# Case Presentation

## Plaque Morphea at Distance from Breast Cancer Radiotherapy: A Cost of the Treatment?

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**Abstract**

*Introduction.* Morphea is a rare dermatological disease with no known cause, characterized by persistent inflammation, collagen deposition, fibrosis, and atrophy, as well as a considerable reduction in quality of life. *Case presentation*. An 89-year-old female patient, with a history of arterial hypertension, right mastectomy, and radiation therapy for breast cancer 10 years before, presented for the appearance of two erythematous plaques in the right submammary groove and right flank. The plaques are well-defined, with irregular margins, and have dimensions of 10/5 cm, and 13/8 cm respectively, were infiltrated, with areas of skin retraction and visible capillary network, itchy and painful. They were observed six months before presentation, as a single hyperpigmented lesion that gradually evolved into its current appearance and was treated as a subcutaneous hematoma, without resolution. Laboratory tests showed a nonspecific inflammatory syndrome and an increase in antinuclear antibodies. By corroborating the clinical and paraclinical data, the diagnosis of plaque morphea was made, and the systemic treatment with Penicillin G 2mil IU/12h, 311nm UVB phototherapy was initiated, with favorable evolution. At the subsequent hospitalization, after noticing the increase in the size of the plaques, with their extension to the left hemiabdomen, it was decided to start treatment with Methotrexate 7.5 mg/week, with a favorable evolution and the disappearance of fibrous bands. *Conclusions.* Although radiotherapy may be the trigger factor of morphea, the time until the onset of the disease (9 years) is consistent with the data presented in the literature (9.4 years).

**Keywords:** morphea, irradiation therapy, breast cancer.

**DOI https://doi.org/10.56082/annalsarscimed.2021.1.35**

## INTRODUCTION

Morphea, also known as localized scleroderma, is a rare inflammatory dermatosis characterized by inflammation, increased fibrosis, and subsequent atrophy in the dermis and subcutaneous tissue, with a relatively benign evolution, but increased alteration of the quality of life [1]. The etiology of the disease is not fully understood; multiple trigger factors are involved, such as radiotherapy, surgery, traumatism, repeated friction in the interested area, bleomycin injection, and Borrelia burgdorferi infection. Even though the mechanisms are not fully elucidated, endothelial activation seems to be the primary event in the scleroderma process' formation [2].

Regarding the epidemiology of the disease, the number of cases varies between 0.34 and

2.7 cases per 100,000 inhabitants, with a predilection for females. Although one-third of the cases start in childhood, the peak incidence occurs between 20 and 40 years of age [3,4]. The variety of clinical forms in terms of distribution, plaque sizes, and shapes of the lesions has led to the necessity of classifying the disease into different clinical forms: circumscribed morphea, linear morphea, generalized morphea, pansclerotic morphea, and mixed morphea. Older classifications, which included other forms such as atrophoderma of Pasini and Pierini, eosinophilic fasciitis, or lichen scleroatrophic, are no longer accepted [5].

## CASE PRESENTATION

A 89-year-old Caucasian female patient presented to our department with two erythematous plaques in the right submammary groove and right flank. The patient's medical history was relevant for breast cancer 12 years before presentation, for which the patient undergone surgical excision (complete right mastectomy) followed by radiotherapy. Two erythematous, infiltrating, painful, and itchy plaques were discovered during the dermatological examination. The lesions were well-defined, with an irregular border and large diameters: 10x5 cm and 13x8 cm, respectively (**Figure 1**).

At the level of the abdominal lesion, we observed the presence of retraction and central atrophic areas, sclerous intermediate area, and red inflammatory peripheric border. The thinning of the cutaneous layers in the central atrophic zone also exposed the underlying capillary network. The other examined parameters were considered normal, taking into consideration the patient's age. The lesions first manifested 10 years after the last radiation session, as a hyperpigmented macula in the right submammary groove, which was misdiagnosed and treated as a local posttraumatic hematoma, that evolved during the prescribed treatment.

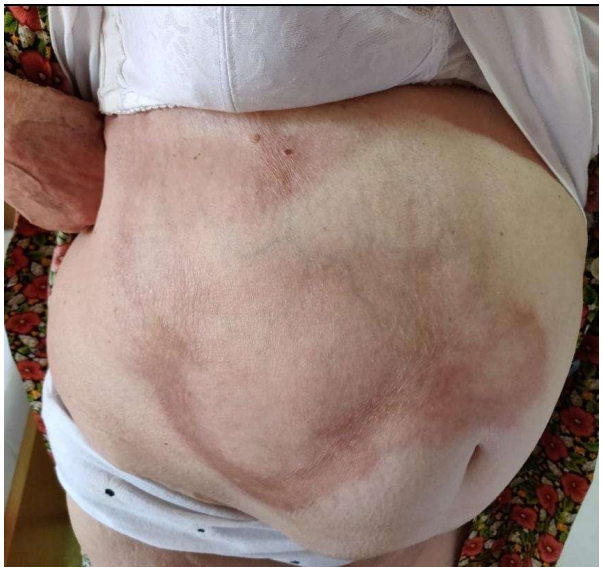

**Figure 1.** The aspect of the lesions at the moment of the presentation: large, well-defined plaques, indurated at palpation, with atrofic center, retraction areas and red inflammatory borders.

The paraclinical tests indicated an inflammatory syndrome (elevated fibrinogen, C-reactive protein, and erythrocyte sedimentation rate) and a positive antinuclear antibody panel. Following a punch biopsy, the histological investigation revealed an atrophic epidermis with reticular dermal sclerosis and perivascular lymphocytic infiltration. Additionally, areas of sclerosis extension in the subcutaneous fat tissue were revealed. The histopathological findings were consistent with cutaneous sclerosis. To confirm the diagnosis of morphea and exclude systemic involvement, a panel of systemic scleroderma antibodies was performed (anti centromere antibodies, anti-topoisomerase I antibodies, and anti RNA polymerase III antibodies), with negative results. Treatment with narrow-band phototherapy and penicillin G (as an anti-fibrosing agent) was initiated, followed by methotrexate therapy 7.5mg/week after three months. The lesions evolved favorably throughout therapy, with significant involution of the inflammatory region (**Figure 2**).

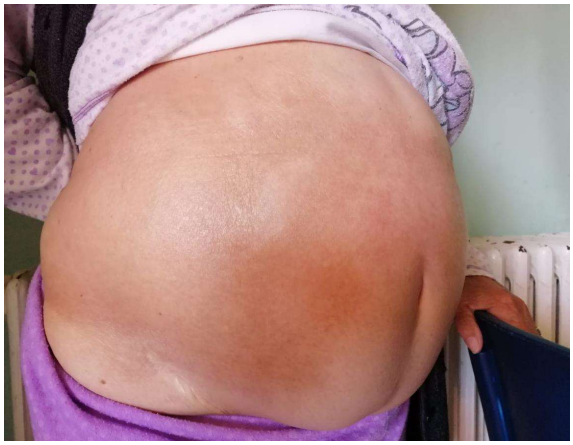

**Figure 2.** The aspect of the lesions after two years of treatment with Methotrexate 7.5mg/week. A reduction in the size of the lesions and of the fibrous, retractile area is observed.

## DISCUSSION

Plaque morphea is the most frequent type of morphea in the elderly. It is characterized by ovalar, well-circumscribed atrophic paches on the trunk or extremities, with the fibrous process restricted to the cutaneous tissue. Although various risk factors have been identified, including surgery and radiotherapy, the disease's pathogenesis remain unknown [1,6]. In the current case, the plaque morphea may have been caused by radiotherapy, the operation itself, or it may have been idiopathic.

Post-irradiation morphea (radiation-induced morphea) is a side effect of radiotherapy that is characterized by the formation of indurated atrophic plaques on the irradiated region or, in rare cases, at a distance from the irradiation field [7]. Numerous examples of breast cancer patients who had adjuvant irradiation and developed scleroderma in the radiation area or surroundings have been reported in the literature. The incidence of postradiotherapy morphea after breast cancer has been found to be about 70 times more than the general population's incidence of morphea [8]. Regarding the time interval between radiation and the beginning of morphea, either localized or widespread, the majority of reported cases indicated a time interval of less than 12 months between treatment and the onset of morphea [9]. As a rare complication, it is difficult to conduct studies on a statistically significant number of patients, with the majority of papers presenting single cases. Diago et al. published a research in 2017 on a group of six patients with breast cancer and subsequent radiation, who developed secondary scleroderma. The average period between treatment and complication was 9.5 years [8]. Another multicentric study on 22 female patients treated with radiation noted a range of time frames for the onset of cutaneous sclerosis from two months to eleven years after radiotherapy. Unfortunately, the majority of patients had a poor treatment response, with the best results being found in patients treated with Methotrexate, as was the situation with our patient [10]. Concerning the spreading of the sclerotic process outside the irradiation area, around 50% of patients developed generalized scleroderma, with a positive ANA panel considered to be a risk factor for the extensive postradiation form [10].

## CONCLUSIONS

Although more common than in the general population, post-irradiation morphea is a rare complication that should be considered in patients who had radiotherapy and developed erythematous-violaceous patches in the treated area, since clinical diagnosis during the disease's incipient inflammatory phases is associated with a favorable treatment response.

**Author Contributions:**

*All authors were responsible for the diagnostic procedures, clinical diagnosis, and treatment decision. All authors contributed to the manuscript and have read and agreed to the published version of the manuscript.*

**Compliance with Ethics Requirements:**

*"The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from the patient included in the study"*

*"No funding for this study"*

"*The authors declare no conflict of interest regarding this article".*

**Acknowledgements:** *None*

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