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CASE REPORT

Case Report: Late complications of radiotherapy for breast cancer [version 1; peer review: awaiting peer review]

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Abstract

The long term functional and aesthetic impact of breast neoplasia treatment partly reflects the consequences of high dose irradiation of the skin and subcutaneous tissue.

This work, based on a case observed in our department and a review of the literature, aims to discuss certain secondary manifestations following breast irradiation and their therapeutic options.

Our work reports the case of a premenopausal 46-year-old patient, treated for a right breast neoplasia. In July 2019, the patient underwent a Patey with simple postoperative follow-up. Histology substantiated the presence of an infiltrating ductal carcinoma SBRI. Mastectomy was followed by locoregional irradiation and adjuvant chemotherapy.

Thirteen months after the end of irradiation, the patient reconsulted for functional impotence and pain at the level of the right upper limb. The clinical examination showed cutaneous sclerosis and lymphedema. An X-ray showing the non-metastatic fracture of the clavicle. The patient underwent physiotherapy sessions with slight improvement on the functional level and clear improvement on the sensory level with progressive disappearance of pain.

Therapeutic options for complications of breast irradiation include massage, bandages, and physical exercise, often used in combination. The precise localization of the tumor bed and the application of appropriate clinical target volumes and planning target volumes are essential, as these concepts are fundamental for partial breast irradiation and avoid the complications of radiotherapy.

Keywords

Key words: breast neoplasia, radiotherapy, lymphedema., case report

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Introduction

The assessment of the long-term effects of breast irradiation is justified by the frequency of breast neoplasias, the role of radiotherapy in their locoregional management, and the importance of aesthetic outcomes. All of these factors are used in the assessment of the quality of care, especially after conservative treatment.

The breast cancer lymphoedema remains a potentially life-altering sequela of breast cancer treatment that affects approximately one in five patients.¹

Here, we report a case of a 46-year old patient who had late complications after undergoing irradiation for breast neoplasia.

Case report

Our work reports the case of a premenopausal 46-year-old patient, house wife, with no relevant personal medical history, sixth gesture fourth barrier, treated for a right breast neoplasia classified as T2 N1 M0. In July 2019, the patient underwent a Patey type mastectomy with axillary lymph node dissection with simple postoperative follow-up. Histology substantiated the presence of an infiltrating ductal carcinoma SBR I of 2.8 cm 5N +/13. Mastectomy was followed by locoregional irradiation and adjuvant chemotherapy. Radiotherapy sessions ended in February 2020.

The subsequent course was marked by the appearance of cutaneous sclerosis affecting the right upper limb nerve root in April 2021 (Figure 1; 13 months after the end of irradiation), significant lymphedema and clavicle fracture. This was confirmed by X-ray (Figure 2), with the site causing total function impotence and permanent pain of the right upper limb. A bone scan ruled out a metastatic origin.

Figure 1. Photograph showing lymphedema and skin fibrosis.

Figure 2. X-ray showing the non-metastatic fracture of the clavicle.

The patient underwent physiotherapy sessions with slight improvement on the functional level and clear improvement on the sensory level with progressive disappearance of pain.

Discussion

Despite constant progress in irradiation techniques, radiotherapy is not without side effects, which can sometimes occur a long time after the end of irradiation. Priority must be given to the early detection of these complications developed in the irradiation zone by close follow-up of the patients, which is not the case for our patient who consulted after 13 months after irradiation.

Complications start most often by the appearance of pain when mobilizing the right shoulder, which was neglected by our patient, and much more rarely by the sudden onset of total functional impotence. In our case, treatment was started directly after the diagnosis with good compliance of our patient with favorable clinical result.

Late cutaneous and subcutaneous manifestations induced by radiotherapy largely determine the aesthetic and functional outcome of local treatment of breast tumors. The administration of a high dose to the skin is difficult to avoid due to its anatomical proximity to the target volume of radiotherapy. If irradiation is not the only determining factor, the technique and treatment methods can be adapted to limit the most harmful consequences.² In our case, the patient underwent loco-regional radiotherapy with a total dose of 66,6 Gy.

Currently, various studies on the *in vitro* radiosensitivity of fibroblasts derived from patients treated with irradiation suggest a correlation between the radiosensitivity of these fibroblasts and the reactions of different healthy tissues to radiotherapy.³ Alsbeih *et al*³ in their work on seven patients treated with radiation reported that this association suggests that the analysis of clonogenic survival, or a more convenient alternative, could be used as a predictive test. The involvement of several tissues and organs suggests the existence of genetic factors which determine, at least in part, the radiosensitivity of the target cells involved in the clinical phenotype of response to radiotherapy in these patients.³ However, given the small number and selection of patients included ($n = 7$), larger studies must be carried out to confirm these results.³

The treatment of radiation induced sequelae is classically disappointing, hence the idea deeply rooted in the minds of clinicians of their irreversibility and a certain reluctance to engage in tiresome therapeutic trials. However, several experimental studies and some clinical studies have indicated that certain treatments can be active on the fibrotic process. In the inflammatory phase, the transition to the stage of fibrosis could be prevented by the use of non-steroidal anti-inflammatory drugs. Corticosteroids, certain antiproliferative substances and phenotypic modulators of endothelial and connective cells (interferons) and low molecular weight heparins for antithrombotic purposes seem less active.² Physiotherapy was the unique treatment carried out in our case.

Different teams have also studied the incidence of lymphedema after radiosurgical treatment of breast neoplasia which varies between 0 and 73%.^{1,4} The National Institute for Clinical Excellence in the UK, for example, reported an incidence of 25% to 28% and recommended its research 1 to 3 years after the establishment of the diagnosis.² Lymphedema appears to be dependent on the type of surgery, adjuvant therapy, and the number of axillary nodes removed during the dissection. "Standard" axillary dissection appears to be responsible for lymphedema in 56% of cases,⁵ which was the case for our patient. The use of less invasive methods such as the sentinel node technique seems to decrease its incidence.⁴

In a large prospective study including 1031 patients, Mansel⁶ found a lymphedema risk reduction of up to 12 months after treatment. The relative risk was 0.37 (95% confidence interval, 0.23-0.6) in favor of the sentinel node technique.

Axillary radiation therapy also appears to increase the risk of developing lymphedema in some studies. In fact, lymphedema occurred in 23 to 58% of patients treated with axillary radiotherapy versus 5 to 12% only in those who had not received this treatment.^{4,7} On the contrary, a large, randomized study found no relationship between breast radiotherapy and upper limb morbidity.⁴

Other risk factors are not well identified. Wounds and skin infections, as well as obesity, could stimulate the development of lymphedema. There were no postoperative complications in our case. The latter is associated with a heavy morbidity such as mobility limitation and weakness of the limb, pain, and paraesthesia.⁸

In a study carried out on 742 patients treated for breast neoplasia, Hiba *et al*⁴ stated that 31.67% of their study population reported the appearance of lymphedema after an average interval of 4.3 years. The medical history of these patients included breast irradiation in all cases. They also reported that 44.3% of patients with a diagnosis of lymphedema

experienced pain at the site of the intervention versus 36.9% of cases in those without lymphedema, in the armpit in 55.3% versus 31.8%, in the arm in 57% versus 28.6%, limitation of limb mobility in 63% versus 31.8%, paresthesia in the armpit in 60.9% versus 36.1%, and in the arm in 47.2% versus 23.5% of cases. The proportion of patients who reported these complications varied between 46 and 90%.

Therapeutic options include massage, bandages, and physical exercise, often used in combination. Compression bandaging alleviates lymphedema by 39%. Bandaging associated with an exercise program can reduce lymphedema by up to 50%.⁴ A prospective randomized study showed that lymphatic drainage associated with compression was of little benefit only in cases of minimal lymphedema. We observed a slight improvement on the functional level and a clear improvement on the sensory level after the physiotherapy for our patient.

The recommendations set out in the guidelines are to take good care of the limb by wearing gloves, for example, while doing house chores or gardening so as to avoid sores and skin infections.

Conclusions

The development of these complications has only been rarely reported. However, this does not appear to be exceptional in our clinical experience, especially after breast cancer.

Strict monitoring therefore seems essential in the face of any symptomatology appearing in the previously irradiated territory. This avoids a worsening of the symptoms which then require specific support.

As many of these women will have long-term survivability, the matter of late radiation-related complications will continue to be clinically relevant, making further exploration into improved strategies for dose reduction imperative.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Consent

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient.

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