ISSN: 2584-0355
DOI: doi.org/10.51219/MCCRJ/Asledin-Mohammed/64

URF PUBLISHERS
connect with research world

Medical & Clinical Case Reports Journal

https://urfpublishers.com/journal/case-reports

Vol: 2 & Iss: 2

Case Report

Radiation Induced Extra Skeletal Soft Tissue Osteosarcoma

Samer Jumean*, Shatha Elemian, Bader Al Omour, Sawjanya Kalluri, Amr Ramahi, Gunwant Guron and Hamid Shaaban

Department of Internal Medicine, Hematology/Oncology, New York Medical College at St.Michael's, NJ State, USA

Citation: Jumean S, Elemian S, Kalluri S, et al. Radiation Induced Extra Skeletal Soft Tissue Osteosarcoma. *Medi Clin Case Rep J* 2024;2(2):240-242. DOI: doi.org/10.51219/MCCRJ/Samer-Jumean/65

Received: 26 April, 2024; **Accepted:** 29 April, 2024; **Published:** 03 May, 2024

***Corresponding author:** Samer Jumean, New York Medical College at St. Michael's Medical center, USA. Email: sjumean1@outlook.com

Copyright: © 2024 Jumean S, et al., This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

ABSTRACT

Radiation-induced sarcoma (RIS) is an aggressive form of cancer, seen in individuals previously treated for breast cancer. Typically associated with unfavorable outcomes The onset of RIS commonly occurs a decade after the initial breast cancer diagnosis, with a potential latency period extending up to 20 years. Angiosarcomas and osteosarcomas are the predominant soft tissue and bone sarcomas arising within the irradiated conserved breast and its surrounding area, respectively. Notably, radiation-induced osteosarcomas predominantly originate from skeletal structures, with only 2-4% being extra-skeletal in nature. Herein, we present a remarkably rare case involving the development of radiation-induced extra-skeletal soft tissue osteosarcoma in the axilla mixed with features of spindle cell sarcoma

Keywords: Sarcoma; Radiation induced sarcoma; Osteosarcoma; spindle cell sarcoma; breast cancer

Introduction

Radiation-induced sarcoma (RIS) is an uncommon and aggressive form of cancer, exhibiting a higher prevalence in individuals previously treated for breast cancer compared to those with other primary solid cancers[1]. Typically associated with unfavorable outcomes[2], RIS often manifests histologically as malignant fibrous histiocytomas, angiosarcomas, and osteosarcomas[3]. The onset of RIS commonly occurs a decade after the initial breast cancer diagnosis, with a potential latency period extending up to 20 years[4-6]. The reported long-term risk of developing sarcoma following radiation therapy for breast cancer is approximately 0.2% over a span of 10 years. Angiosarcomas and osteosarcomas are the predominant soft tissue and bone sarcomas arising within the irradiated conserved breast and its surrounding area, respectively[7]. Notably, radiation-induced osteosarcomas predominantly originate from skeletal structures, with only 2-4% being extra-skeletal in nature[8]. Reported instances of radiation-induced extra-skeletal osteosarcomas are predominantly situated in the chest wall[9,10] and supraclavicular fossa[7]. Herein, we present a remarkably rare case involving the development of radiation-induced extra-skeletal soft tissue osteosarcoma in the axilla mixed with features of spindle cell sarcoma.

Case Presentation

This case involves a 67-year-old female with a medical history notable for asthma, obesity, and hypertension. She had a previous diagnosis of right breast cancer in remission since 2000, classified as stage IIB, T3N0M0, and positive for estrogen and progesterone receptors. received adjuvant radiotherapy, and kept on Tamoxifen for 5 years, then letrozole for another 5 years. In 2023, while the patient was undergoing regular follow up exam, the patient reported the onset of an asymptomatic painless right axillary mass characterized by gradual size increase over several weeks. Upon examination, the mass, measuring 2x2 cm, was found to be posteriorly located, fixed, and exhibited no changes in the overlying skin.

An ultrasonography revealed a multilobulated, well-

defined focus within subcutaneous fat, measuring 2.3 x 1.5 x 2.2 cm. The mass appeared hypoechoic with echogenic areas suggestive of calcification Figure 1. Due to highly suspicious features, an ultrasound-guided biopsy was performed. Initial histopathological examination identified an atypical monomorphic spindle cell neoplasm suggestive of a phylloides tumor, mitotic rates are rare to absent with little pleomorphism and no necrosis, immunohistochemical stains were focally positive for CD31 and CD34 and negative for S100, HMB45, SMA and AE1-AE3. The specimens were sent to a specialized pathology center for second opinion which showed cellular spindle cell neoplasm with mild to moderate cytological atypia and focal hyalinizing stroma. The mitotic count was 5/10 high-power fields, and focal positivity to desmin, muscle-specific action, and myogenin supported skeletal differentiation. The final diagnosis was spindle cell/sclerosing rhabdomyosarcoma, with positive markers for F13A, Ki-67 up to 20%, and vimentin. Conversely, S-100, HMB45, SMA, AE1-AE3, CD 31, and CD 34 were not expressed.

Contrasted computed tomography (CT) of the chest abdomen pelvis revealing no suspicious lesions, the patient was referred to multidisciplinary surgical oncology for excision of the mass. The final pathology diagnosis was high grade (grade 3) sarcoma with feature of osteosarcoma and spindle cell sarcoma, mitotic rate 11 mitoses/ 10 high power fields, with 5-10% necrosis. Immunohistochemical staining showed patchy positive staining for SMA, Demsin in the spindle cell component. Cytokeratin AE1/AE3, CD 34 and STAT6 are negative.

This case underscores the complexity and challenges in the diagnosis of rare malignancies, necessitating a thorough multidisciplinary approach for accurate assessment and appropriate management.

Discussion

Alongside chemotherapy and immunotherapy, radiation treatment plays an essential role in cancer management, which resulted in better outcomes that prolong long term survival rate in different types of cancers. However, it still carrying the risk of developing secondary malignant tumors[11,12]. Radiation induce sarcoma (RIS) is a uncommon and aggressive complication that could raise at the site of radiation after a latency period that can span for decades, with strong dose-response relationship[12,13], for instance patient with breast cancer who treated with ≥ 45 Gy faces a higher risk of developing RIS than patients who received lower doses with estimated 15-year incidence of RIS after breast cancer treatment is 0.3%[14].

The diagnosis of radiation-induced breast sarcoma (RIBS) presents a challenge; as the patients are usually asymptotic and the resemblance of primary sarcomas's characteristics in diagnostic imaging[15] Cahan et al. reported the first 11 cases of radiation-induced osteosarcoma and established criteria for RIS. These criteria include the tumor's development within the radiation field, distinct histology from the initial malignant tumor, a latency period typically exceeding 4 years, and confirmation through histopathological examination that the second malignancy is indeed a sarcoma[2,16]. In a retrospective screening study included patients with primary breast cancer who were treated with radiotherapy and diagnosed between 2000 and 2020, 19 patients were identified with RIBS meeting Cahan criteria, with a median latency period of 112 months[17].

Angiosarcoma was the most common identified histo-type followed by osteosarcoma[17]. In histopathologic analysis, primary sarcomas and secondary sarcomas of the breast exhibit identical morphological characteristics[18,19]. However, RIS usually manifests with a high-grade tumor with variable size upon excision[20,21]. Histopathologic features of RIS may include spindle-shaped tumor cells, hemorrhagic tumor nodules, prominent mitotic figures, and areas of necrosis[20-22]. The importance of whole tissue sampling is well seen in many case reports[23,24], including our case, where the initial core needle biopsies failed to reveal the osteosarcoma component, emphasizing the need for comprehensive sampling to avoid misdiagnosis.

RIS is associated with poor prognosis and lower disease-free survival rate compared with sporadic soft-tissue sarcomas, the reported 5-year survival rates range from 17 to 58% vs 54–76%, respectively[25,26]. Multiple risk factors were associated with poor outcomes such as tumor size and the presence of high-grade features[26, 27].

Treatment RIBS consider a challenge for most clinicians, as patients usually present with advance disease and the lack of standard guidelines for its treatment. However surgical resection with achieving negative margins is the most effective treatment for RIBS to reduce the risk of recurrence[28-30]; the presence of positive margins significantly elevates the risk of local recurrence[31], Thijssens et al.[32] observed that R0 resections (microscopically tumor-free) yield considerably higher survival rates compared to R1 (microscopically positive for tumor) or R2 (macroscopically positive for tumor) resections. Moreover, survival rates did not significantly differ between patients with R1 and R2 resections. For proper disease clearance in RIS patients, retrospective studies indicated that surgical margin of 2-4 cm are necessary[33,34].

Radiotherapy was proposed as part of treatment in RIS to ensure local control after surgery, especially in patients with positive margins and large tumor size (≥ 5 cm)[27, 35, 36], however the effect of radiation treatment on overall survival rate is still uncertain[29, 37]. In addition, second course of radiotherapy raises concerns about toxicities such as rib fracture, pneumonitis, and soft-tissue necrosis. The role of chemotherapy for RIS remains ambiguous. No level 1 or 2 studies are available to address this question for RIS because of the rarity of this disease[38].

Conclusion

Although rare, post-irradiation breast sarcoma should be considered in the differential diagnosis of breast lesions showing malignant osteoid. RIBS tend to be more aggressive than traditional osteosarcomas owing to their deep location, large size, and difficult complete surgical removal. It is imperative to underscore the critical need for enhanced detection and treatment strategies in light of the low survival rates associated with RIBS. The extended latency period observed in many cases further emphasizes the essential role of long-term oncologic follow-up, administered by experienced oncologist's adept in evaluating the radiated breast and chest wall. Additionally due to the observed missed histopathological findings of osteosarcoma in needle biopsies in multiple cases including ours, we emphasize on the importance of opting for complete surgical excision to avoid missing such a diagnosis. Due to the rarity of extra-skeletal breast osteosarcomas, there are no guidelines on the optimal management, but it is agreed that surgical excision is the main key for initial therapy.

Disclosures

Ethics approval and consent to participate: Not Applicable

Consent for publication: Not Applicable

Availability of data and materials: Not Applicable

Conflicts of interest: no conflict of interest

Funding: Not Applicable

Acknowledgements: Not Applicable

Authors Contributions

Writing, Review and Editing: Shatha Elemian, Bader Al Omour, Sawjanya Kalluri, Amr Ramahi,

Supervision and critical review: Gunwant Guron, Hamid Shaaban

References

1. Snow A, Ring A, Struycken L, Mack W, Koç M, Lang JE. 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 2021;70:101857.
2. Yap J, Chuba PJ, Thomas R, et al. Sarcoma as a second malignancy after treatment for breast cancer. Int J Radiat Oncol Biol Phys 2002;52(5):1231-1237.
3. Bjerkehagen B, Smeland S, Walberg L, et al. Radiation-induced sarcoma: 25-year experience from the Norwegian Radium Hospital. Acta Oncol 2008;47(8):1475-1482.
4. Olcina M, Merck B, Giménez-Climent MJ, et al. Radiation-Induced Leiomyosarcoma after Breast Cancer Treatment and TRAM Flap Reconstruction. Sarcoma 2008;2008:456950.
5. Travis EL, Kreuther A, Young T, Gerald WL. Unusual postirradiation sarcoma of chest wall. Cancer 1976;38(6):2269-2273.
6. Cozen W, Bernstein L, Wang F, Press MF, Mack TM. The risk of angiosarcoma following primary breast cancer. Br J Cancer 1999;81(3):532-536.
7. Pendlebury SC, Bilous M, Langlands AO. Sarcomas following radiation therapy for breast cancer: a report of three cases and a review of the literature. Int J Radiat Oncol Biol Phys 1995;31(2):405-410.
8. Wiklund TA, Blomqvist CP, Räty J, Elomaa I, Rissanen P, Miettinen M. Postirradiation sarcoma. Analysis of a nationwide cancer registry material. Cancer 1991;68(3):524-531.
9. Alpert LI, Abaci IF, Werthamer S. Radiation-induced extraskeletal osteosarcoma. Cancer 1973;31(6):1359-1363.
10. Orta L, Suprun U, Goldfarb A, Bleiweiss I, Jaffer S. Radiation-associated extraskeletal osteosarcoma of the chest wall. Arch Pathol Lab Med 2006;130(2):198-200.
11. Mahmood S, Vu K, Tai P, et al. Radiation-induced second malignancies. Anticancer Res 2015;35(4):2431-2434.
12. Virtanen A, Pukkala E, Auvinen A. Angiosarcoma after radiotherapy: a cohort study of 332,163 Finnish cancer patients. Br J Cancer 2007;97(1):115-117.
13. Behjati S, Gundem G, Wedge DC, et al. Mutational signatures of ionizing radiation in second malignancies. Nat Commun 2016;7:12605.
14. Rubino C, Shamsaldin A, Lê MG, et al. Radiation dose and risk of soft tissue and bone sarcoma after breast cancer treatment. Breast Cancer Res Treat 2005;89(3):277-288.
15. Sheppard DG, Libshitz HI. Post-radiation sarcomas: a review of the clinical and imaging features in 63 cases. Clin Radiol 2001;56(1):22-29.
16. Cahan WG, Woodard HQ. Sarcoma arising in irradiated bone; report of 11 cases. Cancer 1948;1(1):3-29.
17. Di Lalla V, Tolba M, Khosrow-Khavar F, Baig A, Freeman C, Panet-Raymond V. Radiation-Induced Sarcomas of the Breast: A Review of a 20-Year Single-Center Experience. Cureus 2023;15(4):e38096.
18. Velaj RH, DeLuca SA. Radiation-induced sarcoma. Am Fam Physician 1987;36(5):129-130.
19. Chen KT, Hoffman KD, Hendricks EJ. Angiosarcoma following therapeutic irradiation. Cancer 1979;44(6):2044-2048.
20. Moskaluk CA, Merino MJ, Danforth DN, Medeiros LJ. Low-grade angiosarcoma of the skin of the breast: a complication of lumpectomy and radiation therapy for breast carcinoma. Hum Pathol 1992;23(6):710-714.
21. Gherardi G, Rossi S, Perrone S, Scanni A. Angiosarcoma after breast-conserving therapy: fine-needle aspiration biopsy, immunocytochemistry, and clinicopathologic correlates. Cancer 2005;105(3):145-151.