

the unusual presence of eccrine squamous syringometaplasia. *Br J Dermatol.* 1995;133:630–2.

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Mixed Panniculitis Secondary to Interferon Beta-1a Therapy in a Woman With Multiple Sclerosis[☆]

Paniculitis mixta secundaria al uso de interferón β 1A en una paciente con esclerosis múltiple

To the Editor:

Interferon beta was approved in Spain in 1995 for the treatment of progressive multiple sclerosis. There are 2 main types, interferon beta-1a and 1b, both of which are sold in a variety of formulations, resulting in a range of responses to the same molecule. Local skin reactions are a common adverse effect, and are usually self-limiting. By contrast, panniculitis and lipoatrophy are very rare, and may necessitate discontinuation of treatment.

We describe the case of a 43-year-old woman who was diagnosed in 2005 with multiple sclerosis, for which she received several disease-modifying treatments. In October 2009, she began treatment with interferon beta-1a (Rebif 44), which was self-administered subcutaneously 3 times a week, with a favorable response. After 18 months of treatment, induration was observed at the injection sites, on the back of the thighs, and on the outer arms. A few weeks later, ulcerated lesions appeared on the front of the thighs and progressively increased in size. The patient reported that the plaques caused severe pain, which made moving and walking difficult. She reported no fever or systemic upset and her neurological status remained unchanged.

Examination revealed 2 ulcers on the front of the thighs of 1 cm diameter. The borders of the ulcers had a scarlike appearance and beneath the ulcers were cavities of about 4 cm in diameter. An indurated plaque of about 15 cm in diameter, with a slightly erythematous surface, surrounded the ulcer and was intensely painful to touch (Fig. 1). These indurated plaques were also present on the external aspect of both arms, although no ulcers were observed.

Tissue culture of the ulcers and an incisional biopsy of a plaque from 1 of the thighs were negative. Histopathology revealed a preserved epidermis, sclerosis of the middle

and deep dermis, and subcutaneous tissue involvement. At higher magnification we detected an infiltrate that primarily affected the lobule, although septal thickening was also observed (Fig. 2a); this infiltrate was composed mainly of neutrophils and lymphocytes (Fig. 2b). No vasculitis or necrosis was observed. Based on these observations, the patient was diagnosed with mixed panniculitis secondary to interferon beta-1a therapy. Upon consultation with her neurologist, it was decided to discontinue interferon beta-1a treatment, mainly due to functional impairment.

Interferon beta-1a was approved for the treatment of progressive multiple sclerosis in Spain in 1995. Its administration decreases the relapse rate by 30% and the appearance of new lesions on magnetic resonance imaging by 66%. Local skin manifestations such as erythema and pain are well-described frequent adverse effects; they occur in 63% to 85% of patients¹ but are usually self-limiting and do not require discontinuation of treatment. However, treatment may need to be discontinued in cases of other more serious reactions such as ulcerations, necrosis,² sclerosis, and induration at the injection site. Other adverse effects such as sarcoid granulomas, lipoatrofia,³ lupus-like lesions,⁴ and septal or lobular panniculitis⁵ are considered very rare. Table 1 summarizes the cases of panniculitis secondary to interferon treatment described to date. Some authors have suggested that this form of panniculitis may be caused by the vascular toxicity of interferon beta.



Figure 1 Indurated erythematous plaques with ulcerated centers on the front of both thighs.

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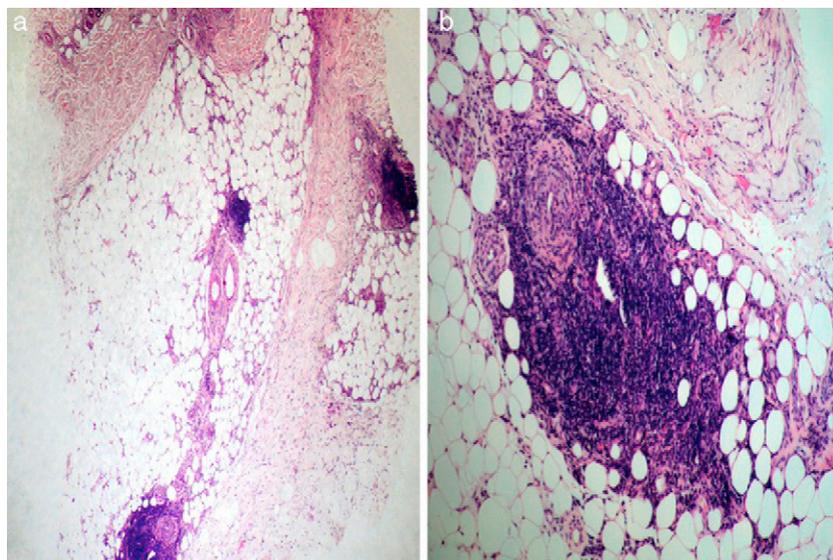


Figure 2 a, An infiltrate affecting the lobule and to a lesser extent, the septum. Septal thickening is also observed. Hematoxylin-eosin, original magnification $\times 40$. b, Mixed infiltrate composed mainly of lymphocytes with some neutrophils. Hematoxylin-eosin, original magnification $\times 200$.

In 2009, Ball and coworkers⁹ reported that interferon beta-induced panniculitis can mimic pancreatic panniculitis; differential diagnosis in such cases may be facilitated by lipase and amylase tests.

Two theories have been proposed regarding the pathophysiology of panniculitis secondary to interferon beta treatment. The first proposes that the stress associated with self-injection plays a key role in triggering this condition. The second theory attributes greater importance to the immunological effects of interferon beta. According to the

latter theory, the resulting symptoms reflect activation of the immune system and may be an indication of treatment effectiveness.⁹

The management of patients with panniculitis secondary to interferon beta treatment remains unsatisfactory. It is essential that patients are shown how to correctly self-administer the injection, which should be subcutaneous and never intradermal, and to rotate the injection sites daily. Application of these measures leads to improvements in the majority of lesions,⁵ although in some cases suspension of

Table 1 Patients Described in the Literature Who Developed Panniculitis After Interferon Administration.

	Age, Sex	Location	Onset of Symptoms	Clinical Symptoms	Pathological Findings
Nakamura et al., ⁵ 2008	43, female	Buttocks	5 y	Erythema, induration, and pain	Perivascular dermatitis and lobular and septal panniculitis with lymphocytic infiltrate
Ziegler et al., ⁶ 1998	41, female	Legs	8 wk	Erythema, induration, and pain	Perivascular infiltrate and lobular panniculitis with lymphocytic infiltrate
Heinzerling et al., ⁷ 2002	44, female	Arms, legs and abdomen	4 y	Painful induration	Septal panniculitis with predominantly lymphocytic infiltrate
O'Sullivan et al., ⁸ 2006	37, male	Left leg	2 y, 3 mo	Erythema and pain	Septal panniculitis with inflammatory infiltrate
Ball et al., ⁹ 2009	46, female	Not recorded	1 y, 10 mo	Pain and induration	Lobular panniculitis with neutrophilic infiltrate
Ball et al., ⁹ 2009	45, female	Not recorded	6 y, 1 mo	Cellulitis	Lipomembranous panniculitis
Poulin et al., ¹⁰ 2009	43, female	Abdomen	9 y	Erythema, pain, and fever	Septal panniculitis with predominantly lymphocytic infiltrate
Present case	43, female	Legs	19 mo	Pain, erythema, induration, and functional impairment	Lobular and septal panniculitis with mixed inflammatory infiltrate (lymphocytes and neutrophils)

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

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Porokeratosis of Mibelli: A New Indication for Photodynamic Therapy?[☆]

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/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

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