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Case Report

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High-Burden Metastatic Prostate Cancer Mimicking Lymphoma: A Case of Extensive Lymphadenopathy

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ABSTRACT

Supradiaphragmatic lymphadenopathy is a rare finding in prostate cancer. The occurrence of multiple lymphadenopathies forming a conglomerate that resembles lymphoma is also rarely encountered in prostate cancer diagnosis. We present the case of a 71-year-old man who has experienced bilateral leg swelling in the last four months. Multiple lymphadenopathies were detected in the intra-abdominal and supradiaphragmatic regions, along with several metastatic bone lesions. Histopathological and immunohistochemical evaluations confirmed a diagnosis of prostate adenocarcinoma, not otherwise specified (NOS), with a Gleason score of 4+3=7, classified as grade group III, indicating high-volume metastatic prostate cancer. The patient was treated with docetaxel and anti-androgen therapy. His condition was improved after eight cycles of chemotherapy, and his prostate-specific antigen (PSA) levels returned to normal.

Keywords: Metastatic prostate cancer; Lymphadenopathy; Chemotherapy; Hormonal therapy; Case report

INTRODUCTION

Prostate cancer is the fifth most common malignancy found in men in Indonesia. Data from National referral hospital showed that 52.2% of prostate cancer cases present at stage IV or with metastasis[1]. Common metastatic sites include bones, regional lymph nodes, liver, and lungs[2]. Metastasis to the peritoneal cavity is rarely seen[3]. Prostate cancer frequently involves regional lymph nodes, with metastasis typically spreading through the lymphatic system involving obturator, internal iliac, external iliac, presacral, and para-aortic nodes. However, lymph node involvement above the diaphragm is uncommon.[4] This case report presents a 71-year-old male patient with prostate cancer, presenting initially with bilateral leg edema, multiple lymphadenopathies extending above the diaphragm, and peritoneal carcinomatosis.

Case presentation

A 71-year-old male patient was referred to the medical oncology clinic with bilateral lower extremities edema since four months ago. He denied experiencing fever, night sweats, weight loss, abdominal pain, or hematochezia, but mentioned occasional difficulty in fully emptying his bladder and experiencing dribbling at the end of urination. He reported that he had history of prostate hyperplasia

seven years ago and received prostate reduction treatment, which had improved his symptoms at the time.

On physical examination, the patient was fully conscious, with blood pressure of 136/77 mmHg, heart rate 87 beats per minute, respiratory rate of 16 breaths per minute, and a temperature of 36.7°C. A firm 1.5 cm left supraclavicular lymphadenopathy was palpated, but no abdominal masses were detected. Bilateral leg edema was found, without tenderness or erythema.

A Doppler ultrasonography of the lower extremities revealed subcutis edema and thrombus in the femoral vein at the inguinal level. Abdominal CT scan showed multiple lymphadenopathy that conglomerated in the abdominal paraaortic, right and left inguinal, right and left iliac, as well as bilateral hydronephrosis, and enlargement of the prostate. A follow-up Prostate-Specific Membrane Antigen Positron Emission Tomography/Computed Tomography (PSMA PET CT scan) detected an irregular mass in the prostate infiltrating the right seminal vesicle and bladder neck. Multiple lymphadenopathies were identified in perivocal, left inferior-supraclavicular jugular, left infraclavicular, paraoesophageal, paraaortic, aortocaval, pericaval, bilateral para iliac communis, bilateral internal and external iliac, and bilateral internal obturator. Additionally, bone metastases lesions were found in the bilateral caput humerus, right scapula, posterior and lateral costae VI-VII, sacral, pelvic and both femurs (as shown in Figure 1).

Laboratory tests revealed anemia with a hemoglobin level of 8.8 g/dL, serum urea at 44.9 mg/dL, serum creatinine at 2.1 mg/dL, and D-dimer level at 2,630 mg/dL. The lactate dehydrogenase (LDH) level was measured normal at 216 mg/dL and the PSA was elevated at 165 ng/mL. The patient subsequently underwent a laparoscopic biopsy of the intra-abdominal mass, prostate biopsy, and DJ stent insertion. Histopathological findings of intra-abdominal mass biopsy showed poorly differentiated carcinoma of unknown origin. Tumor cells form a solid structure with connective tissue stroma in between. Tumor cells have round/oval nuclei, pleomorphic, vesicular nuclei with prominent nucleoli, and eosinophilic cytoplasm. Some of the tumor cells show hyperchromatic nuclei with smaller size and eosinophilic cytoplasm. Mitosis is observed. Fibrotic stroma is infiltrated with chronic inflammatory cells. Immunohistochemical examination showed negative results for CK7, CK20, and chromogranin. Meanwhile, Prostatic Acid Phosphatase (PSAP) expression was diffusely positive in the cancer cells, also AMCR positive and AR positive, which indicate a prostate origin (Figure 2). The prostate biopsy examination confirmed the presence of prostate adenocarcinoma, not otherwise specified (NOS), with a Gleason score of 4+3, classified as grade group III.

The patient was then planned to receive a combination treatment involving Docetaxel chemotherapy and anti-androgen therapy. After completing eight cycles of Docetaxel prednisone chemotherapy along with anti-androgen therapy, the edema reduced, and the PSA level decreased to 1.16 ng/mL (Figure 3).

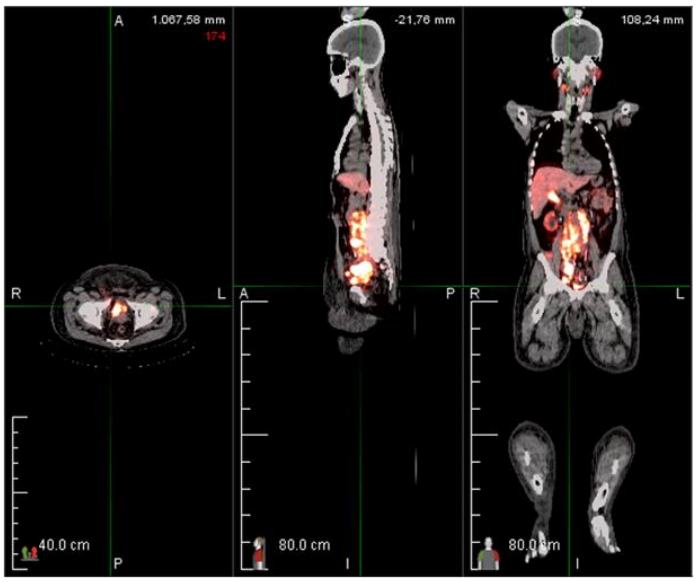

Figure 1. PSMA PET CT scan revealed increased uptake in the prostate, multiple lymphadenopathies, and multiple bone lesions

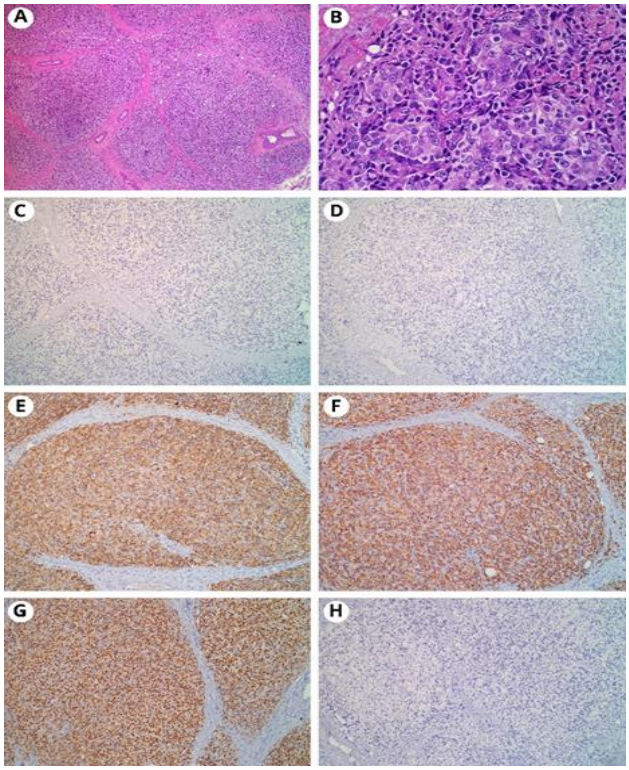

Figure 2. Representative images of patient (A) HE 40x, (B) HE 400x, (C) negative CK7 expression in (IHC 100x), (D) negative CK20 expression (IHC x100), (E) positive PSAP expression (IHC x100), (F) positive AMCR expression (IHC x100), (G) positive AR expression (IHC x100), and (H) negative chromonin expression (IHC x100)

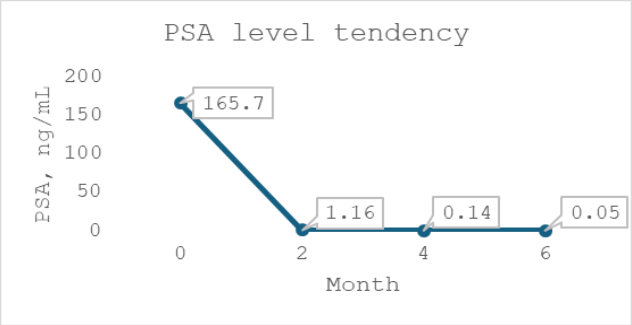

Figure 3. PSA level tendency during treatment showd markedly reduced and sustained after initiation of treatment with hormonal chemotherapy.

DISCUSSION

In this case, the patient initially presented with leg edema resulting from bilateral iliac and inguinal lymphadenopathy compressing the venous vessels. This patient did not complain of any symptoms and signs suggestive of lymphoma such as B symptoms or prolonged fever. PET CT scan revealed multiple lymphadenopathies in the perivocal chord region, left inferior supraclavicular, left infraclavicular, paraoesophageal, paraaortic, aortocaval, pericaval, bilateral common iliac, and bilateral internal and external iliac, as well as bilateral internal obturator regions. Initially, the picture of lymph node spread in this case more likely a lymphoproliferative disorder (lymphoma), infection, or collagen disease[5]. This pattern of lymph node involvement is uncommon in prostate cancer, as bones are typically the most frequently involved organs in prostate cancer metastasis. Moreover, supradiaphragmatic lymph node involvement, particularly in the jugular and suprailiac area, is rarely observed[2, 4]. Generally, such rare metastatic lesions occur alongside bone metastases. Prostate cancer metastasis is initially thought to occur hematogenously through the inferior vena cava, which may explain the frequent involvement of regional lymph nodes. Another hematogenous route could involve the venous system from the prostate to the spine, potentially spreading to the thoracic region[4]. The presence of a bulky intra-abdominal mass in this case could also resemble lymphoma. Prostate cancer generally progresses slowly, although in some cases, it can become aggressive. Up to this point, there has been one case report by Mahjoubi et al.[6] documenting similar case, reporting a 85-year-old man with a pelvic mass resembling intra-abdominal lymphoma.

Based on these findings, the medical team initially suspected lymphoma and decided to obtain representative samples from the intra-abdominal lymph nodes. However, the normal LDH levels and elevated PSA levels in this patient were inconsistent with lymphoma. Ultimately, histopathological results confirmed the diagnosis of high-volume metastatic prostate cancer. Immunohistochemistry examination in this case helped in making the diagnosis. The positive PSAP supports that the cancer cells originated from the prostate. PSAP

examination is important in cases of metastatic adenocarcinoma in the abdominal cavity, with multiple lymph node involvement[5,7]. The Gleason score for this case is 4+3=7, which is classified as grade group III, placing it into the intermediate category with a five-year recurrence-free rate of 65%. Grade group III has a higher mortality risk compared to grade group I (HR 6.0 relative to grade group I)[8,9].

This case is classified as high-volume metastatic prostate cancer according to the CHAARTED criteria, which include the presence of ≥ 4 bone metastases with ≥ 1 lesion outside the vertebrae and pelvis[10, 11]. The treatment for this patient includes administering docetaxel chemotherapy in combination with anti-androgen therapy. CHAARTED study data support this approach, showing that early chemotherapy combined with anti-androgen therapy leads to better survival outcomes (13.6 months) compared to anti-androgen therapy alone[11]. Following eight cycles of docetaxel and prednisone chemotherapy along with anti-androgen therapy, the patient showed improvement, with reduced leg edema and decreased PSA levels. Additionally, the patient received regular bisphosphonate therapy to manage the bone metastatic lesions.

This was a challenging case for the medical team. Initially suspicion of intra-abdominal lymphoma, so medical oncology and digestive surgery evaluation was undertaken. The location of the mass was mainly in the abdomen so laparoscopic biopsy was performed. When the pathologist reported suspicion of a prostate mass, a prostate biopsy by the urologist was carried out. The pathologist's foresight in evaluating histopathology and immunohistochemistry is important in this case. Appropriate diagnosis give a chance for medical oncologist to treat the patient based on the latest guidelines that gives better opportunity of therapeutic success.

Based on these case findings, it is important that we should keep in mind that patients with multiple lymphadenopathies without typical sign and symptoms of lymphoma, one possible differential diagnosis is prostate malignancy. PSAP examination is important in such cases to confirm or rule out malignancy that originated from prostate[5,7].

CONCLUSION

Metastatic involvement of supradiaphragmatic lymph nodes is a rare clinical manifestation in prostate cancer. Multiple bulky and conglomerated lymphadenopathies in the pelvic cavity can also resemble lymphoma, thus histopathological examination plays a crucial role in diagnosing atypical cases. This case was classified as high-volume prostate cancer and treated initially with chemotherapy and antiandrogen therapy.

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