

Breast Cancer Induced by Radiotherapy Following Hodgkin's Disease: A Study of Four Cases and Literature Review

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Abstract: Radiotherapy is a cornerstone in the treatment of Hodgkin's disease but can have long-term consequences, notably the development of secondary malignant tumors. This case study and literature review highlight the imaging characteristics, diagnostic challenges, and clinical outcomes of this late complication. The aim of this article is to underscore the role of imaging modalities in the diagnosis, characterization, and management of this rare and complex condition. We discuss the radiological findings, clinical diagnosis, and therapeutic considerations, thereby providing valuable insights into radio-induced breast cancer in Hodgkin's disease and emphasizing the importance of personalized surveillance in these high-risk patients.

Keywords: Radio-induced breast cancer, Hodgkin's disease, imaging modalities, mammography, ultrasound, magnetic resonance imaging, biopsy.

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INTRODUCTION

Radiotherapy plays a crucial role in managing Hodgkin's disease, offering high cure rates. However, long-term complications such as the development of secondary malignant tumors induced by radiotherapy can occur, with breast cancer being one of the most frequent. Imaging plays a crucial role in detecting and characterizing radio-induced breast cancer, aiding in accurate diagnosis and treatment planning. This retrospective study conducted between 2015 and 2016 in the medical imaging department of the Pierre and Marie Curie Center focuses on young patients under 35 years old presenting with breast cancer, aiming to illustrate the importance of various imaging modalities in assessing and managing radio-induced breast cancer in patients with Hodgkin's disease.

CASE OBSERVATION 1

We present the case of a 33-year-old patient who had previously received radiotherapy and chemotherapy for Hodgkin's disease at the age of 16. The patient was under ovulation induction treatment for primary infertility. She consulted following the appearance of a right breast mass. Clinical examination revealed a mobile nodule concerning both planes; given the suspicious characteristics of the mass, a mammography was performed revealing a suspicious high-density mass with irregular shape and heterogeneous due to the presence of calcifications within, located in the right QME, causing skin retraction in its vicinity (Figure 1). Ultrasound confirmed the presence of a hypoechoic right breast mass with irregular contours measuring 21mm, attenuating, associated with another lobulated mass with microlobulated homogeneous contours of 12mm (Figure 2), classifying the radiological file as BI-RADS 5 by the ACR on the right and BI-RADS 4 by the ACR on the left.

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Microbiopsy under ultrasound control on both masses favored grade II infiltrating ductal carcinoma RE/7 RP/8 Her2/2+ Ki67: 10% on the right and in situ carcinoma on the left. Magnetic resonance imaging (MRI) was then requested given the age and locoregional extension assessment for multifocality and multicentricity, providing additional information on the malign morphology, size was 24 mm, the vascularization of the

lesion was heterogeneous with a type 2 curve and the presence of contralateral lesion searching for additional lesions. The radiological and anatomopathological results were compatible with malignancy (Figure 3). The decision of the multidisciplinary consultation meeting was a mastectomy on the right, lumpectomy under localization on the left followed by chemotherapy and radiotherapy.

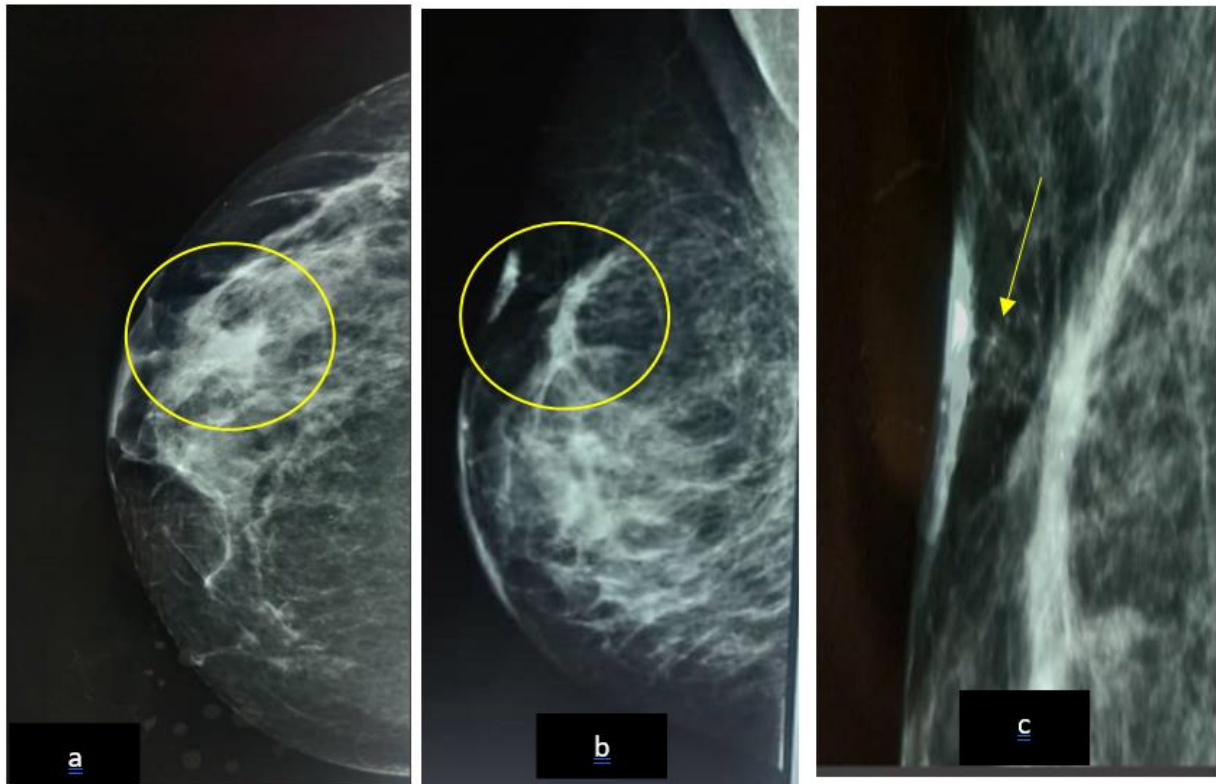


Figure 1: Mammography incidences: front(a), external oblique (b), magnification (c). Mass of high density, irregular in shape, with irregular contours, heterogeneous by the presence of calcifications within it are located at the level of the right QSE

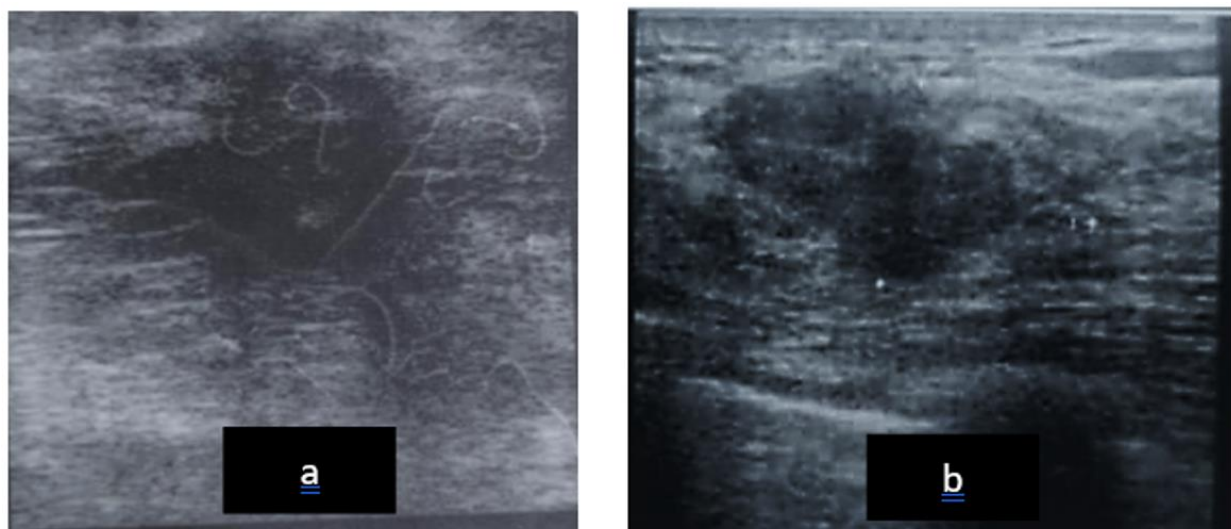


Figure 2: Breast ultrasound. (a) Right breast mass, hypoechoic, with irregular contours, attenuating, heterogeneous, by the presence of echogenic spots. (b) Left breast mass of lobulated shape with micro lobulated contours

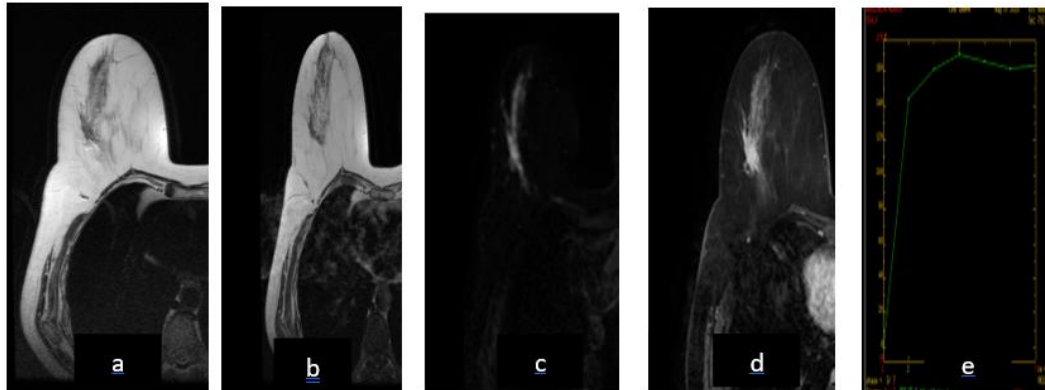


Figure 3: Breast MRI in axial sections. T1 and T2 weighted sequence. (a, b). Breast mass straight, dormant and irregularly contoured, in hyposignal T1, and T2, (c). Diffusion sequence. Hypersignal diffusion, (d). Sequence with injection of contrast media Intense enhancement of the breast mass, (e). Type 2 hemodynamic curve

OBSERVATION 2

We present the case of a 24-year-old patient who had previously received radiotherapy and chemotherapy for Hodgkin's lymphoma, stage II A sub-diaphragmatic, at the age of 17. The patient underwent 04 cycles of ABVD chemotherapy and radiotherapy at a dose of 30 Gy. The patient consulted following the appearance of a right breast mass. Clinical examination revealed a 2 cm induration in the right supero-external quadrant (QSE), highly suspect without axillary lymphadenopathies, thus classified as T2 N0 M0. Breast ultrasound found a hypoechoic right breast mass with irregular contours, roughly round, attenuating heterogeneous, measuring 26mm (Figure 4a), classifying the radiological file as BI-RADS 4b by the ACR on the right and BI-RADS 1 by the ACR on the left. Microbiopsy under ultrasound control of the mass returned in favor of grade II triple-negative infiltrating ductal carcinoma with Ki67 at 40% on the right.

Mammography was performed for an extension assessment to search for microcalcifications, revealing a suspect isodense mass, round in shape with microlobulated contours at places, homogeneous without calcifications within, located in the right supero-external quadrant (QSE) (Figure 4a). Magnetic resonance imaging (MRI) was then requested considering the patient's age and for a locoregional extension assessment to search for multifocality and multicentricity, providing additional information on the irregular morphology, irregular contours, size of 29mm, and the heterogeneous vascularization with a type 2 curve of the lesion and also on the absence of additional lesions (Figure 5). The radiological and anatomopathological results were in favor of malignancy. The decision of the multidisciplinary consultation meeting was neoadjuvant chemotherapy after clip placement followed by lumpectomy under localization on the right and radiotherapy.

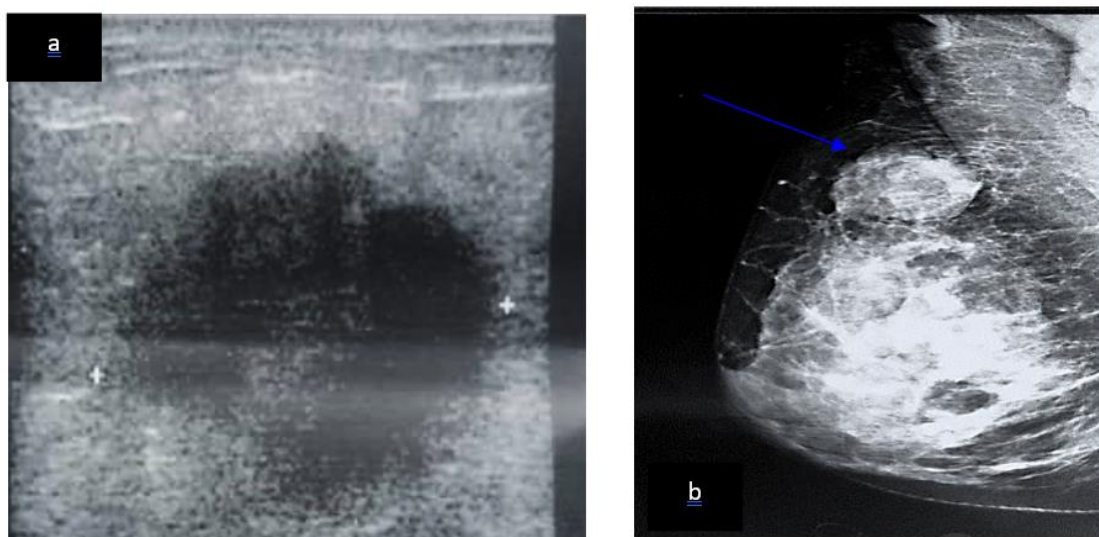


Figure 4a: Mammography external oblique incidence. Iso dense mass, rounded in shape, with micro-lobulated contours, homogeneous without calcifications within it sit at the level of the right QSE

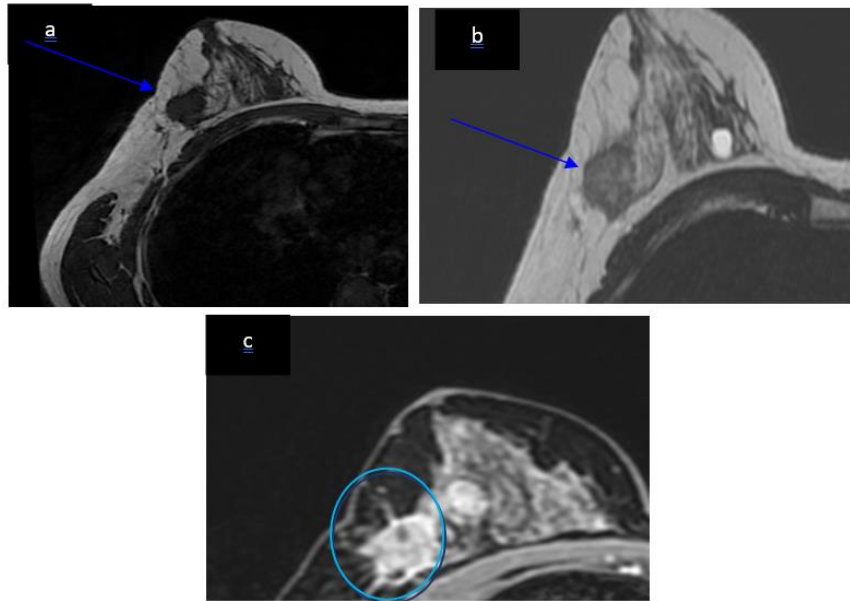


Figure 5: Axial cross-sectional breast MRI weighted sequence T1 (a) and T2 (b) Straight breast mass, irregularly shaped and contoured, in hyposignal T1, and T2, (c). T1 sequence with contrast injection. Intense and heterogeneous mass enhancements

OBSERVATION 3

We present the case of a 33-year-old patient who had previously received radiotherapy and chemotherapy for Hodgkin's lymphoma at the age of 19. The patient underwent chemotherapy and radiotherapy at a dose of 30 Gy. The patient consulted following the appearance of a left breast nodule. Clinical examination revealed a 3 cm mass in the left median-external quadrant (QME), mobile relative to the deep plane, highly suspect with axillary lymphadenopathy thus classified as T2 N1 M0. Breast ultrasound was requested, finding a hypoechoic left breast mass with irregular contours, irregularly shaped, measuring 21mm, attenuating heterogeneous, 26mm (Figure 6a), classifying the radiological file as BI-RADS 4b by the ACR on the right and BI-RADS 1 by the ACR on the left. Microbiopsy under ultrasound control of the mass returned in favor of grade II infiltrating ductal carcinoma

with positive hormone receptors and Ki67 at 50%. Mammography was performed for an extension assessment to search for microcalcifications, revealing homogeneous architectural distortion without calcifications within, located in the left median-external quadrant (QME) (Figure 7). Magnetic resonance imaging (MRI) was then requested considering the patient's age and for a locoregional extension assessment to search for multifocality and multicentricity, providing additional information on the irregular morphology, irregular contours, size of 29mm, and the heterogeneous vascularization with a type 2 hemodynamic curve with the presence of some additional lesions. The radiological and anatomopathological results were compatible with malignancy (Figure 3). The decision of the multidisciplinary consultation meeting was a mastectomy followed by adjuvant chemotherapy under localization on the right followed by radiotherapy.

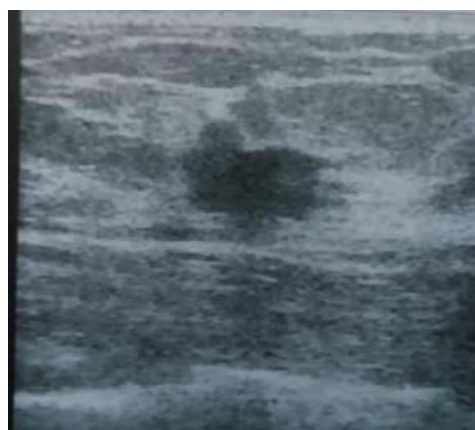


Figure 6: Breast ultrasound. Straight, hypoechoic breast mass with irregular, attenuating contours

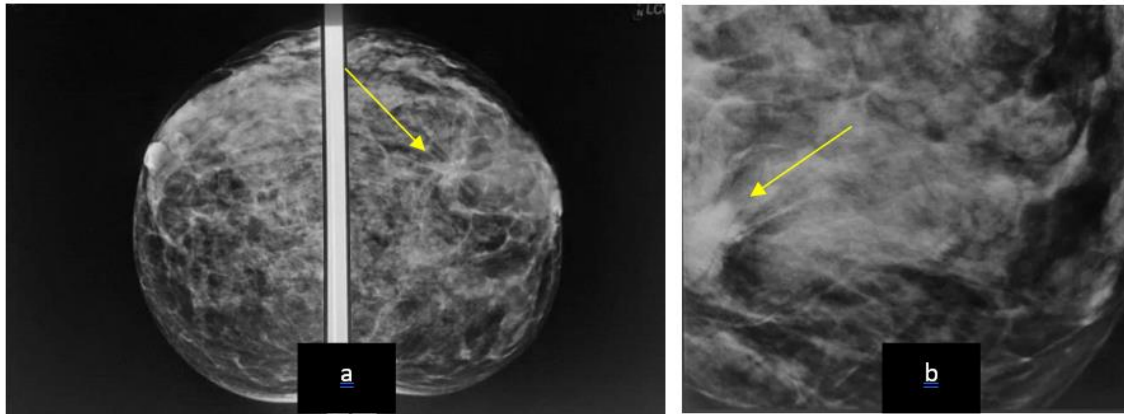


Figure 7: Mammography front incidences (a). Enlargement (b). High-density, speculated mass, irregular contours, homogeneous sit at the level of the left EIQ

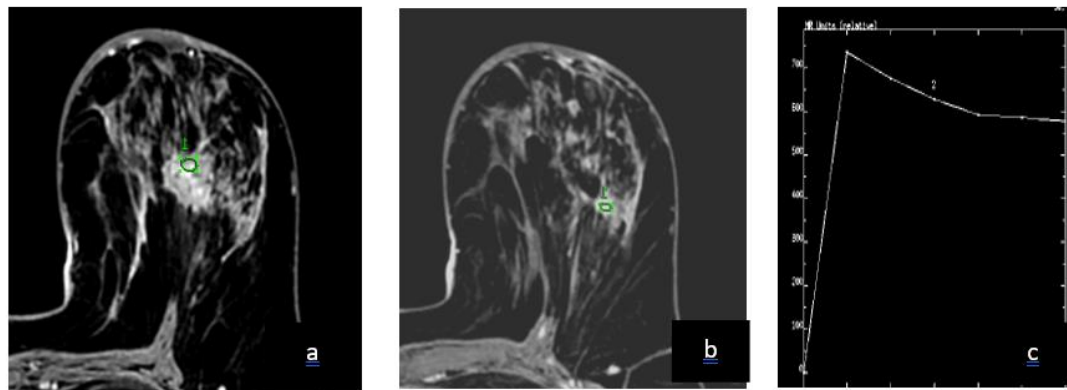


Figure 8: Axial cross-sectional breast MRI sequence injected under T1 (a, b), Mass of multiple spiculated shape and contours (c). Type 3 hemodynamic enhancement curve

Given the extensive and detailed nature of the document, it's important to approach the translation in segments that ensure both accuracy and completeness. Continuing from where we left off:

OBSERVATION 4

We present the case of a 29-year-old patient who had previously received radiotherapy and chemotherapy for Hodgkin's lymphoma at the age of 18. The patient was treated with chemotherapy and radiotherapy. The patient consulted following the appearance of a left breast mass with associated redness. Clinical examination revealed a central inflammatory tumor mass of 10 cm in the left breast with edema and warmth, and suspicious homolateral axillary lymphadenopathies of 6 cm, thus classified as T4d N1b M0. Breast ultrasound found a left breast mass, roughly round in shape with irregular contours, solid-cystic heterogeneous predominantly cystic with a thickened wall measuring 41 mm (Figure 9a), classifying the radiological file as BI-RADS 4 by the ACR on the right and BI-RADS 1 by the ACR on the left. Microbiopsy

under ultrasound control of the mass returned in favor of grade II triple-negative infiltrating ductal carcinoma with Ki67 at 60% on the right, and the cytopuncture of the lymph node was positive. Mammography was performed for an extension assessment to search for microcalcifications, revealing a suspect isodense mass, round in shape with irregular contours at places, homogeneous without calcifications within, located in the left supero-external quadrant (QSE) (Figure 9b). Magnetic resonance imaging (MRI) was then requested considering the patient's age and for a locoregional extension assessment to search for multifocality and multicentricity, providing additional information on the round morphology, irregular contours, size of 49x51mm, and the heterogeneous vascularization with a type 2 curve. There were associated additional lesions of the non-mass enhancement type contiguous (Figure 10). The radiological results were compatible with malignancy. The decision of the multidisciplinary consultation meeting was neoadjuvant chemotherapy after clip placement followed by lumpectomy under localization on the left and radiotherapy.

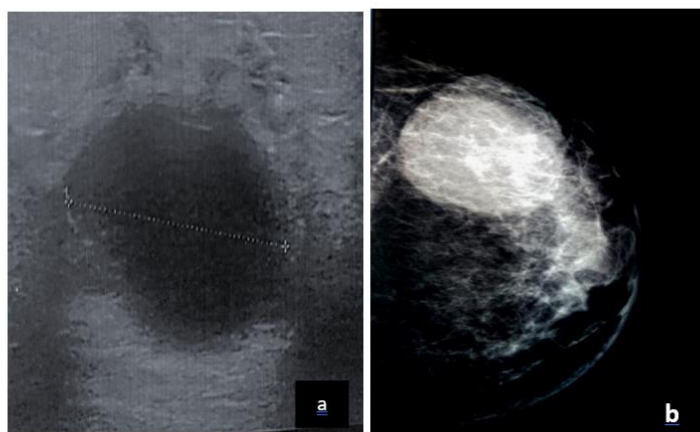


Figure 9a. Mammography facing the front. Dense iso mass, rounded in shape, with circumscribed contours, homogeneous, without calcifications within it sit at the level of the left QSE.
Figure 9b. Breast ultrasound. Left breast mass, very hypoechoic heterogeneous with an anechoic center, with microlobulated contours. with posterior reinforcement

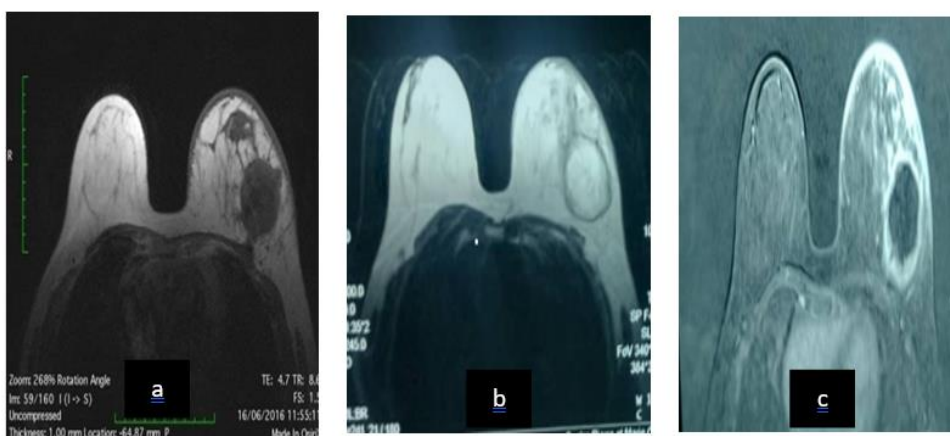


Figure 10: Breast MRI in axial section, T1 (a) and T2 (b) weighted sequence. Right breast mass, round in shape and with irregular contours, in T1 and T2 hyposignal, c. T1 with contrast product injection Fat Sat sequence. Peripheral annular enhancements of the thickened wall and non-enhanced necrotic center

DISCUSSION

Hodgkin's disease (HD) was once a fatal illness. Since the 1960s, its prognosis has changed due to chemotherapy and radiotherapy. However, after several years, side effects, notably chemo and radio-induced cancers, have drawn attention. These are primarily leukemias, non-Hodgkin lymphomas, but also solid tumors [1]. Breast cancer is the most frequent neoplasm among solid tumors in women treated for HD [2, 3]. Radio-induced breast cancer is a long-term complication recognized from radiotherapy in Hodgkin's disease. The latency period may be shortened in young women. The risk of developing breast cancer varies depending on several parameters, notably the age at HD diagnosis, the dose of radiotherapy, especially received by the breast gland, the type of chemotherapy due to the possible aggravating role of certain molecules (alkylating agents), possible genetic factors like BRCA1 and BRCA2

mutations [4]. But also the state of chronic immunosuppression either intrinsic to Hodgkin's disease or induced by treatment [5-7]. The average latency time between secondary breast cancer and Hodgkin's disease is 16 years, with extremes ranging from 7 to 31 years [8]. In our cases, the latency time was entirely comparable to that of other studies. According to various literature data, secondary breast cancer does not seem to have a particular topographic distribution; however, Van Leeuwen *et al.*, [9]. reported a frequency of 50% of central-site tumors and bilateral involvement in young women with family history of breast cancer and/or predisposing genetic factors (BRCA1, BRCA2). These secondary breast cancers are aggressive; the relative risk of radio-induced cancer to develop a cancer is 56 for a therapeutic age under 20 years. This risk aggravates in children or adolescents treated in the prepubertal period

[10-12]. probably corresponding to the maximum radiosensitivity moment of the breast gland [13].

Imaging modalities, notably mammography, ultrasound, and MRI, play a crucial role in the detection, characterization, and management of these malignancies. Ultrasound is the initial screening tool in young women, detecting suspicious anomalies such as masses and non-mass echoes, providing additional information on morphology, contours, and vascularization of the lesion [14]. Mammography searches for microcalcifications or architectural distortion [15]. MRI offers superior tissue contrast and multiplanar imaging capabilities, contributing to precise staging and treatment planning [16].

In our case, mammographic results of masses with spiculated, irregular, and microlobulated contours raised strong suspicion of malignancy. Subsequent ultrasound evaluation revealed an irregularly contoured hypochoic mass, further strengthening the suspicion of breast cancer. MRI provided detailed information on morphology and vascularization of the lesion, contributing to the assessment of tumor extent and surgical planning. However, there is no radiological semiotic difference compared to primary cancers.

Histopathological examination of the biopsy sample confirmed the diagnosis of infiltrating ductal carcinoma. Treatment options were discussed in a multidisciplinary meeting, considering the patient's history of Hodgkin's disease, the extent of breast cancer, and the patient's preferences. A personalized treatment plan including surgery, adjuvant chemotherapy, and radiotherapy was developed [17].

CONCLUSION

Radio-induced breast cancer is a potential long-term complication in patients treated for Hodgkin's disease. Imaging modalities such as mammography, ultrasound, and MRI play essential roles in detecting, characterizing, and managing these malignancies. Accurate radiological evaluation, combined with histopathological confirmation, guides therapeutic decisions and improves patient outcomes. Medical residents must be aware of the unique challenges and considerations associated with radio-induced breast cancer in patients with Hodgkin's disease. Further research is needed to optimize management strategies for this specific patient population.

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