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Linear porokeratosis: a case report

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VERSITA

Abstract

Porokeratosis is a rare genodermatosis based on chronic keratinization disorder histologically characterized by the presence of a cornoid lamella and various clinical manifestations. Five most commonly described types of poroketarosis are porokeratosis of Mibelli or "classic" porokeratosis, disseminated superficial actinic porokeratosis, disseminated palmoplantar porokeratosis, linear porokeratosis, and punctate porokeratosis. In all of the five clinical types of porokeratosis described today, cases of planocellular skin carcinoma are described, except in punctate type cases. Use of topical CO2 laser ablation, cryotherapy and topical use of 5% Imiquimod cream, have shown favorable effects in local treatment of porokeratosis. The authors present a clinical case of a girl suffering from linear porokeratosis over the course of the last four years, spreading on the inside of her right arm along the lines of Blaschko. Linear porokeratosis was histologically confirmed by biopsy of skin lesions and dermoscopy. Dermoscopic findings, used as an auxiliary method, also indicated linear porokeratosis. Successful liquid nitrogen cryotherapy prompted the authors to present a case in which the applied treatment proved to be successful, but also to emphasize the need for timely treatment in order to prevent malignant alterations of these changes.

Key words

Porokeratosis; Dermoscopy; Cryotherapy; Treatment Outcome

The "classic" type of porokeratosis (PK) was first described by Mibelli in 1983 (1, 2), as a condition which usually occurs in childhood, manifesting by one or several discreet keratotic plaques with desquamation, that may be present on any part of the skin and/or mucous membranes (3). That same year, Respighi described the disseminated superficial type of the disease, while the disseminated superficial actinic PK was described by Chernosky in 1967 (4). The linear type of PK was first described in 1918. In 1971, Guss was the first to describe the disseminated palmoplantar PK (5). In 1974, Rahbari defined linear PK as a separate form of the disease (6), and in 1977, the punctate PK was added to other clinical types (7).

Porokeratosis is considered a genetic disorder characterized by autosomal dominant way of transmission, but most cases develop sporadically (8). Generally speaking, "classic porokeratosis" is more common in men, even up to 2-3 times, while the ratio in favor of males in cases of disseminated palmoplantar porokeratosis is 2:1. Disseminated superficial actinic porokeratosis is a female-predominant disease with a female to male ratio of 3:1 (8). According to data provided by The Singapore National Center, the incidence of linear PK, as a clinical type among different clinical types of the disease, is 12.9% and it is most commonly detected in the fourth decade of life (9). Linear type of PK is found/ in: monozygotic twins (10, 11) and families in which other types of PK are present (11, 12); its mode of transmission remains unknown (8, 11); the ratio of male to female porokeratosis cases is 1:1 and it is more common in Caucasians (11).

Porokeratosis commonly affects extremities in the form of small, asymptomatic, distinct keratotic and/

or lichenoid papules or plaques, ranging from brown to skin color, and from one to several centimeters in diameter, with distinct keratotic edges and hypo-or-hyperpigmented slightly depressed atrophic centers. Various skin changes can occur, but the ones typical for linear porokeratosis are localized, unilateral and follow the lines of Blaschko. Cases of malignant alterations have been reported in all 5 clinical types of PK, mostly planocellular skin carcinoma (PSC) within the porokeratosis lesions (8), except in cases of punctate type of PK (11).

In this paper, the authors present a case of a young female patient with linear porokeratosis, present in the course of the last four years, affecting the inside of the right arm following the lines of Blaschko. Successful liquid nitrogen cryotherapy performed in the patient prompted the authors to present a case in which the applied treatment proved to be successful, but also to emphasize the need for timely treatment in order to prevent malignant alterations of these changes.

Case report

We present a case of a 27-year-old pharmacy student, otherwise healthy, who visited the Outpatient Clinic of the Clinical Center of Vojvodina in Novi Sad in 2009, with skin changes in the form of linear keratotic lesions running along the inside of her right arm. These changes first appeared four years earlier on the inside of her right humerus region, gradually spreading to the lower arm, without any subjective symptoms. After clinical examination, dermoscopy was performed, followed by skin biopsy of lesions. The diagnosis of linear porokeratosis was histologically confirmed. With the patient's consent, cryotherapy was applied to all skin lesions on her right arm. Complete regression of skin lesions occurred after 8 weeks of treatment.

Personal history revealed that the patient never had any contraindications for liquid nitrogen cryotherapy.

Family history revealed that none of her relatives had similar skin lesions or suffered from any kind of skin condition. There was no history of malignant tumors among immediate family members.

Clinical examination showed that on the inside of the right arm, particularly on the 2/3 of the entire humerus and forearm, characteristic keratotic papules and/or small plaques were present, 0.5 to 2 cm in

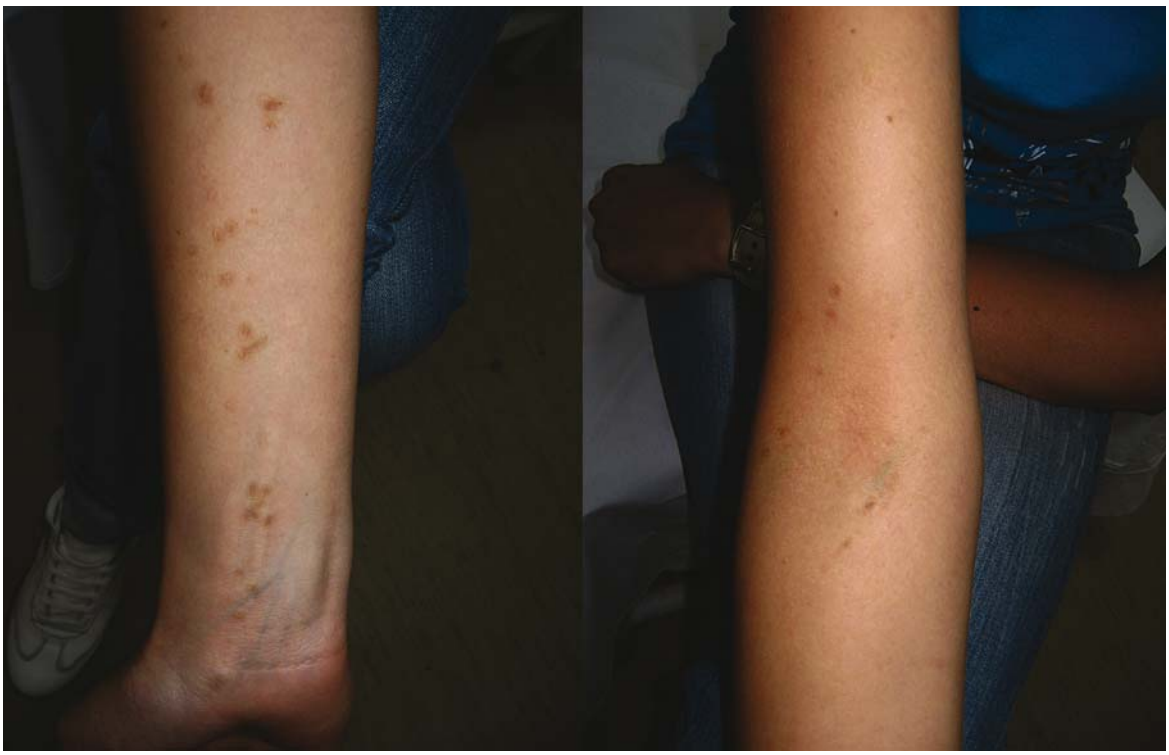

Figure 1. Linear porokeratosis; a) on the forearm b) on the upper arm and cubital fossa

diameter, oval to round shaped, with distinct edges separating them from the surrounding healthy skin, light to dark brown, with accentuated keratotic edges, hard in consistency, with slightly depressed, and a hypo- or hyperpigmented atrophic center. The lesions were located along the inside of the right arm, in a linear arrangement, running parallel within a distance of a few centimeters (Figures 1, and 2.).

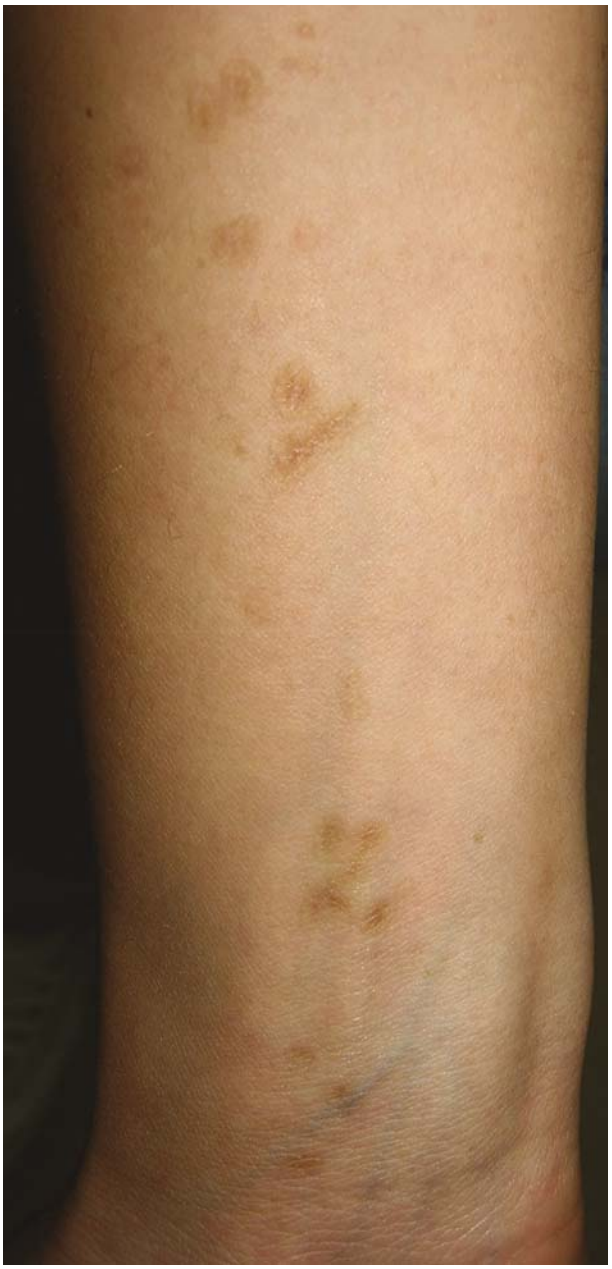

Figure 2. Linear porokeratosis: changes on the forearm (detail/close up)

General examination of all organs and systems was regular.

All the basic laboratory tests and biochemical results were within normal ranges.

Histopathological examination revealed that the skin sample, stained by HE method (hematoxylin and eosin), PAS (periodic acid–schiff stain), and Gomori's and Giemsa methods, was affected by moderate epidermal hyperkeratosis and partial parakeratosis. In this region, epidermis was moderately thickened, with an angular keratotic layer towards the center of the lesion. Dyskeratotic cells were found in the middle layer along the zone affected by porokeratosis (cornoid lamella), while the granular layer of the epidermis was missing. Perivascular mononuclear cells were present in the papillary dermis. The remaining skin showed adequate and age-appropriate morphology (Figures 3. and 4.).

Dermoscopy was performed using a manual dermatoscope Heine Delta 20 (Heine Optotechnik, Kientalsrasse 7, D-82211 Hersching, Germany) with 10 x magnification, using non-polarized light, after covering porokeratosis lesions with ultrasound gel.

Dermoscopy showed round structures in the form of a "white line" along the edge of each porokeratosis lesion, which is a characteristic dermoscopic finding for porokeratosis. They were identified at the periphery of the lesion along with brown pigmentation on the inside and a double "white line" (arrow) in some parts of the lesion. Structures found in the form of a single or a double "white line" at the edge of the PK lesion histologically matched the cornoid lamella (Figure 5.) (13).

Therapy was conducted using the open spray method with the Cry-Ac®-3 Brymill devices (Brymill Cryogenic Systems Bld 2. 105, Windermere Ave., Ellington, CT 06029 USA). The liquid nitrogen application lasted 30 seconds with a 2mm halo, in two cycles with a four-week period in between. Follow-ups were performed every four weeks combined with local application of an antibiotic cream. In addition to the usual post-therapeutic reactions, such as the appearance of small blisters and a light burning sensation during the first 48 hours following the treatment, no other objective and subjective symptoms were reported. After 8 weeks, there was a complete regression of the treated lesions (Figure 6.).

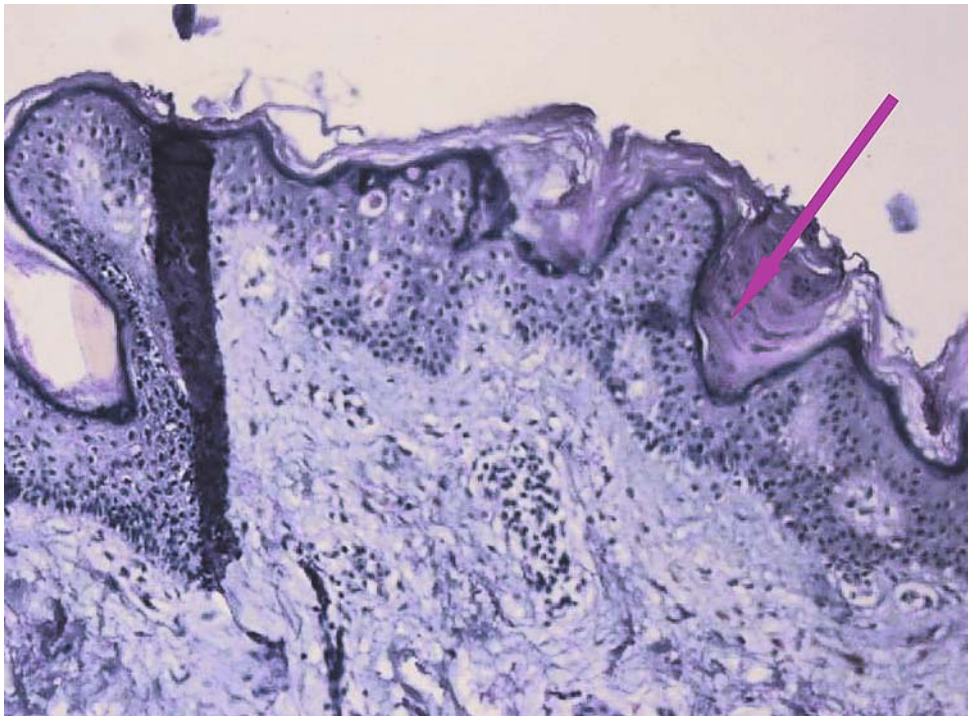

Figure 3. Pathohistological finding: cornoid lamella angulated towards the center of the lesion (hematoxylin and eosin, x200)

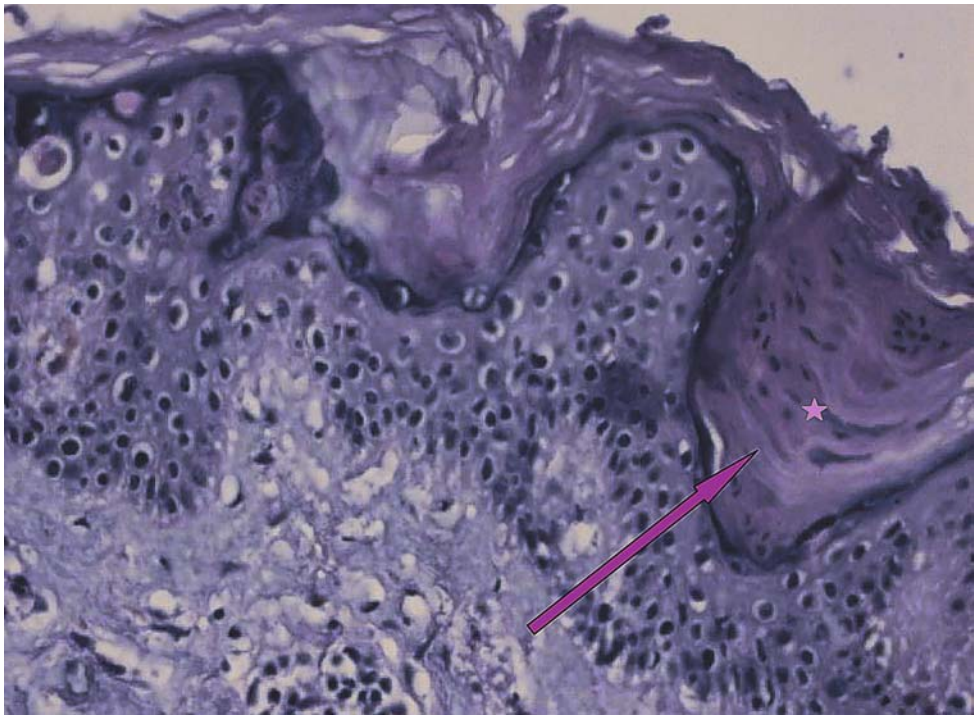

Figure 4. Pathohistological finding of linear porokeratosis: A column of parakeratosis (cornoid lamella indicated by an arrow) angulated towards the center of the lesion (indicated by a star); the underlying epidermis shows focal loss of the granular cell layer (hematoxylin and eosin, x10)

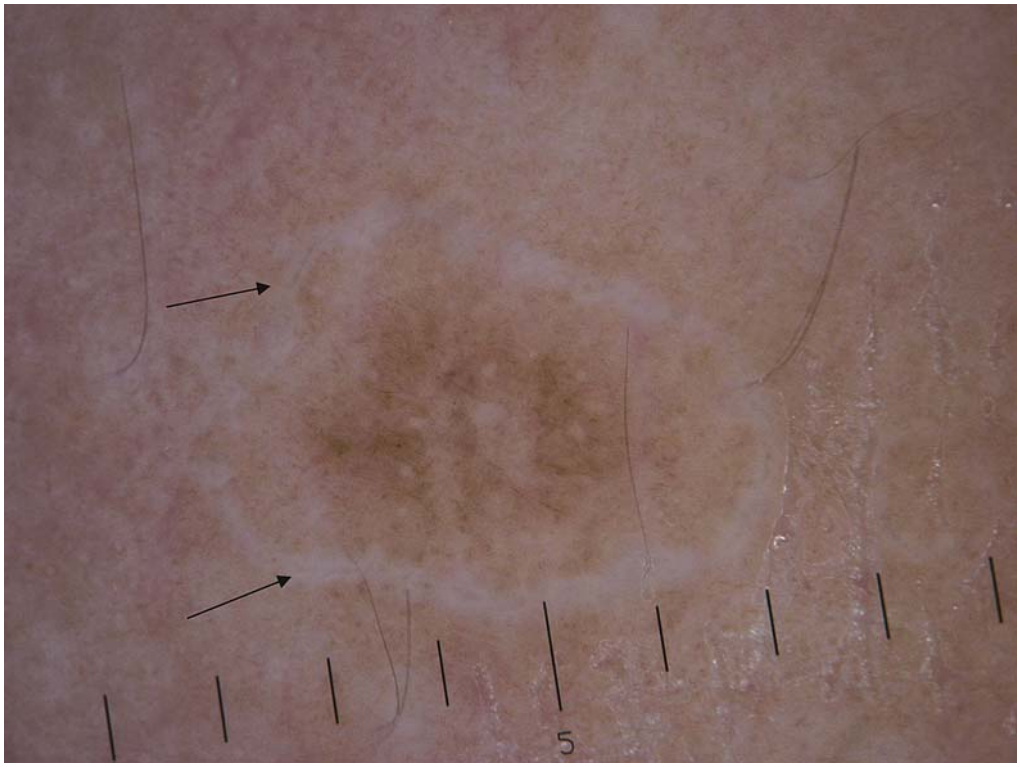

Figure 5. Dermoscopy finding of linear porokeratosis: characteristic annular whitish structure „white track" that sharply demarcates a central scar-like area with "double white track" (arrow) in some parts of the lesion (x10).

Discussion

Porokeratosis represents a whole spectrum of cutaneous/mucous clinical and morphological entities characterized by severe keratinization disorder, typical histological features and predisposition to development of cutaneous malignancies. The exact mechanism of carcinogenesis is still unknown, but it is assumed that the mediator in this process is increased expression of p53 gene, which was immuno-histochemically detected in skin changes of those suffering from porokeratosis (14). The presence of p53 mutations is probably a direct result of UV irradiation (11). Our case was one of linear porokeratosis located on the inside of the right arm in a spot directly exposed to sun during periods when short-sleeve and sleeveless garments are worn.

As a genetically heterogeneous disorder, porokeratosis is characterized by histopathological changes and cornoid lamella formation, which increases the risk of skin cancer (11). At the same time, an important mechanism in the development of many types of cancer is the loss of allelic heterozygosity. Considering the fact that it was recently assumed that linear porokeratosis occurs also due to loss of allelic heterozygosity, it may be expected that linear porokeratosis lesions are particularly prone to malignant alteration. These results have been confirmed by certain studies (14, 15). According to literature data, planocellular skin carcinoma develops in the regions affected by linear porokeratosis (16). Critical review of skin cancer development within porokeratosis lesions showed an incidence of 7% (17).

The literature describes different types of porokeratosis simultaneously affecting one person (12, 18) and immunosuppressed patients after renal or bone marrow transplantation, which refers specifically to the superficial type of the disease (19, 20).

In our case, apart from clinical and pathohistological confirmation of the diagnosis, we additionally performed a dermoscopic examination of porokeratosis linear lesions and the obtained results were consistent with the ones previously published (13).

Various therapeutic modalities that have been successfully applied in the treatment of linear porokeratosis do not favor any method for the time

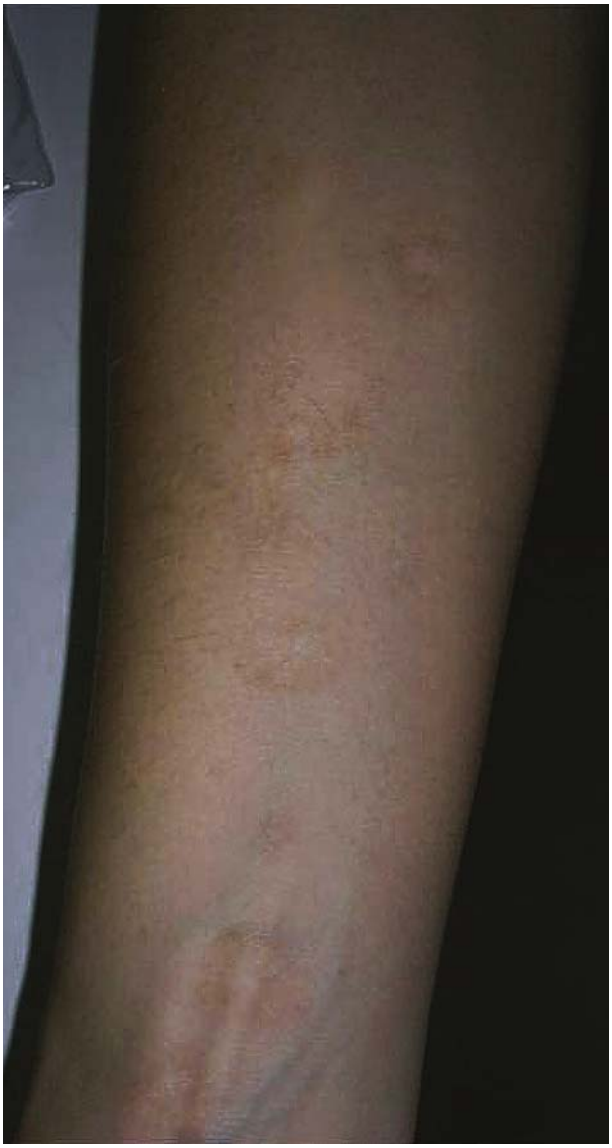

Figure 6. Linear porokeratosis after local cryotherapy

being (3, 9, 11). The efficacy of systemic therapy of PK with Etretinate or retinoids has been previously described (3, 21, 22). In the case described herein, local cryotherapy has proven effective, which was confirmed by the results of other authors (23, 24). Photodynamic therapy has also proved effective (25) as well as local use of CO_2 laser and Imiquimod cream application (26, 27).

Conclusion

In the presented case of linear porokeratosis, which is a rare genokeratosis, the authors emphasize the necessity of timely therapy in order to prevent malignant alterations within the lesions and demonstrate favorable therapeutic effects of a simple and widely available method of cryotherapy.

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Porokeratoza

Sažetak

Uvod: Porokeratoza predstavlja retku genodermatozu u čijoj osnovi se nalazi hronični poremećaj keratinizacije sa karakterističnim histološkim nalazom kornoidne lamele i različitim kliničkim ispoljavanjem. Naj-češće se opisuje 5 tipova porokeratoze: ”klasična” porokeratoza Mibelli, diseminovana superficijalna aktinička porokeratoza, diseminovana palmoplantarna porokeratoza, linearna porokeratoza i punktatna porokeratoza. U svim do danas poznatim kliničkim tipovima porokeratoze, opisani su slučajevi nastanka planocelularnog karcinoma kože, izuzev kod punktatnog oblika. U lokalnoj terapiji porokeratoze, povoljan terapijski efekat su ispoljili: CO_2-laser, krioterapija i lokalna primen 5% imikvimod krema. Prikaz slučaja: Autori prikazuju slučaj devojke sa linearnom porokeratozom prisutnom tokom poslednje četiri godine, koja je zahvatila desnu ruku sa unutrašnje strane, pružajući se duž Blaškovih linija. Nalaz linearne porokeratoze potvrđen je histološki posle uzete biopsije kožnih promena, a urađen je i pregled metodom dermoskopije. Dermoskopski nalaz, kao pomoćni dijagnostički metod, takođe je ukazivao na linearni oblik porokeratoze. Uspešna krioterapija tečnim azotom, koja je sprovedena kod bolesnice, navela je autore da prikažu ovaj slučaj u kome se primenjena metoda lečenja porokeratoze pokazala uspešnom, ali i da bi istakli potrebu blagovremene terapije porokeratoze sa ciljem prevencije maligne alteracije u ovim promenama.
Diskusija: „Klasičan oblik“ porokeratoze (PK) prvi je opisao Mibelli 1893. godine (1, 2) kao oboljenje koje se obično pojavljuje u detinjstvu u vidu jednog ili nekoliko diskretnih keratotičnih plakova sa deskvamacijom, koji se mogu pojaviti na bilo kom delu kože i/ili sluznicama (3). Respighi iste 1893. godine opisuje diseminovani superficijelni oblik PK, a 1967. godine Chernosky daje detaljan opis diseminovane superficijelne aktiničke forme bolesti (4). Linearni oblik PK prvi put je opisan 1918. godine. Guss 1971. godine prvi opisuje diseminovanu palmoplantarnu PK (5). Rahbari 1974. godine izdvaja linearnu PK kao posebnu formu bolesti (6), a 1977. godine kliničkim oblicima PK dodaje punktatni oblik (7).
PK se smatra naslednom bolesti sa autozomnodominantnim načinom prenosa, ali najveći broj slučajeva nastaje sporadično (8). Inače, „klasična“ PK je češća kod muškaraca, čak 2-3 puta, dok je kod palmoplantarne diseminovane PK odnos muškarci : žene – 2:1. Kod diseminovane aktiničke PK postoji predominacija ženskog pola nad muškim u odnosu 3:1 (8). Učestalost linearne porokeratoze kao kliničkog oblika među svim ostalim kliničkim oblicima porokeratoze prema podacima Nacionalnog centra u Singapuru iznosi 12,9 % i obično se otkriva u četvrtoj deceniji života (9). Linearni oblik PK je nađen kod monozigotnih blizanaca (10, 11) i u porodicama u kojima su istovremeno prisutni i ostali oblici PK (11, 12); ostaje nepoznat način prenošenja (8, 11); odnos polova je 1:1 i češći se javlja kod pripadnika bele rase (11).
PK najčešće zahvata ekstremitete u vidu malih, asimptomatskih, keratotičnih i/ili lihenoidnih papula ili plakova smeđe do boje kože, koji su oštro ograničeni,

promera jednog do nekoliko centimetara, sa naglašenom keratotičnom ivicom tvrde konzistencije sa hipopigmentovanim ili hiperpigmentovanim centrom koji se lako uleže; atrofičnog je izgleda. Kod linearne PK mogu nastati multiple promene, zatim lokalizovane i unilateralne, slede Blaškove linije na koži. U svim do danas danas poznatim kliničkim tipovima PK, opisani su slučajevi maligne alteracije i nastanka, najčešće planocelularnog karcinoma kože (PCK) u lezijama PK (8), izuzev kod punktatnog oblika (11).

Zaključak: U ovom radu, autori prikazuju slučaj devojke sa linearnim porokeratozom, prisutnom unazad četiri godine, koja je zahvatila desnu ruku sa unutrašnje strane, pružajući se duž Blaškovih linija, da bi istakli potrebu blagovremene terapije porokeratoze radi prevencije maligne alteracije u ovim promenama.

Ključne reči

Porokeratoza; Dermoskopija; Krioterapija; Ishod lečenja