

## Extragenital Lichen Sclerosus Induced by Radiotherapy<sup>☆</sup>



### Liquen escleroso extragenital inducido por radioterapia

To the Editor:

Lichen sclerosus is a rare, chronic inflammatory skin disease that affects the genital and extragenital regions. It was first described by Hallopeau in 1887 as atrophic lichen planus.<sup>1</sup> The current most widely accepted term for the disease is *lichen sclerosus*. We report a case of lichen sclerosus in which lesions appeared only in a previously irradiated area.

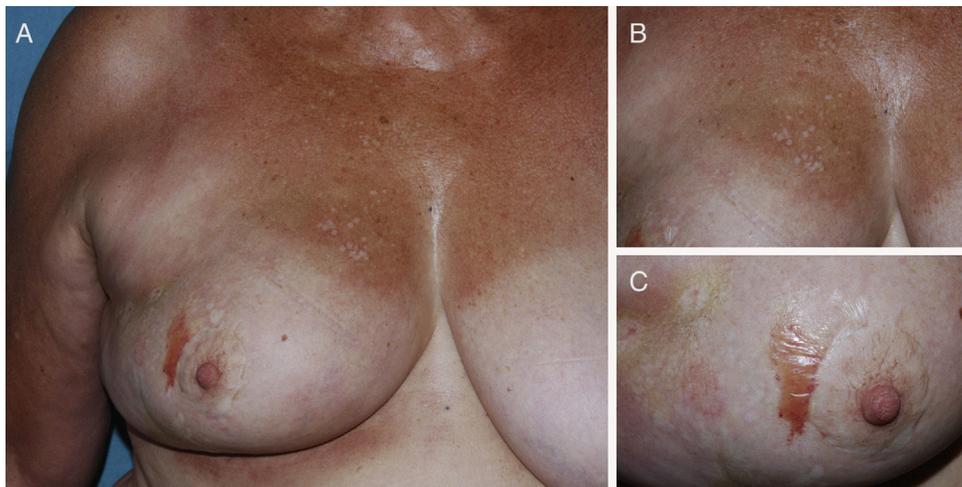
The patient was a 71-year-old woman who had been diagnosed 2 years earlier with an infiltrating lobular carcinoma in the right breast. The tumor was treated with lumpectomy and subsequent radiotherapy. The patient was undergoing treatment with letrozole. Two years after radiotherapy, the patient was referred to us with asymptomatic lesions that had appeared 2 months earlier on the irradiated breast. The physical examination revealed a flaccid blister containing serosanguineous fluid beside the areola of the right breast and small, round, pearly white macules on the right hemithorax and the outer quadrants of the right breast (Fig. 1). The patient presented no associated genital lesions. In light of the suspected diagnosis of lichen sclerosus secondary to radiotherapy, we performed a biopsy of the site of the blister. Histopathology revealed epidermal atrophy and marked dermal hyalinization associated with superficial edema, compatible with lichen sclerosus (Fig. 2A). Secondary subepithelial vesiculation, responsible

for the blister, was also observed (Fig. 2B). Treatment was started with daily application of 0.1% topical tacrolimus, which attenuated the whiteish macules and resolved the blister completely. No subsequent new lesions appeared.

The exact prevalence of lichen sclerosus is unknown. It is markedly more frequent in females and may appear at any age, although peak incidence occurs around the fifth and sixth decades of life. Genital involvement is most frequent (85% of cases), concomitant extragenital involvement can be found in up to 20% of cases, and exclusively extragenital involvement is found in up to 2.5%.<sup>2</sup>

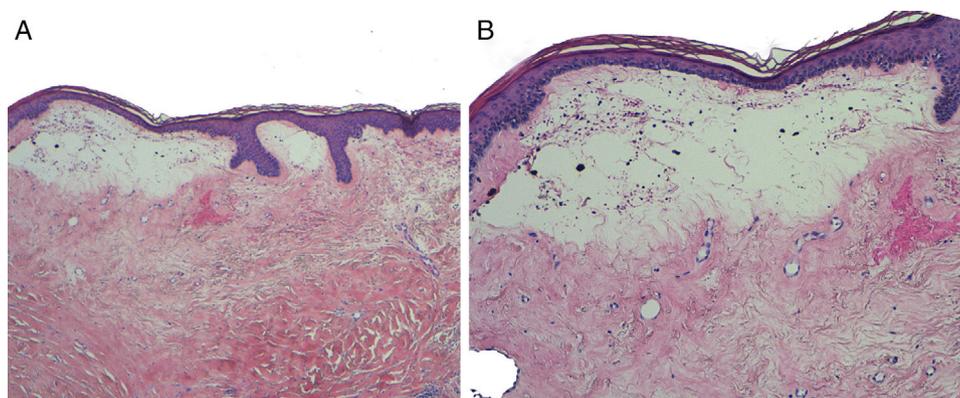
The etiology is unknown, although there appears to be some genetic predisposition. A link with underlying autoimmune mechanisms has also been postulated, as cases have been reported in association with diseases such as vitiligo, alopecia areata, and thyroiditis. What is clear is the presence of the Koebner response in this disease. Cases of lichen sclerosus have been reported in association with jellyfish stings,<sup>3</sup> subcutaneous insulin injections,<sup>4</sup> and chronic pressure sores.<sup>5</sup> The Koebner response may explain the appearance of lesions in previously irradiated areas, as in our case. Although radiotherapy is currently widely used, only 4 cases of lichen sclerosus induced by radiotherapy have been described in the literature (Table 1).<sup>6-8</sup>

Extragenital lichen sclerosus is generally asymptomatic, although it may present with associated dryness and pruritus. It most frequently affects the torso, neck, upper limbs, and flexor surface of the wrists. Lesions initially present as ivory-colored interfollicular polygonal papules that coalesce to form scleroatrophic plaques. Telangiectasia and follicular plugging may be observed in more advanced stages. Hemorrhagic blisters may appear owing to the fragility of the dermal-epidermal junction, as in our case.<sup>2</sup>



**Figure 1** A, Pearly white macules on the right hemithorax and outer quadrants of the right breast. A serosanguineous blister can also be observed beside the right areola. B, Detail of the pearly white macules on the hemithorax. C, Higher magnification of the serosanguineous blister.

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**Figure 2** A, Marked dermal hyalinization and superficial edema (hematoxylin–eosin, original magnification  $\times 40$ ). B, Epidermal atrophy and incipient vesiculation (hematoxylin–eosin, original magnification  $\times 100$ ).

**Table 1** Cases of Lichen Sclerosus Induced by Radiation Therapy Reported in the Literature.

	Type of Tumor	Treatment Received	Latency Period	Location of Lichen Sclerosus
Yates et al. (1985) <sup>8</sup>	Neoplasm of right breast	Surgery + radiation therapy	2 y	Right breast
Yates et al. (1985) <sup>8</sup>	Neoplasm of right breast	Surgery + radiation therapy	9 y	Right breast
Vujovic (2010) <sup>6</sup>	Neoplasm of left breast	Surgery + radiation therapy + hormone therapy	2 y	Left breast
Edwards et al. (2017) <sup>7</sup>	Vaginal squamous cell carcinoma	External radiotherapy and brachytherapy	16 mo	Vulvar region

Diagnosis is essentially based on histologic findings, which show a specific pattern characterized by sclerosis or uniform hyalinization of the superficial dermis, and a lymphohistiocytic inflammatory infiltrate in an underlying band. Other more variable findings include thinning and atrophy of the epidermis, orthokeratotic hyperkeratosis, vacuolar degeneration of the basal layer, and dermal edema. Loss of elastic fibers is frequent in this disease.<sup>9</sup>

Genital lichen sclerosis only requires treatment in the event of associated pruritus or severe sclerosis. The most commonly used treatments are potent topical corticosteroids and topical calcineurin inhibitors. Systemic treatment is generally unnecessary in extragenital lichen sclerosis, as it is a benign skin disease that, unlike genital lichen sclerosis, presents a low risk of malignant transformation of the lesions.

We report a new case for the literature of lichen sclerosis induced by radiotherapy. Although only 4 reported cases of the disease exist in the literature, it is an entity we should be aware of given the current widespread use of radiotherapy.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Milia: An Uncommon Reaction to Photodynamic Therapy<sup>☆</sup>



### Milia, una reacción infrecuente tras terapia fotodinámica

To the Editor:

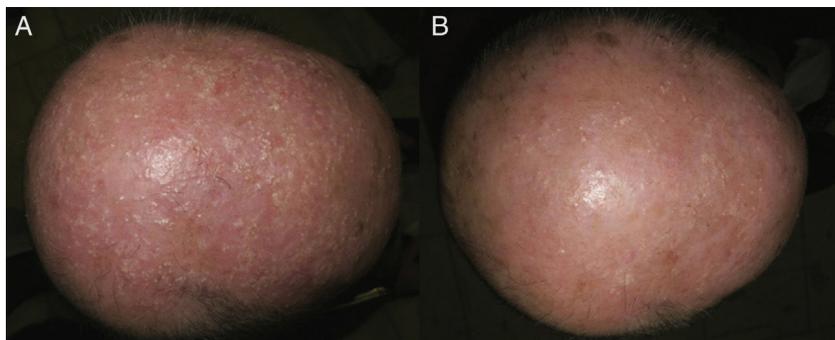
Photodynamic therapy (PDT) is a noninvasive treatment that combines a light source with a topical photosensitizing agent. The technique is widely used in dermatology for treating certain oncologic conditions such as actinic keratosis and superficial basal cell carcinoma. While PDT is safe and effective, an appreciable number of patients present local adverse effects such as erythema, pain, and edema at the treatment site. Isolated incidents of other adverse effects have been described, including transitory hyperpigmentation, cellulitis, and, more rarely, milia.

A 91-year-old man with skin phototype II on the Fitzpatrick scale and a past history of hypertension and hypertensive heart disease visited our department with lesions in the parieto-occipital region of the scalp. The lesions had appeared 3 years earlier and had not improved despite months of keratolytic therapy. Physical examination revealed multiple soft keratotic crusted papules grouped in the parieto-occipital region of the scalp. Shave biopsy of one of the lesions revealed acanthosis with hyperkeratosis, alternating orthokeratosis and parakeratosis, and focal atypia of keratinocytes in the lower third of the

epidermis, confirming the suspected diagnosis of actinic keratosis. PDT was performed using 5-aminolevulinic acid hydrochloride gel (78 mg/g). The area to be treated was covered with an opaque dressing for 3 hours. The area was cleaned using saline solution and exposed to a lamp with red light-emitting diodes at a wavelength of 630 nm (Aktilite CL128, Galderma) and the dosage recommended in the product information sheet (37 J/cm<sup>2</sup>). The patient presented considerable erythema in the treated area at the end of the treatment session.

By the follow-up visit a month after treatment, the actinic keratosis had completely resolved; however, multiple millimeter-sized monomorphous, whiteish papules were observed in the treated area (Fig. 1 A). In light of the suspected diagnosis of milia, a 4-mm punch biopsy was performed. The results of histopathology were compatible with milia: multiple cyst-like structures lined by squamous epithelium with a granular layer and containing orthokeratotic keratin (Fig. 2). Treatment was started with 5% salicylic acid in petroleum jelly, applied once daily, and the lesions improved after 2 months of treatment (Fig. 1B).

Milia are small epidermal cysts that present as firm whiteish papules with a diameter of less than 3 mm; they are thought to originate in the pilosebaceous follicle. Cysts are classed as primary milia when they appear spontaneously, predominantly on the face, and as secondary milia<sup>1</sup> when they are caused by trauma or occur in association with inflammatory skin conditions. Secondary milia have been reported in association with second-degree burns, radiotherapy,<sup>2</sup> porphyria cutanea tarda, and after



**Figure 1** A, Multiple millimeter-sized monomorphous, whiteish papules in the parieto-occipital region. B, Clear improvement of the milia in the parieto-occipital region following application of mild keratolytic agents.

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