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Case Report

A CASE OF PROSTATE ADENOCARCINOMA IN A 67-YEAR-OLD MAN MANIFESTING AS GENERALIZED LYMPHADENOPATHY MIMICKING LYMPHOMA

Abstract

Prostate cancer is predominantly a disease of older men. Patients generally present with urinary symptoms and rarely with metastatic disease. Prostate cancers most often have metastasis in regional lymph nodes, i.e the obturator and internal iliac nodes, by hematogenous or lymphatic spread, but metastasis to the supradiaphragmatic lymph nodes or generalized lymphadenopathy is rare. Generalized lymphadenopathy is seen in many metastatic neoplasms, especially in lymphoma and lung cancer. It is very rare in prostate cancer. We present an unusual case of a 67-year-old male with metastatic prostate cancer with generalized lymphadenopathy mimicking malignant lymphoma or lung cancer. The biopsy result indicated metastatic adenocarcinoma and prostate was found to be the origin. Diagnostic and therapeutic approach in this case is also discussed in the light of the literature.

Key Words: Prostate; Prostatic Neoplasms; Neoplasm Metastasis.

Olgu Sunumu

YAYGIN LENFADENOPATİ İLE SEYREDEN METASTATİK PROSTAT KANSERİ OLGUSU

Öz

Prostat kanseri, çoğunlukla yaşlı erkeklerde görülmektedir. Hastalar genellikle üriner sisteme ait semptomlar ile başvururlar. Nadiren de metastatik evrede gelirler. Prostat kanseri, hematojen veya lenfojen yolla bölgesel lenf nodlarına (yani obturatuar ve internal lenf nodları) ve/veya kemiğe metastaz yapar. Supradiyafragmatik lenf nodlarına metastazı oldukça nadir olmaktadır. Generalize lenfadenopati başta lenfoma, akciğer kanseri olmak üzere birçok metastatik neoplazilerde görülmektedir. Bununla birlikte generalize lenfadenopati prostat kanserinde çok nadir görülür. Bu yazıda, generalize lenfadenopati şikayeti ile başvuran ve lenfoma veya metastatik akciğer kanseri düşünülen 67 yaşındaki erkek hasta sunuldu. Biyopsi sonucu adenokarsinom metastazı gelen ve primeri prostat kanseri bulunan olgunun teşhis ve tedavisi literatür eşliğinde tartışıldı.

Anahtar Sözcükler: Prostat; Prostat Kanseri; Kanser Metastazı.

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INTRODUCTION

Adenocarcinoma of the prostate is the most common form of cancer and the second leading cause of cancer death in men (1). The lymphatic spread of prostatic carcinoma occurs initially in the obturator nodes followed by perivesical, hypogastric, iliac, presacral and para-aortic nodes. The regional lymph nodes are the single most common metastatic site (2-4). Generalized lymphadenopathy has been reported as a site of nonregional, extraskeletal metastasis, generalized lymphatic metastasis as the initial presentation of prostate cancer is extremely rare and a very uncommon manifestation (6-7).

Supradiaphragmatic lymph node spread of prostate cancer has been postulated to be by a hematogenous route via the vertebral venous system (Batson's plexus), accessible via direct extension from the primary cancer site (6-8).

Metastases to generalized lymph nodes can be the initial manifestation of different primary malignancies such as malignant lymphoma or other distant primaries, but the most frequently encountered is from the lungs in elderly individuals (9). In a case of prostate cancer with generalized lymph node involvement, diagnosis of prostate carcinoma is typically made using transrectal core needle biopsies; a histological diagnosis must be established as well.

CASE

A 67-year-old male smoker with generalized lymphadenopathy was referred to our hospital with complaints of vomiting, nausea, weight loss of 10 kg and severe back and leg pain lasting for the last two months. He had no history of previous disease or drug intake. His father was also diagnosed with prostate cancer. Upon admission, he refused the proposed digital rectal examination, but physical examination was normal. The patient's laboratory evaluation was within normal ranges after a serum creatinine test, and no evidence of anemia, leukocytosis, hypoalbuminemia, electrolyte imbalance or disturbed liver function tests was found. A complete metabolic panel was normal except for an elevated alkaline phosphatase 384U/L (reference range 38–126U/L).The patient underwent enhanced computed tomography (CT) scan of the thorax, abdomen and, pelvis. Massive mediastinal, intra-abdominal, retroperitoneal, and inguinal lymphadenopathies were noted (Figure 1). The presence of the above-described enlarged lymph nodes raised the possibility of lymphoma or lung cancer. The patient received tests for lung cancer, lymphoma, disseminated disease, etc. Fine needle aspiration cytology of a hilar lesion under CT-guidance was nonspecific. A bone marrow aspiration biopsy revealed infiltration with neoplastic cells. The patient's prostate specific antigen (PSA) was 240ng/ml. A biopsy of bone marrow was compatible with invasion of adenocarcinoma (Figure 2). The origin of the primary tumor was confirmed by prostate biopsy which revealed prostatic adenocarcinoma with a Gleason's score of 9 (4+5). The histologic picture was similar to that observed for the biopsied bone narrow. A whole-body bone scan revealed evidence of multiple bone metastases. Maximal androgen blockade was performed with adding bicalutamide to bilateral orchiectomy. The patient was treated with radiotherapy for bone metastases. PSA (prostate specific antigen) declined to 0.53 ng/ml in 4 months after orchiectomy. A repeat CT scan of the chest, abdomen and pelvis revealed a remarkable decrease in the sizes and number of the metastatic lymph nodes. At a follow-up 15 months after the initial diagnosis, the patient had urinary tract infection, progressive bone metastases and a serum PSA >200 ng/ml. The PSA continued to rise, indicating

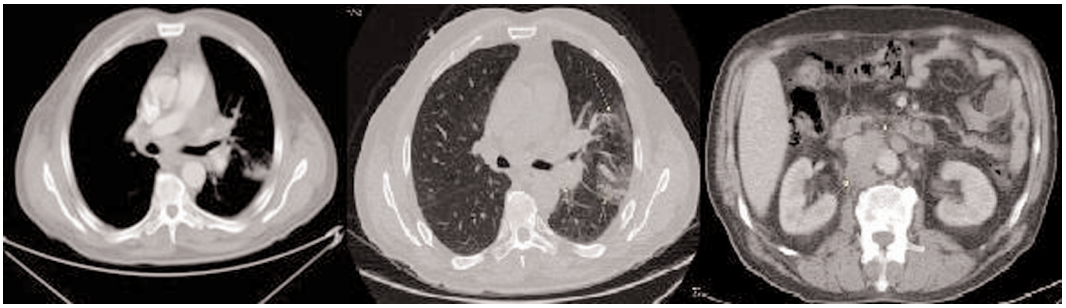

Figure 1— Computed tomography (CT) scan of the thorax, abdomen, and, pelvis, massive mediastinal, intra-abdominal, retroperitoneal, and inguinal lymphadenopathies were noted.

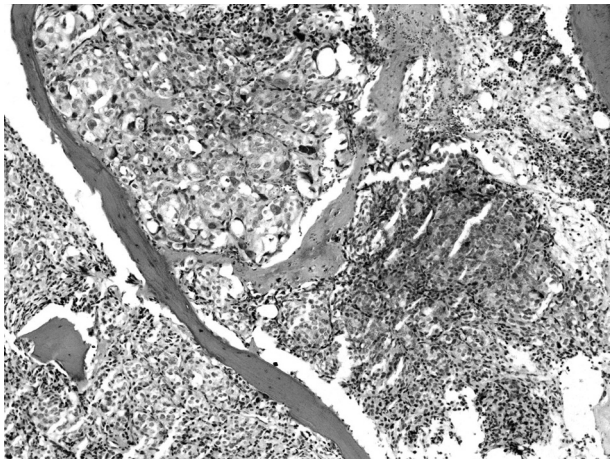

Figure 2— A biopsy of bone marrow was compatible with metastasis of adenocarcinoma.

the development of hormonerefractory disease. Additional treatment measures such as secondary hormonal manipulation, systemic chemotherapy, and radiation for local palliation were discussed with the patient who refused further treatment. Death occurred approximately 20 months after diagnosis.

Discussion

Prostate cancer is the most common solid organ cancer. In developed countries, prostate cancer accounts for about 25% of new cancers in men and is the second most common cause of death from cancer. Age, diet, hormones, sexually transmitted infections, alcohol, vitamins, ethnic origin and positive family history are known probable risk factors. However, risk associations have generally been inconsistent. To date the only 3 well-documented risk factors of prostate cancer are race, a family history of prostate cancer, and older age.

Family history is a well known risk factor for prostate cancer. However, epidemiological studies have consistently noted the familial clustering of the disease. The relative risk for prostate cancer increases in accordance with the number of affected members and the degree of relatedness, and is inversely related to the age at which family members were affected. The risk of prostate cancer in a first-degree relative (father, brother or son) increases a man's lifetime risk of the disease by 2-8 times. Most studies suggest that risks in brothers are greater than in father-son relationships (1-5). The late age of onset of the disease suggests a lack of strong predisposing factors for familial forms of this disease as in our case.

The clinical behavior of prostate cancer ranges from a slow growing, well-differentiated tumor of little clinical importance to an aggressive cancer with substantial invasive and metastatic potential (8,10). However, this tumor is responsible for only 2% of metastatic carcinomas of undetermined origin (11). The most frequent pattern of nonregional metastasis involves bones, lungs, liver and the epidural space, with supradiaphragmatic lymph node involvement being uncommon (1,2,9).

Prostate cancers most often have metastases in regional lymph nodes and bones by hematogenous or lymphatic spread. Primary lymphatic spread of prostate adenocarcinoma is to the obturator and internal iliac nodes. Secondary lymphatic drainage is from the external iliac, hypogastric and sacral lymph nodes. These are the nodes most often evaluated during the initial staging workup. Metastasis to the supradiaphragmatic nodes is rare (6-8). Few patients with prostate cancer present initially with generalized lymphadenopathy without any other concomitant distant dissemination. To the best of our knowledge a few cases have been reported in which generalized lymph nodes have been reported as the presenting sign (6,7,8,12-14).

The prostate is richly supplied with lymphatic vessels that drain into regional lymph nodes. Further spread occurs via the iliac and paraaortic nodes to the cisterna chyli and thoracic duct. Once this level has been reached, the tumor gains direct entry into the systemic blood circulation via the subclavian vein. This fact may explain the occurrence of metastasis in generalized lymph nodes (12-14). This pattern of nonregional lymphatic involvement observed in prostate cancer can clinically and radiologically simulate a malignant lymphoma (9,14,15), a fact impairing diagnosis, as observed in the current case and therefore generalized lympadenopathy is rare at diagnosis.

Diagnosis of metastatic adenocarcinoma was determined with the differential diagnosis for the primary site being lung, pancreas, stomach, and other solid organs (12). Serum PSA, a specific marker of prostatic tissue, permits the definition of the prostatic origin of a metastatic adenocarcinoma. The probability of lymph node lesions being due to distant metastatic disease from the prostate would have been very low; thus, prompting the clinicians to explore other etiologies such as those listed above. In our case, the tumor was initially misdiagnosed as an adenocarcinoma of unknown origin but the ab-

normal serum PSA level suggested the diagnosis of metastatic prostatic adenocarcinoma.

Prostate cancer is usually asymptomatic or may present with local symptoms. Patients generally present with urinary symptoms such as urinary urgency, nocturia, frequency, and hesitancy and rarely with bone pain due to metastasis (8,10). Saeter et al. (4) observed urinary symptoms in only 40% of cases with locally advanced prostate cancer associated with generalized lymphadenopathy. The majority of patients presented with urinary symptoms, prostatism, but our patient did not have these symptoms at initial presentation.

Clinically, prostate cancer is diagnosed as local or advanced, and treatments range from surveillance to radical local treatment or androgen deprivation treatment. Although the possibility of lymph node metastasis in the early stages of prostate cancer is rare, its presence will have important implications for treatment and management, such as the use of hormonal therapy with or without locoregional radiotherapy.

Presently, the primary approach to advanced prostate cancer is hormonal therapy, including orchiectomy, exogenous estrogens, antiandrogens, adrenal enzyme synthesis inhibitors, and gonadotropin-releasing hormone analogues (6,7,9,10). Some studies have shown that the combination of antiandrogen therapy with chemotherapy improves the survival time. Our patient was treated with antiandrogens with clinical response lasting for 15 months but then his disease rapidly progressed to bone metastasis. Generally, chemotherapy is used in patients with advanced prostate cancer when hormonal therapy fails. This failure is established based on clinical criteria and/or progression of PSA during hormonal therapy. In the present case, the patient refused futher treatment.

The presence of generalized lymphatic metastases does not worsen the prognosis of prostate cancer compared to tumors with the same Gleason score because even widespread lymph node involvement can be hormonally responsive. In contrast, bone metastases have been associated with a poor prognosis (6,12). In an observational study on 205 cases of metastatic prostate cancer, including 17 with distant lymph node metastasis, Furuya et al. (11) reported a better prognosis for patients with lymph node involvement only, even if nonregional, compared to those with bone metastasis.

The diagnostic difficulty in the present case was a result of the fact that the patient presented with supraclavicular, mediastinal, hilar, pulmonary and retroperitoneal lymph node involvement as the initial manifestation of prostate cancer. A suspicion of prostate cancer in men with adenocarcinoma of undetermined origin is important for an adequate diagnostic and therapeutic approach. It should be emphasized that male patients with metastatic adenocarcinoma of an unknown primary site should have lymph nodes biopsied.

Another major feature which makes this patient unique in presentation and in difficulty of diagnosis was the presence of distant metastases and lymphadenopathy in the absence of bone involvement. The above-mentioned clinical findings are relatively uncommon upon initial diagnosis (9), and the absence of urinary symptoms might have masked the suspicion of prostate cancer as the primary adenocarcinoma that mimics a metastatic lung cancer or a lymphoma (10). The rapid and dramatic regression of the lung lesions and of the lymph nodes confirms their metastatic nature and shows androgen deprivation to be an effective treatment.

In conclusion, this report emphasizes the difficulty in diagnosing men with adenocarcinoma of unknown origin, which clinically manifests as generalized lymphadenopathy in the absence of urological complaints.

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