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Case Report

Primary Prostatic Lymphoma Presenting with Features of Prostatism Developed Central Nervous System (CNS) Symptoms During Chemotherapy: A Case Report

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Abstract: Primary lymphoma of prostate is rare representing approximately 0.1% of all non-Hogdk in lymphomas. This type of lymphoma is more common in men with an average age of 60 years old. Dysuria is the most common symptom of prostatic lymphoma, which can lead to misdiagnosis of benign prostatic hyperplasia and adenocarcinoma easily. Besides, PSA was widely considered in the normal range in most patients with prostatic lymphoma, only a few patients showed elevated. We report a case of a 72-year-old primary prostatic diffuse large B-cell lymphoma patient with a significant increasing of PSA, developed Central Nervous System (CNS) symptoms after completing a cycle of R-CHOP therapy. Unfortunately, the patients received R-CHP in combination with high dose immunoglobulin, after a brief relief of CNS symptoms, the similar CNS symptoms returning again later. Involvement of CNS symptoms during therapy represents a serious complication of aggressive lymphoma, which is rare occurring nearly 5% of non-Hodgkin lymphoma and is considered as a high-risk model In conclusions, primary prostatic lymphoma with an increasing of prostatic-specific antigen is a rare case that is easily misdiagnosed. R-CHOP is till the recommended regimen, but other safe and effective alternatives are urgently needed when obvious CNS symptoms occurred during treatment.

Keywords: Lymphoma, Prostate, Chemotherapy, Central Nervous System Symptoms

1. Introduction

Primary prostatic lymphoma is rare representing approximately 0.1% of all non-Hogdkin lymphomas which occur in men aged 60 years in average [1, 2] Dysuria is the most common symptom of prostatic lymphoma, which can lead to misdiagnosis of benign prostatic hyperplasia and adenocarcinoma easily. Besides, PSA was widely considered in the normal range in most patients with prostatic lymphoma, only a few patients showed elevated [1, 3]. At present, there is no consensus on the treatment but the recommended treatments included radiotherapy, chemotherapy and prostatectomy referring to the case report [4] We report a case of a 72-year-old primary prostatic diffuse large B-cell lymphoma patient with a significant increasing of PSA, developed CNS symptoms after completing a cycle of R-CHOP therapy. We have discussed the clinical features, diagnosis and treatment of this rare patient in the light of the literature.

2. Case Report

A 72-year-old man presented only dysuria two years ago, however, significantly aggravated near a week, without systemic symptoms (Fever, shudder, weigh loss). He was treated for benign prostate hyperplasia with no improvement. On physical examination, erythematous, bleeding spot and enlarged superficial lymphnodes were not found and there were

not any abnormal findings on lung, liver and spleen. Related blood biochemistry test are shown below: Total prostatic-specific antigen (Total PSA): 19.35ng/mL (control: 0-4ng/mL), Lactate dehydrogenase (LDH): 272μ/L (normal: 109-245μ/mL), Erythrocyte sedimentation rate (ESR): 3mm/h, Tumor specific growth factor (TSGF): 81.6U/mL (control: 25-71U/mL). A computed tomographic (CT) scan showed an increased prostatic tumor measuring 56×58×73mm and rectum, seminal vesicle and bladder were invaded and multiple bone metastases (Figure 1). Prostate biopsy guided by ultrasound revealed diffuse large B-cell lymphoma (DLBCL). Immunohistochemical staining revealed LCA (+), CD20 (+), CD79a (+), MUM-1 (+), PAX-5 (+), CD10 (+), Ki-67 (+), bcl-6 (-), Vim (+) (Figure 2). Bone marrow aspirate and biopsy showed normal hematopoiesis status. After the diagnosis of P-DLBCL, germinal center B cell-like (GCB) type, was confirmed, the patient was treated with a cycle of R-CHOP (Rituximab 500 mg on day 1, Cyclophosphamide 800 mg on day 2, Doxorubicin 40 mg on day 2, Vincristine 4 mg on day 2, and Prednisone 80 mg on day 2 to 6). Twenty-six days later, the patient began to develop a series of neurological symptoms, included hoarseness, blurred vision, ptosis, headache, weakness and numbness of right leg. We checked a CT scan and magnetic resonance imaging (MRI) of skull, only cerebral arteriosclerosis and demyelination of white matter and half oval center in bilateral lateral ventricles was found. Cerebro-spinal fluid (CSF) tests displayed an increasing microprotein (MTP): 1916mg/L (normal: 100-450mg/L) and white blood cell (WBC): 25×10^6/L (98% is mononuclear cell). Lymphoid cells were found under microscope. Combined with the opinions of neurologists, we made the possible diagnoses, included central nervous system invasion of lymphoma, drug related neurotoxic side effects and Gillain-Barre syndrome (GBS). Then the patient was treated with a cycle of R-CHP (Rituximab 500 mg on day 1, Cyclophosphamide 800 mg on day 2, Doxorubicin 40 mg on day 2, and Prednisone 80 mg on day 2 to 6) combined with high dose immunoglobulin (on day 7-11). The neurological symptoms were relieved on day 9. The similar CNS symptoms returned again later. Then, two cycles of ESHAP (Etoposide 100mg/d1-4, Dexamethasone 20mg/d1-4, Cytarabine 1g/d5, Cisplatin 30mg/d1-4) and three courses of CNS prophylaxis (Methotrexate 5mg + Dexamethasone 5mg) were used. Obvious bone marrow suppression occurred after the second cycle of ESHAP. Eventually, the patient was died of CNS relapse and multiple organ dysfunction syndrome (MODS) five months after diagnosis.

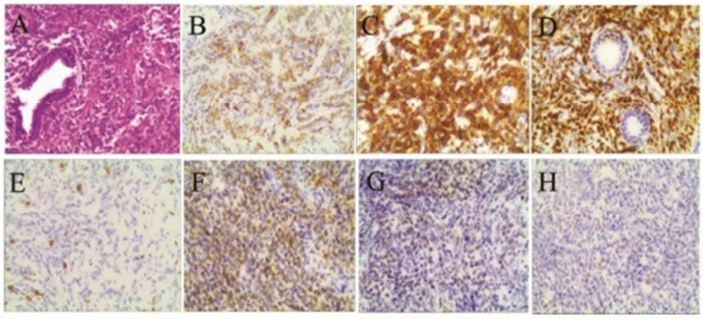

Figure 1. *Pelvic CT scan of the case at the initial diagnosis stage. A: plain scan, B: arterial phase, C: venous phase, D: delayed phase.*

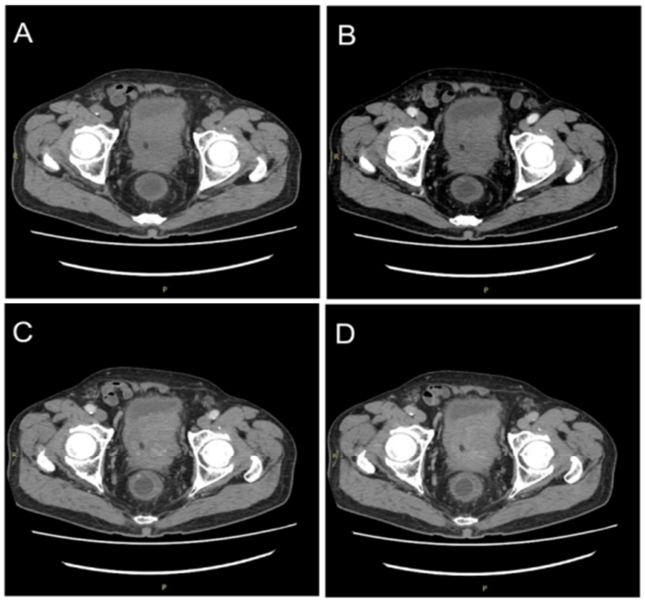

Figure 2. *Immunohistochemical characterization of the prostate biopsy sample. A:HE, x400; B: CD20 (+), x400; C:CD79a (+), x400; D:PAX-5 (+), x400; E:CD3 (+), x400; F:CD10 (+), x400; G:MUM1 (+), X400; H:bcl-6 (+), x400.*

3. Discussion

Lymphoma is a common malignant cancer. However, prostatic lymphoma is rare representing approximately 0.1% of all non-Hogdkin lymphomas [1, 2] Most of these patients are concentrated in elderly men with an average age of 60 years [2, 5]. Dysuria is the most common symptom of prostatic lymphoma, which leading to difficulty in distinguishing clinically from benign prostatic hyperplasia and adenocarcinoma of prostate. Bostwick DG et al believed that fever, anemia and other systemic symptoms might be the characteristic to distinguish with adenocarcinoma of prostate [6, 8]. However, our case does not match. PSA is produced by prostate epithelial cells, while prostate lymphoma is the source of mesophyll and PSA mostly in the normal range. However, Rao, RN et al indicated that nearly 20% of prostatic lymphoma patient with an elevation of PSA [3]. In the early stage, a small number of cases have reported the co-existence of non-hodgkin's lymphoma and prostate adenocarcinoma with an elevation of PSA [7]. In this case, clinical symptoms, serological and imaging examination all misled to the diagnosis of prostate adenocarcinoma. Prostate biopsy and immunohistochemical staining are the most important basis for the identification of prostate lymphoma and adenocarcinoma. Rituximab in combination with CHOP regimen is considered as the standard treatment for patients with advanced stage DLBCL [8]. After the diagnosis of prostate DLBC, the patient was treated with a cycle of R-CHOP therapy. Then, obvious CNS symptoms developed. The symptoms were relieved after a cycle of R-CHP therapy, but the disease progressed soon. Involvement of CNS during therapy represents a serious complication of aggressive lymphoma, which is rare occurring nearly 5% of non-Hodgkin lymphoma and is considered as a high-risk model [9]. According to the NCCN guide, three courses of CNS prophylaxis were used. And two cycle of ESHAP, which is considered as a second-line treatment of lymphomas, were applied. Unfortunately, the patient developed significant bone marrow suppression and died five months after diagnosis. Currently, the treatment of lymphoma has entered immunotherapy, and genetically engineered anti-CD19 chimeric antigen receptor (CAR) T-cells are a more accurate immunotherapy strategy. Multiple clinical studies have demonstrated significant efficacy of CAR-T cells in relapsed/refractory (R/R) B-cell lymphoma [10, 11]. CAR-T are also effective in central involved R/R lymphoma, demonstrating that they can pass through the blood-brain barrier [12]. In addition, Vari et al have shown that a higher proportion of programmed death receptor ligand 1 (PD-L1) is expressed in the nervous system, testicles and the patients with DLBCL, related to prognosis, which demonstrated PD-L1 can be a potential target for the R/R-DLBCL with CNS [13]. However, the clinical application of immunotherapy in primary extra-lymph node lymphoma is still lacking. In conclusion, primary prostatic lymphoma with an increasing of prostatic-specific antigen is a rare case that is easily misdiagnosed. R-CHOP is till the recommended regimen, but other safe and effective alternatives are urgently needed when obvious CNS symptoms occurred during treatment.

4. Conclusion

Primary prostatic lymphoma with an increasing of prostatic-specific antigen is a rare case that is easily misdiagnosed. R-CHOP is till the recommended regimen, but other safe and effective alternatives are urgently needed when obvious CNS symptoms occurred during treatment.

Abbreviations

CNS:	central nervous system
CT:	computed tomographic
CSF:	cerebro spinal fluid
CAR-T:	chimeric antigen receptor (CAR) T-cells
DLBCL:	diffuse large B-cell lymphoma
ESR:	erythrocyte sedimentation rate
GBS:	Gillain-Barre syndrome
LDH:	lactate dehydrogenase
MTP:	microprotein
MRI:	magnetic resonance imaging
PSA:	prostatic-specific antigen
PD-L1:	programmed death receptor ligand 1
TSGF:	tumor specific growth factor
WBC:	white blood cell

Statement

The manuscript has been read and approved by all the authors.

Conflict of Interest

All the authors do not have any possible conflicts of interest.

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