

A case of metastatic prostate cancer and immune thrombocytopenia

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ABSTRACT

Prostate cancer frequently metastasizes to bone, but bone marrow involvement is relatively less common. In advanced prostate cancer, significant bone marrow infiltration can result in hematologic abnormalities such as anemia and thrombocytopenia. We report the case of a patient who presented with a new diagnosis of thrombocytopenia at the same time that he presented with prostate cancer metastatic to bone. He was found to have immune thrombocytopenia (ITP) which responded to treatment with steroids. We discuss this case and review the literature on ITP in the setting of advanced malignancy.

Key Words Prostate cancer, metastatic; immune thrombocytopenia; ITP; case reports

Curr Oncol. 2017 Oct;24(5):e434-e436

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INTRODUCTION

Although bone is the most common site of metastasis from prostate cancer, bone marrow involvement occurs relatively less frequently¹. Infiltration of bone marrow can result in bone marrow failure, manifesting as cytopenias involving multiple cell lines. Severe hematologic involvement of this kind is predictive of poor prognosis².

Isolated thrombocytopenia in the context of advanced metastatic disease attributable to an underlying immunologic cause is rare³. A literature review reveals a small number of cases in which immune thrombocytopenia (ITP) presents simultaneously with advanced metastatic adenocarcinoma. Of the few cases published, only 1 other case has involved a primary carcinoma of the prostate³. Here, with the fully informed, voluntary, and written consent of the patient, we describe an unusual case of ITP presenting with advanced metastatic prostate cancer. As in other cases of carcinoma and ITP discussed in the literature, the patient presented with an isolated thrombocytopenia and responsiveness to prednisone therapy.

CASE DESCRIPTION

An 85-year-old man presented to the emergency department with a year-long history of progressive right groin discomfort, fatigue, and weight loss. His past medical history was significant for hypertension, a multinodular goiter, and a remote history of colon cancer. His medications on presentation were acetaminophen 975 mg 4 times daily and hydrochlorothiazide 12.5 mg daily.

Initial blood work revealed an isolated thrombocytopenia with a platelet count of $40 \times 10^9/L$. Large platelets and immature myeloid cells were seen on peripheral blood smear. No nucleated red blood cells were present [Figure 1(A)]. There was no evidence of microangiopathic hemolytic anemia, disseminated intravascular coagulopathy, or leucoerythroblastic anemia. The patient was on no offending medications. Additionally, the patient had no evidence of vitamin B₁₂ or folate deficiency, infection, hypersplenism, or significant alcohol consumption. Treatment for presumed ITP was initiated. After 2 doses of intravenous immunoglobulin 1 g/kg, the patient's platelet count rose to $74 \times 10^9/L$.

A bone marrow aspirate [Figure 1(B)] and biopsy [Figure 1(C)] were taken from the right iliac crest. Immunostaining performed on the biopsy revealed neoplastic cells positive for prostate specific antigen (PSA), supportive of a metastatic carcinoma originating from the prostate [Figure 1(D)].

A bone scan revealed numerous foci of accumulation in the right hip, both femurs, left humerus, and axial skeleton (Figure 2). Computed tomography imaging showed abnormal areas of mixed sclerosis and lysis over most of the right hemipelvis and axial skeleton. The patient's PSA was elevated at 276 ng/mL, and a digital rectal exam revealed a firm, enlarged prostate.

The patient was started on oral bicalutamide 50 mg daily for 30 days and subcutaneous goserelin acetate 10.8 mg every 3 months for management of his prostate cancer. He received radiation (2000 cGy in 5 fractions) to his hip with palliative intent. The patient responded

well to treatment and experienced a significant decrease in pain.

Three weeks later, the patient's platelet count dropped to $7 \times 10^9/L$. He was unresponsive to pulse dexamethasone (40 mg daily for 4 days). He received intravenous immunoglobulin and began prednisone 1 mg/kg daily, and his platelets increased to $34 \times 10^9/L$ after 3 days and subsequently normalized. Upon prednisone weaning, the patient's platelets dropped to $89 \times 10^9/L$. After an increase in prednisone to 1.5 mg/kg daily, the platelet count again normalized.

Subsequently, a rise in the patient's PSA to 490 ng/mL warranted a change in his prostate cancer therapy. He was

maintained on androgen deprivation therapy with the addition of oral enzalutamide 160 mg daily and subcutaneous denosumab 120 mg monthly.

The patient's platelets have remained within normal range, and prednisone has successfully been tapered. Clinically he is well, and he continues on his current therapy for metastatic prostate cancer with a most recent PSA of 0.55 ng/mL (Figure 3).

DISCUSSION

Prostate cancer carries a high burden of disease, and it is the 5th most common cancer worldwide and the 2nd most common cancer among men⁴. Metastatic involvement continues to be the primary cause of morbidity and mortality, with bone being the most common site of infiltration⁵.

Infiltration of the bone marrow by metastatic tumour cells can result in bone marrow failure and resultant hematologic abnormalities. As cancer cells invade the healthy marrow, they replace hematopoietic stem cells, leading to the depletion of multiple cell lines. Nieder *et al.*² describe a typical pattern of anemia, thrombocytopenia, and increased mortality. All cases of thrombocytopenia described by those authors were preceded by anemia requiring blood transfusion. Those presentations differ from that of our patient, who had isolated thrombocytopenia, suggesting that bone marrow infiltration was not the primary cause of his decreased platelet count.

Although thrombocytopenia in the context of metastatic disease is most often attributable to actual invasion of the marrow by tumour cells, a review of the literature reveals a small number of cases in which an underlying immune component was suspected. Spivack *et al.*³ described 3 cases in which patients presented with both epithelial malignancies and presumed ITP. Of those 3 patients, 1 had adenocarcinoma of the prostate, and as in our patient, all 3 presented with an isolated thrombocytopenia that was

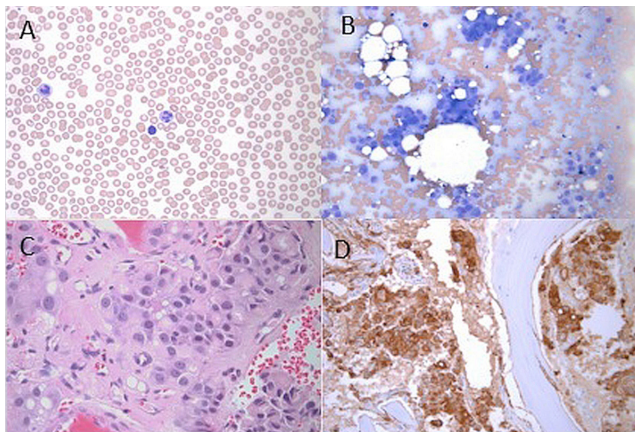


FIGURE 1 (A) Peripheral blood smear showing thrombocytopenia with normal erythrocytes. (B) Bone marrow aspirate showing non-hematopoietic cells with round nuclei, prominent nucleoli, and abundant cytoplasm, in keeping with prostate carcinoma. (C) Bone marrow biopsy showing hematopoiesis and almost complete replacement of the bone marrow by glandular metastatic carcinoma. (D) Bone marrow biopsy showing neoplastic cells positive to immunostaining for prostate specific antigen. 400× original magnification.

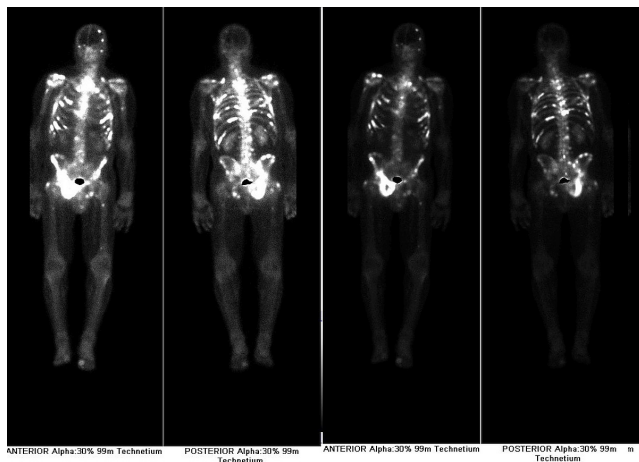


FIGURE 2 Bone scan, with anterior (two panels, right) and posterior views (two panels, left) showing numerous foci of accumulation in the proximal femurs bilaterally, the thoracic and lumbar spine, the left humeral shaft, the proximal humerus bilaterally, the right distal clavicle, and the skull. Significant abnormal accumulation is also seen extending from the right superior inferior pubic ramus to the acetabulum.

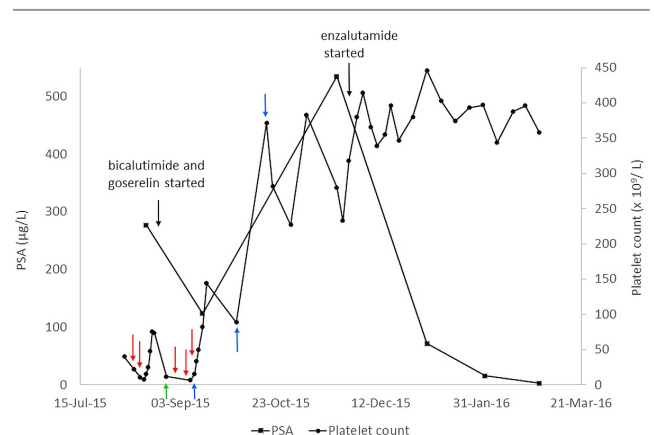


FIGURE 3 The patient's clinical course and response to treatment for prostate cancer and immune thrombocytopenia. Each arrow indicates a point in time at which a specific treatment was administered. Red arrows indicate treatment with intravenous immunoglobulin, green arrows indicate dexamethasone treatment, and blue arrows indicate prednisone treatment (initiation, dose increase, and dose decrease from left to right respectively). PSA = prostate-specific antigen.

responsive to prednisone therapy. Bone marrow analysis in the 3 patients showed no evidence of replacement by metastatic tumour cells, unlike the situation in our patient.

The mechanism of carcinoma-associated ITP has not yet been elucidated. Age might be a contributing factor, given that many of the individuals described in the literature with both ITP and carcinoma are older than the average patient with isolated ITP³. With advanced age comes immune system dampening and modulation that could potentially predispose to both malignancy and thrombocytopenia³. Other theories include an increase in antiplatelet antibody with carcinoma, as well as the presence of immune-modulating oncogenic viruses^{6,7}.

It appears that ITP as part of a paraneoplastic syndrome is an uncommon but well-recognized occurrence. Krauth and colleagues⁸ examined 68 cases of ITP associated with solid tumours and found that the association was most likely to occur in breast and lung cancers and least likely to occur in prostate cancer. In the cases found in the literature, 50% describe ITP presenting simultaneously with malignancy, as in the present case report. Also consistent with our case was the effectiveness of steroid therapy in the treatment of cancer-associated ITP⁸.

SUMMARY

Although thrombocytopenia in the context of metastatic carcinoma is frequently attributed to bone marrow infiltration, an underlying immune component should be considered. In particular, an immune cause should be considered when a patient presents with isolated thrombocytopenia despite histologic evidence of profound marrow replacement by malignant cells. Should patients present with this dual diagnosis, our case supports the general consensus in the literature that the typical treatment regimen for ITP is an effective therapy for cancer-associated ITP.

ACKNOWLEDGMENTS

We thank Dr. Lakshmi Rajappannair for her contributions to this manuscript.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare the following interests: SEZ has attended advisory boards for Amgen, Celgene, Novartis, and Janssen, and has received an honorarium from Pfizer for presenting at a journal club. SEZ has also been a sub-investigator in clinical trials for CSL Behring, Bristol-Myers Squibb, CTI BioPharma, Bayer, Celgene, Janssen, Alexion, Acerta, and Daiichi-Sankyo. SG has attended advisory boards for Sanofi, Amgen, Astellas, and Pfizer. SG has also been a sub-investigator in clinical trials for Daiichi-Sankyo and Amgen. DMB has no conflicts of interest to disclose.

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