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Disseminated Superficial Actinic Porokeratosis in the Elderly: A Case Report

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Abstract

Currently, most authors believe that disseminated superficial actinic porokeratosis (DSAP) is an inherited or acquired dermatologic disorder of keratinization that occurs in genetically predisposed individuals after adequate exposure to ultraviolet (UV) rays, or immunosuppression. Lesions in DSAP start in sun-exposed areas most commonly in the third or fourth decade of life. The lesions are pink to brownish papules and plaques with a raised scaling ridge, histologically seen as a column of parakeratotic keratinocytes, the cornoid lamella. DSAP is not only the most common, but also the most often overlooked form of porokeratosis (P). Here we present a 77-year-old male with DSAP, who sporadically developed initial skin lesions at the age of 67, at the time when his personal and medical history were significantly long for chronic intensive sun exposure and type 1 insulin dependent diabetes mellitus. We established the diagnosis of DSAP based on personal and medical history, clinical presentation, auxiliary methods such as dermoscopy, and confirmed with pathohistological findings. We advised the patient to avoid sun exposure and to apply photo-protective sunscreens, emollients and keratolytics. After five years of monitoring his changes, we continue to control his lesions for any possible alteration. Although mutations in several genes and data on sun exposure may be responsible for the onset of the disease, most cases of DSPA occur sporadically and without involving the facial skin, as in our case. Lesions usually begin in the third or fourth decade of life. In the elderly, an additional trigger may be present, such as e.g. age-related decreased immune competence. Diabetes mellitus may also be associated with immunodeficiency in the elderly. Recently, DSPA has been a special subtype of DSPA in the elderly. Malignant alteration can occur in DSPA, most commonly in lesions that are long lasting, large, in the elderly, or in lesions in immunocompromised individuals. In conclusion, this is the case of a 77-year-old male person, who sporadically developed the so-called subtype DSPA in the elderly. In addition to UV radiation, the relevant suggestive trigger factors were the immunosuppressive effects of diabetes mellitus and chronological aging.

Key words: Porokeratosis; Predisposition to Disease; Ultraviolet Rays; Immunosuppression; Aged; Diabetes Mellitus, Type 1; Dermoscopy; Biopsy; Case Reports

Porokeratosis (P) represents a group of rare, acquired or inherited disorders of keratinization showing circumscribed scaling lesions with a raised ridge edge, which is on histology present as a column of parakeratotic keratinocytes, the so-called cornoid lamella. The underlying lesion begins as a 1-3 mm brown conical papule that spreads to 10 mm or more in diameter, with a sharp, slightly raised 1 mm thick keratotic ridge (1-3). Mutations of several genes have demonstrated to be responsible for P, but the pathogenesis of P remains unclear (1, 4-6). Disseminated superficial actinic porokeratosis (DSAP) is the most common form of P in adults. Although most cases of the disease develop sporadically (7), there is familial DSAP that has an autosomal dominant inheritance pattern with incomplete penetrance (3). Apart from several susceptible genetic loci determined for DSAP that were previously identified (5), mutations in the mevalonate kinase gene (*MVK*) on chromosome 12q24 are present in some patients with DSAP. The *MVK* gen encodes the

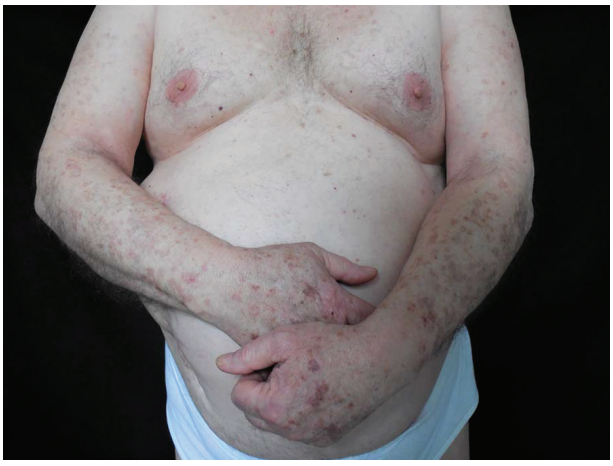

Figure 1. Lesions predominantly in sun-exposed sites of the forearms and hands

synthesis of mevalonate kinase, an enzyme that is part of the cholesterol synthesis pathway which provides protection from UV-induced cell death (6). Thus, DSAP is an inherited dermatologic disorder with lesions appearing in genetically predisposed individuals after adequate exposure to UV radiation or immunosuppression (1, 8).

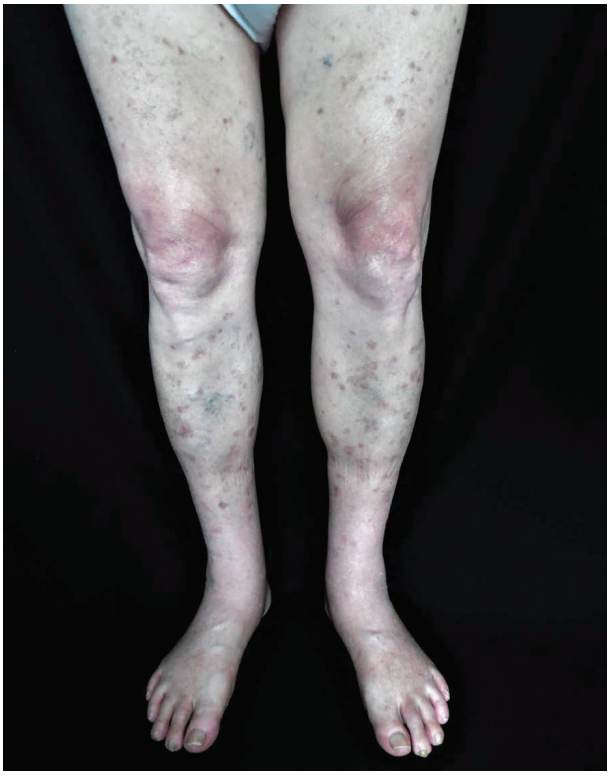

Figure 2. Lesions on the lower limbs

The group of several different porokeratoses includes 6 main types: 1) porokeratosis of Mibelli (PM); 2) linear porokeratosis (LP); 3) disseminated superficial porokeratosis (DSP); 4) disseminated superficial actinic porokeratosis (DSAP); 5) disseminated palmoplantar porokeratosis (DPPP); 6) punctate palmoplantar porokeratosis (PPPP). Besides these main clinical forms, a number of rare morphological forms, such as facial, giant, punched-out, hypertrophic verrucous, reticulate, eruptive pruritic papular, and ptychotropic (manifesting with symmetric verrucous, hyperkeratotic red-brownish plaques of the buttocks and genitalia), has been reported in the literature (9). Different forms of P dermatologists may differentiate solely based on clinical criteria.

Coexistence of several different forms of P has been reported, making final diagnosis somewhat arbitrary (2, 9).

In DSAP, there are numerous skin-colored or brownish-red papules and plaques of variable size, forming a thin peripheral keratotic rim and atrophic hypopigmented center by expanding radially in the sun-exposed sites. It occurs bilaterally and symmetrically. Lesions in DSAP start in sun-exposed areas most commonly in the third or fourth decade of life. The legs, forearms, shoulders, and back are most often affected. The face can rarely be involved. The palms and soles are without lesions. DSAP usually worsens when the affected skin is sun-exposed, and pruritus can intensify (5, 10).

All forms of P can be overlooked, but DSAP, which is also the most common form of P, is most often overlooked (3, 11).

In this case report we present a 77-year-old male with DSAP, who developed initial skin changes at the age of 67, at the time when his medical history was significantly long for type 1 insulin dependent diabetes mellitus

Case Report

A 77-year-old non-atopic Caucasian male was admitted to our Clinic, with a 9-year long history of disseminated skin papules. Widespread lesions first appeared on the lower legs, were initially asymptomatic and then quickly became pruritic. The deterioration occurred a year before admission to the hospital.

The patient denied any personal or family history of previous skin disorders, as well as alcohol intake or cigarette smoking. A review

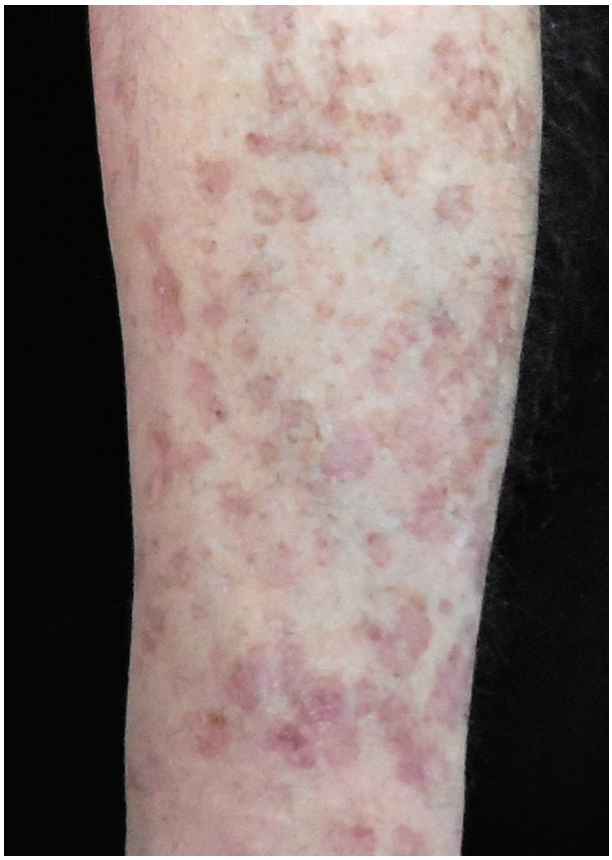

Figure 3. Well-defined erythematous and red-brownish to dark pigmented annular papules and dry plaques up to 1 cm in diameter, with atrophic center

of his medical history was significant for type 1 insulin dependent diabetes mellitus, arterial hypertension, ventricular extra-systolic arrhythmia, and prostate hyperplasia. We continued the treatment of the aforementioned comorbidities at our clinic. The patient also revealed a history of recent and past sun exposure during the performance of his daily activities in the external environment, such as animal husbandry and agriculture for an average of 24 weeks a year for the last 50 years.

At admission, the patient with Fitzpatrick skin phototype II was in good general condition. In addition to the solar lentigines, multiple widespread circular well-defined erythematous and red-brownish to dark pigmented annular papules and dry plaques up to 1 cm and more in diameter were present, with an atrophic center surrounded by a raised, fine keratotic wall and a furrow. The lesions were mostly on the limbs and affected sun-exposed skin of the forearms, upper chest, arms, thighs, buttocks, and legs, sparing the skin of his face, scalp, ears, palms, and soles **(Figures 1-3)**. The diagnosis of DSAP was preliminary considered on clinical ground.

All relevant laboratory findings were within normal limits except for a slight elevation of the erythrocyte sedimentation rate, high blood sugar level, and slightly elevated total prostate specific serum antigen (tPSA).

Additional investigations revealed the following abnormalities: abdominal ultrasound scanning showing calculi in the gallbladder and chest X-rays revealing calcification of the aorta. The cardiologist confirmed the diagnosis of high blood pressure and ventricular extra systolic arrhythmia, and administrated the following therapy: acetyl salicylic acid, propafenone, fosinopril, isosorbide mononitrate, furosemide, and magnesium.

On dermoscopy we saw annular lesions with brown peripheral rim and open pores with plugs, multiple dotted and linear irregular blood vessels, and brown globules in the center. Some lesions had white scar-like center, characteristic annular whitish structures in the form of “white line” or “white track“ along the edge of each lesion. In some parts of the lesion, there was a “double white track” (arrow), sharply demarcated central scar-like area. Tracks were present at the periphery of the lesion along with brown pigmentation (globules and red spots) inside. Structures of single or double “white tracks” and red spots

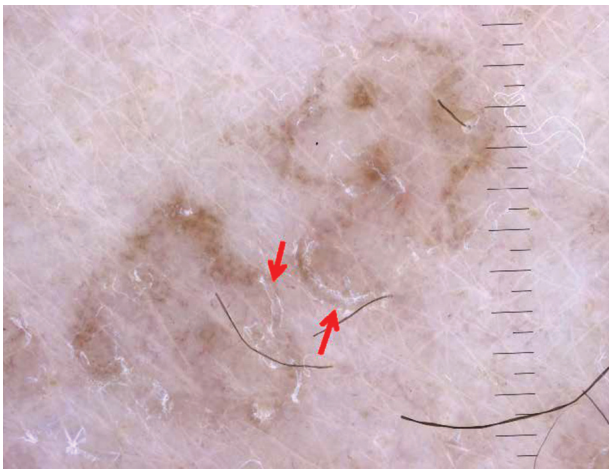

Figure 4. Characteristic annular “white line” or “white track”, along the edge of each porokeratosis lesion and “double white track” (arrow) in some parts of the lesion

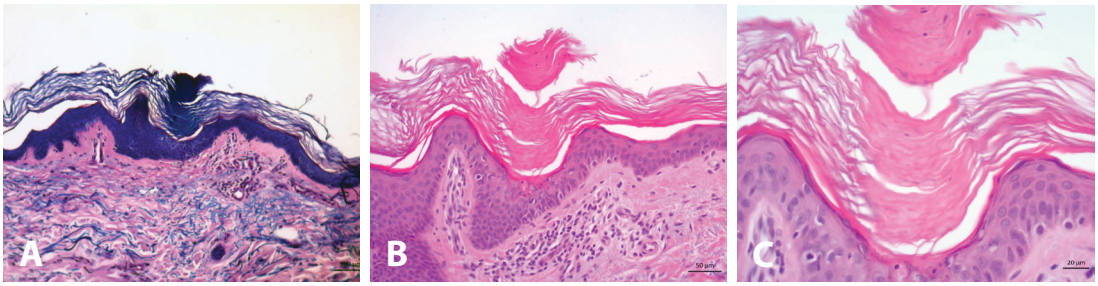

Figure 5. a. The epidermis with slightly flattened rete pegs and orthohyperkeratosis. In the shallowly depressed epidermal part, the thick parakeratotic, vertically oriented column, cornoid lamella. Actinic degenerative changes are present in the dermis (Giemsa x100); **b.** The vertically oriented cornoid lamella without granular layer, with some dyskeratotic and vacuolated keratinocytes. In the dermis variable inflammatory infiltrate is present (HE x200); **c.** At the base of the cornoid lamella, granular layer is absent and some dyskeratotic cells are visible (HE x400)

or globules, corresponded histologically to the cornoid lamella and enlarged blood vessels, respectively **(Figure 4).**

Hystology analysis showed epidermis with slightly flattened rete ridges, orthohyperkeratosis and, a column of parakeratotic stratum corneum cells, the so-called cornoid lamella. The lamella was running vertically through the surrounding cells at the shallowly depressed epidermis, with an almost absent underlying granular zone and some dyskeratotic and vacuolated cells in the spinous and basal layers, respectively. Papillary dermis below lamellae was with extensive actinic degenerative features, dilated capillary blood vessels surrounded with a variably thick dermal lymphocytic infiltrate. Hair follicles and sebaceous glands were missing, while sweat glands extended with regular morphology **(Figures 5a, 5b and 5c).** Clinical, dermoscopic appearance, histological, and laboratory findings were consistent with the diagnosis of DSAP.

Initially, the treatment was topical application of corticosteroids. Although we advised the patient to continue therapy with intermittent systemic retinoid, primarly acitretin and then local calcipotriol or tacrolimus, he was unable to administer this therapy for financial reasons. He no longer had any complaints or subjective problems, and was not worried about his changes even in the cosmetic sense. That is why we recommended him to use emollients and urea-containing keratolytics, avoid sun exposure, and to use photo-protective sunscreens. After 5 years of follow-up, we still regularly control his lesions for any possible alteration.

Discussion

The diagnosis of DSAP encompasses personal and medical history, clinical presentation, auxiliary methods such as dermoscopy, and pathohistological confirmation. Our patient has revealed a history of recent and past sun exposure in his normal daily outdoor activities such as farming. Clinically distinguishing certain forms of disseminated porokeratosis may not be justified (11). Thus, DSP can be clinically similar to DSAP, except that UV rays do not play a role in its formation: the distribution of lesion may be similar to DSAP, but without a history of sun exposure (11). For our patient, chronic intensive sun exposure was a significant risk factor for obtaining DSAP (5). Even more, DSP starts much earlier than DSPA, the former usually between 5-10 years of age and the latter in the third or fourth decade. Our patient developed initial skin changes at the age of 67 years on the photo-exposed skin; however, the skin of his face, palms, and soles was spared. Although changes in DSPA occur on the sun-exposed skin, only 15% of people with DSPA have facial changes (2). The sporadic onset of the disease in our patient may be due to somatic mutations (5).

DSAP occurred at the time when the patient's medical history was significantly long for type 1 insulin dependent diabetes mellitus. P have been associated with hematological malignancies, precancerous diseases, autoimmune diseases, e.g. diabetes mellitus, genetic, and other chronic diseases (4). It is assumed that for the development of DSPA in the elderly, the reported predisposing risk factors are UV radiation, genetic predisposition, immuno-

suppression, infective agents, drugs (e.g. thiazide diuretics), and mechanical trauma (5). It seems that in the case of P of the elderly, in addition to the previously mentioned, the group of other factors can also include age-related decreased immunocompetence (12). Diabetes mellitus may also be associated with deterioration of immune competence of the elderly (13). Thus, apart from UV radiation, immunosuppressive effects of diabetes mellitus and chronological ageing were also present in our patient. Recently, DSPA has been a special subtype of DSPA in the elderly (12, 13). Although the etiology and pathogenesis of P have not been fully elucidated (4-6), it has been proposed that besides genetic predisposition, the proliferation of abnormal clones may be triggered by extrinsic factors such as UV light (5). The centrifugal progress of individual lesions reflects the proliferation and migration of a special clone of abnormal cells (3).

A biopsy of the skin lesion in our patient included the edge of the lesion (1). Histopathological analysis revealed features typical for DSAP, including cornoid lamella, a narrow column of altered or parakeratotic keratin seated in a slight depression in the epidermis. The cornoid lamella is a distinctive feature on the periphery of porokeratotic lesions, but cornoid lamellae may be present in other conditions, e.g. viral warts, some ichthyoses (e.g. hystrix), and naevoid hyperkeratoses. Parakeratotic hyperkeratosis, which is a histological reflection of the cornoid lamella, occurs e.g. in some punctate keratodermas, but the lack of lesions at the margin distinguishes them from true porokeratosis (3). In various forms of P, the epidermal changes (usually of atrophy) are often not striking and the diagnostic cornoid lamella may not be present on the first sections, cut from the block. Therefore, as mentioned previously, all forms of P may be misdiagnosed, but DSAP is the most commonly overlooked one (11).

Dermoscopy can be a useful method for evaluating DSAP, since Nicola et al. proposed dermoscopic features for P lesions: white border circumscribing the lesion; homogenous central white scar-like area; brownish globules or dots; vascular structures: pinpoint vessels or irregular linear vessels crossing the lesion (14). All these criteria were present in dermoscopic finding obtained from our patient.

DSPA usually shows poor therapeutic responses to the applied therapy or, as with our patient, therapy does not seem to be necessary (1, 2, 5, 3). Topical diclofenac shows variable treatment results, but a good safety profile, mostly in the management of P affecting genitalia (1, 5). Ingenol mebutate helps treat hyperkeratosis but not atrophy or hypopigmentation (1). Topical vitamin D analog calcipotriol leads to a favorable response after 6 to 8 weeks (1). 5-fluorouracil produces a robust inflammatory reaction; the clinical response is usually temporal, but a novel approach utilizing 5-fluorouracil chemo-wraps is going on (4). Photodynamic therapy in combination with laser, cryotherapy or other options such as excision, curettage and dermabrasion can give some good results, but not in extensive diseases (1, 15). Lasers, e.g. carbon dioxide laser leaves hyperpigmentation, Q-switched ruby laser does not destroy the cornoid lamella, neodymium:yttrium-aluminum-garnet laser reduces hyperpigmentation and obliteration of the cornoid lamella, fractional photothermolysis does not create too much damage and allows faster healing (16, 17). Grenz ray therapy may help because it blocks cell proliferation by inhibiting DNA synthesis (18). Topical retinoids are preferred over systemic ones due to rapid relapses because of discontinuation of systemic therapy. In addition, oral alitretin caused good therapeutic effects in DSPA, but it is necessary to confirm the duration of the effect even after stopping the therapy (1, 19). Because DSPA is not an inflammatory disease, immunosuppressive agents, such as topical corticosteroids, are usually not effective but may reduce itching (1, 20). Topical cholesterol/lovastatin may prevent the accumulation of toxic products of disturbed mevalonate metabolism (21).

The course of the disease may take a progressive course with potential malignant alteration. Malignant transformation can occur, although its exact cause remains unknown, it may relate to chromosomal instability, reduced immune surveillance, and over expression of mutant p53 in the skin lesions (1, 4). Malignant alteration can occur in DSPA, most commonly in lesions that are long lasting, large, in the elderly, or in lesions in immunocompromised individuals (1, 7). Lesions in DSPA have a 7.5% to 10% risk of malignant

transformation into squamous cell carcinoma or basal cell carcinoma (1, 22). Based on the literature available to us, there are only three published cases of melanoma associated with DSPA (4). Sun protection, use of moisturizers and regular check-ups to rule out malignancy are mandatory as with our patient (5).

Conclusion

This is a case report of a 77-year-old male person, who sporadically developed the so-called subtype DSPA in the elderly. In addition to UV radiation, the relevant suggestive trigger factors were the immunosuppressive effects of diabetes mellitus and chronological ageing.

Abbreviations

P – Porokeratosis
UV – ultraviolet
DSAP – Disseminated superficial actinic porokeratosis
MVK – mevalonate kinase gene
PM – Porokeratosis of Mibelli
LP – Linear porokeratosis
DSP – Disseminated superficial porokeratosis
DPPP – Disseminated palmoplantar porokeratosis
PPPP – Punctate palmoplantar porokeratosis

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Diseminovana superficijalna aktinična porokeratoza u populaciji starih – prikaz slučaja

Sažetak

Diseminovana superficijalna aktinična porokeratoza (DSAP) danas se definiše kao redak genetski determinisani poremećaj keratinizacije pokrenut UV zracima ili imunosupresijom. Započinje u trećoj ili četvrtoj deceniji života pojavom kružnih lezija u vidu ružičastih do smeđih papula i plakova, sa centralnom atrofijom i perifernim keratotičnim rubom sa skvamama koji histološki odgovara stubu parakeratotičnih ćelija tzv. kornoidnoj lameli. Hronična ekspozicija UV zracima u anamnezi i odsustvo lezija na dlanovima i tabanima, odvajaju DSAP od ostalih diseminovanih formi porokeratoze (P). DSAP ne predstavlja samo najčešći oblik P nego i formu bolesti čija se dijagnoza najčešće previdi. Prikazujemo sporadičan slučaj DSPA kod 77 godina starog muškarca, zemljoradnika, kod koga su se prve promene na koži pojavile u 67. godini života. Dijagnoza bolesti je postavljena na osnovu anamneze o hroničnoj ekspoziciji sunčevim zracima, prisustvu diseminovanih promena karakterističnog izgleda sa predilekcijom zahvatanja fotoeksponiranih delova i dermoskopskog pregleda, a potvrđena prisustvom kornoidne lamele u patohistološkoj analizi bioptirane lezije na koži. Promene nisu zahvatale lice, dlanove i tabane, a u anamnezi je dominirao podatak o višedecenijskom prisustvu insulin-zavisnog dijabetesa melitus. Pacijentu je savetovano da izbegava sunce, koristi fotoprotektivne kreme, emolijense i keratolitike. Na regularnim kontrolnim pregledima nisu uočeni znaci alteracije. Iako se smatra da su mutacije opisane na nekoliko gena i genskih lokusa, uz anamnezu o relevantnoj ekspoziciji sunčevim zracima (odgovorni za nastanak oboljenja), najveći broj slučajeva DSAP se javlja sporadično i bez zahvatanja kože lica kao kod našeg pacijenta. Prve lezije se javljaju u trećoj ili četvrtoj deceniji života, a kao najznačajniji deklanširajući faktori, koji mogu izazvati imunosupresiju odgovornu za pojavu oboljenja kod starih osoba, ističu se hronološko starenje i prisustvo dijabetesa mulitus. Nova klasifikacija P podrazumeva postojanje posebnog podtipa DSAP u populaciji starih osoba. Maligna transformacija se može javiti u lezijama DSPA i to najčešće kod starih osoba, u velikim lezijama, onim sa dugim trajanjem ili kod imunosuprimiranih osoba. U zaključku treba istaći da je u radu prikazan sporadičan slučaj muške osobe sa podtipom P nazvanim DSAP u populaciji starih, kod koje su, pored hronične ekspozicije sunčevim zracima, mogući relevantni deklanširajući faktori odgovorni za nastanak oboljenja bili imunosuprimirajući efekti hronološkog starenja i dugogodišnje prisustvo dijabetesa melitus.

Ključne reči: Porokeratoza; Predispozicija za bolest; Ultravioletni zraci; Imunosupresija; Stari; Dijabetes melitus tip 1; Dermoskopija; Biopsija; Prikazi slučajeva

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