

Radiation-Induced Breast Cancer after Treatment of Hodgkin's Disease: A Revealing Case of the Challenges of Long-Term Follow-Up

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Abstract

Case Report

Introduction: Radiation-induced breast cancer is a rare but documented long-term complication of combined chemotherapy and radiotherapy for Hodgkin's disease, especially in young patients. Improved treatments have increased survival rates but also secondary cancer risks, particularly in women irradiated in the mediastinum before age 30, leading to unique diagnostic and therapeutic challenges. **Methods:** This case report describes a 45-year-old woman with a history of Hodgkin's disease treated at age 20 with chemotherapy and radiotherapy. Screening began at age 42 with mammography, followed by biennial assessments. After loss to follow-up, she presented with a right breast nodule. Diagnostic methods included clinical examination, echomammography, micro-biopsy, and multidisciplinary evaluation for neoadjuvant chemotherapy, mastectomy, hormone therapy, and targeted therapy. **Results:** Initial mammography showed ACR2 right and ACR1 left breasts, progressing to ACR4B right (with pleomorphic microcalcifications) and ACR3 left after two years. Re-presentation revealed a 70x50x34 mm irregular mass in the upper-outer right quadrant with axillary adenopathy (ACR5 right, ACR3 left). Biopsy confirmed infiltrating micropapillary carcinoma (SBR grade II, hormone receptor-positive, Ki67 50%, HER2 3+). Extension assessment was negative, leading to neoadjuvant treatment and planned surgery. **Conclusions:** This case underscores the need for early, annual screening (mammography/IRM) starting 8-10 years post-radiotherapy or at age 25 in high-risk patients to prevent delayed diagnosis and advanced presentation. Multidisciplinary surveillance is essential to mitigate risks and improve outcomes in survivors of Hodgkin's disease.

Keywords: Radiation-induced breast cancer, Hodgkin's disease, Mediastinal radiotherapy, Early screening, Micropapillary carcinoma.

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INTRODUCTION

Radiation-induced breast cancer represents a rare but well-documented complication of combined chemotherapy and radiotherapy treatments, particularly in patients treated at a young age for malignant hemopathies such as Hodgkin's disease [1]. The improvement in therapeutic protocols has significantly increased patient survival, but this advancement is accompanied by an increase in long-term side effects, including secondary cancers. Women who received mediastinal irradiation before the age of 30 are particularly at risk of developing radiation-induced breast cancer, with a cumulative risk that increases over time. This type of cancer often presents biological and clinical characteristics different from sporadic cancers, raising specific diagnostic and therapeutic challenges.

CASE REPORT

We report here the case of a 45-year-old patient, followed for a history of Hodgkin's disease treated with chemotherapy and radiotherapy at the age of 20, who developed secondary breast cancer. The patient began her first screening mammography at the age of 42. The initial radiological assessment showed two breasts classified as ACR2 on the right and ACR1 on the left. A second assessment performed two years later showed a focus of round and pleomorphic grouped microcalcifications deep in the right breast, bilateral fibrocystic dystrophy foci: breasts classified as ACR4B on the right and ACR3 on the left. The patient was lost to follow-up. She returned for consultation after one year due to a nodule in the right breast. On examination, it was a nodule in the upper-outer quadrant on the right, irregular, measuring 5 cm, mobile relative to both planes,

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with ipsilateral axillary adenopathy. On echomammography, there was an irregular mass with non-circumscribed contours in the upper-outer quadrant measuring 70x50x34 mm, associated with skin thickening and right axillary adenopathy, a fibrocystic dystrophy focus in the upper-inner quadrant: breasts classified as ACR5 on the right and ACR3 on the left. A micro-biopsy showed an infiltrating micropapillary carcinoma of the right breast with a modified SBR histoprognotic grade II, positive hormone receptors, Ki67 at 50%, HER2 neu overexpressed (score 3+). The extension assessment was without abnormality. The extension assessment was without abnormality. The multidisciplinary staff decision was to initiate neoadjuvant chemotherapy followed by a Patey-type mastectomy on the right, hormone therapy, and targeted therapy.

DISCUSSION

This clinical case highlights the challenges of long-term follow-up for patients treated for Hodgkin's disease at a young age. The literature reports a significant increase in the risk of developing secondary breast cancer in patients who received mediastinal radiotherapy, particularly when performed before the age of 30. In our case, the patient was treated at the age of 20, placing her in a high-risk category [1,2]. Systematic screening in these patients should begin early, often recommended starting 8 to 10 years after the end of treatment or from the age of 30, according to international recommendations. Current recommendations (notably those from the NCCN [3], EUSOBI [4], and the American Cancer Society [5] advocate for annual imaging surveillance (breast MRI and/or mammography) starting 8 to 10 years after thoracic radiotherapy, or from the age of 25 [6]. However, in this case, screening was only initiated at the age of 42, more than two decades after the initial radiotherapy, representing a significant delay in surveillance [2,6]. The radiological evolution observed between the two initial assessments underscores the importance of regular follow-up. The transition from ACR2 to ACR4B indicates the appearance of suspicious elements, particularly pleomorphic microcalcifications. Unfortunately, the loss of follow-up for one year led to an advanced clinical presentation at the time of diagnosis, with a large palpable mass (70 x 50 x 34 mm), associated with axillary adenopathy. Indeed, radiation-induced breast cancers often exhibit aggressive biological and anatomopathological characteristics, which may correlate with faster tumor evolution in some cases. However, rapid evolution depends on multiple factors (age, hormonal status, molecular subtype, time since irradiation, etc.), and is not systematic [7].

The histological analysis revealed an infiltrating micropapillary carcinoma, a rare subtype known for its aggressiveness and tendency toward lymph node dissemination [8,9]. The immunohistochemical profile shows a luminal B HER2-positive tumor, with a high Ki-67 at 50%, suggesting significant proliferative

behavior. Although the extension assessment was negative, the tumor volume and axillary lymph node invasion indicate a locally advanced stage. The chosen therapeutic strategy – neoadjuvant chemotherapy followed by a Patey-type mastectomy – aligns with recommendations for locally advanced tumors with lymph node involvement. It optimizes local control while facilitating an evaluation of tumor response, which is an important prognostic factor [10].

This case illustrates several key points:

1. Secondary oncogenic risk after treatment for Hodgkin's disease, particularly related to thoracic radiotherapy.
2. Importance of early and tailored screening for high-risk patients, which differs from standard screening in the general population.
3. Impact of irregular surveillance, which can lead to a late diagnosis with significant prognostic implications.
4. Therapeutic challenges related to managing a new cancer in the context of prior therapeutic sequelae (cumulative toxicity, cardiovascular risks, post-radiation fibrosis...). It is therefore crucial to inform patients treated in childhood or adolescence for Hodgkin's lymphoma about the risk of secondary cancer and to integrate them into personalized and multidisciplinary surveillance programs.

CONCLUSION

This case highlights the importance of early screening and rigorous follow-up in patients treated with radiotherapy for Hodgkin's disease at a young age. The risk of radiation-induced breast cancer, although rare, is real and underestimated, particularly in the absence of awareness and adapted surveillance protocols. The late and advanced presentation of the cancer in this case illustrates the consequences of diagnostic delay. A multidisciplinary approach, including oncologists, radiologists, and general practitioners, is essential to ensure early detection, improve prognosis, and optimize the management of these high-risk patients.

“The authors declare that they have no conflicts of interest to disclose.”

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