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## Metastatic prostate carcinoma: A rare presentation initially misdiagnosed as a rib fracture ☆☆☆☆

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### ABSTRACT

Metastatic prostate carcinoma mainly occurs in bone as an osteoblastic lesion or lesions in the pelvis, spine, or chest wall. We present a unique case of a singular metastatic osteolytic lesion in the rib initially misdiagnosed as a fracture in a 61-year-old male. A single rib fracture in a patient with no history of trauma should raise suspicion for metastatic disease. We would encourage prostate cancer to be included in the differential diagnosis for an osteolytic lesion in a male over the age of 40. We review the current literature on this rare presentation of bone metastasis as well as the pathogenesis of metastatic prostate carcinoma as it relates to a solitary metastatic osteolytic lesion.

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### Introduction

Prostate cancer is one of the most common malignancies and causes of cancer mortality in men. Metastatic bone deposits classically present as multiple osteoblastic lesions in the pelvis, ribs and/or vertebral column [1]. The percentage of bone metastases from prostate disease that are purely osteoblastic has been reported to be 70.9%, while 16.4% of bone metastases actually present as osteolytic lesions, and 12.7% present as mixed osteoblastic and osteolytic lesions [2]. It is extremely rare for primary prostate cancer to present as a singular osteolytic lesion. We present an unusual case of metastatic prostate carcinoma presenting initially as a rib

fracture, and we review the literature regarding the pathogenesis of metastatic prostate carcinoma.

### Case

A 61-year-old man with a history of obstructive sleep apnea, hypertension, hyperlipidemia, and severe obesity presented to the emergency department with spontaneous pleuritic left chest pain. The patient denied recent history of trauma as well as dyspnea or coughing. Computed tomography (CT) imaging showed a minimally displaced fracture of the seventh rib shown in Fig. 1. Supportive measures for rib fracture were

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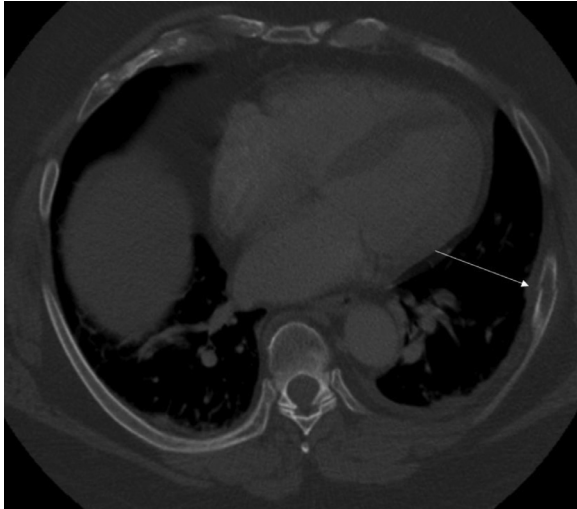
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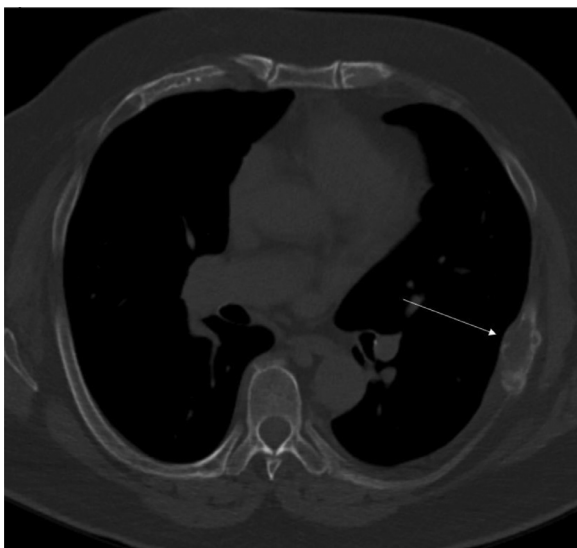
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**Fig. 1 – Initial CT of a 61-year-old male. The white arrow points to the posterolateral seventh rib fracture.**



**Fig. 2 – CT 4 months post the image in Fig. 1. The white arrow now points to a notable lytic lesion present.**

recommended to the patient, including pharmaceutical pain management and rest.

The patient was referred to orthopedic oncology clinic at 2 months reporting increased pain (8/10) with movement, breathing and coughing over the past week. His referral was initiated by a persistently positive bone scan ordered by his primary physician showing increased uptake in his left seventh rib (Fig. 3). Pain was noted on the left lateral side and posterior spine near the seventh rib. The patient denied fevers, chills, and unintentional weight loss. Repeat CT exposed a single lytic, aggressive-appearing lesion of the left lateral seventh rib as shown in Fig. 2.

Given the appearance on the repeat CT and lack of trauma, a pathologic fracture was suspected, and a core-needle biopsy was recommended. On questioning, the patient stated he

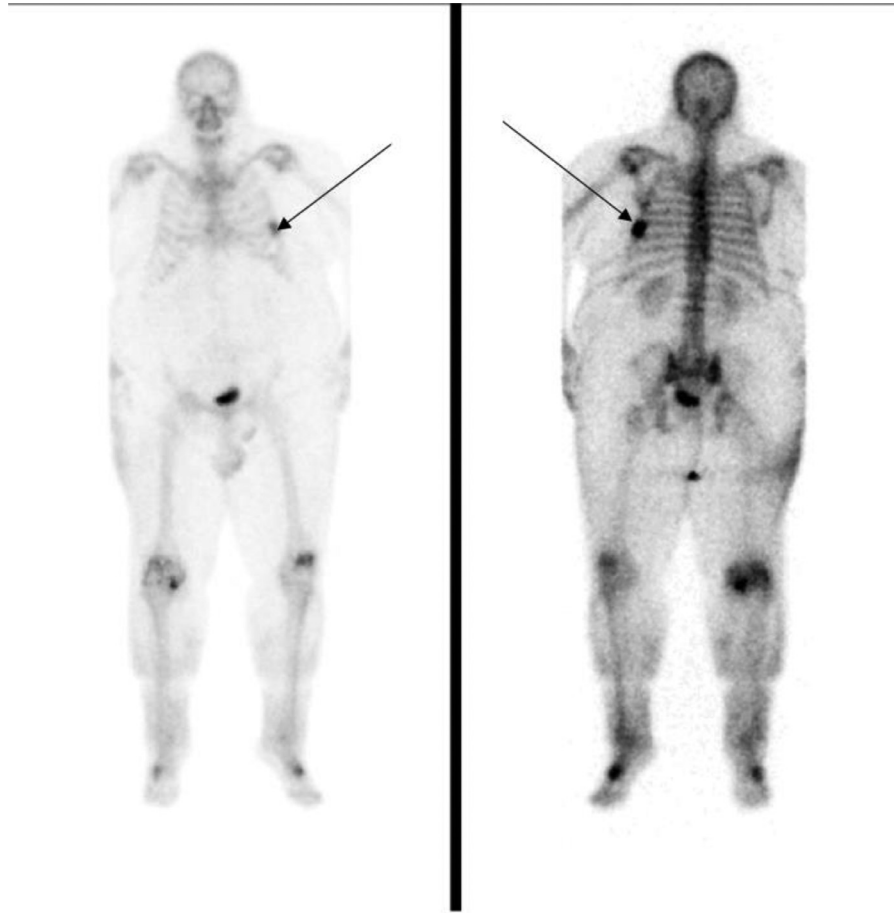
had a previous detected elevation of prostate-specific antigen (PSA) at 5.1 ng/mL and had been recommended for a prostate biopsy that he deferred. Repeat PSA was now 16.8 ng/mL, leading to an magnetic imaging resonance of the pelvis that showed a normal-sized prostate (28.34 cc) with a large (2.4 cm) left lateral peripheral zone lesion extending from the apex to the base of the gland performed prior to this evaluation. A broad base of contact and focal capsular bulge were noted, as well as enlarged left internal iliac and presacral lymph nodes. No definite extracapsular extension was visualized although these findings suggested clinically significant malignancy. Rib biopsy revealed glandular differentiation that stained positive for AE1/AE3, PSAP, and focally positive for PSA. The PSA staining pathologic slide is shown in Fig. 4. Considering the pelvic magnetic imaging resonance findings and lymphadenopathy, this was diagnostic of metastatic prostate carcinoma and no prostate biopsy was recommended by the urology and oncology teams.

We recommended radiation for local control and referral to medical oncology for systemic treatment. The patient was started on androgen deprivation therapy, including a GnRH analog and first-generation androgen blocker, as well as calcium and vitamin D. After 30 days of treatment with the first-generation androgen blocker, the patient will receive a second-generation drug such as apalutamide or enzalutamide. He is scheduled to receive stereotactic body radiation therapy for his rib metastasis (7 Gy treatments over 5 fractions). He will also undergo stereotactic body radiation therapy with supplemental image-modulated radiation therapy for his prostate primary and pelvic lymph node metastases.

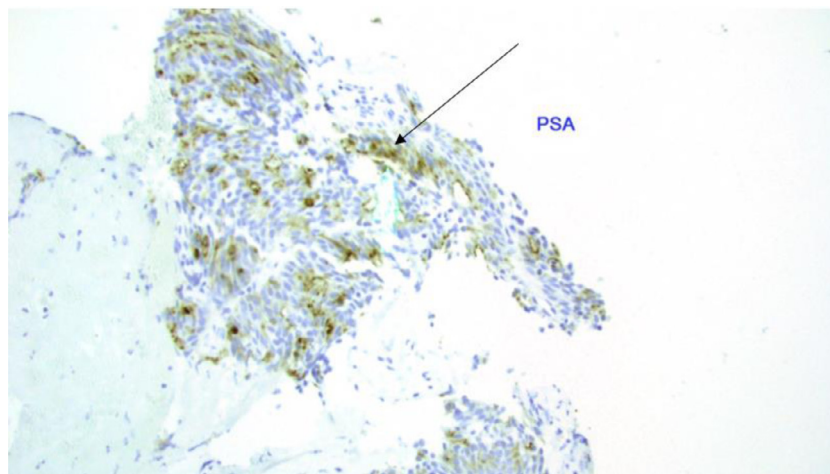
## Discussion

Prostate cancer is the most common cancer in American men. Morbidity and mortality are consequences of bone metastases, which occur in approximately half of men diagnosed with prostate cancer. There are occasional documented cases of patients presenting with a solitary osteoblastic lesion that were found to be due to primary prostate carcinoma, but a single osteolytic metastasis as the presenting finding is extremely rare. More common etiologies for a single osteolytic rib lesion in patients over the age of 40 include metastasis from renal cell, thyroid, lung, breast cancer, myeloma or lymphoma. Primary bone neoplasms of the rib in adults would include benign lesions such as fibrous dysplasia or enchondroma and malignancies such as chondrosarcoma [3].

We report a rare case of prostate carcinoma presenting with a singular, osteolytic bony metastasis to the rib. To our knowledge, few published reports exist documenting similar, confirmed occurrences. Ansari et al. in 2003 first reported a case of an osteolytic solitary radial head metastasis, presenting clinically with wrist drop [4]. Agheli et al in 2009 documented a case of a single osteolytic lesion spanning the femoral head to the proximal shaft of the femur. This patient presented with progressive severe hip stiffness and pain [5]. There has also been a report of a single osteolytic lesion as the presenting finding for metastatic prostate carcinoma in the left hallux distal phalanx [6]. We present a documented



**Fig. 3 – Bone scan showing uptake in the seventh rib indicated by the black arrows.**



**Fig. 4 – PSA staining of the glandular lesion from the rib core needle biopsy confirming metastatic prostate carcinoma.**

and confirmed case of a solitary osteolytic bone lesion from metastatic prostate carcinoma and per our literature review the first such lesion described in the rib.

In the early stages of advanced prostate cancer, malignant cells spread from their primary origin and invade local structures and blood circulation, such as Batson's plexus,

which helps explain prostate cancer's frequent involvement of the vertebral column. As illustrated by Paget's "seed and soil" theory, bone provides a preferential microenvironment "soil" for prostate cancer cells to "seed." Red marrow is abundant in the bones of the axial skeleton, such as the pelvis, spine and in our case, the ribs, providing an adequate envi-

ronment for hematogenous prostate cells to deposit. Although hemodynamic theories alone cannot explain the frequency and location of bone metastases in prostate cancer, slow blood flow in the axial skeleton as well as nutritional and anatomically functional vascularization promotes prostate cancer embolization to these locations [1].

Though classically thought to generate a purely osteoblastic response in bone, prostate cancer cells are now known to promote both osteoblastic and osteolytic activity. The osteolytic effect of prostate cancer cells relies on their ability to secrete factors that promote osteoclast differentiation. The receptor activator of nuclear factor kappa-B ligand (RANKL) and its receptor RANK stimulate osteoclast formation, activation and survival. Osteoprotegerin (OPG) acts as a decoy receptor for RANKL to offset bone resorption effects of RANK stimulation. Prostate cancer expresses both RANKL and OPG, and it is hypothesized that an unbalanced ratio of RANKL to OPG secreted by malignant cells is responsible for the appearance of osteolytic bone lesions [7]. Production of parathyroid hormone-related peptide (PTHrP) by prostate cancer cells may also play a role in the pathogenesis of lytic metastases. PTHrP is known to directly bind the PTH receptor and trigger both osteoblastic and osteoclastic effects via the RANK/RANKL/OPG system. As a mediator of prostate cancer skeletal progression, PTHrP in the absence of secreted osteoblastic factors may explain the predominance of osteoclastogenesis in some lesions [8]. Processes and mechanisms that control osteoclastogenesis via the expression of soluble factors secreted by prostate cancer cells are largely unknown. More recent studies have explored how the macroH2a histone variant attenuates prostate cancer-induced osteoclastogenesis [9]. Another recent study identified early-growth-response-1 transcription factor as having a direct effect on prostate cancer metastasis, acting as a regulator of angiogenic and osteoclastic factors in the formation of osteolytic lesions [10].

Treatment of metastatic prostate cancer involves a combination of chemotherapy including hormonal therapy, radiation, and in some instances, surgical treatment. Skeletal complications from bone metastases can include pathologic fractures, hypercalcemia, cord compression, and severe bone pain refractory to analgesics [1]. Patients with metastatic lesions require routine radiographic and clinical follow-up to ensure complications such as pathologic fracture or neurologic compromise in the spine do not occur. Surgery is occasionally indicated for impending or pathologic fracture. Area of involvement, quality of bone involved and involvement of soft tissue should be considered prior to surgical management for fracture stabilization or reconstruction [4]. It should be noted that poor prognostic factors in the treatment of prostate carcinoma include: higher Gleason score, bone metastasis, and time interval to surgery following recognition of metastatic disease [2]. The last point is likely due to the fact that this implies treatment failure with chemotherapy and radiation with progression of disease necessitating surgical intervention late in the disease course [2].

In conclusion, primary prostate carcinoma presenting as solitary metastatic osteolytic lesion is extremely uncommon [4–6]. This case is the first reported that initially presented as a pathologic fracture of a rib. Further research is required to clearly determine the pathogenesis of this lesion; however, it likely involves abnormal concentrations of secreted factors that control the bone microenvironment. In addition, we would recommend utilizing a thorough differential including pathologic fracture for patients who present with a clinical history absent of trauma and bony pain. This case shows such an example of an uncommon presentation of prostate carcinoma initially misdiagnosed. Consideration of pathologic fracture from prostate carcinoma should be in the differential for a fracture failing to clinically improve following adequate time for healing in a male patient over the age of 40.

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