CLINICAL VIGNETTE

How to Make a Scary Situation Less Scary… Prostate Cancer Gone Awry, a Remarkable Case Report

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Case Vignette

The following case report illustrates a common disease, prostate cancer, with a recurrence of a rare and potentially life threatening high high-grade neuroendocrine tumor treated with a combination of standard chemotherapy and radiation therapy as well as a novel use of a biologic inhibitor treated.

Case

The patient currently is a 73-year-old male who was originally diagnosed with prostate cancer in 2002 (at age 58) after presenting with asymptomatic elevated prostate specific antigen (PSA) of 4.5 and having undergone a radical prostatectomy. Pathology showed a pT2b lesion, with a Gleason score of 7 (3+4), perineural invasion and clear margins. Pelvic lymph nodes were negative and his PSA became undetectable for about one year before rising. There was no evidence of metastatic disease and he was treated with radiation therapy with curative intent to the prostate bed and surrounding lymph node region. His PSA decrease to less than 0.1 and he was then followed with surveillance PSA tests. He did well for more than eight years and remained very active.

At age 68, he developed low back and pelvic pain. Evaluation revealed an 8.5 cm mass in the pelvis, lesions in the liver and a single T5 bony lesion. Biopsy showed poorly differentiated carcinoma, favoring a high-grade neuroendocrine tumor. The patient received 6 cycles of cisplatin and etoposide, with a significant decrease in the size of the pelvic mass to about 3 cm. The response was consolidated with stereotactic body radiation therapy (SBRT) to the residual mass, followed by off-label use of maintenance pazopanib, which he continued at 200 mg/day. He had also been on denosumab and androgen deprivation therapy (ADT) with leuprolide given his history of prostate cancer. Serial scans have shown stable small residual pelvic mass. The patient has been off maintenance pazopanib for two years.

Surveillance scans demonstrate continued remission, and the patient remains clinically well and active more than five years after neuroendocrine tumor diagnosis.

Prostate cancer is the most common nondermatologic cancer in men worldwide with estimated incidence of 1,600,000 cases/ year and more than 300,00 deaths annually.[1] In the United States, there will be 161,000 new cases, and 26,700 deaths in 2017.[2] For localized prostate cancer, surgery and radiation are two accepted treatments with curative intent.

Neuroendocrine cells occur though out the human body. Malignant transformation can lead to a variety of neuroendocrine carcinomas including gastrointestinal neuroendocrine carcinoma, carcinoid disease, and adrenocortical carcinoma. Small cell carcinoma is a rare and distinct neuroendocrine carcinoma that often begins in the lungs but can also arise in extra-pulmonary sites. Extra-pulmonary small cell carcinomas (ESCCs) are very uncommon and have been reported in the urinary bladder, prostate, esophagus, stomach, colon and rectum, gallbladder, larynx, salivary glands, cervix, and skin. Although the initial clinical symptoms of ESCCs are usually from locoregional disease, they are naturally aggressive and have early, widespread metastases. Some patients can be cured by aggressive therapy; however, the overall prognosis is poor.

The initial assessment of ESCCs include evaluation of the primary tumor and regional lymph nodes to determine the extent of locoregional disease and CT of the chest to rule out a primary small cell lung cancer (SCLC). Initial treatment of patients with locoregional disease is similar to that for other tumor types of the same extrapulmonary site, with adjuvant systemic chemotherapy. Despite adjuvant therapy, most patients develop metastatic disease. Prophylactic cranial radiation therapy is offered to patients with primary pulmonary small cell carcinoma due to a prevalence of brain disease either at diagnosis or at recurrence ranging from 15% to over 50%, whereas extrapulmonary small cell neuroendocrine carcinoma in one study had a prevalence of 2.5%. Management of systemic disease with palliative chemotherapy uses a combination of a platinum compound and etoposide with a goal of symptom management as well as prolongation of life. Systemic therapy rarely effects a curative result in this disease with reported 12.6 percent 5-year survival and a median survival of 10 months.[3]

Discussion

Our patient was diagnosed with prostate cancer that was treated with radical prostatectomy in April 2002 and subsequent local radiation therapy for biochemical relapse of prostate cancer. He did well for the next decade before developing metastatic high-grade neuroendocrine tumor with a large pelvic mass and multiple metastatic sites including liver and bone.

Development of metastatic neuroendocrine tumor from a primary prostate cancer is rare. This recurrence is unusual because small cell neuroendocrine prostate cancer typically presents as de novo pure disease or mixed histology with adenocarcinoma in varying degree of involvement. Literature review regarding this type of presentation confirms this is a rare presentation, and raises the question, i.e., Is this a recurrence of his original prostate cancer versus de novo disease versus possibly secondary malignancy after radiation treatment given the location of the prior radiation treatment? His tumor underwent molecular analysis (Cancer Type ID, Biotheranostics, Inc. San Diego, Ca.) revealing with high probability (over 90%) prostate as origin in addition to immunostaining of his tumor of prostatic acid phosphatase. PSA expression was relatively low (0.35-0.40) at time of recurrence and responded to primary hormonal therapy. Further, review of the radiation oncology literature illustrates that secondary cancers after radiation treatment are very rare with prostate radiation and those secondary cancers are most commonly noted to be rectal and bladder carcinomas not neuroendocrine carcinomas. Thus, these clinicopathologic factors are suggestive of recurrence of primary prostate cancer in a very unusual manner, as a rare case of high-grade neuroendocrine carcinoma.

He received standard palliative systematic cisplatin etoposide for treatment of metastatic high-grade neuroendocrine carcinoma, with excellent partial response, and consolidation radiation to the large pelvic mass. The liver and bony disease resolved on imaging. Despite the excellent response, there remained a significant risk of relapse, and a novel approach at suppressive/maintenance therapy was pursued. He was started on off-label maintenance pazopanib, an oral multitargeted tyrosine kinase growth factor inhibitor. He completed two years of therapy without signs of recurrent disease. His scans continue to show no signs of disease five years after diagnosis.

Summary

We present a rare case of prostate cancer with recurrent metastatic high-grade neuroendocrine carcinoma. The excellent and durable treatment response illustrates the value of multidisciplinary management of cancer, as well as creative use of novel therapy. This case raises a potential use of pazopanib maintenance therapy, however, the tumor may have remained in remission without use of maintenance therapy.

We believe this is one of the first reports of malignant neuroendocrine recurrence after nonneuroendocrine primary prostate adenocarcinoma.

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