usually appears after contact with infected animals or ingestion of contaminated milk; dissemination from a pulmonary focus is less common. *Mycobacterium bovis* is a member of the *M. tuberculosis* complex, which includes the species *M. tuberculosis*, *M. bovis*, *Mycobacterium africanum*, *Mycobacterium microti*, and *Mycobacterium canetti*, the causative agents of tuberculosis in humans and animals.

Our review of the literature identified 4 cases of lupus vulgaris caused by *M. bovis* in the past 20 years (Table 1). In 2005, Meyer et al. described the case of a 69-year-old woman who had contracted pulmonary tuberculosis as a child. In 2009, Tar et al. and Flohr et al. presented cases of patients suspected of having been infected with *M. bovis* through contact with cattle or by ingesting unpasteurized milk. In 2010, Twomey et al. described a case of occupational infection with *M. bovis* in a veterinarian.

As a result of efforts to eradicate bovine tuberculosis and due to the prevalence of milk pasteurization, lupus vulgaris caused by *M. bovis* is now very rare. Nevertheless, it should be considered, primarily in patients who live in rural areas or work in high-risk occupations such as livestock rearing or veterinary medicine.

In conclusion, we present a case of lupus vulgaris caused by *M. bovis*, now regarded as a very rare pathogen. This case involved a considerable delay in diagnosis, as the lesion had been present since childhood.

References


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Systemic Follicular Lymphoma With Cutaneous Manifestations and Exclusively Cutaneous Recurrence

**Linfoma folicular sistémico con afectación cutánea y recidiva únicamente cutánea**

To the Editor:

Follicular lymphoma (FL) constitutes approximately 30% of all non-Hodgkin lymphomas in Western countries. Clinical presentation is typically in the form of lymphadenopathy, hepatomegaly, splenomegaly and bone marrow infiltration.1,2 Extranodal involvement is less frequent than in large B-cell lymphoma3 and does not appear to affect prognosis; this is not the case with B-cell lymphoma.

We report the case of a patient diagnosed with FL who developed skin nodules in the course of her disease. The lymphoma recurred after treatment, but it was exclusively limited to the skin, an unusual observation in this disease.

The patient was a 54-year-old woman who was referred to the hematology department in August 2004 for thrombocytopenia detected during a routine blood analysis (platelet count 70 × 10^9/L). Monoclonal B-cell lymphocytosis in the peripheral blood and bone marrow, enlarged subcentimeter abdominal lymph nodes and splenomegaly were observed during the study. The diagnosis was chronic B-cell lymphoproliferative syndrome and the patient was offered splenectomy, which she refused at that time. At follow-up in January 2007, enlarged mediastinal and retroperitoneal lymph nodes (<5 cm in diameter) were observed, prompting the performance of diagnostic and therapeutic splenectomy. Histologic study of the spleen showed a proliferation of small lymphoid cells, with a micronodular growth pattern, predominantly in the germinal centers of the white pulp, with infiltration of the red pulp. The cells had a CD20+, Bcl2+, Bcl6+, IgD+CD23+, cyclin D1+ and p53– phenotype and a low proliferative index, findings which were consistent with the diagnosis of FL.

In March 2007, the patient was referred to the dermatology department due to the gradual appearance of

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*Please cite this article as: Palacios Abufón A, et al. Linfoma folicular sistémico con afectación cutánea y recidiva únicamente cutánea. Actas Dermosifiligr. 2012;103:253–55.*
asymptomatic subcutaneous nodular lesions on the face, chest and back. The nodules had an erythematous-violacious appearance, were slightly raised, and had diameters ranging between 8 mm and 20 mm (Fig. 1). Biopsy of the lesions showed a lymphoid infiltrate composed of small monomorphous cells, compatible with FL infiltration (CD20+, Bcl2+, Bcl6+) (Fig. 2). Reassessment of the disease at this time also demonstrated the development of lymphadenopathy, for which chemotherapy was started with a rituximab-CHOP schedule (cyclophosphamide, vincristine, adriamycin and prednisone). Complete remission was achieved after 6 cycles, with clearance of the subcutaneous nodules and the enlarged lymph nodes; subsequently, the patient was placed on maintenance therapy with rituximab administered every 3 months. In December 2009, the patient again presented with cutaneous lesions, predominantly facial, similar to those previously described; biopsy reconfirmed the diagnosis of infiltration by FL. The rituximab maintenance treatment ended in June 2010; the skin lesions were still stable and there was no evidence of disease spread to other areas (peripheral blood immunophenotyping and cervical-thoracic-abdomen CT scan were normal).

FL is characterized by an indolent course and has no standardized treatment; a variety of approaches are used, including simple observation, radiotherapy, immunotherapy, polychemotherapy, maintenance treatment with rituximab, and even the application of various hematopoietic stem cell transplantation treatment modalities. As in other lymphoid malignancies, patients with FL can have extranodal involvement affecting the skin in up to 3.8% of cases. Extranodal involvement in FL does not generally affect overall survival, unlike the case with large diffuse B-cell lymphoma; these 2 diseases constitute the majority of B-cell lymphomas in Spain. It is therefore important to rule out transformation of FL to more aggressive forms as these are associated with significantly decreased survival. For this reason, lesions should be biopsied whenever a patient experiences relapse or disease progression.

Differential diagnosis is particularly important in primary cutaneous follicular center lymphoma, since it shares histologic features with FL. In addition to systemic involvement, Bcl2 negativity, which is common in cases primarily involving the skin, may be of use in differentiating the 2 diseases.

FL usually responds well to treatment, although relapses are common and usually affect the lymph nodes, bone marrow or peripheral blood. What is unusual is recurrence being limited to the skin, as in our patient. At present, and after more than 6 years of follow-up, the patient’s disease remains limited to the skin. The persistence of cutaneous disease reflects a lack of complete control of the disease, and it is therefore likely that the patient will develop systemic disease in the future.

References

Short-Contact Therapy With Topical Tazarotene in Darier Disease

Terapia de contacto corto con tazaroteno tópico en Darier segmentaria

To the Editor:

We read with interest the clinical science letter by de la Hera and coworkers and wish to share our positive experience with topical tazarotene in the treatment of linear Darier disease. Our good results contrast with the weak efficacy and poor tolerance described by those authors.

Mild Darier disease is treated with topical retinoids, although the use of such therapy is limited by local irritation.

Tazarotene is a retinoid indicated for the treatment of psoriasis. Isolated cases have been reported in which tazarotene was used to treat acne, lichen planus, keratosis pilaris, ichthyosis, confluent and reticulated papillomatosis, keratoderma blennorrhagica, discoid lupus erythematosus, and Darier disease.

We present the case of a 48-year-old woman with a 20-year history of linear Darier disease, who was being treated with topical corticosteroids. She reported poor control of lesions for a period of over 1 year, prompting her referral to our service. At the time of the consultation the patient presented brownish keratotic lesions on the left side of her forehead, the back and left side of her neck, and her lower back. These clinical signs were indicative of Darier disease and the diagnosis was subsequently confirmed by biopsy and histological analysis (Fig. 1).

As the lesions were localized to the areas described, therapy with 0.1% tazarotene was prescribed. The treatment was applied nightly and washed off with water 15 minutes after application.

The lesions disappeared after 1 month of treatment (Fig. 2).

The neck lesions did not recur during 1 year of follow-up, even during the summer. Lesions in the lumbar and frontal regions persist, although to a lesser degree, and are controlled by the patient with topical tazarotene. The patient reported no irritation at any stage of the treatment.

Tazarotene is a third generation retinoid. This prodrug is rapidly converted by skin esterases to its active metabolite, tazarotenic acid. Systemic exposure to the drug is low due to its rapid metabolism. Its greatest affinity is for the retinoic acid receptors RAR-β and RAR-γ, through which it exerts its biological effect. These receptors interact with genes and influence their expression. Although the mechanism of action of tazarotene in Darier disease is unknown, it may be similar to that underlying its therapeutic effect in the treatment of psoriasis, another differentiation and keratinization disorder. Studies in psoriasis have shown that tazarotene exerts a potent antiproliferative effect by normalizing the differentiation and proliferation of keratinocytes. It also decreases markers of inflammation and regulates cytokine and gene expression by interacting specifically with RAR-β and RAR-γ receptors. Analyses of other retinoids in the treatment of Darier disease have also demonstrated altered expression of cytokeratin, which is associated with clinical and histopathological improvements and a reduction in acanthosis and hyperkeratosis.

Figure 1 Multiple keratotic lesions on the back and side of the neck.

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doi:10.1016/j.adengl.2012.04.009

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Please cite this article as: Sanz-Sánchez T, et al. Terapia de contacto corto con tazaroteno tópico en Darier segmentaria. Actas Dermosifiliogr. 2012;103:253-6.