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### Title

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### Permalink

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### Journal

Dermatology Online Journal, 26(9)

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### Publication Date

2020

### DOI

10.5070/D3269050162

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Peer reviewed

# Annular erythema as a cutaneous sign of recurrent ductal breast carcinoma, misdiagnosed as erythema chronicum migrans

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## Abstract

Annular erythema as a clinical manifestation of locoregional recurrence of breast cancer is extremely rare. Only three papers with the description of five cases have been published in the current literature to our knowledge. Herein, we describe two additional cases of annular erythema as a cutaneous sign of recurrent ductal breast carcinoma; both were misdiagnosed as erythema chronicum migrans.

**Keywords:** annular erythema breast cancer, metastasis, erythema migrans

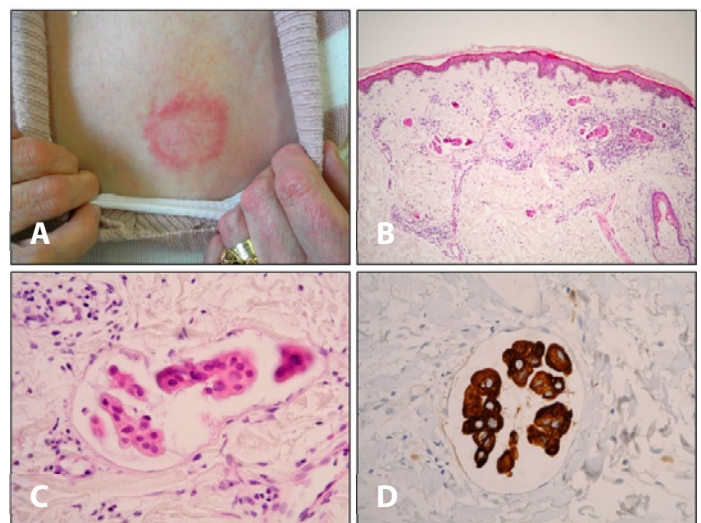
## Introduction

Annular erythema as a clinical manifestation of locoregional recurrence of malignant tumor disease is extremely rare. Only three reports describing five cases of breast cancer have shown cutaneous recurrences that manifested in the form of annular erythema [1-3]. Herein, we describe two further cases of annular erythema as a cutaneous sign of recurrent ductal breast carcinoma; both were misdiagnosed as erythema chronicum migrans.

## Case Synopsis

In our first case, a 62-year-old woman presented with high-grade invasive ductal carcinoma of the left breast with metastases in the lymph nodes of the left

axilla. After mastectomy, dissection of axillary lymph nodes, radiotherapy, and chemotherapy, the patient was in complete remission on long-term tamoxifen treatment. Five years later, a solitary 6×6cm annular erythematous plaque with a raised red border was detected in the left pectoral area (**Figure 1A**). The patient reported a tick bite at the site of the lesion; serological examination (ELISA method) detected IgM positivity and IgG negativity of anti-*Borrelia* antibodies. The dermatologist diagnosed erythema chronicum migrans and put the patient on oral doxycycline with a dosage of 200mg daily for 21

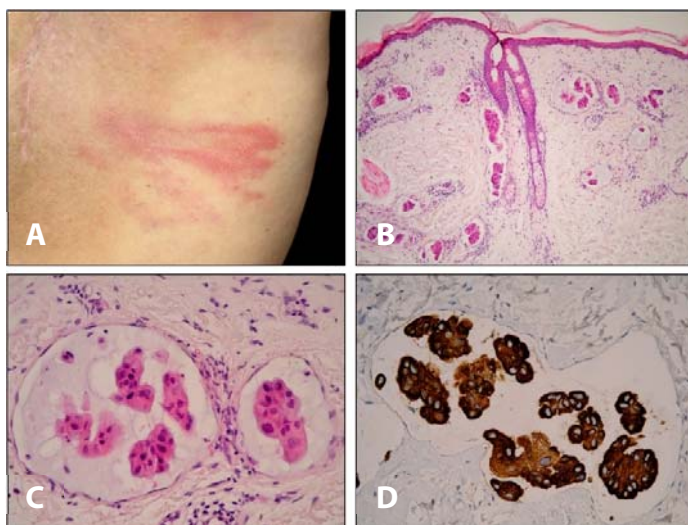


**Figure 1.** **A)** A solitary annular erythematous plaque in the left pectoral area. **B)** Histological finding from the annular edge of the lesion. H&E, 100×. **C)** Breast cancer cells in lymphatic capillaries of the dermis. H&E, 400×. **D)** Positivity of tumor cells for cytokeratin 7 immunohistochemistry, 200×.

days, with no response. The Western blot confirmation test did not confirm the occurrence of active or retreated borrelia infection.

In the second case, a 60-year-old woman was diagnosed with high-grade invasive ductal carcinoma initially in the left breast and a year later in the right breast. After bilateral mastectomy and dissection of axillary lymph nodes, she underwent several cycles of radiotherapy and chemotherapy with herceptin and capecitabine. A year later, a solitary 12×6cm oval-shaped annular erythematous plaque with a raised red border developed in the left lateral side of the thorax (**Figure 2A**). Her physician based his diagnosis of erythema chronicum migrans on the clinical picture. Amoxicillin therapy lasting for 14 days produced no response.

In both the above-mentioned case reports an incisional biopsy of the lesion through the annular margin yielded identical histological and immunohistochemical findings. In the hematoxylin and eosin stained sections, solid groups of atypical cancer cells with rare mitoses in the lumens of dilated capillaries of the upper and middle dermis were detected (**Figure 1B, C; Figure 2B, C**). Immunohistochemically, cancer cells were CK7 positive (**Figure 1D, Figure 2D**), GATA3 and E-cadherin positive and CK20, ER, and PR negative. The endothelial cells of



**Figure 2. A)** A solitary oval-shaped annular erythematous plaque in the left lateral side of the thorax. **B)** Histological finding from the annular edge of the lesion H&E, 100×. **C)** Breast cancer cells in lymphatic capillaries of the dermis. H&E, 400×. **D)** Positivity of tumor cells for cytokeratin 7 immunohistochemistry, 200×.

capillaries showed podoplanin positivity and CD31 and CD34 negativity. Dual in situ hybridization analysis of HER2 gene amplification confirmed the positive HER2 status in both cases. Both patients were referred to an oncologist to undergo chemotherapy and radiotherapy.

## Case Discussion

Breast cancer is the most frequent source of skin metastases in women (69%); in 86% of cases local metastases were diagnosed [4]. Cutaneous breast carcinoma metastases have several clinical manifestations: nodular, inflammatory, telangiectatic, sclerodermoid, and en cuirasse. Other forms include alopecia, Paget disease, carcinoma of the inframammary crease, and histoid carcinoma of the eyelid [1-4]. Annular erythema as a clinical manifestation of locoregional recurrence of breast carcinoma is extremely rare: to our knowledge only three papers with the description of five cases have been published [1-3]. In those cases, the primary diagnosis was a high-grade ductal breast carcinoma. In four cases its local recurrence manifested as annular erythema with localization on the anterior chest wall at the site of the breast previously affected [1,2]. However, one case in which the localization of annular erythema was on the back has been published [3]. The annular erythema in these cases was clinically diagnosed as dermatitis and tinea corporis [1], subacute cutaneous lupus erythematosus [1], erythema annulare centrifugum [3], and in two cases as non-specific annular erythema [1,2].

In our first case, the dermatologist at first made the diagnosis of erythema chronicum migrans on the basis of positive anti-*Borrelia* IgM antibodies by the ELISA method. Inefficacy of antibiotic treatment and a negative Western blot confirmation test ruled out borreliosis. IgM positivity of anti-*Borrelia* antibodies detected by the ELISA method may result in false positivity; thus, it is recommended to use a two-tier serologic testing protocol (ELISA plus Western blot test), [5]. In the second case, the diagnosis was made on the basis of the clinical picture with no serological examination performed.

Immunohistochemically, the positivity of CK7, GCDPF-15, GATA3, ER, and PR and negativity of CK20 are significant for a breast origin of cutaneous metastasis [4]. Lobular breast carcinoma is E-cadherin negative; ductal breast carcinoma is E-cadherin positive. The risk of locoregional breast carcinoma recurrences is higher in ER-/PR- and HER2- tumors than in HER2+ or ER+/PR+ tumors [1].

The clinical differential diagnosis includes erythema gyratum repens, erythema annulare centrifugum, tinea, subacute cutaneous lupus erythematosus-like gyrate erythema, and drug-induced subacute cutaneous lupus erythematosus [1-3]. The above-mentioned diseases can be differentiated from the annular cutaneous metastases of breast carcinoma by histological examination. The most appropriate

site for the incisional biopsy is through the raised annular border of the lesion.

## Conclusion

Our two cases demonstrated the importance of careful evaluation of medical history, clinical dermatological examination of the skin lesions, cautious interpretation of *Borrelia* serology, and histological and immunohistochemical examination of skin biopsies to determine the correct diagnosis of these annular erythemas.

## Potential conflicts of interest

The authors declare no conflicts of interests.

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