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Post Radiotherapy Leiomyosarcoma of the Prostate: Can Radiation Therapy Induce a Secondary Cancer? A Case Report

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ABSTRACT

Sarcoma of the prostate is a rare neoplasm, accounting for less than 0.1% of prostate malignancies. There are only a few cases reported in the literature. The prognosis for this cancer is poor and the average survival is variable. The authors present a case report on a patient diagnosed with prostate sarcoma following initial diagnosis and treatment for adenocarcinoma of the prostate. What makes this case interesting is that the patient had a history of failed treatment for prostate adenocarcinoma that consisted of external beam therapy and palladium seed implants. Eight years later, the patient was diagnosed with leiomyosarcoma of the prostate. There may be a causal relationship between radiation therapy to the prostate and the development of the leiomyosarcoma.

KEYWORDS: Prostate cancer; Prostate leiomyosarcoma; Sarcoma; Radiation induced sarcoma; Prostate adenocarcinoma; Secondary prostate cancer; Secondary prostate leiomyosarcoma.

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INTRODUCTION

Sarcoma of the prostate is a rare neoplasm, accounting for less than 0.1% of prostate malignancies. There are only a few cases reported in the literature. As a whole, sarcomas account for 1% of all malignant tumors; less than 5% of the sarcomas arise from the genitourinary system [1]. The two most common subtypes are leiomyosarcoma (usually found in adults) and rhabdomyosarcoma (usually found in children) [2]. Leiomyosarcoma accounts for 38% to 52% of primary prostatic sarcomas and the etiology remains unknown [3]. The survival rate is variable, but the prognosis for this cancer is poor and the median length of survival is 17-24 months [4,5]. The authors present a case report on a patient diagnosed with prostate sarcoma following initial diagnosis and treatment for adenocarcinoma of the prostate.

CASE REPORT

A 75-year-old male with a history of diabetes, hypertension, hyperlipidemia, and coronary artery disease presented with hematuria and had a mass on digital rectal examination (DRE). There was no family history of any genitourinary cancer. The patient was a former smoker and denied alcohol abuse.

The patient had a history of prostate adenocarcinoma, which was diagnosed 8 years before this examination and staged at T2b. At the time of initial diagnosis, he was treated with external beam radiation therapy and brachytherapy that consisted of palladium seed implantation. Both treatments locally failed with an increasing prostate-specific antigen (PSA). Four years later, the patient underwent cryosurgical ablation without complications for a recurrent, poorly differentiated

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Figure 1. Spindle Cell Neoplasm/High Grade Leiomyosarcoma; High Power Photograph (400x) Shows 3 Mitoses in 1/40x HPF.

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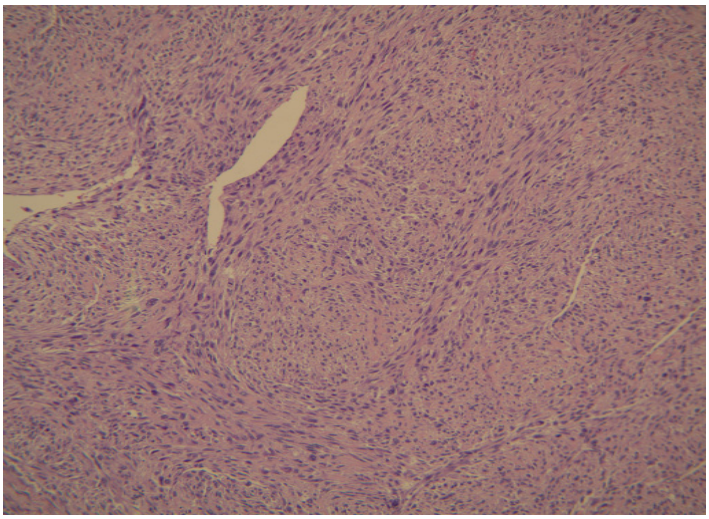

Figure 2. Positive Immunohistochemical Staining of Tumor Cells with Desmin, Confirming the Diagnosis of Leiomyosarcoma (Photograph at 200x).

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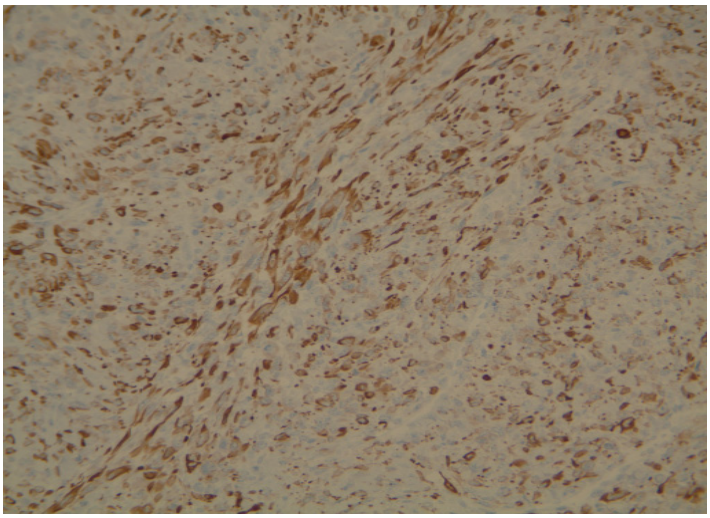

adenocarcinoma that had a Gleason score of 4+5=9 and was clinically staged as T2b. Body bone scan and CAT scan of the abdomen and pelvis were negative for metastases. DRE prior to cryoabation revealed a small, irregular prostate with mild induration over both lobes. PSA at that time was 11.4 with a prostate volume of 26 cc. After cryoablation, PSA decreased to 0.2.

The PSA progressed upward to 1.5 one year later and to 2.7 two years after cryoablation, with a questionable induration at the prostatic base on DRE. A CAT scan confirmed a 2.3 cm mass along the anterior surface of the rectum just posterior to the seminal vesicles. Hormonal therapy was initiated and consisted of leuprolide depot 30 mg every 4 months and bicalutamide 50 mg. This therapy resulted in a PSA decline to 0.1 after 8 months. DRE at that time was negative with a flat, benign-feeling prostate. The patient's PSA remained at 0.1 on hormone therapy, but 2 years after starting hormone therapy the patient complained of gross hematuria. On DRE, the prostate was indurated and slightly enlarged at 30 grams; PSA was 0.1. Cystoscopy revealed a large median lobe that was necrotic and oozing blood. A CT urogram revealed a marked increase in the size of the pelvic neoplasm with direct invasion of the rectum measuring 8.3 x 5 cm. There was no pelvic sidewall or retroperitoneal lymphadenopathy. Prostate biopsies revealed infiltrative, interlacing fascicles of spindle cells with eosinophilic cytoplasm characterized by high cellularity, marked nuclear atypia, and numerous atypical mitosis. These signs were strongly suggestive of prostate sarcoma. Immunostaining of the biopsies were negative for PAS, PCA3, CK A1/A3, CK903, PSA, and hormone receptor ER/PR, ruling out any residual epithelial prostate adenocarcinoma. Immunostains for leiomyosarcoma were positive. Desmin and smooth muscle actin were weakly positive; vimentin was strongly positive. Thus, a diagnosis of prostate leiomyosarcoma was confirmed.

The patient underwent a radical cystoprostatectomy, bilateral pelvic lymph node dissection, resection of the left sigmoid and rectum, ileal conduit urinary diversion, and colostomy. The surgery was uneventful.

Pathology revealed a high-grade leiomyosarcoma of the prostate. The tumor completely replaced the prostate and extended into the periprostatic adipose tissue and bladder wall. Perineural invasion was present without angiolymphatic invasion. The tumor extended posteriorly into the deep pelvic tissue including the full thickness of the rectum. The tumor was present at the posterior margin of the prostate and subsequent rectal deep margin. However, additional deep margin was taken separately, which was free at the designated ink margins. The prostatic apex was also positive and no additional tissue was submitted. The resected rectum specimen showed diffuse infiltration by high-grade leiomyosarcoma, with tumor infiltration throughout the full thickness of the bowel wall and presence of ulcerations through the free mucosal surface (Figure 1). The sigmoid colon and pelvic lymph nodes were negative for tumor. A panel of immunohistochemical stains supported the diagnosis of a malignant smooth muscle neoplasm based

on positive staining for smooth muscle actin and desmin (Figure 2). The other malignant entities in the differential, including other mesenchymal neoplasms and a sarcamatoid carcinoma, were ruled out with negative staining for myogenin, S100, CD34, HMW cytokeratin, and pancytokeratin.

Three months after the surgery, a CT of the abdomen, chest, and pelvis with contrast showed a new 3 mm nodule in the right middle lobe, representing metastasis. In addition, there was soft tissue in the region adjacent to the prostate bed and rectal stump that was suspicious for tumor recurrence. Chemotherapy was initiated consisting of Doxil (Centocor Ortho Biotech Inc, Horsham, PA) every 2 weeks; dosage was adjusted according to weight and height. A CT with contrast several months later showed increased findings. The soft tissue located near the prostate bed had a marked increase in size. The mass invaded the perineum and abdominal wall that led to a cutaneous fistula. There were also numerous new pulmonary metastases identified in the lung bases. Twenty-five months after surgery and chemotherapy, the patient is alive although the overall prognosis is poor.

DISCUSSION

Leiomyosarcoma of the prostate is a rare prostate malignancy with a poor prognosis because of the aggressiveness of tumor growth, lack of early symptoms, and late presentation. However, the survival rate is variable and can range from 0 to 60%; survival length ranges from months to years. It is reported that 50% to 75% of patients die of prostatic leiomyosarcoma after 2-5 years [6].

Recommended treatment for prostate leiomyosarcoma is surgery involving a cystoprostatectomy, followed by chemotherapy or radiotherapy [2]. Surgery may provide symptomatic relief and be a palliative option for patients (as opposed to a cure), because local recurrence and metastasis is common. There is no optimal form of therapy, but Mansouri et al [7] state that radical surgery with complete resection offers a chance for prolonged survival when the tumor has low mitotic activity. Additionally, Dotan et al [8] demonstrated that complete surgical resection can lead to decreased local recurrence and decreased metastasis, which prolong survival. Unfortunately, prostate leiomyosarcoma is often caught late in the disease process so tumor size at the time of surgical resection is commonly extensive. This was true in the present patient and in cases reported by Cheville et al [9], in which complete excision was difficult and did not result in a cure. Thus, it is believed that variables affecting disease survival are tumor margins, size, grade, histology, and complete tumor resection. However, further research is needed because there is contradictory evidence in the literature. Sexton et al [10] reported no association between survival and negative surgical margins, tumor size, and staging.

With respect to adjuvant therapy, Sexton et al [10] and Janet et al [4] showed that there may be a survival advantage for a combined multimodality approach versus surgery by itself. Therefore, these authors recommended optimizing multimodality treatment strategies to improve prognosis. Nonetheless, studies have shown that rare prostatic carcinomas that develop after radiation therapy are usually aggressive tumors that present with secondary deposits, for which the outcome is generally poor regardless of treatment. Additionally, because sarcomas have a high recurrence rate, it is recommended that patients be followed closely with chest, abdominal, and pelvic imaging. Primary sites of metastases in order of frequency are lung, bone, lymph nodes, and brain [11].

There is no definitive etiology for prostate leiomysarcoma, and there has been an ongoing debate about whether radiation therapy to the prostate can induce a secondary cancer. In the present case report, leiomyosarcoma of the prostate was discovered 8 years after treatment for prostate adenocarcinoma that consisted of a failed brachytherapy and failed external beam therapy, and eventually cryoablation. It is interesting to note that this patient is not the only one to have developed a leiomyosarcoma of the prostate after various radiation therapies to the prostate. In fact, a handful of cases in the literature were found associating adenocarcinoma with leiomyosarcoma of the prostate. Moreira et al [12] suggest a causal effect of leiomyosarcoma of the prostate following brachytherapy to the prostate. The authors discuss complications after brachytherapy, in which 3 patients developed cancer of the prostate following brachytherapy. One developed recurrence of the adenocarcinoma, and 2 others developed secondary cancers (a neuroendocrine tumor of the rectum and leiomyosarcoma of the prostate). In addition, McKenzie et al [13] reported 3 cases of postirradiation sarcoma that arose in the pelvis 8, 15, and 16 years after external beam therapy to treat localized adenocarcinoma of the prostate. Prevost et al [5] reported 1 case of postirradiation sarcoma that developed in the right inguinal region 8 years after external beam therapy for localized prostate adenocarcinoma. Mazzucchelli et al [11] conducted a study on histological variants of prostatic carcinoma. They reported that half of the cases of sarcomatous component (SC) carcinosarcoma of the prostate developed after hormonal or radiation therapy that followed an initial diagnosis of acinar adenocarcinoma. However, they suggested that SC status after radiation therapy is not necessarily the only cause, because SC can develop de novo.

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Leiomyosarcomas can develop in other regions of the body after local radiation. Grabowska et al [14] reviewed 11 cases of leiomyosarcoma of the head and neck that developed after irradiation to those areas. In addition, Olcina et al [15] described the development of radiation-induced sarcoma after mastectomy treatment. The authors reported that the frequency of newly diagnosed sarcomas is rising as breast cancer patients treated with adjuvant radiation therapy survive for longer periods of time.

Further studies are needed to assess whether there is a link between radiation therapy to the prostate and the development of leiomyosarcoma of the prostate. If such an association exists, it would be beneficial to closely monitor patients treated with radiation for prostate cancer who may appear to be locally controlled. An early rebiopsy may be needed. Studies have shown that the PSA level proves to be a poor marker of screening for prostate leiomyosarcoma. For example, the patient discussed in this article had a PSA of 0.1 on diagnosis of leiomyosarcoma. Therefore, initial suspicion for prostate leiomyosarcoma should be based on symptoms such as hematuria, pelvic and back pain, and mass on DRE. Screening does not appear warranted because of the rarity of the cancer and little evidence in the literature. Nonetheless, leiomyosarcoma of the prostate is an aggressive tumor, and the best treatment outcomes depend upon early detection.

REFERENCES

[1] Vandoros GP, Manolidis T, Karamouzis MV, Gkermpesi M, et al. Leiomyosarcoma of the Prostate: Case Report and Review of 54 Previously Published Cases. *Sarcoma*. 2008:458079.

[2] Agarwal NK, Dorairajan LN, Kumar S, Murthy C, Krishnan R. Primary prostatic leiomyosarcoma in an adult. *Indian J Urol*. 2006;22:66-67.

[3] Mondalni N, Palli D, Saieva C, et al. Clinical characteristics and overall survival in genitourinary sarcomas treated with curative intent: a multicenter study. *Eur Urol.* 2005;47(4):468-473.

[4] Janet NL, May AW, Akins RS. Sarcoma of the prostate: a single institutional review. *Am J Clin Oncol*. 2009;32(1):27-29.

[5] Prevost JB, Bossi A, Sciot R, Debiec-Rychter M. Post-irradiation sarcoma after external beam radiation therapy for localized adenocarcinoma of the prostate. *Tumori.* 2004;90(6):618-621.

[6] Miedler JD, MacLennan GT. Leiomyosarcoma of the prostate. *J Urol*. 2007;178(2):668.

[7] Mansouri H, Kanouni L, Kebdani T, Hassouni K, Sifat H, El Gueddari B. Primary prostatic leiomyosarcoma. *J Urol.* 2001;165(5):1676.

[8] Dotan ZA, Tal R, Golijanin D, et al. Adult genitourinary sarcoma: the 25-year memorial sloan-kettering experience. *J Urol*. 2006;176(5):2033-2039.

[9] Cheville JC, Dundore PA, Nascimento AG, et al. Leiomyosarcoma of the prostate report of 23 cases. *Cancer.* 1995;76(8):1422-1427.

[10] Sexton WJ, Lance RE, Reyes AO, Pisters PW, Tu SM, Pisters LL. Adult prostate sarcoma: the MD Anderson Cancer Center experience. *J Urol*. 2001;166:521-525.

[11] Mazzucchelli R, Lopez-Beltran A, Cheng L, Scarpelli M, Kirkali Z, Montironi R. Rare and unusual histological variants of prostatic carcinoma: clinical significance. *BJU Int*. 2008;102(10):1369-1374.

[12] Moreira SG Jr, Seigne JD, Ordorica RC, Marcet J, Pow-Sang JM, Lockhart JL. Devastating complications after brachytherapy in the treatment of prostate adenocarcinoma. *BJU Int.* 2004;93(1):31-35.

[13] McKenzie M, MacLennan I, Kostashuk E, Bainbridge T. Postirradiation sarcoma after external beam radiation therapy for localized adenocarcinoma of the prostate: report of three cases. *Urology*. 1999;53(6):1228.

[14] Grabowska SZ, Zimnoch L, Hubert E, Duraj E, Wincewicz-Pietrzykowska A. Radiation induced leiomyosarcoma. Review of literature and case report [article in Polish]. *Otolaryngol Pol*. 2007;61(5):744-749.

[15] Olcina M, Merck B, Giménez-Climent MJ, et al. Radiation-induced leiomyosarcoma after breast cancer treatment and TRAM flap reconstruction. *Sarcoma*. 2008:456950.

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