, small to medium sized cells with centrocyte-like characteristics were also apparent in some infiltration areas (Figure 1B). In these areas lymphoepithelial lesions (LELs) were also observed.

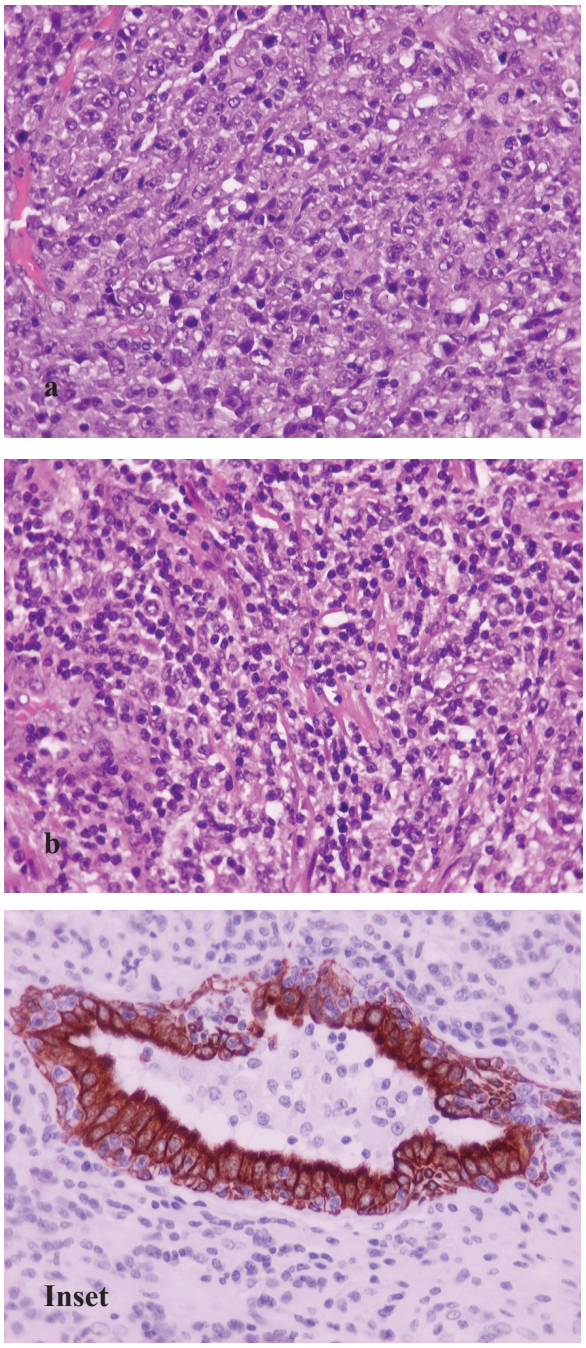

Figure 1: Infiltration of prostate gland by large lymphoid cells, H&Ex400 (a).
Area with MALT lymphoma, H&Ex400(b).
(inset) Lymphoepithelial lesion (epithelial cells highlighted by CAM5.2), IHCx400.

Immunohistochemical analysis was performed, using a standard streptavidin-biotin method. The lymphoid cells were positive for CD45, CD20 (Figure 2A), CD79α and bcl2. Additionally, a smaller proportion of the large cells were also positive for MUM1/IRF4, bcl6 and p53 (Figure 2B). On the contrary, the neoplastic cells were negative for CD45RA, CD45RO, CD3, CD5, CD10, cyclin D1, kappa and lambda light chains. Stains for cytokeratin CAM5.2 and CK7 highlighted the LELs (Figure 1B, inset). Ki67 staining index was approximately 70%. The above mentioned findings indicated the diagnosis of a DLBCL with a MALT lymphoma component.

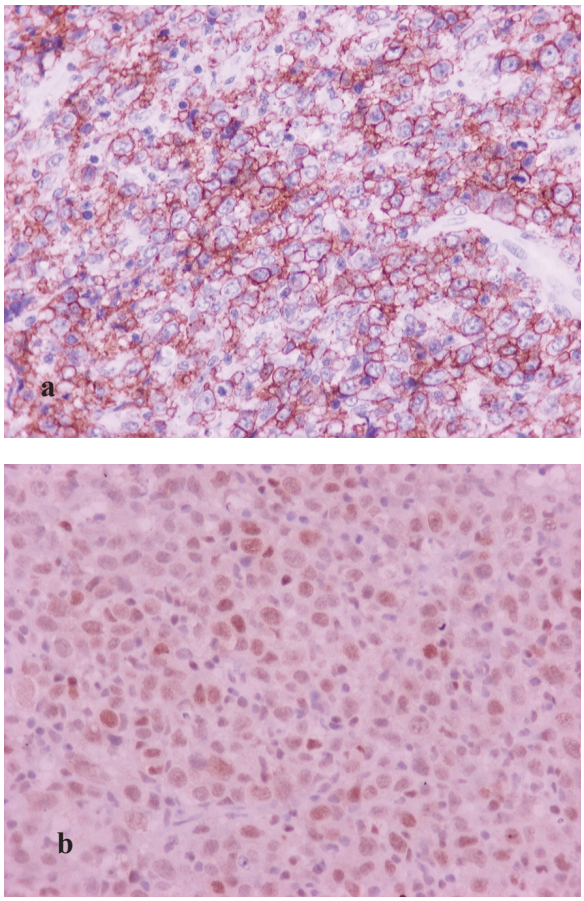

Figure 2: Neoplastic lymphoid cells positive for CD20 (a) and p53 (b), IHCx400

Bone marrow aspiration and trephine biopsy were suggested for completion of staging but were not performed due to patient's refusal. Thus, his disease was staged as a presumed stage Ie and he was treated with 6 cycles of cyclophosphamide, epirubicin, vincristine, prednisone plus rituximab (R-CEOP) combination chemotherapy without any complication. The patient is now free of disease in the post treatment follow up.

Discussion

A total of 165 cases of primary and secondary lymphomas involving the prostate has been reported[2-4]. The majority of them were NHL, whereas Hodgkin lymphoma of the prostate seems to be an extremely rare entity[3,6].

The largest series of the literature concerning prostatic lymphomas are those of Bostwick et al and Chu et al[2,6]. In the first study Bostwick et al classified 62 prostatic lymphomas as primary (22/62), secondary (30/62) and indeterminate (10/62). In the second more recent study, Chu et al presented 29 cases of incidental (18/29) and concurrent (11/29) prostatic lymphomas of B-cell origin. The incidental lymphomas consisted of 13 SLL/CLL

(Small lymphocytic lymphoma/B-chronic lymphocytic leukemia), 3 Marginal Zone Lymphomas (MZL), 1 Mantle Cell Lymphoma (MCL), 1 DLBCL and the concurrent ones of 4 SLL/CLL, 4 Follicular Lymphomas (FL), 2 MCL, 1 DLBCL.

The most common histologic types of prostatic NHLs are DLBCL and B-CLL/SLL[6]. On the other hand, only eight cases of primary MALT lymphoma of the prostate have been reported[2,10-15], without any evidence of transformation. The clinicopathological features of these eight cases are presented in Table 1.

In our case the presence of DLBCL with a MALT lymphoma component raised the question of transformation. Although there is actually no consensus on the definition of transformation, the presence of more than 20% of large lymphomatous cells and increased proliferation index has been proposed[16-20]. Ghesquieres et al proposed three patterns of morphologic transformation that could be observed: a) DLBCL with presence of low-grade lymphoma in a distinct area; b) colocalization, in the same biopsy specimen, of DLBCL and a lesion of low-grade lymphoma; c) aspect of low-grade lymphoma with an increased number of large cells and mitoses or increased proliferation index, or with sheets of large B cells[21]. Taking these three patterns into consideration, we considered that our case belongs to the second (b) pattern. Moreover, the large neoplastic cells in our case were positive to p53 antigen. It has been proposed that p53 mutations play a role in the pathogenesis of MALT lymphoma and predispose the cells to subsequent genetic alterations that may eventually lead to neoplastic transformation. Besides, Tai et al found that p53 gene mutations were more common in DLBCL with MALT lymphoma than in DLBCL without MALT lymphoma or in pure MALT lymphomas[22].

Primary NHL of the prostate share common clinical presentation with prostate adenocarcinoma and thus it is difficult for these entities to be distinguished on clinical grounds. The majority of the patients present with symptoms of urinary obstruction[6,23], renal failure[24], while other symptoms include haematuria, pain and rarely loss of weight[6,23]. B-symptoms may also be present[6,24]. Notably, concurrent prostatic adenocarcinoma has been reported in 10 cases[25].

Diagnostic approach includes medical history, physical examination (digital rectal examination), transrectal ultrasound, CT or Magnetic Resonance Imaging (MRI) scans and finally prostate biopsy. Digital rectal examination may reveal an abnormal prostate gland which can be hyperplastic, nodular or of hard consistency[6,23,26]. PSA levels usually are within normal range[6,23,26]. CT or MRI scans may reveal a heterogeneous mass or infiltrative lesions causing urinary obstruction[26]. Final diagnosis will be made by histological examination following prostate biopsy.

As has been mentioned above, primary lymphoma of the prostate is a rare disease and as such it is difficult to formulate guidelines, regarding the best treatment modality. Several treatment modalities have been reported in the literature, including radical prostatectomy, chemotherapy, radiotherapy or concurrent chemoradiotherapy. Currently, the treatment of choice is considered to be the standard cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) regimen. In a Japanese study, 22 cases of primary prostate NHL were discussed. All cases were treated with CHOP chemotherapy and complete response has been reported in 69% of them[27]. In another smaller study from M. D. Anderson 3 patients treated with doxorubicin based regimen achieved complete remission and remained free of disease after a follow up of 3 years[28]. Positive outcomes using the CHOP regimen have also been reported in sporadic isolated case reports[26,29]. Furthermore, the use of monoclonal anti-CD20 antibody (rituximab) has been employed in the treatment of primary prostate NHL and seems promising in those tumors expressing the CD20 antigen[26,30].

Finally, it should always be kept in mind that adenocarcinomas are not the only malignant entities encountered in the prostate gland and thorough histological examination is the only safe way, in order to avoid diagnostic mistakes, especially in the absence of elevated PSA levels.

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