

8. Mendes-Bastos P, Coelho-Macias V, Moraes-Fontes MF, Milheiro A, Rodrigues AM, Cardoso J. Erythema annulare centrifugum during rituximab treatment for autoimmune haemolytic anaemia. *J Eur Acad Dermatol Venereol*. 2014;28:1125–7.
9. Valla DC. Primary Syndrome de Budd-Chiari. *J Hepatol*. 2009;50:195–203.
10. Martens P, Nevens F. Síndrome de Budd-Chiari. *United European Gastroenterol J*. 2015;3:489–500.
11. Motohashi N, Satoh T, Yokozeki H, Nishioka K. Annular erythema associated with essential thrombocythemia. *Acta Derm Venereol*. 2002;82:390.

A.S. Borges,<sup>a,\*</sup> A. Brasileiro,<sup>a</sup> S. Santos,<sup>b</sup> J. Saiote<sup>b</sup>

<sup>a</sup> *Unidad de Dermatología y Venereología, Hospital Santo António dos Capuchos, Centro Hospitalar de Lisboa Central, Lisboa, Portugal*

<sup>b</sup> *Unidad de Gastroenterología, Hospital Santo António dos Capuchos, Centro Hospitalar de Lisboa Central, Lisboa, Portugal*

\* Corresponding author.

E-mail address: [a.sofia.r.borges@gmail.com](mailto:a.sofia.r.borges@gmail.com) (A.S. Borges).

© 2018 Elsevier España, S.L.U. and AEDV. Published by Elsevier España, S.L.U. All rights reserved.

## Successful Suppression of Recurrent Zosteriform Mycosis Fungoides With Maintenance Valacyclovir<sup>☆</sup>



### Supresión de un cuadro de micosis fungoide recurrente con distribución zosteriforme mediante tratamiento de mantenimiento con valaciclovir

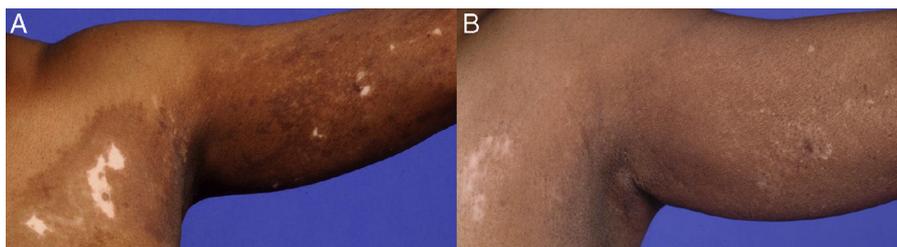
To the Editor

Mycosis fungoides (MF) is a cutaneous T-cell lymphoma (CTCL) that typically presents as patches or plaques in sun-protected areas. However, MF frequently exhibits clinical variability, and its atypical presentations can make the diagnosis difficult. Histopathology classically shows an atypical, superficial lymphoid infiltrate with epidermotropism. In addition, molecular assays can demonstrate a dominant T-cell clone in the skin, and flow cytometry can illustrate immunophenotypic abnormalities characteristic of MF. Zosteriform MF is an exceedingly rare variant in which lesions occur in a dermatomal distribution.<sup>1–3</sup> We describe the first case of zosteriform MF that responded to antiviral therapy.

Interestingly, the patient's MF recurred on four occasions when antiviral therapy was discontinued or the dose was reduced.

A 69-year-old African-American female presented in October 2002 with a one-month history of erythema, pruritus, and hypo- and hyperpigmentation that began on her left upper back and spread down her arm onto her left chest in a dermatomal distribution. She denied pain, anesthesia, or history of herpes zoster. Physical examination revealed hypo- and hyperpigmented patches on left upper back (9 × 8 cm), left upper chest (8 × 7 cm), and left arm (9 × 4 cm) with 3% total body surface area (BSA) involvement (Fig. 1A; Fig. 2A). There were no bullae present. Wood's light examination showed depigmentation consistent with vitiligo.

Biopsy of the left upper back showed a dermal CD4+ and CD8+ atypical lymphoid infiltrate with focal epidermotropism (Fig. 3A–B). Immunohistochemical studies (Fig. 3C–F) demonstrated CD3+ T cells in the epidermis and dermis with predominance of CD4 over CD8 in the dermis, with a CD4:CD8 ratio of approximately 4:1. In the epidermis, there was a subset of atypical lymphocytes negative for CD4 and CD8. There is loss of CD7 expression. Rare cells were reactive for CD30. The majority of the lymphocytes were positive for TCR beta (BF1) and negative for TCR gamma. Monoclonal T-cell receptor gamma-chain gene

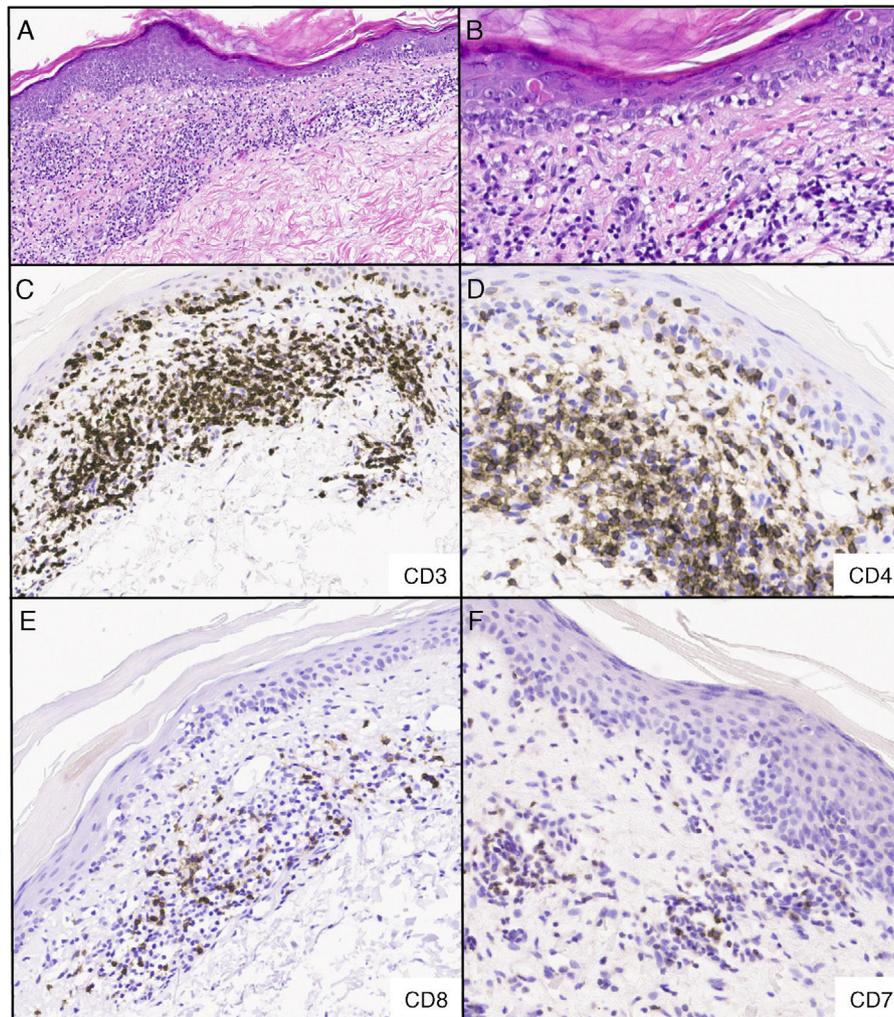


**Figure 1** Área con hypo- e hiperpigmentación en región superior del torso y brazo A) como presentación inicial B) y pigmentada en el 90% con tratamiento con valaciclovir.

<sup>☆</sup> Please cite this article as: Lewis DJ, Hinojosa T, Chan WH, Wu JH, Duvic M. Supresión de un cuadro de micosis fungoide recurrente con distribución zosteriforme mediante tratamiento de mantenimiento con valaciclovir. *Actas Dermosifiliogr*. 2018;109:757–760.



**Figure 2** Área con hipo- e hiperpigmentación en parte superior de la espalda A) como presentación inicial, B) repigmentada al 90%, C) y repigmentación casi completa con el tratamiento con valaciclovir.



**Figure 3** Infiltrado linfoide dérmico atípico para las células CD4+ y CD8+ con epidermotropismo focal; los estudios inmunohistoquímicos realizados confirmaron presencia de células T CD3+ en dermis y epidermis con predominancia de células CD4 sobre células CD8 en la dermis, en una proporción CD4:CD8 de, aproximadamente, 4:1. En la epidermis, se observó un subgrupo de linfocitos atípicos negativos para CD4 y CD8. Hay pérdida de expresión de CD7. Pocas células fueron reactivas al marcador CD30. La mayoría de los linfocitos dieron positivo para el receptor de la cadena beta de linfocitos T (BF1) y negativo para el receptor de la cadena gamma de linfocitos T. A) Tinción hematoxilina y eosina, 40x. B) Tinción hematoxilina y eosina, 200x C-F) inmunohistoquímica, 200x.

rearrangements were detected by polymerase chain reaction, suggestive of MF. There were 42.2% of CD4+ CD26-cells by flow cytometry, suspicious for CTCL involvement of the blood. The patient was given triamcinolone cream 0.1% and bexarotene gel after a diagnosis of stage IA MF.

She demonstrated minimal improvement with topical agents. Because of the zosteriform pattern, the patient was given valacyclovir 1000 mg daily. On extended antiviral therapy, her erythema and pruritus resolved within two months, leaving only pigmentary changes in a zosteriform distribution. Subsequently, she continued to receive valacyclovir, though the dose was halved to 500 mg daily in January 2005.

By September 2006, 90% repigmentation was noted with maintenance therapy (Fig. 1B; Fig. 2B). However, the patient discontinued valacyclovir in May 2008 and one month later reportedly developed bullae with erythema, and so valacyclovir 500 mg daily was resumed. She experienced additional flares in April 2009, May 2011, and May 2012, each about one month after an attempt to taper or discontinue the valacyclovir. On valacyclovir 500 mg daily, she has maintained repigmentation with no additional flares in the last four years, with 0.75% BSA involvement at last follow-up in August 2016 (Fig. 2C).

A number of dermatoses may follow a dermatomal distribution. Although zoster and herpes simplex are the most common, MF should be considered in the differential diagnosis of zosteriform eruptions. Our patient represents the fourth case of zosteriform MF.<sup>1-3</sup> Her dermatomal MF lesions might have occurred via lymphocytic invasion of perineural lymphatic vessels or the fenestrated vasculature of the dorsal root ganglion.<sup>4,5</sup> Alternatively, she may have experienced recurrent zoster with histology mimicking MF, although the plausibility and frequency of recurrent zoster have been debated.<sup>6</sup> She never developed vesiculobullous lesions that would suggest recurrent zoster. Furthermore, her lesions fulfilled the Pimpinelli algorithm for a diagnosis of early MF.<sup>7</sup>

In making a diagnosis of zosteriform MF, it is important to consider the histopathology given that it is a histopathological diagnosis. In the early lesions of vitiligo, there may be lichenoid inflammation that can clinically and histopathologically mimic MF.<sup>8</sup> There can be dense band-like lymphocytic infiltrates with exocytosis of cells into the lower layers of the epidermis.<sup>8</sup> Since these lymphocytes are usually CD8+ cytotoxic T cells, they can make a diagnosis of MF very difficult. Moreover, cutaneous herpes zoster and herpes simplex virus infection can present with atypical histologic features—dense lymphoid infiltrates, angiotropism, and atypical lymphocytes—that resemble MF.<sup>9</sup> In these cases, the typical clinical and histopathological characteristics of viral infection may be absent, although histopathology may demonstrate the typical cytopathic changes of herpetic infection, which can be confirmed by PCR.<sup>9</sup>

Our case is extraordinary in that her MF and segmental vitiligo not only demonstrated a near-complete response to valacyclovir, but also, peculiarly, recurred after each of four attempts to taper or discontinue the medication. She represents the first case of a patient with zosteriform MF that responded to antiviral therapy. In addition, her condition

improved over time on maintenance therapy since it was initiated in 2002. Her response to suppressive antiviral therapy, which poses minimal risks, spared her from the adverse effects of more advanced treatments.

Evidence of clinical activity of antiviral agents in MF remains very limited. Burg et al. and Resnick et al. found that, of 30 MF patients treated with acyclovir, one exhibited a complete response and six showed a partial response.<sup>10,11</sup> Potential mechanisms for the effect of antiviral agents on MF are via direct cytopathic action or activation through thymidine kinase.<sup>10</sup> Levin et al. noted that acyclovir has an inhibitory effect on the phytohemagglutinin blastogenic response of human blood mononuclear cells.<sup>12</sup> In addition, antiviral agents act as a substrate for thymidine kinase, whose isoenzymes have high activity in peripheral mononuclear cells of some subtypes of lymphoma.<sup>10</sup> Although their mechanism of action in MF remains unknown, antiviral agents may represent an appropriate treatment, particularly for its zosteriform variant.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Bibliografía

1. Williams LR, Levine LJ, Kauh YC. Cutaneous malignancies mimicking herpes zoster. *Int J Dermatol.* 1991;30:432-4.
2. Ricci RM, Latham PL, Soong V, Mullins D. Zosteriform cutaneous T-cell lymphoma. *J Am Acad Dermatol.* 1995;32:127-8.
3. Rieger KE, Kim J, Kim YH. Zosteriform mycosis fungoides: A new clinical presentation with a dermatomal distribution. *Am J Dermatopathol.* 2017;39:e17-8.
4. Johnson PC. Hematogenous metastases of carcinoma to dorsal root ganglia. *Acta Neuropathol.* 1977;38:171-2.
5. Braverman IM. *Cancer Skin metastases and related disorders. Skin signs of systemic disease.* 2. nd ed Philadelphia, PA: WB Saunders; 1981. p. 1-14.
6. Heskell NS, Hanifin JM. Recurrent herpes zoster: An unproved entity? *JAAD.* 1984;10:486-90.
7. Pimpinelli N, Olsen EA, Santucci M, Vonderheid E, Haeflner AC, Stevens S, et al., International Society for Cutaneous Lymphoma. Defining early mycosis fungoides. *J Am Acad Dermatol.* 2005;53:1053-60.
8. El-Darouti MA, Marzouk SA, Azzam O, Fawzi MM, Abdel-Halim MR, Zayed AA, et al. Vitiligo vs hypopigmented mycosis fungoides (histopathological and immunohistochemical study, univariate analysis). *Eur J Dermatol.* 2006;16:17-22.
9. Leinweber B, Kerl H, Cerroni L. Histopathologic features of cutaneous herpes virus infections (herpes simplex, herpes varicella/zoster): a broad spectrum of presentations with common pseudolymphomatous aspects. *Am J Surg Pathol.* 2006;30:50-8.
10. Burg G, Klepzig K, Kaudewitz P, Wolf H, Braun-Falco O. Acyclovir in lymphomatoid papulosis and mycosis fungoides. *JAMA.* 1986;256:214-5.
11. Resnick L, Schleider-Kushner N, Horwitz SN, Frost P. Remission of tumor-stage mycosis fungoides following intravenously administered acyclovir. *JAMA.* 1984;251:1571-3.
12. Levin MJ, Leary PL, Arbeit RD. Effect of acyclovir on the proliferation of human fibroblasts and peripheral blood mononuclear cells. *Antimicrob Agents Chemother.* 1980;17:947-53.

D.J. Lewis,<sup>a,b,\*</sup> T. Hinojosa,<sup>c</sup> W.H. Chan,<sup>a</sup> J.H. Wu,<sup>a</sup>  
M. Duvic<sup>b</sup>

<sup>a</sup> *Facultad de Medicina, Universidad de Baylor, Houston, Texas, Estados Unidos*

<sup>b</sup> *Unidad de Dermatología, MD Anderson Cancer Center, Universidad de Texas, Houston, Texas, Estados Unidos*

<sup>c</sup> *Centro para Estudios Clínicos, Houston, Texas, Estados Unidos*

\* Corresponding author.

E-mail address: [daniel.lewis@bcm.edu](mailto:daniel.lewis@bcm.edu) (D.J. Lewis).  
1578-2190/

© 2018 Elsevier España, S.L.U. and AEDV. Published by Elsevier España, S.L.U. All rights reserved.

## Facial Calcinosis Cutis in a Woman with Paraneoplastic Dermatomyositis<sup>☆</sup>



### Calcinosis cutis facial en una paciente con dermatomiositis paraneoplásica

To the Editor:

Calcinosis is an infrequent complication of adult dermatomyositis (DM) and a very rare complication of paraneoplastic DM that predominantly affects areas of the limbs that are frequently exposed to pressure. Descriptions of facial calcinosis are very scarce.<sup>1</sup> We describe the case of a patient with paraneoplastic DM and calcinosis cutis of the face.

The patient was a 50-year-old woman who was being followed for DM, which had been diagnosed 8 years earlier. She had extensive DM skin lesions on the face, trunk, and limbs, and electromyography and muscle biopsy revealed involvement of the scapular and pelvic girdles. The results of the antinuclear antibody test were positive. An autoimmunity test for DM revealed positivity for anti-SAE1 (small ubiquitin-like modifier activating enzyme 1) antibody. Treatment with systemic corticosteroids, azathioprine, and methotrexate controlled the myositis but not the skin lesions, which worsened and progressed to necrotic lesions in the lumbar and gluteal regions. Mammography revealed an increase in focal density in the right retroareolar region that was difficult to evaluate; a breast biopsy was not performed until microcalcifications appeared on the breast 3 years after the onset of DM. At this point, the patient was diagnosed with grade III invasive ductal breast carcinoma. Complete remission was achieved following surgery and chemotherapy. The patient's skin condition markedly improved after breast cancer treatment. The only persisting lesions were mild poikilodermal lesions on the face and trunk that did not require immunosuppressive therapy. About 4 years after diagnosis of DM, the patient developed painful, indurated nodules, some of which were ulcerated, first on the arm and subsequently on the biopsy scar, both malar regions

(Fig. 1), and the forearms, legs, and gluteal region. Radiography confirmed the presence of calcium in these locations. Craniofacial computed tomography showed thickening of the periorbital soft tissue and the presence of subcutaneous calcifications in both malar regions and the left preauricular region (Fig. 2). Skin ultrasound showed thickening of the dermis and the presence in the subcutaneous cellular tissue of hyperechoic deposits that produced posterior acoustic shadow, with no increase in vascularization evident on Doppler ultrasound (Fig. 3). Analysis of phosphocalcic metabolism revealed no findings of interest. At the time, the patient was being treated with diltiazem, colchicine, and alendronic acid (70 mg/wk), which prevented progression of calcification. Several flare-ups of skin lesions, without myositis, were effectively controlled with methotrexate and cycles of intravenous immunoglobulin. The patient's breast cancer remains in complete remission and no new tumors have been detected.

Dystrophic calcinosis cutis is a relatively common complication of juvenile DM (45%–75% of cases), but is uncommon in adult DM (19%–20% of cases).<sup>1</sup> It usually appears in patients with intense DM skin lesions, as in our patient. It is extremely rare in patients with paraneoplastic DM. No cases of calcinosis were reported in one of the largest published series of patients (N = 12) with paraneoplastic DM.<sup>2</sup> We have found reports of this association only in isolated cases in the literature.<sup>3</sup>

According to Callen and Wortmann,<sup>4</sup> the course of paraneoplastic DM may not be dependent on the underlying tumor, but usually is. Our patient's DM did not fully resolve after treatment of the underlying tumor. However, the change in the intensity of the clinical picture and the



**Figure 1** Stony-hard plaques in both malar regions of about 3 cm in diameter with well-defined borders.

<sup>☆</sup> Please cite this article as: Herrero-Moyano M, Martínez-Mera C, García-García C, Dauden E. Calcinosis cutis facial en una paciente con dermatomiositis paraneoplásica. *Actas Dermosifiliogr*. 2018;109:760–762.