

LETTER - THERAPY

Successful treatment of eosinophilic cellulitis with a short course of Dupilumab[☆]



Dear Editor,

Eosinophilic diseases comprise a heterogeneous group of diseases characterized by tissue eosinophilia that may be accompanied by peripheral eosinophilia.^{1,2} Eosinophilic cellulitis (Wells' syndrome) is a well known condition which can be mistaken for bacterial infections,^{3,4} and histopathology is essential for its definitive diagnosis.¹ Other primary eosinophilic diseases are granuloma faciale, eosinophilic fasciitis (Shulman syndrome), and eosinophilic folliculitis (Ofuji disease).²

Histopathology varies according to disease stage: in the acute phase there are more eosinophils; in the sub-acute phase, histiocytes and "flame figures" are well evident and in the chronic phase a granulomatous reaction predominates.¹ Flame figures occur due to the adhesion of eosinophilic degranulation material to collagen, but are not always present^{2,5} and occur in other conditions such as pemphigoid, Churg-Strauss syndrome, herpes gestationis, eczema, prurigo, drug-related eruptions, and follicular mucinosis. Clinical and laboratory correlation is necessary for the diagnosis.¹

The present report describes a 50-year-old female patient, a biochemist, who presented with an erythematous infiltrated painful plaque on her left leg of eight weeks duration (Fig. 1). Histopathology of an incisional biopsy revealed a diffuse inflammatory infiltrate and edema in the upper dermis (Fig. 2A), extending to the dermal-hypodermal junction (Fig. 2B). On high power many eosinophils were evident (Fig. 3) and the diagnosis of eosinophilic cellulitis was made.

The patient was treated with oral prednisone, at an initial dose of 40 mg, together with topical tacrolimus 0.1%. There was a good initial response, with decrease in pain and erythema. Recurrence occurred after the gradual withdrawal of prednisone. Due to refractoriness to previous interventions, subcutaneous dupilumab was started, with a 600 mg loading dose followed by two doses of 300 mg, with a 15-day interval. The treatment, therefore, consisted of only four 300 mg syringes, as this was the available quantity since the patient had financial difficulties to acquire a larger quantity of the medication.

There was a gradual decrease in erythema and pain in the subsequent weeks, and there was no recurrence after ten months of follow-up. Although there was residual hyperpigmentation (Fig. 1) there were no other side effects to the treatment.

The standard treatment for eosinophilic cellulitis is systemic corticosteroids, but recurrence is frequently observed when they are discontinued.⁶ Other medications reported to be effective include methotrexate,⁷ colchicine, dapsone, hydroxychloroquine, and azathioprine.²

Dupilumab has already proven effective in several eosinophil-mediated diseases, such as eosinophilic esophagitis,⁸ with four reports of its use in eosinophilic cellulitis, three in the United States^{6,9,10} and one in Germany,¹¹ all of which were patients resistant to conventional therapy. Interestingly, one case in the United States was treated with only four doses, due to financial difficulties in obtaining the drug, and with doses of 200 mg (400 mg loading dose followed by two doses of 200 mg, every 15 days), with a response similar to the case described herein.⁹

Other immunobiologicals have also been successfully reported, such as omalizumab (anti-IgE) and mepolizumab (anti-IL-5), as well as adalimumab, an anti-TNF- α .¹

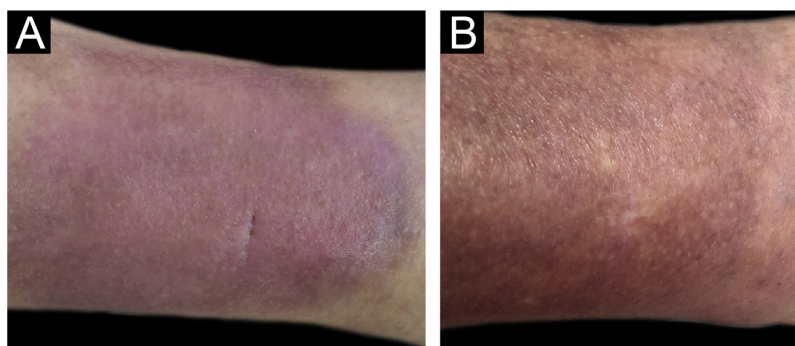


Figure 1 (A) Erythematous infiltrated plaque on the left leg. (B) Appearance after treatment, with residual hyperpigmentation.

[☆] Study conducted at the Universidade Católica de Pelotas, Pelotas, RS, Brazil.

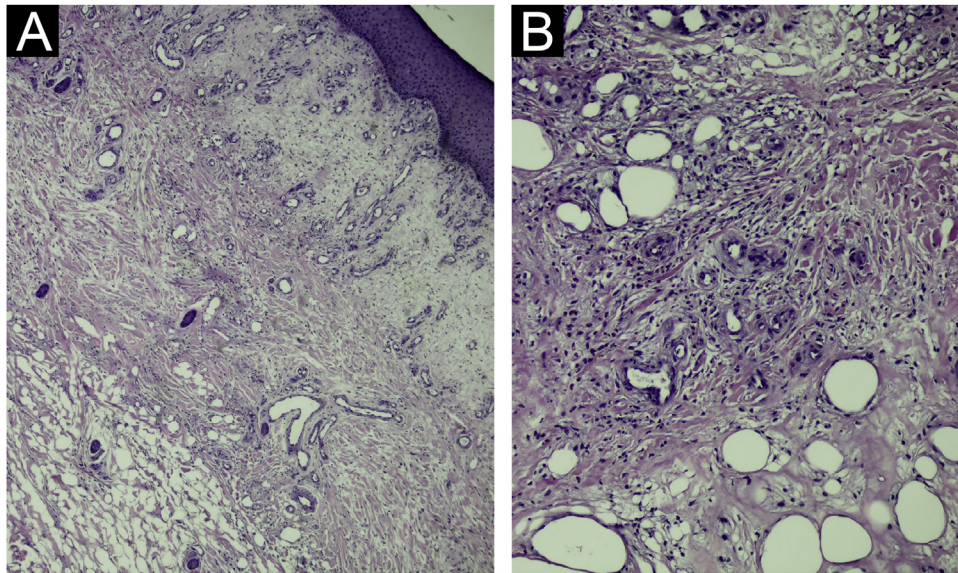


Figure 2 Histopathology: (A) Diffuse inflammatory infiltrate with edema in the upper dermis (Hematoxylin & eosin, $\times 100$). (B) The infiltrate extends to the dermal-hypodermal junction (Hematoxylin & eosin, $\times 200$).

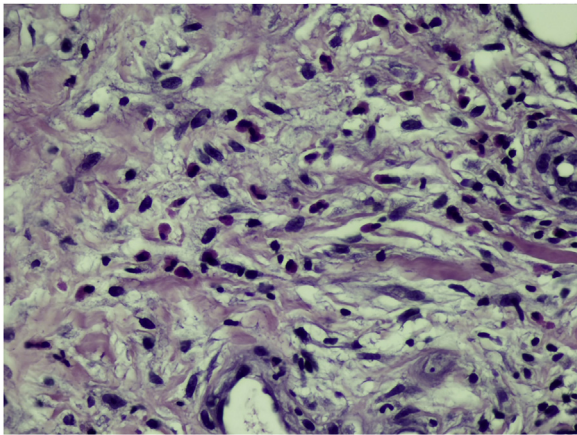


Figure 3 Histopathology: high magnification showing numerous eosinophils (Hematoxylin & eosin, $\times 400$).

Dupilumab targets the IL-4 alpha receptor, interfering with IL-4 and IL-13 signaling involved in eosinophil activation.⁹ This is a relevant alternative in the treatment of diseases mediated by this cell. Possibly, short treatments may be sufficient to interrupt its activation in the skin.

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Authors' contributions

Hiram Larangeira de Almeida Jr: Approval of the final version of the manuscript; design and planning of the study; drafting and editing of the manuscript; collection, anal-

ysis, and interpretation of data; effective participation in research orientation; intellectual participation in the propaedeutic and/or therapeutic conduct of the studied cases; critical review of the literature; critical review of the manuscript.

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Conflicts of interest

None declared.

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Zosteriform cutaneous metastases of HER-2 positive breast carcinoma resolved after treatment with lapatinib[☆]



Dear Editor,

Cutaneous Metastases (CM) represent 1% to 4.3% of all metastatic occurrences and 2% of all skin cancers. Breast cancer is the most common tumor associated with CM in women and usually portends a poor prognosis. Metastases can manifest with various morphological and clinical features, occasionally resembling other dermatological conditions, with nodules being the predominant presentation.^{1,2} More rarely a zosteriform pattern has been described with only a few reports in the literature.³ Herein, we report a case of zosteriform cutaneous metastases from breast carcinoma successfully treated with lapatinib.

A 44-year-old Latin-American woman was referred from the oncology clinic for a three-week evolution dermatosis on the left thoracic wall. Five years prior, she was diagnosed with stage IIIA right breast cancer, HER2-enriched, BRCA wild-type, with metastases to the central nervous system and lymph nodes. Her treatment included a right radical mastectomy, chemotherapy with trastuzumab, pertuzumab, and docetaxel, followed by capecitabine, whole-brain radiation, and lymph node dissection. Despite undergoing extensive chemotherapy, her carcinoma spread to the left breast nine months before her dermatology consultation, leading to the initiation of a trastuzumab monotherapy regimen. Examination revealed a painful and pruritic dermatosis characterized by erythematous plaques and nodules, arranged in a dermatomal distribution on the posterolateral region of the left thorax (Fig. 1A and B). Dermoscopy of the plaques showed a pink background

with polymorphous vessels (Fig. 1C). A skin biopsy was performed, and histopathology demonstrated dermal infiltration by neoplastic cell clusters dispersed among collagen fibers and infiltrating lymphatic vessels (Figs. 2 and 3). These findings were consistent with a metastatic carcinoma from the breast tumor, leading to the diagnosis of zosteriform cutaneous metastases from breast carcinoma.

Consequently, a new monotherapy regimen with oral lapatinib 1 g/day was initiated. The skin metastases disappeared after one month of lapatinib administration, and the patient was considered to be in partial response after completing four months with this treatment (Fig. 4A and B). Dermoscopy revealed only a few structureless whitish areas with a pinkish hue (Fig. 4C). After 14 months of follow-up, no skin lesions or significant adverse effects were observed.

A zosteriform pattern in breast carcinoma skin metastasis has been seldom described in the literature.³ It typically manifests as hardened lesions and may appear as papules, nodules, or pseudo-vesicles arranged in a dermatomal distribution, usually misdiagnosed as herpes zoster. The chest wall and abdomen are the predominant locations for these metastases. In more than 50% of cases, skin metastases develop ipsilateral of the primary tumor. That is not the case for our patient, where her metastases appeared on the contralateral breast. Several theories have been postulated to elucidate the pathogenesis of this uncommon distribution. These include a Koebner-like reaction occurring at the site of a previous herpes zoster infection, perineural lymphatic dissemination, and spread through the vessels associated with the dorsal root ganglion. However, the exact mechanism is still speculative.⁴ The presence of CM, particularly originating from breast adenocarcinoma, indicates a poor prognosis.²

There is limited evidence on the dermoscopy of cutaneous metastases from breast cancer.^{5–7} In our case, we report findings consistent with the literature with the presence of branching linear or polymorphic vessels and structureless erythematous areas. Additionally, we observed that following the clinical resolution of the lesions, dermoscopy showed a significant reduction in erythema and

[☆] Study conducted at the Department of Dermatology, Hospital Universitario “Dr. José Eleuterio González” Universidad Autónoma de Nuevo León, Monterrey, N.L. México.