Generalized lymphadenopathy as the first manifestation of prostatic cancer

Sharon Saada, Tony Hayek, Eugene Vlodavsky, Yaron Ofer, Anat Ilivitzky and Shadi Hamoud

Department of Internal Medicine E, Pathology unit, Urology Department, Department of Medical Imaging, Rambam Medical Center, Haifa, Israel

Corresponding address: Dr Shadi Hamoud, Internal Medicine E Department, Rambam Medical Center, Haifa, Israel.
Email: s_hamoud@rambam.health.gov.il

Date accepted for publication 23 August 2010

Abstract

A 72-year-old male was admitted with painful swelling of his left arm. Physical examination revealed supraclavicular lymphadenopathy with swollen left arm and a stony-hard prostate on rectal examination. Routine blood tests were normal. Doppler test showed deep vein thrombosis in the left arm. Tomography of chest, abdomen and pelvis showed generalized lymphadenopathy, suggesting lymphoma. Biopsy of a left supraclavicular node revealed adenocarcinoma of unknown origin. Colonoscopy and gastroscopy revealed no mass lesions. Total serum prostate-specific antigen (PSA) was 1000 ng/ml. Neoplastic cells were positively stained for PSA. Bone scintigraphy revealed abnormal uptake in T5 vertebra and sacrum. The patient was treated with subcutaneous enoxaparin and referred to oncologic care.

Keywords

Prostate carcinoma; generalized lymphadenopathy; metastasis.

Case report

A 72-year-old patient was admitted with a 1-day history of painful swelling of his left arm, following weight loss of 2 kg in the previous months with no anorexia or night sweats. The patient was known to have essential hypertension and hyperlipidaemia treated with enalapril, simvastatin and aspirin. Physical examination revealed non-tender swelling and redness of the left arm and enlarged left supraclavicular lymph nodes. Blood tests showed mild leukocytosis of 12,200 cells/μl and mild hyponatraemia (131 mmol/l). Lactate dehydrogenase (LDH) was within normal range. Chest radiograph was normal. Ultrasound Doppler of the left arm revealed thrombosis in the upper veins of the arm and enlarged jugular lymph nodes. Subcutaneous enoxaparin was started. Total body computed tomography (CT) showed generalized lymphadenopathy at the base of left neck and in the mediastinal, hilar, retroperitoneal and para-aortic areas (Fig. 1A–C).

A biopsy of a left-sided jugular lymph node revealed adenocarcinoma cells of undetermined origin. Colonoscopy and gastroscopy were performed and revealed one benign polyp in the right colonic flexure and antral ulcer, respectively. Rectal examination revealed a stony-hard prostate.
However, there were no symptoms of prostatism. Total serum prostate-specific antigen (PSA) was 1000 ng/ml. Neoplastic cells stained for PSA in immunohistochemical staining (Fig. 2A and B). Bone scintigraphy revealed abnormal uptake in T5 vertebra and sacrum. Enoxaparin treatment improved the swelling in the left arm, along with his general condition. Metastatic dissemination of prostatic carcinoma was confirmed and the patient was referred to the oncology clinic.

**Literature review**

Prostate cancer is the second most frequent cancer in males in the United States, with an estimated 232,090 new cases and approximately 30,350 deaths in 2005\[^1\]. However, it is responsible for only 2% of metastatic carcinomas of undetermined origin\[^2\]. It is generally slow growing and therefore symptoms are unlikely before disseminated disease appears. One-third to one-half of patients have metastatic spread at presentation\[^3\].

The most common sites of metastasis are bones and regional lymph nodes, followed by lung, liver, brain and the epidural space. Supradiaphragmatic lymph node involvement is uncommon\[^2\]. The regional lymph nodes most often involved are the obturator, internal and external iliac nodes, followed by the presacral and para-aortic nodes\[^4\]. Distant metastases are relatively rare at diagnosis, and include supraclavicular, mediastinal, pulmonary and retroperitoneal nodes\[^5\], a pattern that clinically and radiologically simulates malignant lymphoma.

The prostate is supplied with lymphatic vessels that drain into the obturator-hypogastric and presacral nodes. Further spread occurs via the iliac and para-aortic nodes to the cisterna chyli, thoracic duct, and then into the systemic blood circulation via the subclavian vein. The left supraclavicular lymph nodes are located close to the entry of the thoracic duct into the left subclavian vein, into which they drain (via the left jugular trunk). It is possible that tumour cells lodge in these nodes by retrograde spread\[^6\].

The distant lymph nodes most commonly affected are the left supraclavicular nodes\[^6\]. A retrospective survey of 250 cervical lymph node biopsies yielded 11 cases of metastatic prostate
carcinoma (4.4%), all on the left side\[^{4}\]. Metastatic involvement of the right cervical lymph nodes has been described, but is extremely rare\[^{7}\].

Mediastinal lymph node involvement has been reported in approximately 10% of autopsy cases of prostate carcinoma, but is rare during the early stages of the disease\[^{8}\]. Pulmonary metastases are common in advanced disease with autopsy studies showing an incidence of 25% to 50%, but are rare at diagnosis\[^{9}\]. A review of 178 cases of carcinomatous lymphangitis has shown that only 7 patients (3.9%) had prostate carcinoma as the primary focus\[^{9}\]. Abdominal metastases have only been reported in isolated cases\[^{10–12}\].

Clinical symptoms of prostatism (dysuria, nocturia and urinary retention) are poor predictors of prostate carcinoma. Saeter et al.\[^{13}\] observed urinary symptoms in only 40% of cases of locally advanced prostate cancer associated with generalized lymphadenopathy.

Serum PSA level is a specific marker of prostatic tissue that permits the definition of the prostatic origin of a metastatic adenocarcinoma. High levels of PSA may also be observed in benign prostatic hyperplasia and may be normal in poorly differentiated metastatic prostate carcinoma. Epstein and Eggleston\[^{14}\] showed that prostate tumours with normal or slightly increased PSA are more aggressive than other types. Normal levels of serum PSA and/or free/total PSA fraction are not sufficient to exclude the diagnosis of prostate carcinoma. Jones and Anthony\[^{5}\] observed an increase in PSA in only 5 (45.5%) of the 11 cases reported with prostate carcinoma and cervical lymphadenopathy.

The primary approach to advanced prostate carcinoma is hormone therapy, which includes orchiectomy, antiandrogens, adrenal enzyme synthesis inhibitors and gonadotrophin-releasing hormone analogues. Large-scale randomized trials have shown that when used alone, these methods are comparable in their antitumor effects, differing only in terms of side effects and costs\[^{2}\]. Chemotherapy is used in patients with advanced prostate carcinoma after hormone therapy has failed\[^{6}\]. Failure of hormone therapy is established based on clinical criteria and/or increase in PSA level during hormone administration\[^{15,16}\].

The prognosis of patients with disseminated disease is difficult to assert because of the relatively small number of patients with prostate cancer and non-regional lymph node involvement, and because data regarding their prognosis are limited\[^{6}\]. Evidence suggests that the presence of generalized lymphatic metastases does not worsen the prognosis compared with tumours with the same Gleason score because even widespread lymph node involvement can be hormonally responsive\[^{13,17,18}\], unlike bone metastases, which have been clearly associated with a poor prognosis\[^{17,18}\].

**Teaching point**

A suspicion of prostate cancer in men with adenocarcinoma of unknown origin is important to consider, even in patients with generalized lymphadenopathy suggesting lymphoma. Because of the risk of prostate cancer, along with the relative accessibility of immunohistochemical staining for PSA of biopsied lymph nodes, which has been suggested for all cases of adenocarcinoma of unknown origin\[^{19}\], this test should be performed routinely.
References