Oncology

Case report: Adenosquamous carcinoma of the prostate with greater than 20 month response to multimodal therapy

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ABSTRACT

Adenosquamous carcinoma is an extremely rare and lethal subtype of prostate cancer affecting an estimated 0.03 per million men annually. It has been associated with prior hormone therapy for prostate adenocarcinoma. We present a case of de novo adenosquamous carcinoma of the prostate treated with a multimodal approach including surgery, androgen-deprivation therapy, chemotherapy, and radiation.

Introduction

Adenosquamous carcinoma (ASC) of the prostate is rare with an estimated incidence of 0.03 million cases annually. Prior exposure to androgen deprivation therapy (ADT) has been postulated as a possible etiology. The clinical course is commonly marked by early development of metastatic disease; however, a paucity of data exists regarding optimal treatment strategies. We present a patient with no prior history of ADT diagnosed with locally advanced, lymph node positive prostate ASC treated with a multimodal approach including aggressive surgical resection, chemotherapy, ADT, and radiation.

Case presentation

A 66 year-old gentleman presented with urinary frequency and nocturia. Serum prostate-specific antigen (PSA) was 12.7 ng/mL. Digital rectal exam documented a prostate with moderate enlargement and right-sided induration. 12-core transrectal ultrasound-guided prostate biopsy showed Grade Group 4 adenocarcinoma (PCa) in four cores and Grade Group 5 PCa with squamous differentiation in eight cores. Staging MRI demonstrated no evidence of bladder/rectal involvement, nor pelvic lymphadenopathy. A bone scan was negative for metastasis. The patient elected to undergo robotic prostatectomy with bilateral pelvic lymphadenectomy.

During surgery, nodular-appearing lesions in the bladder neck and trigone were consistent with local invasion of PCa at frozen section (Fig. 1). Because the tumor involved a significant portion of the bladder neck and trigone including the right ureteral orifice, a complete resection with radical prostatectomy alone was not feasible. After extensive discussion with the family, the decision was made to proceed with open radical cystoprostatectomy and urinary diversion. During apical dissection, the prostate was markedly adherent to the anterior rectal wall suggesting local tumor extension. The specimen was removed en bloc with a portion of the anterior rectal wall. The rectum was repaired primarily in two layers with colorectal surgical assistance. Given anticipated need for post-operative radiation, a diverting colostomy was created.

Final pathology revealed Grade Group 5 ASC involving 80–90% of the prostate with extraprostatic extension and bilateral seminal vesicle invasion (Fig. 2). There was local extension into the bladder neck, trigone, and rectal wall. Surgical margins were positive. Seven of 11 lymph nodes were positive for metastatic adenocarcinoma with extranodal extension (Fig. 2). The final pathologic stage was pT4pN1M0 (Stage IVA).

The patient started a 2-year course of ADT with leuprolide to treat the adenocarionomatous component of his PCa. Radiation oncology
initiated treatment with adjuvant pelvic intensity-modulated radiation therapy (IMRT) with 30 fractions (total dose 6000 cGy). After counseling regarding the extent and aggressive nature of disease, he elected to proceed with docetaxel 75mg/m2 intravenously every 21 days for six cycles. His colostomy was reversed 12 months post-operatively and he is clinically well with normal bowel function 20 months postoperatively. PSA remains undetectable (on ADT) and surveillance imaging demonstrates no evidence of recurrence or metastasis at 20-months postoperatively.

Discussion

The estimated incidence of prostate ASC is 0.03 cases/million/year. Review of all SEER database PCa cases between January 1973–December 2006 found only 25 cases of prostate ASC.

Histologically, both glandular and keratinizing squamous patterns are present. Squamous components are often negative for PSA and PSAP immunostains; patients with large squamous fractions may have normal PSA. The tumors are usually large, sometimes replacing a substantial portion of the prostate. Men may present with urinary retention or dysuria due to local invasion and distortion of the urethra and trigone.

Several mechanisms have been proposed for the development of prostate ASC (Table 1). Squamous histology may represent a collision tumor developing from squamous metaplasia after radiation or hormonal therapy. The first documented report of prostate squamous metaplasia occurred following estrogen therapy; prostate ASC has also been associated with leuprolide and 5-alpha reductase inhibitors.

However, the literature demonstrates five early cases that lack a history of hormonal or radiation therapy (Table 1). Similar to our case,
Prostate ASC in the absence of prior hormonal or radiation therapy may be derived from resident pluripotent cells capable of multidirectional differentiation.

Prostate ASC is clinically aggressive. Locally advanced disease may be common at relatively low PSA levels depending on the extent of the squamous component. Therefore, preoperative counseling regarding the possibility of adjacent organ involvement and need for extensive resection should be considered even if disease appears to be clinically localized.

Prostate ASC generally confers poor prognosis. Retrospective analysis of prostate ASC cases showed a median cancer-specific survival of 16 months. Patients presenting with distant metastases had only 20% 6-month survival rates, and all died within 1 year of diagnosis. A notable survival benefit was noted among those undergoing surgery (5-year overall survival of 63%) compared to those who did not receive surgery. This likely represents a selection bias with less advanced disease in the surgery group.

The aggressiveness of ASC is attributed in part to variable response to systemic ADT and chemotherapy. Response to ADT may be related to whether these tumors have been exposed to prior hormonal therapies since lack of response to ADT has been associated with previous receipt of ADT. There is a paucity of data regarding systemic chemotherapy or immunotherapy. While no regimens are currently recommended, a recent case report demonstrated short-term response at 6 weeks to external beam radiation therapy (EBRT) and PD-1 inhibitor therapy. 

Our patient has no evidence of disease recurrence at 20 months post-operatively following multimodal therapy, including extensive surgical resection, adjuvant radiation, ADT, and systemic chemotherapy. Therefore, there may be a role for multimodal therapy consisting of extirpative surgery with adjuvant radiation and ADT with or without chemotherapy in the treatment of de novo prostate ASC. 

Consent

The patient has consented to publication of this case.

Disclosure

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Declaration of competing interest

None.

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