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CASE REPORT

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Intracranial metastasis from prostate adenocarcinoma: a case report and literature review

Suhu Liu, Ahmed Hassaan Qavi, Yoel Kim, Prasanta Basak and Stephen Jesmajian

Department of Internal Medicine, Albert Einstein College of Medicine, New Rochelle, NY, USA

ABSTRACT

Intracranial metastasis from prostate adenocarcinoma is rare. A 70-year-old African American male with a history of prostate adenocarcinoma for the last 14 years, presented to our hospital complaining of generalized weakness for the past 2 weeks. He was found to have fever with left ptosis and mild eyelid edema. Brain MRI showed dural metastasis. Two months after the first presentation, he was readmitted with a suspected acute cerebral vascular accident (CVA). CT brain showed vasogenic edema in the right subcortical, likely from intracranial metastasis. His acute neurological symptoms improved with intravenous dexamethasone. This case highlights the possibility of intracranial metastasis from prostate adenocarcinoma. With the advent of novel therapies for prostate cancer, which prolong life expectancy, intracranial metastasis from prostate adenocarcinoma may become an increasingly frequent clinical scenario.

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Intracranial metastasis; prostate adenocarcinoma; dural metastasis

1. Introduction

Aside from non-melanoma skin cancer, prostate cancer is the most common cancer among men in the USA and one of the leading causes of cancer death among men [1]. In most articles, the term 'prostate cancer' has been used interchangeably with 'prostate adenocarcinoma'. Some rare prostate tumors such as small cell carcinoma, stromal neoplasms, and lymphomas are not discussed here.

Unlike lung, breast, melanoma, colon, and kidney cancers, which commonly spread to the brain, intracranial metastasis from prostate adenocarcinoma is rare. In addition, unlike other malignancies where brain metastasis may occur at any stage of the diseases, intracranial metastasis from prostate adenocarcinoma typically occurs in the setting of widely disseminated bone and soft tissue disease. Most patients with intracranial metastasis from prostate adenocarcinoma are initially asymptomatic. Literature regarding clinical presentation of intracranial metastasis from prostate adenocarcinoma is limited to case reports with patients presenting with variable neurological symptoms. We present a unique case of intracranial metastasis from prostate cancer.

2. Case presentation

A 70-year-old African American male presented to the emergency department for generalized weakness. The weakness started about 1 year ago. Though he was able to ambulate, he felt that his legs did not have enough strength. During this period, he also had a feeling of tiredness and loss of appetite. He had a history of prostate adenocarcinoma diagnosed 14 years ago, initially treated with radiotherapy and leuprolide for 1 year. His cancer remained dormant for 10 years after which it metastasized to the bone and liver. He was then treated with bicalutamide and leuprolide, to which he responded well. He continued on abiraterone and enzalutamide in addition to leuprolide and denosumab for up to 1 year ago when he became lost to follow up. He was last seen by his oncologist 5 months prior to presentation for symptomatic severe anemia requiring multiple blood transfusions. His PSA at that time had risen to 96 ng/mL. Surveillance PET/CT scans at that time showed stable bone metastasis compared to PET/CT done 1 year ago. No hypermetabolic adenopathy was then identified.

On review of system, the patient reported chronic multiple bone and joint pain, which he attributed to his 'osteoarthritis'. He did not endorse cough, dysuria, headache, or focal neurological symptoms. On examination, temperature was 103.8 F, BP 102/69 mmHg, HR 102 BPM, RR 21 breaths/min and SpO2 98% on room air. He had poor oral hygiene and dentition. Pupils were equal, round, and reactive to light. Left ptosis and mild eyelid edema were noted. Peripheral neurological examination revealed no motor or sensory defects and deep tendon reflexes were normal.

CONTACT Suhu Liu liusuhu1@yahoo.com Department of Internal Medicine, Albert Einstein College of Medicine, New Rochelle, NY 10801

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Complete blood count revealed moderate normocytic anemia with Hb 7.3 g/dl. There was no leukocytosis or thrombocytopenia. Chemistry was significant for hypocalcemia (6.4 mg/dl) and elevated alkaline phosphatase (572 IU/L). A chest X-rayshowed no infiltrative pulmonary process, but extensive osteoblastic metastases with aggressive periosteal reaction was seen in multiple ribs and both scapula (Figure 1). He was empirically treated for sepsis with intravenous antibiotics. The fever, left eyelid ptosis, and swelling resolved after 2 days of intravenous piperacillin and tazobactam. Blood cultures were sterile. Due to lack of a clear source of infection, a contrast enhanced brain MRI and a lumbar puncture were performed. The lumbar tap was benign with a normal cerebrospinal fluid pressure, cell count, and chemistries. Brain MRI however showed leptomeningeal enhancement with a large area of dural and epidural hyperintensity (Figure 2), which was highly concerning for dural metastasis from disseminated prostate adenocarcinoma. The patient was subsequently discharged to short-term rehabilitation for physical therapy pending further workup and treatment. In the interim, two attempted bone marrow biopsies by hematologists and radiologists failed due to extremely sclerotic metastasis with no bone material retrieved.

Two months later, the patient was readmitted for an acute left sided facial droop, left hemiplegia, and urinary incontinence. He had no headache, syncope, fever, chills, nausea, or vomiting. On examination, he was febrile up to 100.6 F, HR 123 BPM, BP 112/74, RR 19 breaths/min and saturating at 100% on room air. Pupils were equally round and reactive to light. No ptosis was seen. Neck was supple. He had tachycardia with no murmurs or gallops. Lungs were clear to auscultation bilaterally. Patient was awake, alert, and oriented to the person, place, and time. Extraocular movements were intact and there was no gaze preference. He had a flattened left nasolabial fold and left sided facial droop. No tongue deviation was seen. Motor strength was decreased 3/5 on the left upper and lower extremities. Sensations were intact. Initial head CT was negative for hemorrhagic or ischemic stroke. However, serial CT scans revealed a focal area of right frontal cortical and subcortical hypodensity, either from vasogenic edema from brain metastasis or ischemia. The patient received aspirin and dexamethasone. Repeat brain MRI confirmed that the area of restricted diffusion likely represents tumor infiltration of cortex from adjacent dural metastasis rather than ischemic in nature. His facial drooping and left sided weakness significantly improved on day 3 of dexamethasone, which also supported that his acute neurological manifestation was more likely from vasogenic edema. Due to his debilitated general condition and overall poor prognosis, the patient decided to receive palliative care

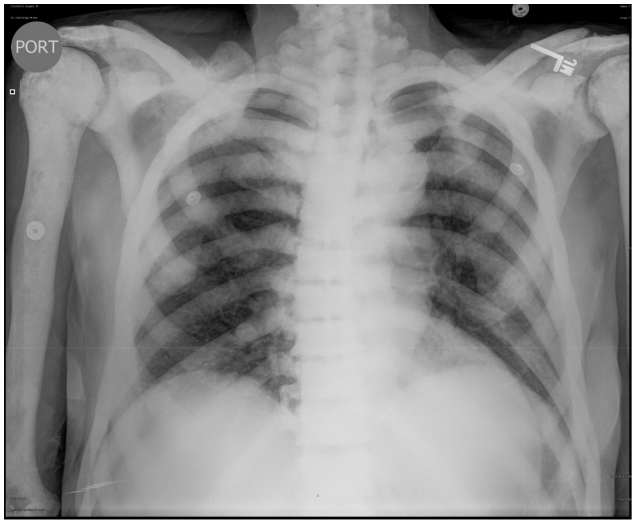

Figure 1. Extensive osteoblastic metastases from prostate adenocarcinoma.

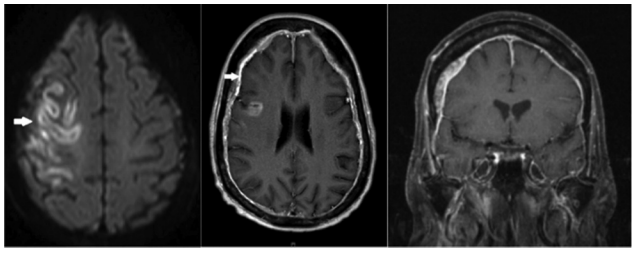

Figure 2. MRI Axial T1 Flair C+ post gadolinium contrast..

instead of radiotherapy for brain metastasis. He passed away 5 months after the diagnosis of brain metastasis.

3. Discussion

Clinically significant intracranial metastasis from prostate adenocarcinoma is extremely rare, with an incidence ranging from 0.04%-2% [2,3]. Although prostate adenocarcinoma is the main histological subtype of prostate tumor (>99%) [4], there are other rare tumor types arising from prostate tissue such as small cell carcinoma, squamous cell carcinoma, neuroendocrine carcinoma, stromal neoplasms, and lymphoma. Although intracranial metastasis from prostate adenocarcinoma is extremely rare, brain metastasis from other types of prostate tumors is much higher. In a retrospective study of patients with prostate carcinoma at MD Anderson cancer institute, CNS metastasis occurred in 119 of 15,359 patients with prostate adenocarcinoma (0.7%), versus 6 of 38 (15.8%) patients with prostate small cell carcinoma [2]. In another retrospective 11-year analysis in the MRI era, 0.13% (18 of the 13,547) of patients with prostate adenocarcinoma developed metastasis to the brain. The other histologic subtypes that metastasized to the brain at a higher rate include 1 of 10 small cell carcinoma patients (10%), 1 of 4 neuroendocrine patients (25%), and 1 of 1 osteosarcoma patient (100%) [3].

Advances in molecular medicine and development of new drugs have significantly altered the natural history and prolonged the life expectancy of patients with prostate adenocarcinoma. Prostate adenocarcinoma relies on androgen for its continued growth and the androgen signaling axis plays a pivotal role in its pathogenesis [5]. Androgen pathway modulatory therapy has been the backbone of treatment of primary and metastatic prostate adenocarcinoma. Hormone therapy includes androgen-deprivation therapy (ADT) with antiandrogens such as bicalutamide, or gonadotropin-releasing hormone (GnRH) agonist such as leuprolide. When prostate adenocarcinoma becomes unresponsive to ADT (castration-resistant prostate adenocarcinoma), addition of novel drugs that either inhibits androgen biosynthesis (such as abiraterone) or interferes androgen-receptor signaling (such as enzalutamide), improve survival and quality of life. Additionally, docetaxel combined with ADT has been shown to prolong survival in patients with prostate adenocarcinoma [6,7]. Immunotherapy with Sipuleucel-T, an autologous dendritic cell vaccine, is typically reserved for men who are minimally symptomatic with slow progression of diseases. Bone health is an additional therapeutic focus in the treatment of metastatic prostate adenocarcinoma. Denosumab, a human monoclonal antibody that inhibits osteoclasts, reduces bone metastasis without effects on overall survival [8]. Radium-233 is an alpha-particle-emitting radiopharmaceutical used in patients with symptomatic bone metastases and no known visceral metastases [9]. However, none of the novel therapies penetrates the blood–brain barrier.

With the above novel life-prolonging therapies, it is conceivable that an increasing number of intracranial metastatic diseases from prostate adenocarcinoma may be identified. For instance, in another single institute retrospective observational study, incidence of intracranial metastasis between the pre- and post-docetaxel era was analyzed. In the pre-docetaxel era, 0.8% of prostate adenocarcinoma patients developed intracranial metastasis, compared to 2.8% in post docetaxel era [10]. Since brain metastasis from prostate adenocarcinoma most frequently occurs in the setting of widely disseminated bone and soft tissue disease, this increase in the frequency of intracranial metastases from prostate adenocarcinoma is believed to be a consequence of prolonged survival.

Dural metastasis is a unique feature of intracranial metastasis from prostate cancer. Among all the patients with dural metastasis, the main primary tumor is prostate cancer [11]. Unlike other primary cancers, such as lung and breast, which are more likely to present as intraparenchymal metastases, the most common intracranial sites of prostate adenocarcinoma metastasis are the leptomeninges (67%), cerebrum (25%), and cerebellum (8%) [12]. In another recent retrospective institutional review to examine prostate cancer brain metastasis, 31 out of 6,595 cases (0.47%) were confirmed brain metastasis from prostate cancer. Among them, 19 of these were dural (61.3%) and 12 (38.7%) were intraparenchymal metastases. Gadolinium-enhanced MRI is essential to exclude or confirm the presence of brain metastases, although biopsy is sometimes needed to confirm the diagnosis, especially in patients with no known history of malignancy or history of multiple malignancies. When histology is not available, there are reports that CSF PSA level may be useful in identifying intradural metastasis from prostate adenocarcinoma [13].

In our patient, we were not able to obtain histological evidence despite multiple attempts to retrieve bone tissue due to extremely hardened bone. This finding is consistent with the character of bone metastasis from prostate cancer, which is well known to produce pro-osteoblastic factors to promote bone mineralization [14]. Cerebrospinal fluid (CSF) exam is of limited utility in diagnosing brain metastasis and is generally not necessary. Cerebrospinal fluid (CSF) examination in our patient was for the purpose of infectious disease work up. The results of a completely normal CSF analysis are

typical of patients with prostate adenocarcinoma brain metastasis. Although we do not have pathological evidence of leptomeningeal involvement with the widespread bony metastases, diagnosis of brain metastasis from prostate adenocarcinoma was circumstantial. In this case, the differentials on the acute CVA like presentation should always include vasogenic edema from metastasis versus ischemic events.

In conclusion, intracranial metastasis from prostate adenocarcinoma is rare. However, with novel therapies that significantly prolonged life expectancy, intracranial metastasis from prostate adenocarcinoma is becoming an increasingly frequent clinical scenario. Physicians should consider CNS metastasis in the differential diagnosis of various neurological presentations in men over 50 years of age. Gadolinium-enhanced MRI is essential if intracranial metastasis is suspected.

Disclosure statement

The authors report no conflict of interest.

ORCID

Ahmed Hassaan Qavi http://orcid.org/0000-0003-2219-2536

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