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Sarcoma of the Penis Following Pelvic Radiotherapy for Prostate Cancer: A Case Report

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Abstract

We present a case report of an 82-year-old patient with a history of prostate cancer treated by prostatectomy, radiotherapy, and hormonal therapy. He developed afterwards an indurated penile mass with urinary obstruction. Biopsy confirmed the diagnosis of leiomyosarcoma. Radiotherapy is a well-known risk factor for sarcomas. Post-radiation sarcoma is defined as the appearance of a sarcoma within the field of previous therapeutic irradiation, histologically different from the treated tumor. The latency period is not well defined, but a long latency period is considered as a risk factor for sarcoma, as well as advanced age, and lymphedema. The relationship between radiation dose and sarcoma risk remains debated. Leiomyosarcoma of the penis is very rare and can present with symptoms of dysuria or urinary obstruction. Post radiation sarcomas are hard to treat, and surgical treatment remains a mainstay of treatment. The prognosis varies depending on tumor location and size but is often poorer compared to sporadic primary sarcomas. Secondary malignancies after radiotherapy are a growing problem because of the increased number of long-term cancer survivors, and it should be included in management discussion. Further studies on the risk and latency period are required to develop better strategies for patient care.

Keywords: Post-Radiation Sarcoma; Leiomyosarcoma; Penis Sarcoma; Prostate Cancer; Radiotherapy.

Introduction

Radiotherapy is a well-known risk factor for sarcomas, but it is difficult to distinguish between radiation-induced sarcomas and unrelated forms. In the context of radiotherapy for prostate cancer, the occurrence of penile sarcomas remains extremely rare, with only limited documented cases in the medical literature. Similarly, non-radio-induced leiomyosarcomas of the penis are uncommon. Within the evolving landscape of prostate cancer management, which has shown substantial enhancements in patient survival rates, there is an emerging concern surrounding the potential development of secondary malignancies, including post-radiation sarcomas within the irradiated field.

This case highlights the importance of recognizing and understanding the risks associated with post-radiation sarcomas, particularly in long-term cancer survivors, and the need for a deeper understanding of their risk factors, molecular pathogenesis, and therapeutic strategies. This case also explores specific considerations related to penile leiomyosarcomas, a particularly rare malignancy.

Case Presentation

An 82-year-old patient was admitted to the emergency department with lower abdominal pain and an indurated mass at the base of the penis. His medical history included an open radical prostatectomy performed in 2000, followed by radiotherapy 6 months later for detectable postoperative PSA. A total dose of 46.8 Gy was delivered over the entire pelvis in 1.8 Gy fractions. A

higher dose was performed on the prostatic bed up to a total dose of 70.2 Gy (Figure 1). From 2004 to 2013, he received Depo-Eligard hormone therapy. In 2021, following a re-increase in PSA at 0,77 µg/L and a positive common iliac lymph node on PET PSMA, the patient underwent stereotactic radiotherapy to the common iliac lymph node at a total dose of 24 Gy (3 x 8 Gy). His PSA decreased well afterwards and was rechecked at 0,11 µg/L at admission. He has no other relevant medical history.

Clinical examination revealed a normal abdomen, but painful hypogastric palpation. Presence of an indurated mass at the base of the penis, in front of the pubis, with no inflammatory signs and no external wound. No inguinal pathological nodes upon examination. Blood tests showed normal leukocytosis at 9.03/nL, creatinine at 2.6 mg/dl, normal ionogram, and CRP at 27.9 mg/L. NSE was measured at 14.5 µg/L (normal value <17 µg/L). Urinalysis showed 149 white blood cells/µL and 0 red blood cells/µL. Culture showed polymicrobial flora, making the result uninterpretable. An abdominal CT scan without injection of contrast showed a nodular swelling measuring 8x4 cm, in the upper part of the penis, responsible for a compression of the urethra, which was dilated upstream with a diameter of 12 mm and a bladder globe. No lymph node or visceral metastases.

An additional magnetic resonance showed a tumoral process measuring 82 x 58 x 42 mm, with intermediate T2 signal and T1 hypo signal infiltrating the base and the 2/3 proximal part of the penile corpus over ¾ of its circumference. Invasion of the corpus spongiosum with consequent stenosis of the urethra was noted. Presence of change in the corpus cavernosum signal, which does not allow formal exclusion of infiltration, despite absence of macroscopic interruption of the albuginea/Buck's fascia in T2 hypo signal. Bilateral inguinal nodes with small infracentimetric axes (Figure 2). A bladder catheter was placed, and the lesion was biopsied percutaneously by a thru-cut needle to assess the histopathological diagnosis. Pathological analysis led to the diagnosis of smooth muscle sarcoma of the leiomyosarcoma type. One month later, the patient underwent total penectomy with perineal urethrostomy (Figure 3). Final pathological analysis confirmed the presence of an FNCLCC grade I leiomyosarcoma measuring 10 x 6 x 5.2 cm.

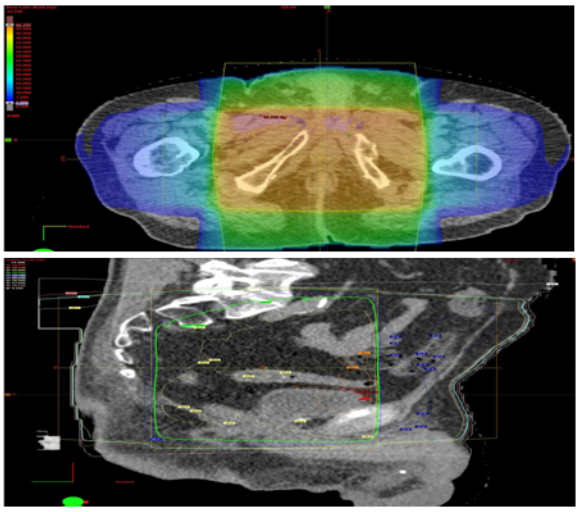

Figure 1: Radiotherapy dosimetry.

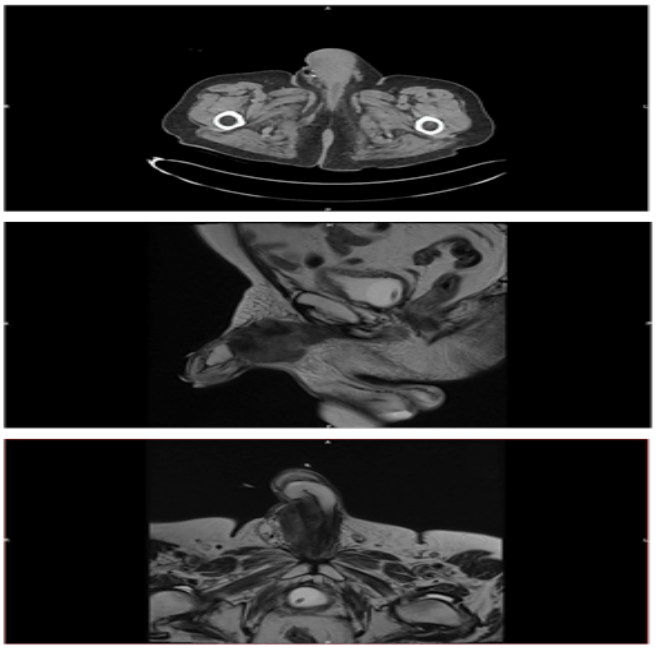

Figure 2: MRI of pelvis.

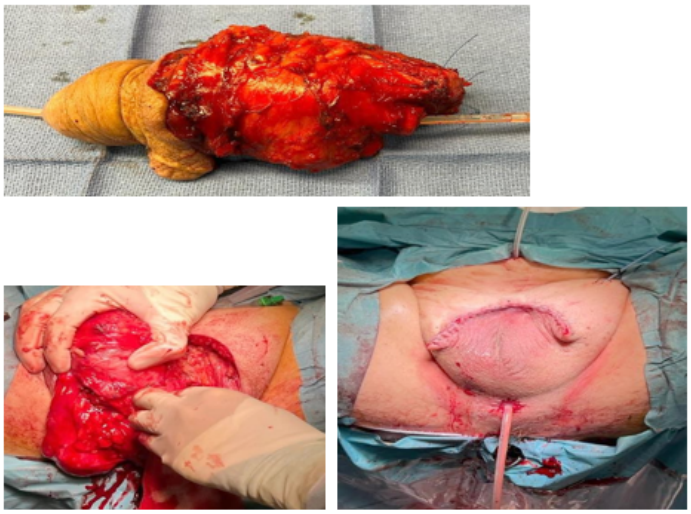

Figure 3: Total penectomy with perineal urethrostomy.

Discussion

Post-radiation sarcoma is defined as the appearance of a sarcoma within the field of previous therapeutic irradiation, histologically different from the treated tumor [1-4], and the tissue where the secondary tumor originates had to be metabolically normal prior to irradiation [4]. Time must elapse between the date of exposure to radiation and the development of a secondary cancer, but the latency period is not well defined [2-8].

Sarcomas are among the first solid tumors to be associated with this radiotherapy exposure [1], but the risk of developing sarcoma following radiotherapy is estimated to be less than 1% [1,2,3,6,8]. In prostate cancer patients treated by radiotherapy, one in 70 patients with prostate cancer treated with radiotherapy will develop a secondary tumor if they survive more than 10 years, but only 0.16% are considered therapy induced [1]. As radio-induced neoplasm in case of radiotherapy for prostate cancer, bladder and rectal cancer are the most frequent [4,7], penile sarcomas are extremely rare with only few cases reported in the literature [4].

The median age of patients with radiotherapy induced sarcoma is 60, but the range is wide because of the variable latency period between initial and secondary malignancy, and the diverse patient population who receives radiotherapy [3,8].

As we know, radiotherapy is a risk factor for the development of neoplasm [4]. One proposed mechanism for radiation carcinogenesis involves [2]:

1) A direct ionizing radiation event leading to DNA damage and to the release of reactive oxygen species [2,3];

2) radiation-induced bystander events that release inflammatory mediators;

3) decrease in DNA repair and cell cycle checkpoint from inflammatory mediators;

4) Cell death and a primary instability event that leads to carcinogenesis.

Compared with non-radio-associated tumors, radio-induced tumors show a greater number of small deletions, and an enrichment of balanced inversion as DNA structural damages [3].

In radio-induced sarcomas, p53 mutation seems to be significantly higher than in sporadic carcinomas [6]. Therefore, the inactivation of p53 could be a consequence of irradiation, and an early trigger event in radio-induced sarcomas [6].

Irradiation of the prostate might contribute to carcinogenesis outside the irradiated area through radiation scatter and increased reactive oxygen species who cause genetic alterations without direct exposure [7].

Elucidating risk factors for the development of post-radiation sarcomas has been difficult given its rare occurrence [2]. Lymphedema, a common complication of cancer, has been linked as a possible risk factor in the development of sarcomas [2]. Radio-induced neoplasms seem to increase with a longer latency period [4,7], and advanced age could also be a risk factor [2,8].

Some authors suggest that there is no relationship established between radiation dose and appearance of radiation-induced sarcoma [1,2]. But a few studies do suggest higher rates of post- radiation sarcoma with higher doses of radiation [1,2,3,6]. However, radiation doses, techniques and treatment modalities, are constantly changing for all cancer types [2,3], which complicates the extrapolation of prior radiation-induced cancer risk factors with future risk [3]. For prostate cancer, brachytherapy seems to be a lower risk of secondary malignancies than external beam radiotherapy, because of less integral radiation to normal tissues [7]. Radiation doses above 50 Gy cause cell death, while lower doses (<30 Gy) cause genomic instability and damage cell repair mechanisms.

Radio-induced sarcoma typically occurs within or at the edge of the radiation field. At the edge of the radiation field, the dose of radiation is not homogeneous and may be less than the tumor killing dose. This may enable surviving genetic mutations to progress into developing tumors [9].

Several hereditary cancer syndromes and defects in DNA-repair mechanism (ex: BRCA1) have been suggested to play a role in the risk of radiation-induced sarcoma [2,3]. Although data on the genetics of radiation-induced sarcoma exists, the research is in its early stages [2]. The combination of radiation and chemotherapy together has been demonstrated to increase the rate of secondary malignancies, including radiation-induced sarcomas (2).

Leiomyosarcoma of the penis is very rare [10,11,12]. Leiomyosarcoma can arise from different sources, like the dartos muscle layer of the prepuce and shaft, the arrector pili muscles associated with lanugo hairs on the penile shaft, and the muscular walls of superficial vessels situated outside of the tunica albuginea, from where superficial lesions are originating [4,10,11,12]. The deep lesions are those arising from the muscular walls of the deep vascular complex that make up the corpus cavernosum and corpus spongiosum [4,10,11,12]. Superficial tumors are usually asymptomatic and present as a small subcutaneous nodule in the distal shaft or the penile prepuce [4,12], while deep-seated tumors present as a non-tender infiltrating mass which can provide symptoms of dysuria or obstruction like in our case [4,10], and penile deviation or erectile pain [4].

Post-radiation sarcomas are hard to treat [2] and are often locally aggressive [8]. Surgical treatment with complete excision and clear margins remains a mainstay of treatment [3,5,8] In case of leiomyosarcoma of the penis, superficial tumors can be treated by wide local resection with fully documented resection margins and long-term follow-up [10,11,12]. Deep-seated tumors are treated by partial or radical penectomy [4,10,11]. Regional lymph node dissection is usually not indicated, as nodal metastasis is uncommon and generally limited to very late stages of disease [10].

Adjuvant radiotherapy and chemotherapy have no clear value as primary treatment of penile leiomyosarcoma [10,11]. Sarcomas are generally poorly radiosensitive and chemo sensitive neoplasms [4], and post-operative chemotherapy doesn't seem to have an association with higher survival rate [8]. Post-radiation tumours are also considered resistant to radiotherapy [1,8].

Post-radiation malignant pelvic sarcoma is associated with a poor outcome [1,2,3,6,8] and has a poorer disease-specific survival compared to sporadic primary sarcoma [2,6]. Some series have shown a maximum survival rate of 15% for pelvic sarcoma developing on a previous tumour bed radiation, compared to 50-80% in primary sarcoma [1]. In case of penile sarcomas, deep-seated tumours can grow rapidly and give metastases with a high mortality rate, especially large tumours or located at the root of the penis [4,11,12], while superficial tumours have a higher relapse rate after resection but a much better prognosis [11,12]. The most common metastatic sites are lung (90%) [4,11] and bone (8%) [4], regional lymph node metastases are uncommon [4,11].

Conclusion

Post-radiation sarcoma is a growing problem because of the increased number of long-term cancer survivors. It would be interesting to study further the genetic landscape of radiation-associated sarcomas to be able to distinguish true radio-induced sarcomas from primary sarcomas. It is also important to learn more about molecular pathogenesis to find effective therapeutic agents in case of advanced disease. The possibility of secondary malignancy related to radiation needs to be included in management discussion, in particular for patients with a long-life expectancy. There is a need for future studies assessing the risk of secondary malignancy after radiotherapy, and additional enlightenment on the expected latency period for individual conditions, to develop an efficient strategy for patient education and surveillance.

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References

1. Lopez-Torres II, Calvo-Haro JA, Mediavilla-Santos L, Perez-Mananes R, Cuervo-Dehesa M, et al. (2018) Post-radiation pelvic sarcomas after radiotherapy treatment of prostate adenocarcinoma. Arch Clin Exp Surg. 7:94-9.
2. Snow A, Ring A, Struycken L, Mack W, Koç M, Lang JE. (2021) Incidence of radiation induced sarcoma attributable to radiotherapy in adults: A retrospective cohort study in the SEER cancer registries across 17 primary tumor sites. Cancer Epidemiol. 70:101857.
3. Mito JK, Mitra D, Doyle LA. (2019) Radiation-Associated Sarcomas: An Update on Clinical, Histologic, and Molecular Features. Surg Pathol Clin. 12:139-48.
4. Arenas J, Hoyos JG, Catano JG, Serrano J, Meek E. (2022) Primary Radiation-Induced Sarcoma of the Penis: Case Report and Review of the Literature. Int Arch Urol Complications. 8:085.
5. Nazemi A, Daneshmand S. (2020) Adult genitourinary sarcoma: A population-based analysis of clinical characteristics and survival. Urol Oncol. 38:334-43.
6. Horiguchi H, Takada K, Kamihara Y, Ibata S, Iyama S, et al. (2014) Radiation-induced leiomyosarcoma of the prostate after brachytherapy for prostatic adenocarcinoma. Case Rep Oncol. 7:565-70.
7. Wallis CJ, Mahar AL, Choo R, Herschorn S, Kodama RT, et al. (2016) Second malignancies after radiotherapy for prostate cancer: systematic review and meta-analysis. BMJ. 352:i851.
8. Joo MW, Kang YK, Ogura K, Iwata S, Kim JH, et al. (2018) Post-radiation sarcoma: A study by the Eastern Asian Musculoskeletal Oncology Group. PLoS One. 13:e0204927.
9. Labidi-Galy SI, Tassy L, Blay JY, Esun A. (2011) Radiation-Induced Soft Tissue Sarcoma. A Resource from The Liddy Shriver Sarcoma Initiative. Corpus ID: 51842679.
10. Fetsch JF, Davis CJ Jr, Miettinen M, Sesterhenn IA. (2004) Leiomyosarcoma of the penis: a clinicopathologic study of 14 cases with review of the literature and discussion of the differential diagnosis. Am J Surg Pathol. 28:115-25.
11. Romero Gonzalez EJ, Marenco Jiménez JL, Mayorga Pineda MP, Martínez Morán A, Castiñeiras Fernández J. (2015) Leiomyosarcoma of the Penis, an Exceptional Entity. Urol Case Rep. 3:63-4.
12. Nanri M, Kondo T, Okuda H, Tanabe K, Toma H. (2006) A case of leiomyosarcoma of the penis. Int J Urol. 13:655-8.