Porokeratosis of Mibelli: A New Indication for Photodynamic Therapy? *

Poroqueratosis 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 atrophic patch surrounded by a clearly defined hyperkeratotic border. The results of a skin biopsy revealed cornoid lamellae with some risk of malignant transformation. Large, long-standing, or linear lesions and those that present in elderly 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 (Aktilite, 37 J/cm²) 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. 1,2 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...
or immunocompromised patients have the greatest risk of malignant transformation. Reported neoplasms, in order of frequency, are Bowen disease, epidermoid carcinoma, and basal cell carcinoma. Because of the risk of malignancy, it is important to consider the best approach to take when 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. Usual treatments include the following: calcipotriol, tacalcitol, 5-fluorouracil, imiquimod, topical and systemic retinoids, laser therapy, cryotherapy, dermabrasion, and surgical excision. 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. 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 (δ-aminolevulinic acid, MAL, and hypericin), all with poor results. The lesions resolved in only 1 case, and improved slightly or remained unchanged in the others. 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. 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 therapeut-ic response with just 1 session. Ulceration is a rare adverse event, 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


Fabry Disease and the Clinical Spectrum of Angiokeratomas

Enfermedad de Fabry: espectro clínico de los angiokeratomas

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. Diagnosis is thus challenging and often delayed. The average time from onset of symptoms to a diagnosis of Fabry disease is around 10 years. 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. 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. It is highly characteristic of Fabry disease, but can also be seen in other lysosomal storage diseases. Angiokeratomas, which can appear in childhood or adulthood, develop in 66% of male patients with Fabry disease and in 36% of female patients. 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

 table 1

<table>
<thead>
<tr>
<th>Clinical Variant</th>
<th>Number of Patients</th>
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<tbody>
<tr>
<td>Classic bathing trunk</td>
<td>2</td>
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<tr>
<td>Angiokeratomas on the left side of the vulva</td>
<td>2</td>
</tr>
<tr>
<td>Small isolated lesions on the anterior surface of the trunk</td>
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