DISSEMINATED SUPERFICIAL ACTINIC POROKERATOSIS: A CASE REPORT

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Summary

Introduction: *Disseminated superficial actinic porokeratosis (DSAP) is a keratinization disorder and the most common variant form of porokeratosis. UV radiation, immunosuppression, radiotherapy, trauma, and genetic factors are all risk factors for DSAP. Porokeratosis usually affects sunexposed skin, and it appears as multiple pink macules, with hypertrophic, well-defined borders and an atrophic center.*

Clinical case: *We present the case of a 70-year-old patient, with a history of left mastectomy and radiotherapy for breast cancer, who came to the Dermatology Clinic, for a bilateral eruption on the calves, consisting of multiple pinkish-brown, itchy macules. A diagnosis of DSAP was established based on clinical examinations, the dermoscopic pattern of "volcanic crater", and the histopathological identification of the" cornoid lamella". Laboratory tests showed high values of fasting blood glucose and positive results for IgG antibodies against HSV type 1, toxoplasma and rubella. Following topical treatment with 0.2% polyvinyl A, 0.02% tretinoin, 4% glycolic acid gel and 5% diclofenac gel the lesions regressed.*

Conclusions: *Multiple treatment options are available for DSAP, no standard care being recognized. Such cases should be followed-up clinically and dermoscopically considering the potential for malignant transformation of such cases.*

Key words: *disseminated superficial actinic porokeratosis, cornoid lamella, radiotherapy, breast cancer.*

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Introduction

Disseminated superficial actinic porokeratosis (DSAP) is the most common subtype of porokeratosis [2]. The onset of porokeratosis is tied to risk factors such as ultraviolet radiation, genetics, trauma, infection, and immunosuppression [2]. Both DSAP and linear porokeratosis are more frequently found in females, while men are more likely to be affected by porokeratosis palmaris and plantaris or by Mibelli's porokeratosis [3]. Female patients are more likely to develop DSAP in their 30s or 40s [4]. DSAP is much more likely to develop Caucasians. It's rarely found in people with Fizpatrick skin types IV or V [5].

In DSAP, clinically we will see pruritic erythematous macules, round-oval in shape, scaly, with well-defined hyperkeratotic margins and an atrophic center [1]. The skin lesions appear on the sun-exposed regions; they are symmetrical, bilateral, and most frequently found on the distal extremities of the lower limbs [1]. Palms, soles, and mucous membranes are typically spared [4], and lesions on the face are found in about 15% of patients [6]. Although the etiopathogenesis of porokeratosis is not fully understood, it seems that a mutation of

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mevalonate kinase in association with ultraviolet radiation exposure are involved in the process and could lead to increased cell death and the clinical onset of the lesions [7].

Clinical case

We report the case of a 70-year-old patient, who presented to the Dermatology Clinic with some intensely itchy lesions on her calves. The dermatological examination revealed a symmetrical rash on the anterior and lateral sides of the calves consisting of multiple erythematous-scaly macules with well-defined margins and an atrophic center [Figure 1]. After using methylene blue 1% for staining the lesions and wiping it off with an alcoholic solution, the hyperkeratotic collar, that histopathologically corresponds to the column of parakeratotic cells located next to the epidermal atrophy area, also known as the "cornoid lamella", was highlighted [Figure 2].

Dermoscopy identified multiple yellowish-white clods in the center of the lesion, indicating the follicular involvement, while white rosettes, due to the degradation of the dermis due to UV exposure, were also seen. Additionally, the "volcanic crater" mark was noticed. [Figure 3].

A punch skin biopsy was performed from a pinkish-brown macule from the anterior calf. The histopathological examination revealed a keratinized stratified squamous epithelium, with orthokeratosis and parakeratosis, an atrophic spinous layer consisting of 3-4 layers of cells, first-degree dermal elastosis, and a chronic inflammatory infiltrate in the superficial dermis. The cornoid lamella, a hallmark of porokeratosis, was also identified [Figure 4].

Laboratory blood analysis revealed high values for fasting blood glucose (117 mg/dl), triglycerides (178 mg/dl), erythrocyte sedimentation rate (ESR) (50 mm/h). Previous herpetic infection (positive IgG antibodies against HSV type 1), Toxoplasma Gondii infection (positive IgG antibodies against Toxoplasma Gondii-7.40 IU/ml, negative IgM antibodies against Toxoplasma Gondii 0.11 S/CO) and Rubella infection (positive IgG antibodies against Rubella-96.70 IU/ml, negative IgM antibodies against Rubella 0.14 S/CO) were identified. The other laboratory findings were withing limits.

Based on the clinical, dermoscopic and histopathological examination, a diagnosis of DSAP was established.

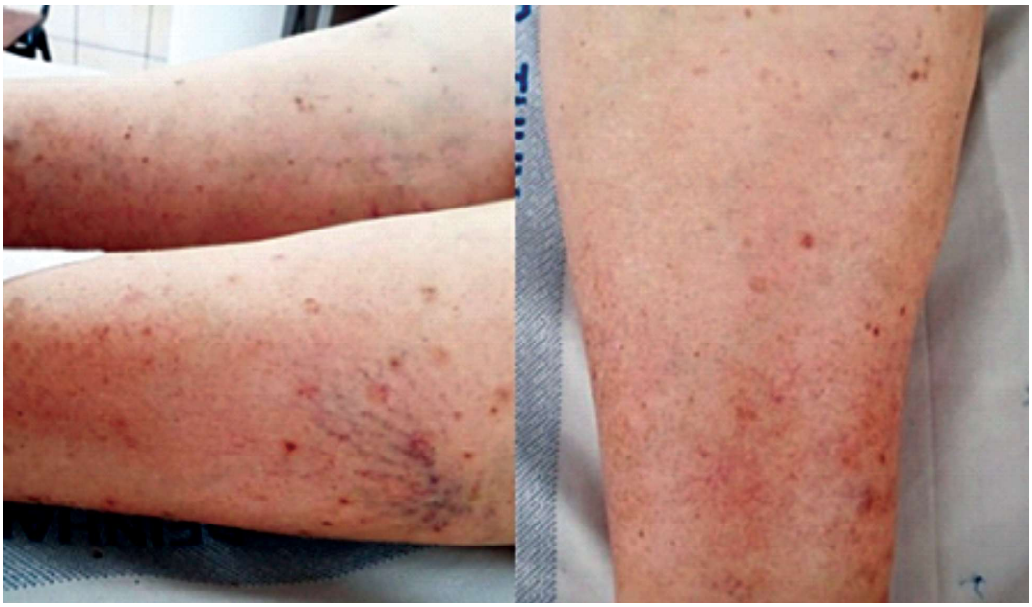

Figure 1. Clinical appearance of DSAP lesions: on the antero-lateral sides of the calves - erythematous macules, with well-defined margins, atrophic center.

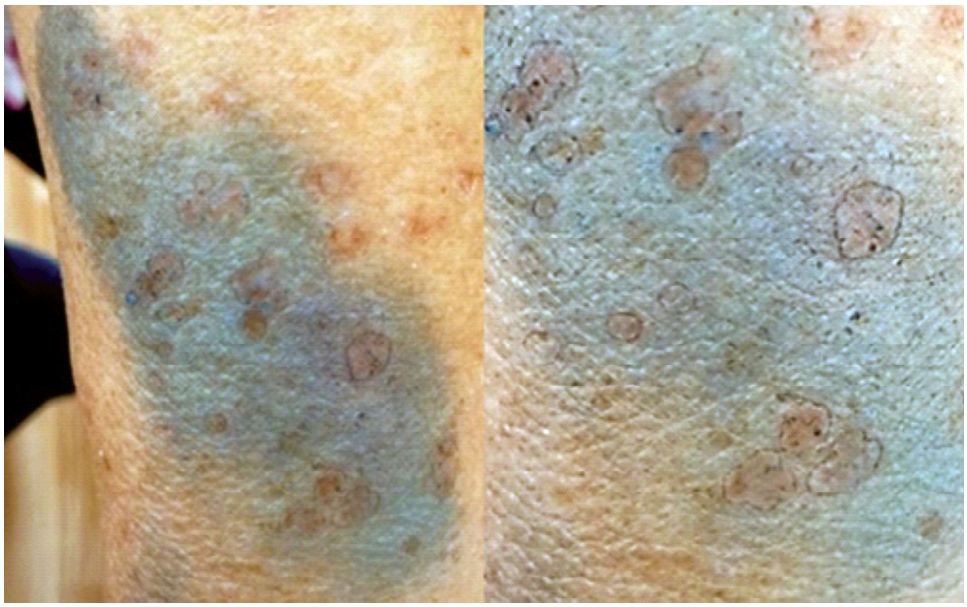

Figure 2. Clinical appearance of DSAP lesions after staining with methylene blue 1%. The "hyperkeratotic collar" is highlighted.

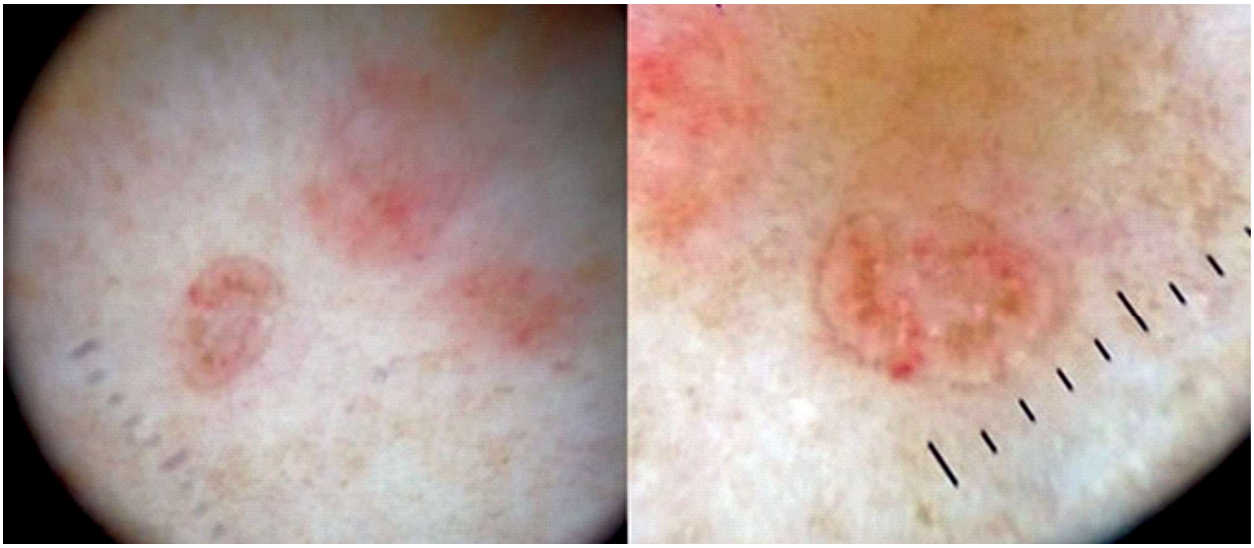

Figure 3. Dermoscopy of porokeratosis lesions: yellow-white lumps ("clods") and white rosettes can be observed in the center of the lesion. The "volcano crater" is observed.

Topical treatment with 0.2% polyvinyl A, 0.02% tretinoin, 4% glycolic acid gel twice a day and 5% diclofenac gel b.i.d. lead to complete clinical remission after 5 weeks. Daily photoprotection has been recommended as well. The patient was carefully followed up for 2 years, with no further treatment needed and no malignant transformation of the lesions.

Discussions

Clinically, porokeratoses are classified as Mibelli's porokeratosis, DSAP, linear porokeratosis, punctate porokeratosis, porokeratosis plantaris, palmaris et disseminata (PPPD), ptycotropic porokeratosis and disseminated eruptive porokeratosis [5].

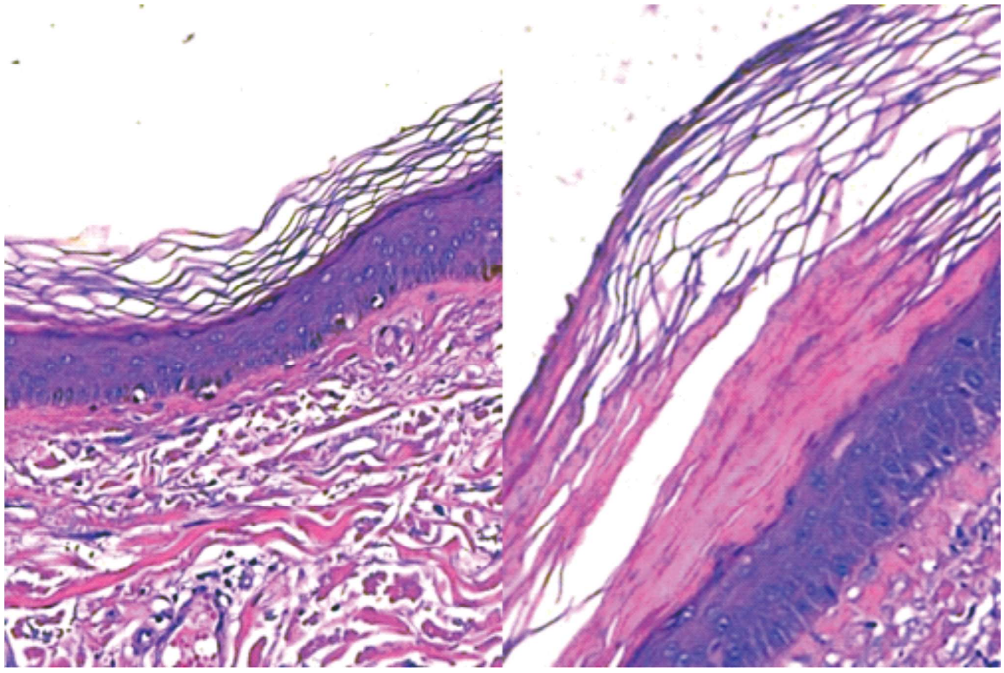

Figure 4. Histopathological aspect in Hematoxylin-Eosin stain, 20x magnification: orthokeratosis and porokeratosis, atrophic spinous layer, cornoid lamella, grade I elastosis in the dermis, and chronic inflammatory infiltrate in the superficial dermis.

There are some triggering factors that may contribute to the onset of the disease. Herpes simplex virus infection is found in approximately 20% of patients with disseminated eruptive porokeratosis [6], but there are no cases reported in patients with DSAP. Also, no cases of porokeratosis and coinfection with Rubella or toxoplasma gondii have been identified.

The specific dermoscopic marker of porokeratosis is known as the "volcanic crater" pattern [8], consisting of a peripheral ring that corresponds to the hyperkeratotic, elevated, usually hyperpigmented, well-defined margin, which can be broken in some places. Dermoscopy of the porokeratosis macules of our patient detected the "volcanic crater" pattern, as well as follicular involvement (white lumps in the center of the lesions). A small number of DSAP cases with follicular involvement have been reported [8].

The onset of superficial disseminated actinic porokeratosis (PSAD) is often associated with kidney transplantation, diabetes mellitus exacerbations, and autoimmune diseases [9], abnormal keratinisation being linked to immunosuppression [5]. For our patient, the diagnosis of DSAP raised awareness for early detection of pre-diabetes, the patient presented high values of fasting blood glucose (117 mg/dl), therefore she was referred to a diabetologist. Radiotherapy and phototherapy are the most common therapies associated with the onset of porokeratosis [2]; in our case, radiotherapy can be considered as a triggering factor of the disease given the patient's history (radiotherapy associated with mastectomy for the treatment of breast cancer).

The literature indicates the association between toxoplasmosis and Nekam's striated porokeratosis[9], but there are no cases involving DSAP and toxoplasma infection.

Keratosis pilaris (discrete perifollicular papules with a central plug of keratin, seen on the extensor surface of the limbs, each papule is surrounded by erythematous margins [10]), Stucco keratosis (white hyperkeratotic papules more frequently found on the limbs and predominantly affects the males [11]), disseminated eruptive porokeratosis (acute onset with numerous keratoses starting on the lower limbs, and then spreading to the upper part of the body, it does not affect only the skin damaged by

ultraviolet light, histopathologically there are signs of porokeratosis, the diagnose may be excluded based on the clinical presentation) [3] are the main differential diagnosis options for DSAP.

Porokeratosis lesions are considered extensions of field cancerization [12,13] through the evolutionary potential towards squamous cell carcinoma [1] or Bowen's disease [14]. This link is justified by the identification of the "cornoid lamella" on the histopathological examination of squamous cell carcinoma lesions in patients with porokeratosis which undergo malignant transformation [1].

Microfluorometric analysis of keratinocytes' DNA of a patient with disseminated superficial actinic porokeratosis and multiple Bowen's disease lesions showed DNA abnormalities in the epidermal cells of the porokeratosis lesions, with elevated DNA index values [14]. Porokeratosis skin lesions progressed, subsequently developing Bowen's disease [14]. These observations suggest the direct and sequential growth of neoplastic clonal cells and the malignant potential of the porokeratosis skin lesions, and their tendency to progress to Bowen's disease [14].

Malignant transformation has been documented in linear porokeratosis, DSAP, Mibelli's porokeratosis, and porokeratosis plantaris palmaris et disseminata (PPPD) [15,16,17,18]; it is more common in Mibelli's porokeratosis [16].

In DSAP, most cases were described in patients who had many lesions in the distal regions of the limbs, suggesting the negative impact of UV exposure on porokeratosis lesions, which undergo malignant transformation [18].

The treatment of porokeratosis does not follow a standardized pattern. There are multiple choices of topical, systemic, surgical treatment. Phototherapy and laser therapy can also be used in the treatment of the disease [19].

Vitamin D analogs are frequently used due to their regulatory properties on the keratinization and epidermal cell proliferation processes [20]. Topical retinoids have been successfully used in the treatment of porokeratosis, due to their positive effects on epidermal proliferation, desquamation, and inflammation [21].

Imiquimod is an immune modulator that enhances the innate immune system [22]. Topical application in DSAP leads to superficial ulcerations, that will later heal with superficial scars and residual erythema [18]. It is necessary to use it with caution to avoid unwanted adverse effects; monitoring may be required during the treatment [18].

3-5% Topical diclofenac gel can be used due to its anti-inflammatory effects, by blocking COX2, limiting cell proliferation and angiogenesis [23]. Topical diclofenac provides an improvement in itching; the most common adverse effects are local erythema and irritation, with a possible evolution to contact dermatitis [21].

The CO2 laser is used to treat porokeratosis; variable clinical responses have been seen. There are cases of DSAP with complete resolution of the lesions, but there are also cases with poor or no response to laser treatment [24]; also, cases of Mibelli's porokeratosis with unsatisfactory results to laser treatment have been reported [25].

Cryotherapy with liquid nitrogen showed favourable results in porokeratosis affecting the genital area [26]. Studies report unsatisfactory results for disseminated superficial actinic porokeratosis [27].

There are multiple reports of surgical interventions in DSAP, like complete surgical excision [28], dermabrasion [29] and radiofrequency surgery [30].

In our case, clinical resolution was observed following the use of 0.02% tretinoin, 4% glycolic acid 4% (which offers better penetration of tretinoin at the follicular level), 0.2% polyvinyl A. 0.2% (which offers a gradual release of its active substance) gel and 5% diclofenac gel.

Conclusions

We reported the case of a 70-year-old female patient, diagnosed with DSAP, who presented a rapid and sustained response with topical combined treatment (0.02% tretinoin, 4% glycolic acid, 0.2% polyvinyl A as gel and 5% diclofenac gel). The patient is being followed up to prevent the recurrence of porokeratosis lesions and their potential malignant evolution.

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Conflict of interest
NONE DECLARED

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