Acute aortic dissection in a hypertensive patient with prostate cancer undergoing chemotherapy containing bevacizumab

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To the Editor

Acute aortic dissection is a fatal life-threatening condition, effectively diagnosed even by non-invasive means [1]. Hypertension remains one of the strongest predisposing factors to the development of aortic dissection [2]. Bevacizumab, a recombinant humanized anti-vascular endothelial growth factor (VEGF) monoclonal antibody that functions as an angiogenic inhibitor, is known to increase the risk of development of hypertension or worsening of preexisting hypertension [3]. Increased awareness of this possible complication in patients undergoing bevacizumab-contained chemotherapy should prompt early recognition of the complications of poorly controlled hypertension. We present a case of an acute aortic dissection in a patient with metastatic prostate cancer being treated in a clinical trial with an investigational regimen [4], including bevacizumab.

A 70-year-old African American male with metastatic castrate resistant prostate cancer (CRPC) who had been on the trial for 18 months presented with right shoulder pain, shortness of breath, and a blood pressure of 180/70 mm Hg. His prostate cancer was diagnosed 8 years ago and was treated with a radical prostatectomy, followed by a total of four years of hormonal deprivation therapy. His metastatic CRPC was found 9 months prior to his enrollment onto the clinical trial [4] at the National Cancer Institute utilizing a treatment combination of bevacizumab (15 mg/kg dose every 21 days as a cycle), docetaxel

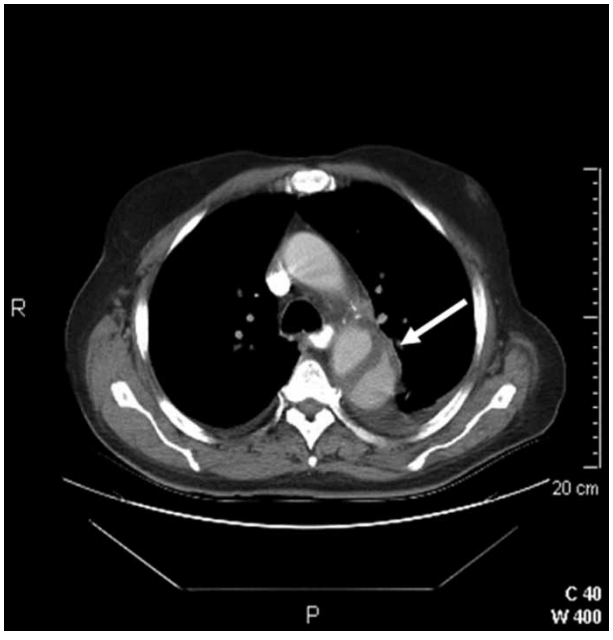

Figure 1. Patient's CT scan of the chest showing aortic dissection (arrow).

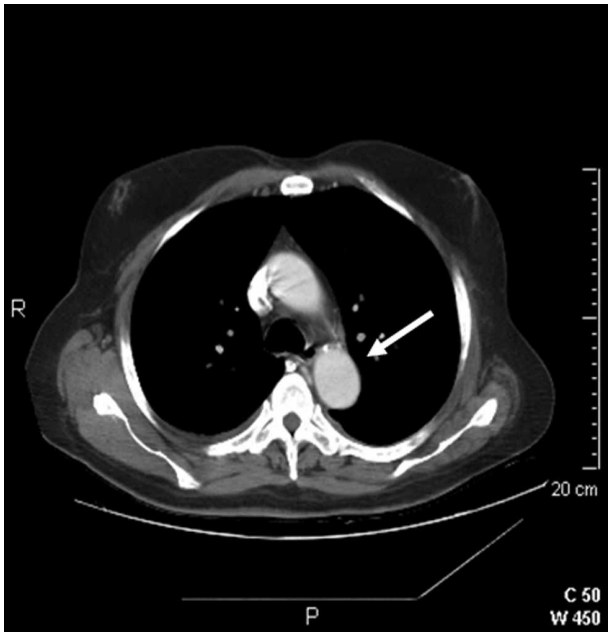

Figure 2. Patient's previous CT scan of the chest showing no evidence of dissection (arrow).

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(75 mg/m^2 every 21 days), thalidomide (200 mg daily), and prednisone (10 mg daily). He had an on-study prostate specific antigen (PSA) of 123 ng/ml and positive metastases on bone scan. He had a good response to chemotherapy with a PSA nadir of 13.4 ng/ml and no progression in staging scans. He also had pre-existing hypertension of 25 years. Prior to the treatment for his metastatic CRPC, his hypertension had been fairly well controlled with diuretics and calcium-channel blockers. However, he developed a grade 3 hypertension (using the National Cancer Institute Common Toxicity Criteria version 3) after 10 months of being on-study. With a negative cardiovascular work-up, his antihypertensive regimen was optimized with an increase in calcium channel blocker dose and addition of hydralazine. His blood pressure control improved.

He presented with the above symptoms after cycle 28 of the trial treatment. CT scan of the chest revealed acute descending aortic dissection up to the level of the renal arteries (Figure 1). Comparison was made against his previous CT scan of the chest which confirmed this as a new finding (Figure 2). He was started on labetalol nitrite drip and his course was complicated by acute tubular necrosis and contrast-induced nephropathy, both of which completely resolved after conservative measures. He was taken off the study thereafter and was optimally managed with four anti-hypertensive medications with a blood pressure of 126/70 on his last follow-up visit. The plan was for him to continue with standard treatment of docetaxel and prednisone alone, without bevacizumab and thalidomide.

Angiogenesis inhibition has emerged rapidly in the field of cancer therapy as frontline treatment, usually in combination with cytotoxic chemotherapy. The most frequent toxicity encountered with the use of bevacizumab is hypertension, occurring in up to 32% of patients [5]. Other anti-angiogenic agents such as sunitinib and sorafenib also have hypertension as a commonly observed toxicity. Patients are most commonly treated with oral agents, such as diuretics or calcium channel blockers, but a minority of patients will not respond and hence, bevacizumab treatment needs to be discontinued [6]. Our patient already had pre-existing hypertension which gradually worsened with continued administration of bevacizumab, although was intermittently controlled by variable combinations of antihypertensive medications.

The use of bevacizumab is currently indicated in colorectal cancer, lung, and renal cell cancer, and increasingly used off-label in different malignancies, which occur predominantly in the elderly population, for whom the incidence of hypertension is also more prevalent. The addition of bevacizumab in different chemotherapy combinations such as in this trial appears to be promising in enhancing efficacy, as reflected by both our patient's good overall responses and the reported results of the trial [4]. Thus, it may have an increasing role in a variety of cancers. However, extreme caution should be undertaken, and rigorous monitoring employed, to prevent possible complications that could ensue as a result of poorly controlled hypertension.

In summary, this case illustrates the need for aggressive monitoring and management of patients with hypertension or those who develop hypertension while angiogenesis targeted agents are used for treatment of malignancies. As the use of bevacizumab and other antiangiogenic agents gains approval and increasing use in the clinics, physicians taking care of patients receiving these agents must be aware of the potential life-threatening complications associated with their use.

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