

interferon beta treatment may be necessary, a decision that should be made in collaboration with the other specialists treating the patient.

## References

- Gaines AR, Varricchio F. Interferon beta-1b injection site reactions and necroses. *Mult Scler*. 1998;4:70.
- Aguilar G, Serrano C, Carmona M, Linares J, Serrano S. Necrosis cutánea por interferón alfa en paciente con melanoma. *Actas Dermosifiliogr*. 2006;97:539–42.
- Beiske AG, Myhr KM. Lipoatrophy: a non-reversible complication of subcutaneous interferon-beta 1a treatment of multiple sclerosis. *J Neurol*. 2006;253:377–8.
- Arrue I, Saiz A, Ortiz-Romero PL, Rodríguez-Peralto JL. Lupus-like reaction to interferon at the injection site: report of five cases. *J Cutan Pathol*. 2007;34:18–21.
- Nakamura Y, Kawachi Y, Furuta J, Otsuka F. Severe local skin reactions to interferon beta-1b in multiple sclerosis-improvement by deep subcutaneous injection. *Eur J Dermatol*. 2008;18:579–82.
- Ziegler VR, Kranke B, Soyer P, Aberer W. Extensive cutaneous-subcutaneous infiltration as a side-effect of interferon beta injection. *Hautarzt*. 1998;49:310.
- Heinzerling L, Dummer R, Burg G, Schmid-Grendelmeier P. Panniculitis after subcutaneous injection of interferon beta in a multiple sclerosis patient. *Eur J Dermatol*. 2002;12:194–7.
- O'Sullivan SS, Cronin EM, Sweeney BJ, Bourke JF, Fitzgibbon J. Panniculitis and lipoatrophy after subcutaneous injection of interferon beta-1b in a patient with multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2006;77:1382–3.
- Ball NJ, Cowan BJ, Hashimoto SA. Lobular panniculitis at the site of subcutaneous interferon beta injections for the treatment of multiple sclerosis can histologically mimic pancreatic panniculitis. A study of 12 cases. *J Cutan Pathol*. 2009;36:331–7.
- Poulin F, Rico P, Côté J, Bégin LR. Interferon beta-induced panniculitis mimicking acute appendicitis. *Arch Dermatol*. 2009;145:916–7.

L. Cuesta,<sup>a,\*</sup> M. Moragón,<sup>a</sup> M. Pérez-Crespo,<sup>a</sup> J. Onrubia,<sup>b</sup> M. García<sup>a</sup>

<sup>a</sup> *Servicio de Dermatología, Hospital Clínico Universitario San Juan, Alicante, Spain*

<sup>b</sup> *Servicio de Anatomía Patológica, Hospital Clínico Universitario San Juan, Alicante, Spain*

\*Corresponding author.

E-mail address: [lcuestamontero@hotmail.com](mailto:lcuestamontero@hotmail.com) (L. Cuesta).

## Porokeratosis of Mibelli: A New Indication for Photodynamic Therapy?<sup>☆</sup>

### Porokeratosis de mibelli, ¿una nueva indicación de la terapia fotodinámica?

To the Editor:

Porokeratosis is a skin keratinization disorder that gives rise to a number of clinical variants; the underlying disorder can be acquired or hereditary. Clinically, it presents as a macule or annular plaque characterized by a central atrophic patch surrounded by a clearly defined hyperkeratotic border. Histology shows a compact parakeratotic column known as a cornoid lamella. The various clinical forms of the disease are defined by the number and distribution of the lesions: porokeratosis of Mibelli, disseminated superficial actinic porokeratosis, linear porokeratosis, porokeratosis palmaris et plantaris disseminata, and punctate porokeratosis. Although the lesions are benign, some of their characteristics are associated with a greater risk of malignant transformation, hence the importance of deciding how to approach these lesions and knowing the different therapeutic options available.

We report the case of an 82-year-old woman with no relevant personal medical history, who visited our department with a skin lesion on the anterior aspect of her left leg that had grown gradually over 2-3 years. The solitary,

erythematous, rounded plaque measuring 4 × 3 cm had well defined margins and was covered by a whitish scale (Fig. 1). The results of a skin biopsy revealed cornoid lamellae with no signs of cellular atypia (Fig. 2). On the basis of both the clinical examination and histology report, a diagnosis of porokeratosis of Mibelli was established. Because of the size and location of the lesion, photodynamic therapy (PDT) was proposed as a good therapeutic option. A cream containing methyl 5-aminolevulinate (MAL) was applied to the lesion, which was then covered with occlusive dressings for 3 hours. The cream used was Metvix. Upon removal of the dressings, the whole surface of the lesion was observed to emit intense red fluorescence under ultraviolet light. The lesion was then exposed to red light from an LED lamp (Aktelite, 37 J/cm<sup>2</sup>) for 9 minutes. Two weeks later, the area of treated skin was ulcerated, perhaps as a result of exposure of the lesion to sunlight a few hours after the treatment; a new session of PDT was therefore ruled out and local therapies were prescribed. Three months after the PDT session, the lesion had almost completely resolved and only a slightly erythematous, crusted area remained (Fig. 3).

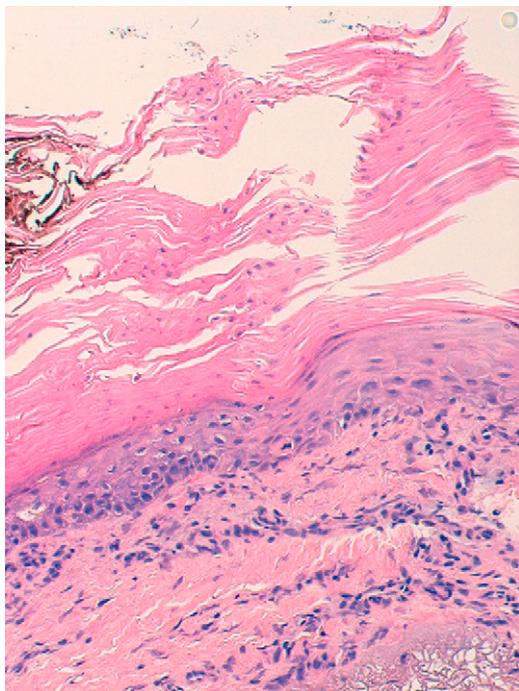
The pathogenesis of porokeratosis is still poorly understood and the disorder is thought to be the result of the proliferation of abnormal clones of keratinocytes induced by the interaction of genetic factors, immunosuppression, and environmental triggers such as exposure to sunlight. The association with irradiation explains why the lesions are more often located in sun-exposed areas of the body and are more evident in summer.<sup>1,2</sup> Although these chronic lesions are benign, all clinical forms of porokeratosis are associated with some risk of malignant transformation. Large, long-standing, or linear lesions and those that present in elderly

<sup>☆</sup> Please cite this article as: Gutiérrez Paredes E, et al. Porokeratosis de mibelli, ¿una nueva indicación de la terapia fotodinámica? *Actas Dermosifiliogr*. 2013;104:259–61.



**Figure 1** Erythematous plaque measuring 4 × 3 cm, covered with a thick, whitish scale.

or immunocompromised patients have the greatest risk of malignant transformation.<sup>2</sup> Reported neoplasms, in order of frequency, are Bowen disease, epidermoid carcinoma, and basal cell carcinoma.<sup>1,2</sup> Because of the risk of malignancy, it is important to consider the best approach to take when



**Figure 2** Hematoxylin-eosin, original magnification ×20. Cornoid lamella (column of parakeratosis associated with hypogranulosis and dyskeratosis).



**Figure 3** Mild erythema and desquamation 3 months after the photodynamic therapy session.

presented with this dermatosis and to know the different therapeutic options available.

The fact that many different therapies are used is indicative of the lack of an ideal treatment that is safe and effective; each case should therefore be evaluated on an individual basis. In the case of multiple, disseminated lesions, the most appropriate approach may be watchful waiting and biopsy of the lesions in which malignant transformation is suspected.<sup>2</sup> Usual treatments include the following: calcipotriol, tacalcitol, 5-fluorouracil, imiquimod, topical and systemic retinoids, laser therapy, cryotherapy, dermabrasion, and surgical excision.<sup>1,2</sup> PDT is approved for the treatment of actinic keratosis, superficial and nodular basal cell carcinoma, and Bowen disease. Its use has recently been extended to a number of infectious and inflammatory skin disorders and certain cancers; the results reported to date indicate varying degrees of efficacy.<sup>3</sup> PDT has been used to treat porokeratosis on the basis of the clinical and histological similarities between this disorder and actinic keratosis. Moreover, it is a safe, well tolerated technique associated with good cosmetic results and minimal side effects. However, the results of the few documented cases are contradictory. Most studies have been carried out in patients with disseminated superficial actinic porokeratosis and various photosensitizing agents have been used ( $\delta$ -aminolevulinic acid, MAL, and hypericin), all with poor results. The lesions resolved in only 1 case,<sup>4</sup> and improved slightly or remained unchanged in the others.<sup>5-7</sup> In the literature, we found only 1 case of porokeratosis of Mibelli that had been successfully treated with PDT. Unlike our case, those authors used a single session of PDT with MAL and blue light in combination with daily application of 5-fluorouracil cream.<sup>1</sup> While the normal PDT regimen in the treatment of most skin disorders involves more than 1 session, we were

only able to apply a single session in the present case owing to the appearance of side effects, and this may explain the incomplete response obtained. However, it is also possible that the immunomodulatory effect of PDT and the inflammation already present in the lesion (visible in the clinical and histological images) may have favored a good therapeutic response with just 1 session. Ulceration is a rare adverse event,<sup>8</sup> and its appearance was probably due in some measure to the fact that the patient was an elderly woman and the leg was exposed to sunlight after treatment, contrary to express instructions.

In conclusion, we report a case of porokeratosis of Mibelli in which treatment with PDT obtained a partial response. Nevertheless, because the results achieved with photodynamic therapy in the treatment of porokeratosis are highly varied, we believe that further studies with larger series of cases are needed if we are to reach clear conclusions regarding its utility in this setting.

## References

1. Levitt J, Emer JJ, Emanuel PO. Treatment of porokeratosis of Mibelli with combined use of photodynamic therapy and fluorouracil cream. *Arch Dermatol*. 2010;146:371–3.
2. Ruiz de Casas A, Moreno-Ramírez D, Camacho-Martínez F. Poroqueratosis actínica superficial diseminada. *Piel*. 2006;21:193–6.
3. Fernández-Guarino M, García-Morales I, Harto A, Montull C, Pérez-García B, Jaén P. Terapia fotodinámica: nuevas indicaciones. *Actas Dermosifiliogr*. 2007;98:377–95.
4. Nayeemuddin FA, Wong M, Yell J, Rhodes LE. Topical photodynamic therapy in disseminated superficial actinic porokeratosis. *Clin Exp Dermatol*. 2002;27:703–6.
5. Cavicchini S, Tournalaki A. Successful treatment of disseminated superficial actinic porokeratosis with methyl aminolevulinate-photodynamic therapy. *J Dermatolog Treat*. 2006;17:190–1.
6. Fernández-Guarino M, Harto A, Pérez-García B, Martín-González M, Urrutia S, Jaén P. Photodynamic therapy in disseminated superficial actinic porokeratosis. *JEADV*. 2009;23:176–7.
7. Boiy A, de Witte PA, Roelandts R. Topical treatment of disseminated superficial actinic porokeratosis with hypericin-photodynamic therapy: a case report. *Photodiagnosis Photodyn Ther*. 2010;7:123–5.
8. Strauss RM, Ogden S, Sheehan-Dare RA, Goulden V. Leg ulceration after aminolaevulinic acid photodynamic therapy in a patient with peripheral vascular disease. *Dermatology*. 2003;207:85.

E. Gutiérrez Paredes,\* R. Bella Navarro,  
E. Montesinos Villaescusa, E. Jordá Cuevas

*Servicio de Dermatología, Hospital Clínico Universitario de Valencia, Universidad de Valencia, Valencia, Spain*

\*Corresponding author.  
E-mail address: [ev\\_gutierrez@hotmail.com](mailto:ev_gutierrez@hotmail.com)  
(E. Gutiérrez Paredes).

## Fabry Disease and the Clinical Spectrum of Angiokeratomas<sup>☆</sup>

### Enfermedad de Fabry: espectro clínico de los angioqueratomas

To the Editor:

After Gaucher disease, Fabry disease is the most common storage disease caused by the progressive accumulation of glycosphingolipids in multiple organs. Clinical presentation is very varied, and furthermore, the manifestations in many of the organs affected are nonspecific.<sup>1</sup> Diagnosis is thus challenging and often delayed. The average time from onset of symptoms to a diagnosis of Fabry disease is around 10 years.<sup>2</sup> Cutaneous involvement is common and is one of the key signs that can lead a physician to suspect the disease. Skin manifestations include angiokeratomas, telangiectasias, abnormal sweating, and lymphedema. Recent studies of cutaneous involvement in Fabry disease have shown that the clinical spectrum of angiokeratomas is also varied.<sup>3</sup> We performed a retrospective review of skin lesions in 5 patients (4 males and 1 female) with Fabry disease, with a particular focus on the clinical variants of angiokeratomas. The main clinical

features are shown in Table 1. The majority of patients, including the only woman, had classic extracutaneous manifestations. The mean age at onset of angiokeratomas was 17.2 years. Patients #4 and #5 had a classic bathing trunk appearance, and patient #5 also had less hyperkeratotic vascular lesions on the palms of both hands. The other 3 patients had less characteristic angiokeratomas. Patient #1 had small, isolated lesions around the mouth and the umbilicus (Fig. 1), while patient #3 had extensive angiokeratomas distributed almost exclusively on the left side of the body. Finally, patient #2, who was heterozygous, had lesions in the form of angiokeratomas on the left side of the vulva (Fig. 2) and small isolated lesions on the anterior surface of the trunk. Just 2 of the patients had hypohidrosis. With the exception of patient #1, all the patients were receiving enzyme replacement treatment, with a mean uninterrupted treatment period of 9 years; there had been no signs of the angiokeratomas disappearing or becoming smaller or any improvements in the other skin manifestations.

Angiokeratoma corporis diffusum is one of the 5 known types of angiokeratoma.<sup>4</sup> It is highly characteristic of Fabry disease, but can also be seen in other lysosomal storage diseases.<sup>5,6</sup> Angiokeratomas, which can appear in childhood or adulthood, develop in 66% of male patients with Fabry disease and in 36% of female patients.<sup>7</sup> While the term *angiokeratoma corporis diffusum* suggests the presence of multiple angiokeratomas, this is not always the case. Furthermore, as seen in 3 of the 5 cases we describe, the lesions

<sup>☆</sup> Please cite this article as: Guinovart RM, et al. Enfermedad de Fabry: espectro clínico de los angioqueratomas. *Actas Dermosifiliogr*. 2013;104:261–3.