

## SHORT COMMUNICATION

**Cutaneous Rosai-Dorfman Disease Located on the Breast: Rapid Effectiveness of Methotrexate After Failure of Topical Corticosteroids, Acitretin and Thalidomide**Marion Nadal<sup>1</sup>, Thibault Kervarrec<sup>1</sup>, Marie-Christine Machet<sup>2</sup>, Tony Petrella<sup>3</sup> and Laurent Machet<sup>1,4</sup>Departments of <sup>1</sup>Dermatology, <sup>2</sup>Pathology, CHRU de Tours, FR-37044 Tours, <sup>3</sup>Pathology, CHU de Dijon, and <sup>4</sup>Inserm U930, Université François Rabelais de Tours, Tours, France. \*E-mail: machet@univ-tours.fr

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An erythematous cutaneous plaque on the breast with no signs of infection requires a skin biopsy to rule out dermal extension of an underlying mammary adenocarcinoma, primary skin tumour (e.g. angiosarcoma or malignant lymphoma) (1), or inflammatory lymphoedema of the breast (2). It can more rarely reveal location on the skin of systemic disease.

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy, is a benign proliferative disorder of histiocytes first described in 1965 by Destombes on nodal biopsy (3). It was subsequently recognised as a distinct clinicopathologic entity by Rosai & Dorfman (4).

Cases of RDD located solely on the skin have rarely been reported, and thus treatment is not well-codified (5). We report a case of RDD on the breast which showed rapid partial response to methotrexate.

## CASE REPORT

A 72-year-old woman with no personal medical history but with a familial history of breast cancer, consulted for cutaneous lesions located on the right breast (Fig. 1). Erythematous, infiltrated papules had appeared 8 months earlier and slowly extended to reach an area of 9 × 6 cm. Mammography and ultrasound imaging showed normal breast parenchyma. An initial skin biopsy showed mixed dermal infiltration of lymphocytes, histiocytes and neutrophils consistent with pseudolymphoma or true lymphoma. Routine blood tests, myelogram and CT-scan were normal, except for skin infiltration (Fig. 2). A second skin biopsy showed a polyclonal and polytypic lymphoid cell population, and a histiocytic population showing some intra-



Fig. 1. Papules located on the right breast. A: Before starting methotrexate. B: after treatment with methotrexate for 3 months.

cellular debris. Histiocytes expressed PS100, CD68, CD163 but were negative for CD1a (Fig. 3). This was consistent with RDD.

Treatment with superpotent topical corticosteroid (clobetasol propionate) for 2 months and later combined with acitretin 25 mg/day for 3 months, was ineffective. Response to thalidomide, 50 mg/day for the first month and 100 mg/day for further 5 months was minimal. Methotrexate started at 10 mg/week and increased to 20 mg/week (0.25 mg/kg) showed a significant response within 1 month with good clinical and biological tolerance. The size of the plaque was unchanged but the lesion was less infiltrated (Figs 1 and

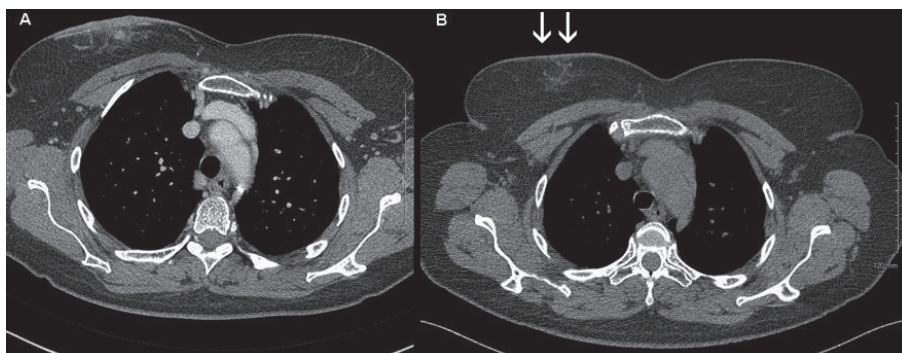


Fig. 2. CT-scan showing improvement of breast skin infiltration after 3 months of methotrexate (arrows).

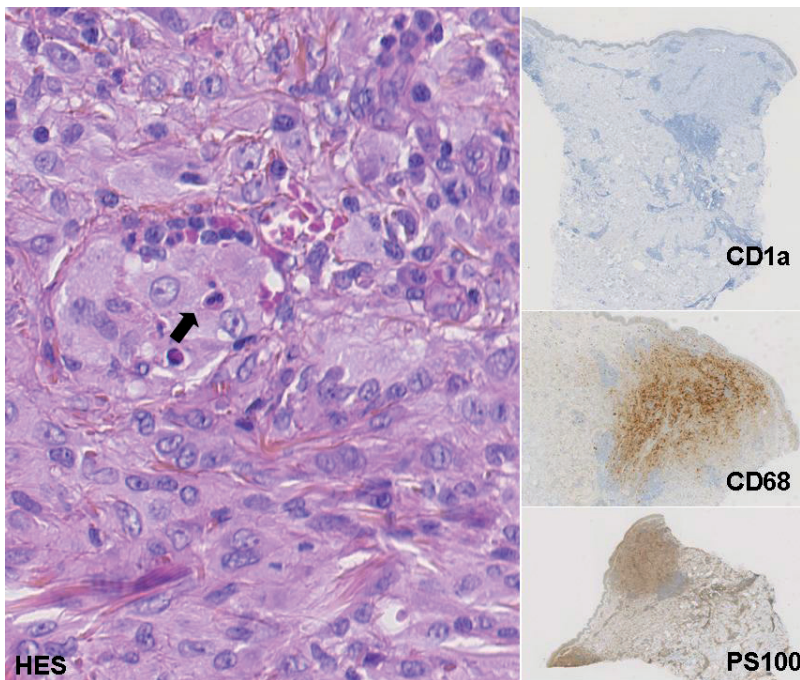


Fig. 3. Skin biopsy showing dermal infiltrate with intracellular debris (emperipolesis, arrow) and immunostaining of histiocytes with PS100, CD68, but not CD1a.

2). Follow-up 3 and 6 months later showed sustained partial response.

## DISCUSSION

RDD is a rare benign non-Langerhans histiocytosis of unknown cause. Extranodal locations are frequent, including the skin which can reveal the disease, despite difficult and often delayed diagnosis. The histological aspect of emperipolesis (phagocytosis of lymphocytes, neutrophil polymorphonuclear cells or plasma cells) is suggestive but not totally specific.

A systematic literature review identified 72 cases of cutaneous RDD in 2006 (6). A French series of 7 cases (diagnosed over a period of 21 years) and a Chinese series of 25 cases were published later (5, 7). Lesions are usually located on the face. Single localisation on the breast skin is exceptional. Another case of perinipple location has been reported (5).

Due to the normally self-limited course aggressive therapies are not recommended. The skin involvement may even regress spontaneously in several months. Thus, a proportion of patients with this disorder will not require treatment (8). For patients requiring treatment, surgery is an appropriate option for disease that can be excised, including single nodal areas, or localised primary cutaneous RDD (8). In more extensive forms of

cutaneous RDD, local therapy (topical or intralesional corticosteroids, cryotherapy, radiotherapy) and systemic treatment (corticosteroids, dapsone, thalidomide, isotretinoin, acitretin,  $\alpha$  interferon, imatinib) have been reported, with variable efficacy (5–11).

Methotrexate was rapidly effective in our case. A review of the cases of RDD treated with methotrexate (alone or in combination with systemic corticosteroids or 6-mercaptopurine) identified 9 cases of systemic RDD and 3 cases of cutaneous RDD with partial to complete response in most of the cases (9–11).

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