

CASE LETTER

Multiple seborrheic keratoses in a previously irradiated site ☆☆☆



Dear Editor,

Breast cancer is the second most common malignancy worldwide. In Brazil, 59,700 new cases were estimated for 2019. It predominantly affects women in their 50s, and the most common histological subtype is invasive ductal adenocarcinoma.¹

Treatment is associated with dermatological complaints in 74%–100% of cases.² Therapy involves surgery and locoregional radiotherapy, in addition to chemotherapy and hormone therapy for systemic treatment.³

Seborrheic keratosis is the most common benign cutaneous tumor, being predominantly observed in Caucasian adults. It originates in the epidermis, and a proliferation of immature keratinocytes is observed. Clinically, it is characterized by brownish, well-defined papules with greasy surface.^{4,5} Based on clinical suspicion, dermoscopy helps in its diagnosis, which is confirmed by histopathology.⁵

A case of multiple seborrheic keratoses restricted to the site of previous breast cancer radiotherapy is described.

A female patient, 73 years old, white, was diagnosed four years ago with invasive micropapillary carcinoma in the left breast, which required surgical intervention (quadrantectomy), chemotherapy (adriamycin, cyclophosphamide, and paclitaxel) and 30 adjuvant radiotherapy sessions. Six months ago, she noticed the onset of brownish, asymptomatic, slowly evolving papules, restricted to the skin adjacent to the surgical scar, an area previously irradiated (Figs. 1 and 2). In 2019, she sought dermatological care, and the clinical examination and dermoscopy showed lesions suggestive of seborrheic keratoses, on the left breast only. At the moment, the patient is in remission and is being followed-up every six months. The histopathology of a lesion was compatible with the diagnosis, due to the presence of basaloid cells, hyperkeratosis, and formation of horn pseudocysts (Fig. 3).

By 2015, over 1.3 million people had been diagnosed with breast cancer worldwide.¹ The invasive micropapillary subtype, diagnosed in this case, is rare, representing 0.9%–2% of breast carcinomas; it is associated with aggres-

sive clinicopathological characteristics.¹ Radiotherapy has numerous effects on skin tissue, ranging from acute (up to six months after therapy initiation) to chronic; depending on the location, size, and depth of the irradiated tumor, these effects can be classified as mild, moderate, or severe.^{2,3,5} The patient presented chronic symptoms.

The severity of the skin lesions caused by radiation is dependent on factors related to the treatment and the patient.² Those linked to treatment include the total dose and the irradiation site, fractionation time, volume and area of irradiated tissue, and the use of chemotherapy.^{2,3} Among the patient-related factors, smoking, malnutrition, obesity, autoimmune diseases, and genetic factors are noteworthy.^{2,3} The only risk factors for the present patient were multiple radiotherapy and chemotherapy sessions.

The sign of Leser-Trélat is rare, and characterized by the abrupt eruption of multiple seborrheic keratoses, usually on the back, which may precede or occur after the diagnosis of the malignancy, especially lung and gastrointestinal adenocarcinoma.⁴ The patient presented progressive lesions only at the irradiated site.

The mechanism of lesion determined by radiation is not fully understood; however, it is known that the skin is an organ in constant renewal, consisting of cells with rapid proliferation and maturation, making them vulnerable to this therapy.² Basal keratinocytes and hair follicles are highly radiosensitive. Moreover, radiation damage causes inflammation, cell recruitment, DNA damage, and cytokine generation.^{3,5}

The etiology of seborrheic keratosis remains unknown. Recently, it has been postulated that epidermal growth factors (oncogenes [PIK3CA] and fibroblast growth factor receptor 3 [FGFR3]) may participate in 32% and 48% of cases, respectively. Recent studies demonstrated that other oncogenes (TERT and DPH3) are also involved in the genesis of the lesions.⁵

Eczemas and chemotherapy can trigger or increase inflammation in pre-existing seborrheic keratoses, differently from the case presented.³

The diagnosis of seborrheic keratosis is clinical, and dermoscopy is useful for differentiating it from other pigmented lesions. The dermoscopic pattern is polymorphic; the most characteristic finding is horn pseudocysts, as observed in the present case. In case of diagnostic doubt, histopathology becomes indispensable.⁵ In our patient, due to the presence of multiple lesions, the authors decided to excise one of them for histopathological examination, confirming the clinical diagnosis.

☆ How to cite this article: Chagas DF, Diniz LM, Badaró BA, Lucas EA. Multiple seborrheic keratoses in a previously irradiated site. An Bras Dermatol. 2020;95:773-775.

☆☆ Study conducted at the Hospital Universitário Cassiano Antônio Moraes, Vitória, ES, Brazil.

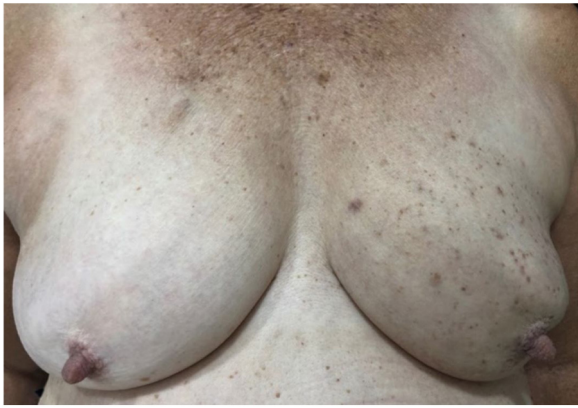


Figure 1 Multiple seborrheic keratoses restricted to the previously irradiated site.



Figure 2 Detail of multiple brownish, rounded, well-defined papules with a greasy surface, restricted to the left breast.

Treatment is indicated for aesthetic purposes; some options include curettage, application of trichloroacetic acid, and cryotherapy with liquid nitrogen.⁵ In the present case, cryotherapy was applied in two sessions; a reduction in the greasy surface of seborrheic keratoses and hyperpigmentation was observed in the first session.

In the literature review, no studies on seborrheic keratosis induced by radiotherapy were retrieved; the authors concluded that radiation triggered the proliferation of keratinocytes, probably through mediators that lead to the production of melanogenesis-stimulating cytokines, activation of oncogenes, and epidermal growth factors.

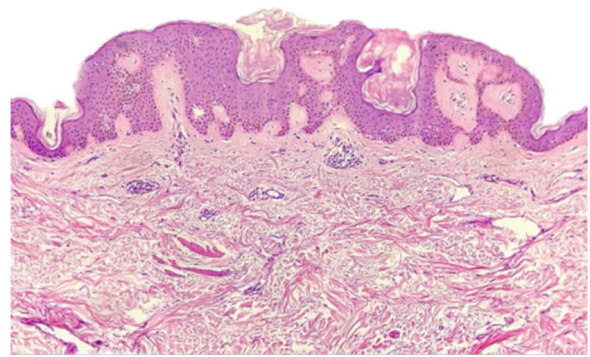


Figure 3 Histopathological examination of one of the breast lesions, showing proliferation of uniform basaloid cells, elongation of the rete ridges, and hyperkeratosis. Keratin pseudocysts and melanic hyperpigmentation of the epidermis are also observed (Hematoxylin & eosin, $\times 10$).

Financial support

None declared.

Authors' contributions

Danielle Ferreira Chagas: Drafting and editing of the manuscript; intellectual participation in the propaedeutic and/or therapeutic conduct of the studied cases; critical review of the literature.

Lúcia Martins Diniz: Approval of the final version of the manuscript; intellectual participation in the propaedeutic and/or therapeutic conduct of the studied cases; critical review of the manuscript.

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Conflicts of interest

None declared.

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Received 12 December 2019; accepted 10 February 2020

<https://doi.org/10.1016/j.abd.2020.02.014>

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Dermoscopy of late-onset nevus comedonicus^{☆☆}



Dear Editor,

Nevus comedonicus (NC) is a rare hamartoma of the pilosebaceous unit, a subtype of epidermal nevus first described by Kofmann in 1895.¹ NC manifests with linear or grouped papules and dilated follicular openings with keratotic plugs (resembling comedones) particularly on the face, trunk, and neck; in 50% of cases, it is present at birth, but can also develop during childhood (most commonly before the age of 10 years). The rare presence of skeletal and neurological abnormalities describes the nevus comedonicus syndrome.² Histopathology shows keratin-filled invaginations of the epidermis, with absent or rudimentary sebaceous glands. Inflammation and subsequent dermal infiltrate have been described in some cases.² Rarely, NC may present in adults; recently Zaniello et al., reporting an additional case of late-onset NC, reviewed the few cases described.³

A 72-year-old man with a previous history of stage IB cutaneous melanoma on the trunk in 2013 and prostate carcinoma presented in June 2019 with a keratotic plaque (2 × 1 cm in diameter) and a small comedo-like nodule (almost 1 cm in diameter) on the left calf, following a Blaschko line (Fig. 1). The lesions had appeared almost 25 years before, and the patient had been asymptomatic until the week before, when the lesions became very itchy. Dermoscopic examination showed a central keratotic plug surrounded by a white structureless area with scales and focal pale structureless red area without clear vessels (Fig. 2). The patient had been taking candesartan, hydrochlorothiazide, bicalutamide, simvastatine, and rabeprezole for years. General physical and neurological examinations were normal, and the patient denied a family history of analogous lesions. Histopathology demonstrated a cyst-dilated follicular opening filled with keratin, slight acanthosis of the epidermis, and hyperkeratosis with ortho- and parakeratosis. The follicular epithelial wall and the epidermis showed EHK with hypereosinophilic keratohyalin granules in the granular cell layer and perinuclear vacuolization (Fig. 3). Sebaceous and eccrine glands were not present. A focal discrete lymphohistiocytic infiltrate was

present in the papillary dermis. Upon clinicopathologic correlation, the diagnosis of late-onset NC with EHK was made. The main differential diagnosis was inflammatory linear verrucous epidermal nevus (ILVEN), which typically presents in the first 6 months of life as a pruritic linear eruption on the lower limbs, arranged along the Blaschko lines. At histopathology, ILVEN shows psoriasiform epidermal hyperplasia with parakeratosis, alternating with orthokeratosis. Beneath the orthokeratosis, hypergranulosis is observed, while the parakeratosis overlies areas of agranulosis. Focal mild spongiosis with some exocytosis and even vesiculation may be present, together with a mild perivascular lymphocytic infiltrate in the upper dermis.³ The infiltrate observed in the present case was probably caused by irritation. EHK is characterized by compact hyperkeratosis with granular and vacuolar degeneration of the cells of the spinous and granular layers. It may be an incidental finding or may be observed in different settings, such as bullous ichthyosis, epidermal nevi variant, palmoplantar keratoderma variant, or disseminated epidermolytic acanthoma.³

EHC in a NC has been reported in few cases in the literature reviewed by Zanniello et al.,³ who reported a peculiar case with late onset (55-year old woman). The present patient is an additional case of this rare histopathological variant of NC.

Dermoscopy of NC was reported in detail for only two young patients. Vora et al. described multiple, well-defined, structureless brown homogenous circular areas surrounding the keratin plugs.⁴ Kamińska-Winciorek et al. reported numerous circular and barrel-shaped, homogenous areas in light and dark-brown shades, with remarkable keratin plugs.⁵ In the present case, a central keratotic plug was observed, surrounded by a white structureless area with scales and focal pale structureless red area without clear vessels. The following dermoscopic differential diagnoses were considered for the present case: squamous cell carcinoma/keratoacanthoma, which shows an amorphous, yellow-white central mass of keratin, hairpin vessels, and/or serpentine vessels; common wart, which at dermoscopy presents multiple densely packed papillae, with a central red dot or loop, surrounded by a whitish halo; molluscum contagiosum, which displays a central pore in association with polylobular white-to-yellow amorphous structures, surrounded by blurred telangiectasia.

A topical treatment with methylprednisolone aceponate 0.1% for on week and urea 10% ointment twice a day as maintenance therapy was prescribed, with fast improvement of the pruritus and slight decrease of keratotic component.

[☆] How to cite this article: Massone C, Javor S, Sola S. Dermoscopy of late-onset nevus comedonicus. *An Bras Dermatol.* 2020;95:775–776.

^{☆☆} Study conducted at the Galliera Hospital, Genoa, Italy.