

CASE REPORT

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# Secondary breast cancer after treatment for Hodgkin's disease: A clinical case

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## ABSTRACT

**Introduction:** Improved survival of patients treated for Hodgkin's disease has been increased at the cost of late complications, the most frequent of which are secondary neoplasias such as breast cancers, which account for 6–9% of these neoplasias after treatment for MDH. The most favorable factors are mainly young age and radiotherapy. **Case Report:** We report the observation of a patient treated for Hodgkin's disease at the age of 17 years and after 17 years, she was diagnosed with right breast cancer, triple negative and then benefiting from breast-conserving surgery treatment and adjuvant chemotherapy and radiotherapy. **Conclusion:** We represent a general review of the risk factors and diagnostic, prognostic and therapeutic choices modulated according to the treatment received for the Hodgkin's disease of these secondary mammary cancers. Survivors of Hodgkin's disease may have a long life expectancy nowadays and it is important to

develop appropriate methods for estimating the risk of late breast cancer.

**Keywords:** Hodgkin's disease, Radio induced neoplasms, Radiotherapy, Secondary breast cancer

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## INTRODUCTION

The use in Hodgkin's disease of extensive and sustained diaphragmatic irradiation combined with multidrug therapy has resulted in dramatic improvements in patient survival but at the price of an increased incidence of secondary neoplasia including breast cancer in women, accounting for 6–9% of neoplasias secondary to Hodgkin's disease. Our objective; Based on clinical observation; is to take stock of breast cancers occurring after Hodgkin's disease while underpinning the characteristic, therapeutic and prognostic modalities.

## CASE REPORT

A 34-years-old female, married, and mother of one child, menarcheal age at 13 years old, not menopausal and she took oral contraceptives for about four years; there is no known family history of breast or ovarian cancer.

She was treated at the age of 17 for Hodgkin's disease initially classified as stage III supra and

under diaphragmatic with first-line chemotherapy: cyclophosphamide, vincristine, prednisone and procarbazine hydrochloride (8 cures) followed by diaphragmatic irradiation mantle; 36 Gy in 18 sessions and irradiation of the lomboatric and the spleen at a dose of 36 Gy at five fractions per week ended on 04 August 1998; The patient was followed regularly and then lost sight of, and come back 17 years later for a right breast nodal in external super-quadrant, 3 cm in size, classified IV according to American College of Radiology; associated with an axillary ganglion infracentimetric. The extension report was normal (computed tomography thoracic-abdominal-pelvic and bone scan).

After the multidisciplinary consultation meeting, a breast-conserving surgery was performed and the lymph node dissection performed nine free lymph nodes and the final anapathological examination was in favor of a slightly differentiated ductal adenocarcinoma infiltrating grade III of Scarff-Bloom-Richardson grading system; triple negative. Subsequently, the patient was treated with three-cure of 5 fluorouracil, epiadriamycin and cyclophosphamide adjuvant chemotherapy and three docetaxel cures and then received external adjuvant radiotherapy 3D; a dose of 50 Gy in 25 sessions at 2 Gy by fraction, followed by a boost on the tumor bed by 10 Gy photons in five sessions (Figure 1). The films of the field involved were first examined carefully by the radiotherapist to assess the risk of breast irradiation.

After a regularly follow-up of two years she is asymptomatic with no evidence of recurrence and in complete remission.

## DISCUSSION

The strongly elevated risk of breast cancer after radiotherapy for Hodgkin's disease has become a major concern for female survivors of this disease and the combination of chemotherapy and radiotherapy in patients with Hodgkin's disease increased the rate of long survivors; exposed to high risk of the occurrence of

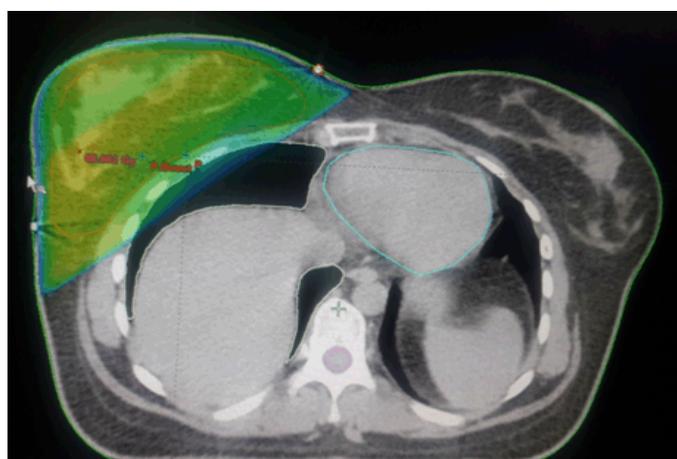


Figure 1: Dosimetric image showing the distribution of the dose on the mammary gland.

secondary neoplasia, including radiation-induced breast cancer in women, whose peak is 5–20 years after the last treatment given for DH. The relative and absolute risks of radiation-induced breast cancer are inversely proportional to the age at the time of exposure. Women treated with radiotherapy for Hodgkin's disease before the age of 41 experiences a high risk for breast cancer. They are maximal for irradiations occurring in the prepubertal and pubertal periods and then decrease regularly [1–7].

The increased risk during this period suggests that the carcinogenic role of ionizing radiation would be maximal on breast tissue in full proliferation.

In the series of 387 children treated at the St Jude Children's Research Hospital from 1968 to 1990, 14 secondary tumors (4%) were reported with average surveillance duration of 15.1 years [6]. In the Stanford series of 694 children followed on average for 13 years, 56 (8%) had 59 secondary tumors, including 48 solid tumors [8]. Breast cancer (16 cases) and sarcomas (13 cases) were the most frequent.

The mean latency between secondary breast cancer and Hodgkin's disease is 16 years with extremes between 7 and 31 years [1]. For our patient the latency period was 17 years. Some studies performed so far show an increased risk for breast cancer up to 30 years after treatment and a strong risk increase in women who received radiation at young ages [9–11]. In a Finnish study, the cumulative risk of second cancer is 17% at 20 years after initial diagnosis [8], and this cumulative incidence increased with decreasing age at first treatment for Hodgkin's disease [12].

Many reports are published on assessment of the risk factors, which are mainly the age at diagnosis of Hodgkin's disease, the dose of radiotherapy received by the mammary gland and the type of computed tomography scan administered. However, the quantification of the risk according to the dose is still imprecise, many factors such as the shape, the volume of the breasts and the shape of the caches that can interfere with the dose distribution at the mammary level during mantle irradiation [13–16]. The risk of breast cancer after Hodgkin's disease has been mainly attributed to supradiaphragmatic radiation therapy. Women treated with mantle field radiation experience up to 30 fold increased risks for breast cancer compared with their peers in the general population [17]. For Hill et al. the risk of breast cancer is 2.7 times higher in women who received a dose of more than 5 Gy in the breast compared to those receiving less than 5 Gy at this level. For Travis et al. the risk varies according to the age at diagnosis of Hodgkin's disease of the total dose of irradiation and the duration of follow-up. Dose response relationships have been shown for the radiation dose to the area of the breast where the tumor developed [18, 19]. In fact, there is a potentiation of the effect of radiotherapy by chemotherapy in radiation-induced tumors. The risk of secondary tumor after chemotherapy appears to be directly proportional to the total dose received and duration of exposure to drugs. And it was found that alkylating

chemotherapy decreases the risk of breast cancer among female Hodgkin's disease survivors, it is thought that the protective effect of alkylating chemotherapy is mediated through induction of premature menopause. Gonadotoxic treatment can also reduce the future risk for breast cancer especially when menopause occurs relatively shortly after treatment; the beneficial effect of gonadotoxic treatment is present in women treated before age 31, women treated between age 31 and 40 do experience an increased risk for breast cancer but this risk is not reduced by gonadotoxic treatment possibly because there are fewer years before natural menopause; but the hypothesis of risk reduction by therapy induced menopause is still controversial [12].

Another factor supported by Bruin is the hypothesis that reducing the proportion of breast tissue exposed to radiation will indeed decrease the future risk for breast cancer. An important issue involves the volume of breast tissue exposed to radiation and its effect on risk of breast cancer [20, 21]. Bruin also showed by his study that reduction of radiation volume can lower this risk [12].

Clinically and histopathologically, Yahalom et al. [22] found that of the 45 secondary breast cancers in 37 patients, of which eight were bilateral, there were no differences in the histological type, histopronostic Scarff-Bloom-Richardson grading system and axillary lymph node invasion compared to 935 primary breast cancer treated at the same time. However, these secondary breast cancers occurred earlier (median age: 43 years) and there were more bilateral cases and central seat tumors.

The treatment of secondary breast cancer is controversial and needs to be discussed collegially about the options available to each woman before deciding on the best therapeutics; the radiotherapist reviews the details of the previous irradiation to assess the dose received by the breast, lungs and heart. Alm El-Din et al. agreed [23] that mastectomy should be the surgery of choice for patients with a history of irradiation and who develop breast cancer. However, other research groups reported spectacular results with breast-conserving surgery followed by breast irradiation. In the series of Cutuli et al. [1] 44 patients had a breast-conserving treatment.

The prognosis of these cancers is generally unfavorable; the median survival in the Stanford study was 12.5 months after the diagnosis of secondary cancer [24]. The significant risk of developing secondary breast cancer after treatment for Hodgkin's disease raises the need for an earlier surveillance and screening strategy than in the normal population. The National Comprehensive Cancer Network [23] proposes an annual clinical examination before 25 years, then twice a year after 25 years according to clinical data and individual risk. More recent studies [25, 26] show that magnetic resonance imaging may be of interest in these high-risk patients, especially since it is not irradiating and performs well in young patients with dense breast.

## CONCLUSION

The occurrence of secondary breast cancer after Hodgkin's disease treatment is a fairly common event that involves a breast screening that must be started in the following decade, for survivors information about risk should be provided, relevant screening made available and any emerging symptoms investigated without delay in order to rule out a second cancer diagnosis. So the management of breast cancer after Hodgkin's disease requires a multidisciplinary consultation in order to appreciate the treatment already received with the modality of a re-irradiation and the place of the prophylactic surgery.

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## Author Contributions

Loubna Belhajjam – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Zineb Alami – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Asmaa Kouadir – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Abderahmane Elmazghi – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Touria Bouhafa – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Khalid Hassouni – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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