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## Dermatology Online Journal

### Title

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### Permalink

<https://escholarship.org/uc/item/2tr4496q>

### Journal

Dermatology Online Journal, 22(2)

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### Publication Date

2016

### DOI

10.5070/D3222030094

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Peer reviewed

## Case presentation

### Generalized morphea as the first sign of breast carcinoma: a case report

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Dermatology Online Journal 22 (2): 10

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## Abstract

Generalized morphea is a rare idiopathic form of scleroderma that literally means “hard skin.” Morphea is usually considered an isolated event that is not associated with malignancy. However, case reports of lung, hematologic, and breast cancer occurring simultaneously with large plaque morphea have caused dermatologists to question whether a work-up for malignancy is appropriate. We highlight a case of generalized morphea that preceded invasive ductal carcinoma of the breast and provide a discussion about the possible paraneoplastic origin of generalized morphea and systemic sclerosis (SSc).

**List of Abbreviations:** SSc: systemic sclerosis

## Introduction

Morphea is a fairly uncommon diagnosis, with an incidence of approximately 0.4-2.7 per 100,000 people in the United States [1]. It is not usually associated with underlying or systemic conditions and almost never progresses to SSc. The “generalized” variant of morphea tends to be more widespread and diffuse than guttate or linear subtypes but does not involve internal organs. There have been reports of outbreaks of morphea and/or SSc preceding or coinciding with solid organ (especially lung) and breast cancer diagnoses suggesting a paraneoplastic etiology [2-8]. This is a subject of ongoing debate, although most dermatologists agree that a complete cancer workup is unwarranted for every patient with hyperpigmented, shiny, and hard-indurated plaques. We present a case of a relatively healthy, active female with remarkable skin changes only months prior to a cancer diagnosis.

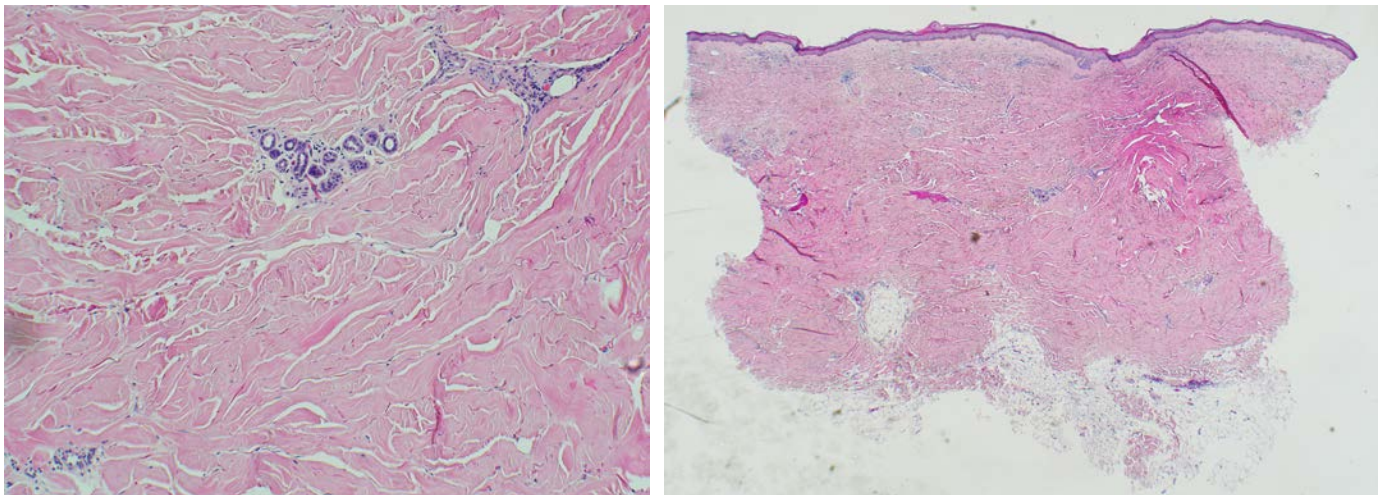
## Case synopsis

A 56 year old female who had recently been diagnosed with HER2/neu-positive, hormone receptor positive invasive ductal carcinoma presented to the clinic at the request of her oncologist for evaluation of atrophic patches with a violaceous border on her upper back, entire abdomen, and underneath the breasts (Figure 1,2). She denied dysphagia, Raynaud’s, and physical exam did not reveal sclerodactyly. Biopsies taken from the upper back and abdomen revealed perivascular and interstitial infiltrate of lymphocytes along with classic morphea signs of collagen trapping glands and “squaring off” of the gross specimen (Figure 3,4).

The patient reported that the aforementioned skin findings had suddenly appeared 2-3 months prior to her diagnosis of breast cancer. She denied a history of autoimmune disease, chronic health problems, or exposure to ticks or biting insects, making *Borrelia*-induced morphea unlikely.



**Figure 1 & 2.** Atrophic patches with a violaceous border on her upper back, entire abdomen, and underneath the breasts



**Figure 3.** Atrophic eccrine glands trapped within the middle of the thickened dermis as subcutaneous fat is replaced by collagen (Hematoxylin & eosin; Magnification 10x) **Figure 4.** Thickening of preexisting collagen bundles and deposition of fine, wavy fibers of newly formed collagen. Flattening of rete ridges, absence of inflammatory infiltrate, and “squaring off” of the gross specimen (Hematoxylin & eosin; Magnification 4x)

Oncology initiated intravenous chemotherapy with trastuzumab and anastrozole after the patient underwent mastectomy with immediate reconstruction. The patient tolerated the chemotherapy fairly well although she reported new onset hot flashes and some morning stiffness and joint aches. Topical clobetasol was prescribed for the morphea with mild improvement of lesions. At 3-month follow-up, the morphea has halted progression and “burnt out” throughout the course of chemotherapy. Her breast cancer is now in remission, and she is continuing to follow closely with both oncology and dermatology.

## Discussion

The association between SSc and cancer is well documented, but whether generalized or localized morphea are a preemptive sign of malignancy remains unknown. The prevalence of cancer in patients with SSc is estimated to be between 3 and 11%, but on average, the neoplastic manifestations do not occur until 13 years after diagnosis [9]. This implies that SSc may lead to malignancy, rather than being an underlying sign of concomitant cancer. Studies show that SSc is most strongly associated with the development of lung cancer (RR 4.35; 95% CI 2.08, 9.09) and hematological neoplasms (RR 2.24; 95% CI 1.53, 3.29) [10]. Previous reports have also suggested an increased risk of breast cancer, but this remains unconfirmed by any large studies (RR 1.05; 95% CI 0.86, 1.29) [11]. To date, there are no well-documented studies linking morphea to underlying solid organ or breast malignancy.

One case of morphea that occurred following the treatment of small cell lung cancer with radiotherapy and chemotherapy has been described [11]. Radiotherapy is a known etiologic factor for morphea, but the patient developed scattered lesions in areas that

were not irradiated [11]. The patient's malignancy rapidly progressed to involve bone, liver, and bilateral suprarenal gland metastasis soon after the onset of morphea [11]. Consequently, morphea may represent an additional distinct paraneoplastic manifestation of small cell lung cancer.

Our patient was unique because she was middle aged and had no evidence of Raynauds, esophageal involvement, or sclerodactyly. In fact, she was not believed to have SSc, but instead, a rapidly progressing generalized morphea immediately preceding a diagnosis of highly aggressive ductal carcinoma of the breast. Following treatment for breast cancer, the morphea started to resolve, which suggests a paraneoplastic origin of disease. Therefore, an age appropriate evaluation for underlying neoplastic disease should be considered for any patient presenting with sudden onset of large plaque or generalized morphea.

## Conclusion

Dermatologists should be aware that SSc is associated with an increased risk of developing lung and hematological malignancies over time [10]. Likewise, an eruption of generalized morphea may indicate a concomitant malignancy. Therefore, a sudden eruption of morphea should prompt age appropriate malignancy screening. Some cases of SSc and possibly generalized morphea may be of paraneoplastic origin and regression of morphea with treatment of cancer suggests a paraneoplastic relationship. Further studies are needed to accurately assess the relationship between generalized morphea and the development of malignancy.

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