Case Report

Dramatic mixed response of lymphangitic pulmonary metastases in newly diagnosed prostate cancer

Elan Gorshein, Robin Burger[1], Anna Ferrari[2], Tina Mayer[2]

Departments of Hematology and Oncology and [1]Pathology and Laboratory Medicine, Rutgers Robert Wood Johnson Medical School, [2]Department of Medical Oncology, Rutgers Cancer Institute of New Jersey, New Brunswick, New Jersey, USA

Abstract

Prostate adenocarcinoma, the most common cancer in males in the United States, is often diagnosed in the nonmetastatic setting. The prognosis with metastatic prostate cancer is less favorable, though treatment options are typically effective in controlling the disease for an extended period. Hormonal therapy is the backbone to the management of prostate cancer metastases, decreasing the level of the prostate-specific antigen and reducing the patient's cancer-related symptoms. Pulmonary metastases, a relatively uncommon initial site of disease involvement, are expected to respond in a similar fashion to hormonal therapy as other organ or bone involvement. This report describes a patient with a newly diagnosed metastatic prostate cancer and a dramatic mixed response to hormonal therapy. This case should remind clinicians that pulmonary disease from prostate cancer may be an early metastatic finding, and can potentially progress even in the setting of an otherwise appropriate response to treatment.

Keywords: Androgen deprivation therapy, lymphangitic carcinomatosis, prostate cancer

Address for correspondence:
Dr. Elan Gorshein, Departments of Hematology and Oncology, Rutgers Robert Wood Johnson Medical School, One Robert Wood Johnson Place, Medical Education Building, 3rd Street, New Brunswick, New Jersey, USA. E-mail: elang@rwjms.rutgers.edu
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INTRODUCTION

Metastatic prostate cancer typically connotes a poor prognosis, and 90% of the time involves skeletal metastases.[1,2] Pulmonary involvement, while noted in approximately 2% of patients with metastases, has been documented as high as 40% in postmortem cases.[3] Lymphangitic spread is the most common radiographic pattern in this setting. Nodules, masses, and effusions have also been documented.[4] The pathogenesis occurs through tumor embolism to the pulmonary microvasculature followed by infiltration of the lymphatic vessels, leading to fluid accumulation and tissue obstruction.[4] We present a case of *de novo* metastatic prostate adenocarcinoma with a dramatic mixed response to androgen deprivation therapy (ADT).

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CASE REPORT

A 62-year-old male with no prior medical history presented with progressive generalized bone pain and a fifty-pound weight loss over the prior 3 months. He was noted to have a prostate-specific antigen (PSA) level of 4100 ng/mL, a testosterone level of 135 ng/dL, and an alkaline phosphatase level of 3800 IU/L. Other than a hemoglobin level of 10.9 g/dL, the complete blood count, prothrombin time, and partial thromboplastin time were normal. A nuclear

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medicine whole body bone scan was consistent with a Superscan, showing diffuse skeletal radiotracer uptake and minimal activity in the genitourinary tract. A computed tomography (CT) of the chest, abdomen, and pelvis was significant for diffuse osseous metastatic disease, hepatic metastases, and mediastinal lymphadenopathy. There were scattered nonspecific pulmonary micronodules measuring up to 3 mm [Figure 1]. The patient was admitted to the hospital for pain management and failure to thrive and was started on ketoconazole, hydrocortisone, and bicalutamide. The following day, he received a loading dose of degarelix. Ketoconazole and hydrocortisone were subsequently discontinued. Within 24 h, the patient reported significant improvement in his symptoms. Approximately 3 days later, he began to experience dyspnea and hypoxemia, while the bone pain remained well controlled. The PSA level was down to 2476 ng/mL, and the testosterone level was <7 ng/dL. The hemoglobin was 6.8 g/dL, platelet level was 52,000/μl, and nucleated red blood cell count was 5/100/white blood cells. The clotting parameters were consistent with disseminated intravascular coagulation (DIC). The patient was afebrile during the development of these symptoms. A ventilation/perfusion scan demonstrated a low probability for acute pulmonary embolism. A chest CT was significant for stable findings of the osseous lesions, lymphadenopathy, and liver disease. However, there were increased bilateral lung opacities and pleural effusions [Figure 2]. These findings represented a significant change from prior CT chest performed 4 days prior. A bronchoscopy with bronchoalveolar lavage showed normal respiratory flora with cytology negative for malignancy, but a right middle lobe transbronchial biopsy with immunohistochemistry staining noted high expression of the androgen-dependent gene, NK3 homeobox 1 (NKX3.1), and low expression of the neuroendocrine tumor markers synaptophysin and chromogranin A, consistent with lymphangitic carcinomatosis from metastatic prostate adenocarcinoma. The patient's clinical status continued to decline, and he expired despite intubation and vasopressor therapy.

DISCUSSION

The dependence of prostate cancer on androgenic hormones is a well-established phenomenon. Despite significant responses in most patients treated with ADT, the majority will only temporarily benefit before disease recurrence. On average, this initial response to ADT lasts approximately 2 years.[5] Patients diagnosed with low baseline serum testosterone levels often present with a more aggressive disease.[6]

Our patient was diagnosed with prostate cancer in a hypogonadal state and in the metastatic setting. He was promptly started on aggressive systemic therapy and noted an immediate and significant improvement in bone pain. His PSA and testosterone levels were responding favorably. Nonetheless, he developed rapid respiratory distress from lymphangitic spread of the prostate cancer as well as DIC and passed away 2 weeks following the initiation of treatment. One explanation for this seemingly paradoxical finding may be evolving cancer cells that acquire a variant clone due to tumor-stroma interactions, which leads to androgen independence and disease progression.[7]

DIC is the most common coagulation disorder in patients with metastatic prostate cancer, described in up to 30% of cases, but often subclinical and rarely noted to have a clinical expression.[8] It occurs primarily in the setting of hormone refractory, high-risk disease, and suggests a poor prognosis.[8] Therapy focuses on treating the underlying malignancy, and the DIC typically responds favorably to

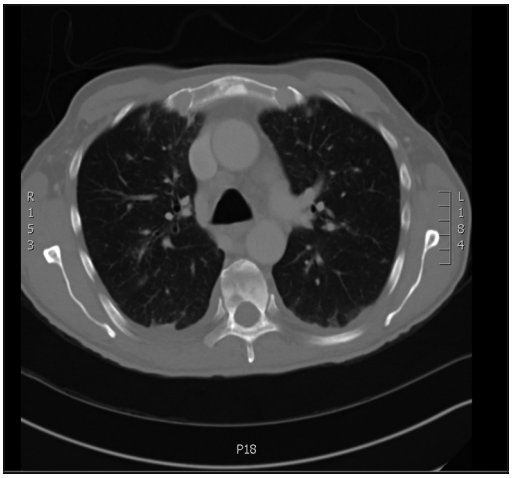

Figure 1: Computed tomography scan of the chest on admission

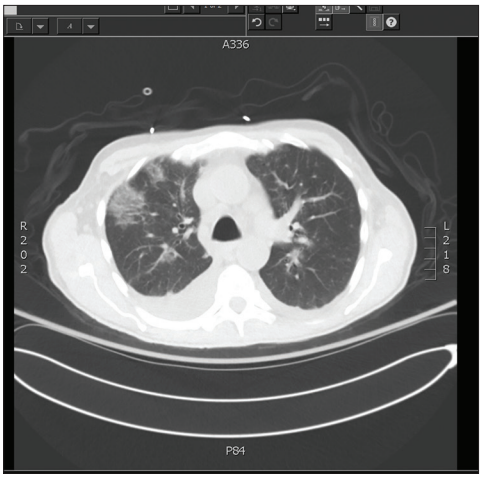

Figure 2: Computed tomography scan of the chest upon disseminated intravascular coagulation manifestation

ADT.[9] Lymphangitic carcinomatosis of prostate cancer is generally a late presentation of metastases for patients with documented castrate resistant disease following a course of ADT.[10] Typically, more than 75% of patients with pulmonary metastases experience significant disease improvement with ADT.[5,10] This case of a newly diagnosed, castrate-sensitive metastatic prostate cancer should alert clinicians that pulmonary lymphangitic spread and DIC may rapidly develop in a castrate-sensitive setting despite an otherwise anticipated response to ADT.

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Conflicts of interest

There are no conflicts of interest.

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