

CASE REPORT

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Pancytopenia as an initial manifestation of prostate cancer: a case report

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Abstract

Background: Prostate adenocarcinoma is the most frequent cancer type among men, followed by skin cancer. Patients with prostate cancer usually present lower urinary tract symptoms due to tumor involvement. Bone marrow invasion is associated with prostate cancer metastasis and is common if blastic lesions in bones are present but is very rare without a large bone involvement and uncommon as initial presentation.

Case presentation: We present a case of an 86-year-old Caucasian man with bone marrow invasion of prostate cancer without urological or bone-related symptoms and without prostate nodules. His findings were dyspnea, fatigue, and tachycardia. We detail the complete investigation of the case until we found the accurate diagnosis. The patient started treatment, but he had no response and so the oncology team started palliative care.

Conclusion: Bone marrow invasion as an initial manifestation of prostate cancer is not common, especially if no prostatic lesions are found. This report is important to provide additional information about prostate cancer management.

Keywords: Prostate cancer, Bone marrow invasion, Metastasis

Background

Cancer is a world health problem. Cancer is the second leading cause of deaths globally according to the World Health Organization (WHO). In 2013, the International Agency on Cancer Research (IARC) estimated that there would be 18.1 million new cancer cases and 9.6 million cancer deaths in 2018 [1].

Prostate cancer is the most common cancer among men, followed by skin cancer, and the second most frequent cause of cancer death among men [1]. In 2018, 1,276,106 cases occurred and 358,989 deaths due to prostate cancer were registered. Prostate adenocarcinoma is the most frequent cancer in men in Brazil. The National

Institute of Cancer (INCA) estimated that there were 68,220 prostate cancer cases in 2018–2019 [2].

The main risk factors for development of prostate cancer are age >50 years [3] or age >45 years with a family history of prostate cancer [4] and being African-American [5]. Furthermore, men with prostate-specific antigen (PSA) levels >1 ng/mL at 40 years and >2 ng/mL at 60 years are also at increased risk of metastasis and death [6, 7].

Prostate cancer is initially suspected by digital rectum examination and/or PSA levels. Definitive diagnosis depends on histopathological verification of adenocarcinoma in prostate biopsy [8].

Metastatic prostate cancer is usually common in bones, lung, and liver and has a 5-year survival rate of 29.3% [9]. Androgen deprivation therapy (ADT) has been traditionally used for the treatment of newly diagnosed metastatic prostate cancer [10]. More recently, some trials have incorporated early chemotherapy with taxanes along with ADT. Zhu et al. [11] showed a synergistic effect of

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taxanes and ADT, blocking microtubule activity mediated by androgen receptors.

Here, we present the case of an 86-year-old man with an atypical presentation of prostate cancer with biopsy-proven bone marrow invasion without huge involvement of bones and without visible prostate nodules.

Case report

An 86-year-old Caucasian man presented to the emergency department with a chief complaint of worsening dyspnea.

One month prior to admission, he started with progressive dyspnea on minimal effort, fatigue, and palpitations. He had undergone examinations and consultation with a cardiologist, who identified arrhythmia and started medication (metoprolol 25 mg). Because of the continuation of symptoms, after 1 week, a geriatrician performed general examinations, like a hemogram, PSA, urea, creatinine, and albumin. The examinations evidenced hemoglobin 12.0 g/dL, total PSA was 130 ng/mL, and free PSA >20 ng/mL. The patient stated that the last PSA done 2 years ago was normal. Because of this, he was referred to a urologist, who requested kidney and urinary tract ultrasound (US) and bone scintigraphy. US showed normal prostate size (10 cm³) and no nodularity. Scintigraphy showed probable bone metastases in the blades and spinous process of L4 vertebra and right iliac crest.

Because of persistent symptoms, he underwent new tests 1 month later; these showed that hemoglobin was 6.2 g/dL, platelets 51,000/μL, leukocytes 3950/μL, total PSA 84 ng/mL, and free PSA >20.0 ng/mL. Because of these examinations, he was referred to an oncologist, who prescribed degarelix (240 mg—first dose and 80 mg once per week for maintenance) as palliative treatment for metastatic prostate cancer and indicated transfusion.

The patient attended the emergency department with frank dyspnea 15 days after degarelix initiation. Tests

were performed that showed pancytopenia, and blood transfusion was indicated (2 units of red blood cells). The patient was hospitalized in the Medical Clinic Nursery for investigation of the condition.

The patient was evaluated by the hematology team, who performed a peripheral blood smear that showed marked anisocytosis at the expense of macrocytosis and elliptocytes, thrombocytopenia, and hypogranulation of neutrophils with segmentation failure. Examinations requested for pancytopenia investigation revealed the following: normal vitamin B₁₂ (482 pmol/L), normal folic acid (7.6 ng/mL), reticulocytosis (5.2%), and increased lactate dehydrogenase (LDH) (350 IU/L)

To assess the etiology of the pancytopenia, bone marrow aspiration and biopsy were performed. Myelogram showed markedly increased cellularity in clumps, cell conglomerates with non-hematological characteristics, suggestive of spinal infiltration due to non-hematological neoplasia and the bone marrow biopsy showed diffuse bone marrow replacement by metastatic adenocarcinoma (Fig. 1). PSA stain was consistent with tumor cells of prostatic origin (Fig. 2).

Prostate examination revealed normal prostate, without nodularity and normal consistency. Because of this, another kidney US and abdomen CT were performed. US showed non-obstructive nephrolithiasis on the left and diffusely thickened walls of the bladder. CT of the abdomen showed areas of increased density, mainly in L4 vertebra posterior elements, in the context suggestive of secondary neoplastic involvement. Lymph node metastasis in the para-aortic, interaortocaval, and right iliac chains. The largest of them, near the confluence of the right common iliac vein with the inferior vena cava, measured 1.7 × 3.1 × 3.8 cm. Pulmonary nodules—the largest of them 1.0 cm in the middle lobe.

The disease staging was TXN1M1. He was evaluated by an oncologist and then started docetaxel and leuprolide.

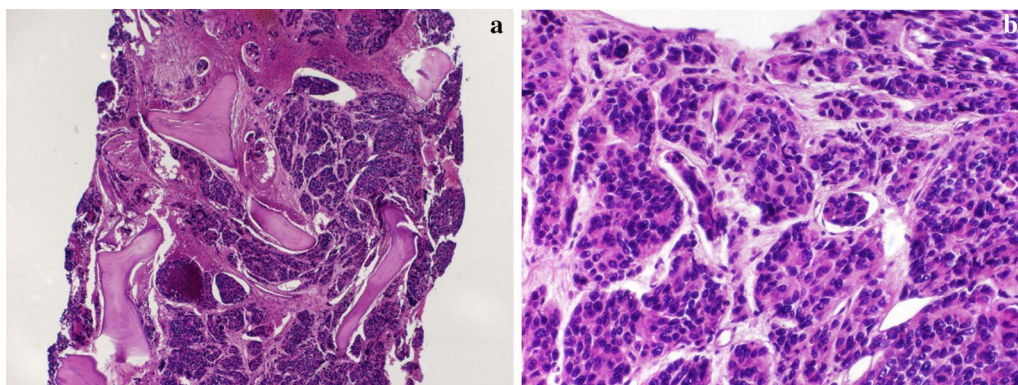


Fig. 1 a, b Bone marrow biopsy demonstrating diffuse bone replacement by metastatic adenocarcinoma. a (×10), b (×20)

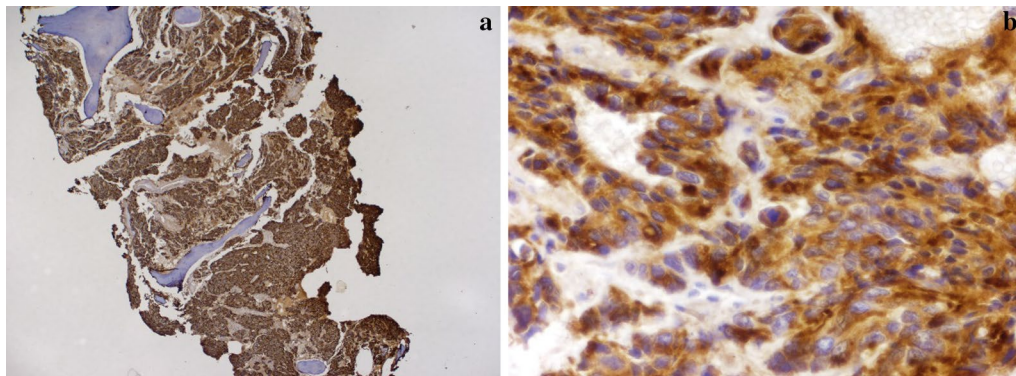


Fig. 2 a, b Bone marrow replacement by prostate adenocarcinoma. Prostate-specific antigen stains were positive. a ($\times 10$), b ($\times 20$)

Additionally, zoledronic acid was started intravenously. He had no significant improvement of symptoms after four cycles and the oncology team decided to initiate palliative care. In the follow-up, the patient needed hemotransfusion support twice.

The patient is still alive 1 year after the presentation.

Discussion

Prostate adenocarcinoma is the most frequent cancer type among men in Brazil, followed by skin cancer [2]. Prostate cancer is frequently asymptomatic, but the most frequent symptoms of prostate cancer are dysuria, increased urinary frequency, and urinary retention secondary to obstruction from prostate nodules.

This case is an interesting report for several reasons.

First, the patient did not present any urinary symptoms. The patient did present other signs and symptoms secondary to metastasis involvement; in this case, bone marrow invasion causing pancytopenia.

Second, bone, lung, and liver are the most common metastatic sites for prostate cancer [12]. When bone metastases are present, in large quantity, bone marrow invasion could happen and cause pancytopenia. In this case, the patient had bone marrow invasion without large involvement of bones. The suppression of blood cell lines causing a pancytopenia is less common and generally a later finding in the disease course when compared to osteoblastic/osteoclastic activity [13].

Third, the patient had a normal prostate examination, and both US and CT did not reveal any prostate nodule. If a patient has increased PSA levels and an abnormal digital rectal examination, transrectal US is performed for diagnostic management [14]. Nevertheless, the detection of prostate cancer has limited diagnostic accuracy, with 40% sensitivity and 50% specificity for detecting prostate cancer on the basis of PSA levels [14]. For image diagnostics, magnetic resonance

imaging (MRI) may have prognostic value in prostate cancer. A negative MRI had a negative predictive value of 84% in a large prospective study [15].

The prognosis of patients with prostate cancer with diffuse bone marrow involvement is very poor. A retrospective analysis of patients with metastatic prostate cancer, bone metastasis, and pancytopenia showed that the median survival was 3 weeks to 4 months [16].

Kunthur reported the successful treatment of a patient with castrate-resistant metastatic prostate cancer and severe pancytopenia with docetaxel chemotherapy [17]. In this case, our patient was transfusion dependent because of severe pancytopenia and there was a concern about docetaxel chemotherapy causing further worsening of cytopenia, but he still needed transfusion support and was unresponsive to docetaxel therapy.

Conclusions

This report has scientific interest because of the pancytopenia as an initial manifestation of prostate cancer in a man without urinary symptoms and no prostate nodularity. The diagnosis was evaluated by bone marrow biopsy and positive PSA stain, and he then started treatment. On the basis of history and physical examination, complementary examinations were performed, supporting the diagnosis.

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Authors' contributions

MACNS designed and wrote the manuscript. LGJ and VPRM contributed to medical record analyses. DMLT and CAL revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data and materials are available from the medical patients record at Clinical Hospital of State University of Campinas.

Declarations**Ethics approval and consent to participate**

The Statement of Informed Consent Form was presented to the patient and signed in accordance with Resolution No. 412/12.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal

Competing interests

The authors declare that they have no competing interests.

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