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POROKERATOSES- A COMPREHENSIVE REVIEW

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ABSTRACT

Porokeratoses are a group of uncommon hereditary or acquired keratinization disorder of unknown aetiology. It is of autosomal dominant inheritance. The known clinical variants include classic porokeratosis of mibelli, disseminated superficial actinic porokeratosis, disseminated superficial porokeratosis, linear porokeratosis, Palmaris plantaris punctata, Palmaris plantaris disseminate. The most common one is disseminated superficial actinic porokeratosis (DSAP) which is more commonly seen in women. Porokeratosis of mibelli shows a male predominance. Different variants can coexist in the same patient. Some rare variants have also been reported in the literature which includes PK ptychotropica, follicular porokeratosis, prurigo nodularis like PK, bullous PK, pustular PK, genital PK, seborrheic keratosis like PK, ulcerative PK, eruptive pruritc PK, porokeratoma or porokeratotic acanthoma. The lesions have a predilection for extremities and trunk, but the face, genito-gluteal regions, scrotum, perianal regions are rarely involved. Clinically it is characterized by an atrophic centre surrounded by an elevated keratotic rim. Histologically it is characterized by the presence of cornoid lamellae. Porokeratotic lesions have a greater risk of malignant transformation, localized destruction causing functional impairment. There are several therapeutic options for porokeratoses which helps in the symptomatic improvement and clearance of lesions, but none of them has shown consistent and long-lasting efficacy. In this article, we will discuss about different clinical and rare variants of porokeratosis and the medical efficacy of different therapeutic approaches and also about newer therapeutic options in the treatment of porokeratoses.

KEYWORDS: Porokeratoses, cornoid lamellae, keratinization, variants, laser therapy.

1. INTRODUCTION

Porokeratoses are a group of hereditary or acquired disorders of keratinization characterized clinically by hyperkeratotic papules or plaques surrounded by a thread like elevated border that expands centrifugally. Histologically it is characterised by cornoid lamella, which is a thin column of closely stacked parakeratotic cells extends through out stratum corneum. The term porokeratosis was coined and described by Vittoria Mibelli in 1893.[1] It is usually asymptomatic, but some cases are associated with mild pruritus.[2] Porokeratoses are mostly inherited in an autosomal dominant form.[3] The lesions have a predilection for the extremities and trunk, but face, natal cleft, genito crural and perianal regions, and scrotum are also rarely involved.[4] Studies also reported multiple porokeratotic lesions with bilateral symmetrical involvement over the ala of the nose, which is a rare variant.[5] Sporadic adult onset cases are associated with immuno suppression, long-term use of corticosteroids, post-transplantation, AIDS, haematological malignancies, autoimmune diseases, immunodeficiency, exposure to ultraviolet light.[6] Frameshift mutations that are associated with porokeratosis, have been identified.[7,8] Instability of chromosome 3 has been reported and may be a factor to develop squamous cell carcinoma of the skin. Studies reported the occurrence of cranial synostosis, anal anomalies and porokeratosis in two male siblings.[9] Porokeratoses affects both sexes and it has no ethnic predilection. Porokeratoses can be classified into localized and disseminated forms. There are six clinical variants of porokeratosis. Localized forms include classic porokeratosis of Mibelli, linear porokeratosis, palmaris plantaris punctata. Disseminated forms include disseminated superficial actinic porokeratosis (DSAP), disseminated superficial porokeratosis, porokeratosis palmaris et plantaris disseminate.[3] The most common clinical variant is disseminated superficial actinic porokeratosis which is more commonly seen in women. Porokeratosis of Mibelli is more frequent in males starting in childhood or adolescence. These variants can coexist in the same patient.[1] Other atypical types are facial and giant porokeratosis, porokeratosis ptychotropica (hypertrophic or verrucous) and porokeratoma. Rare forms of porokeratosis include porokeratotic eccrine ostial and dermal duct nevus and porokeratotic eccrine and hair follicle nevus, porokeratotic adnexal ostial nevus, punched-out and

reticulate porokeratosis. Earlier studies had reported many cases of follicular parakeratosis which have distinctive clinical and histopathological presentation. But there is no proof regarding follicular porokeratosis as an independent clinical variant.[10]

2. Epidemiology

Porokeratoses is a rare disorder. But its precise incidence is not known. It has no obvious ethnic predilection, but actinic porokeratoses is found to be seen more common in those with high sun exposure and fair-skinned individuals. There are only limited reports of the occurrence of Porokeratosis of Mibelli and DSAP in dark-skinned individuals.[12] They affect both sexes with the slight predilection of porokeratoses of Mibelli in men and DSAP in women. The age of onset depends on the clinical form of porokeratoses. Porokeratoses of Mibelli usually starts in childhood.[1]

3. Pathophysiology

Porokeratoses is mostly inherited in an autosomal dominant form.[3] Sporadic cases are found to be associated with immunosuppression and exposure to ultraviolet light.[5] DSAP has been mapped in Chinese pedigrees to 12q, 15q, 18p and 16q.[8] Loss of heterozygosity at 12q and sequence variations in genes at this locus has also been reported.[13] Heterozygous mutations in the MVK gene has also been reported to cause Porokeratosis of mibelli and DSAP. MVK seems to regulate keratinocyte differentiation.[14] Cytogenetic abnormalities in fibroblasts in chromosome 3, over expression of tumour suppressor protein p53 in the cornoid lamella are also found to be associated with porokeratoses.[15] But in another study, they found no evidence of p53 mutations in DSAP.The centrifugal progress of lesions is due to migration of a clone of abnormal cells. There is keratinocyte dysplasia, aneuploidy, and chromosomal abnormalities in lesional keratinocytes which have been reported in the literature.

Porokeratoses has also been found to be associated with immunosuppression. HPV infection with types 66 and 14 have been reported in patients with porokeratosis of Mibelli.[16] Some cases of DSP has been found to be associated with exposure to drugs and chemicals like diuretics, treatment with steroids, antibiotics, TNF a-inhibitors, hydroxyurea, and benzene exposure.[1] Porokeratoses has been found to occur on a burn scar and on localised access region for hemodialysis which explains a role of koebner phenomenon in the genesis of lesions.[11,17]

4. Associated Diseases

Porokeratosis has been seen in immunocompromised patients such as, those with hematological malignancies, HIV patients, Diabetes mellitus, liver cirrhosis, Crohn's disease, acute pancreatitis, solid malignancies, administration of immunomodulating agents to treat auto immune diseases, those who have undergone chemotherapy, radiotherapy and corticosteroid therapy, post transplants. Many cases are found to be developed following kidney transplantation.[18,21] Only a few cases have been reported following bone marrow transplantation in Myelodysplastic syndrome.[22] DSAP lesions have been reported in a patient with immunosuppression due to cystic fibrosis.[23] DSP lesions were also found to be associated with dermal amyloidosis.[24] Porokeratosis developed in immunocompromised patients is typically seen as a disseminated superficial form which occurs in multiple sites like arm, leg, and trunk. An atypical mixed type of porokeratosis of Mibelli and DSP has also occurred in immunocompromised patients. In immunocompromised patients who developed porokeratosis, the possibility of malignant transformation should be considered. Linear porokeratosis has been found to be superimposed with disseminated superficial actinic porokeratosis, which is an autosomal dominant disorder and linear porokeratosis represents the segmental form of the disease. [25]

5. Clinical Features

Porokeratotic lesions are characterized clinically by annular or linear well limited erythematous to brownish papules or plaques. The center of the plaque is slightly atrophic and depressed, and there will be a thread like the elevated border that expands centrifugally. There may be itching associated with the lesion. Most common sites are the extremities and trunk. Pathologically, porokeratosis is characterized by the presence of a thin column of hyperproliferative parakeratotic keratinocytes called the cornoid lamella.[2]

Figure 1

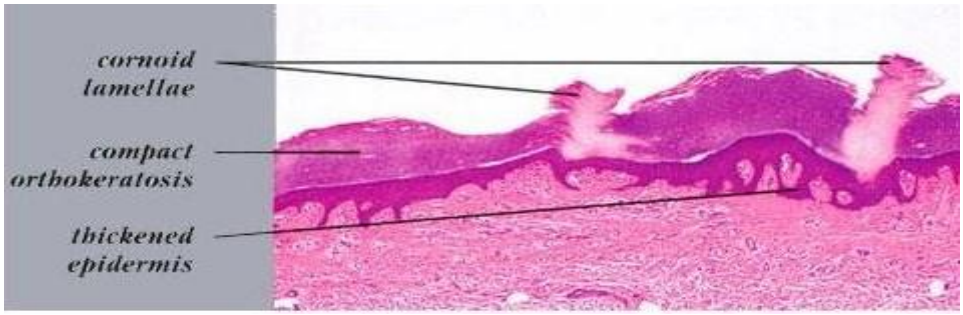

Fig. 1: Histopathology showing a thin column of hyperproliferative parakeratotic keratinocytes called cornoid lamellae.

6. Clinical Variants

6.1 Porokeratosis of Mibelli

Porokeratosis of Mibelli or classic porokeratosis is a chronic progressive dermatoses with a male predilection. The condition may be familial, inherited as an autosomal dominant trait with childhood-onset or sporadic which is of later onset.[1] It is more frequent in Caucasians. These develop as annular dry plaques surrounded by a raised fine keratotic elevated border with a central groove. The center of the lesion is usually atrophic but may be hyperkeratotic. It can occur anywhere in the body, but most commonly seen in the limbs with unilateral distribution. The rare occurrence of facial, mucosal lesions and genito-gluteal lesions have also been reported.[6,26] The lesions are usually asymptomatic with an indolent evolution. But cases with aggressively evolving lesions have also been reported in the literature.[3] The hyperkeratotic variant of Porokeratosis Mibelli as a distinct entity has been reported.[27] Another morphological variant, Porokeratosis Mibelli Gigantea has also been reported.[28] Squamous cell carcinoma, Basal cell carcinoma, Bowen's disease can occur in the lesions. SCC is the most commonly associated tumor.[29,30]

Figure 2.

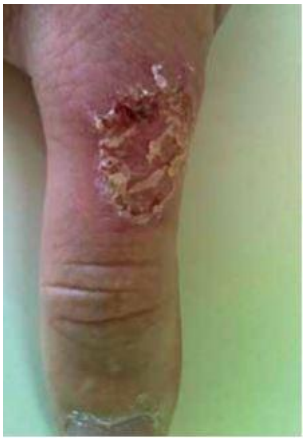

Fig. 2: Showing porokeratosis of mibelli over the thumb.

6.2 Linear Porokeratosis

Linear porokeratosis is a rare variant. It can be present at birth or can develop in adulthood. Linear porokeratosis following the lines of Blaschko usually appear in childhood. Lesions probably result from an abnormal clone of epidermal precursors. Lesions are commonly seen in proximal areas than distal areas.[30,31] Atypical presentations in which lesions were predisposed to distal areas have also been reported. Segmental, zosteriform, and generalized forms have also been found in some patients.[1,25] Malignant transformation and metastasis have been reported in this variant. Linear porokeratosis with squamous cell carcinoma has been reported. Cancer proneness of linear porokeratosis has been explained by the allelic loss. A patient with a linear form of porokeratosis since birth was found to develop disseminated superficial actinic porokeratosis at a later age.[31,32]

Figure 3.

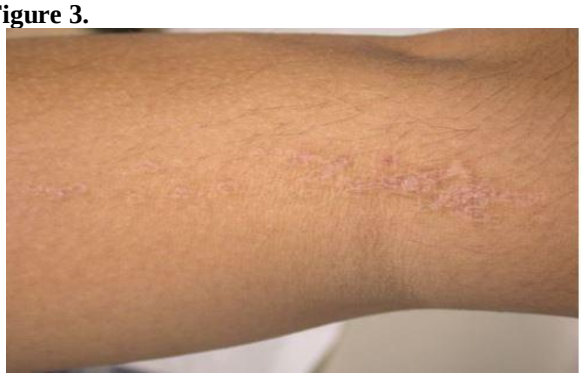

Fig. 3: Showing linear porokeratotic lesions over the thighs.

6. 3 Palmo Plantar Porokeratosis Punctata

It is characterized by multiple punctate lesions that are commonly seen over the palms and soles. It may be associated with porokeratosis of mibelli and linear porokeratosis.[1]

Figure 4

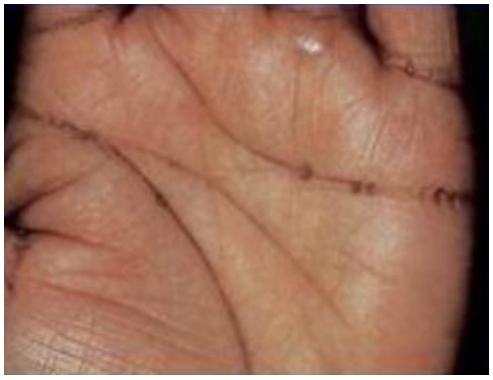

Fig. 4: Showing palmo plantar porokeratosis punctata.

6.4 Disseminated Superficial Actinic Porokeratosis (Dsap)

DSAP was first described as a clinical entity by Chernosky in 1966. It is the most common form seen in women. It can occur in any age group, but commonly seen in the third or fourth decade of life.[33] It is characterized by multiple annular lesions of almost 2 -5 mm in diameter distributed in a bilateral and symmetrical fashion over the sun-exposed areas, particularly over the extremities. It is common in fair-skinned individuals. DSAP can also occur in type VI skin which is a rare presentation.[34] It is characterized by annular keratotic lesions with the atrophic center and raised margin. The lesions are most commonly seen in the forearm, legs, back, and shoulder. DSAP has not been reported in sun-protected areas like perineum and axilla. It is rarely seen in the face. But certain studies suggest that initial origin of DSAP in Chinese population is face which differs from Caucasian.[30] Pathogenesis of DSAP is not clearly understood. Lesions tend to worsen following exposure

to sunlight, radiation therapy, photochemotherapy.[35,36] Squamous cell carcinoma developed over DSAP lesions has also been reported. But lesions are not induced by artificial light exposure. All reported squamous cell carcinoma arising from DSAP was found to be located in the distal extremities which indicates a significant role of UV light in the pathogenesis. The prognosis of squamous cell carcinoma over the DSAP lesions has not been studied yet. Also, there are no studies reporting the recurrence after the excision of the cancerous lesions.[37] A histo-pathological variant of DSAP, punched out porokeratosis has been reported in a previous study, in which there were areas of full-thickness coagulative epidermal necrosis were seen.

Figure 5

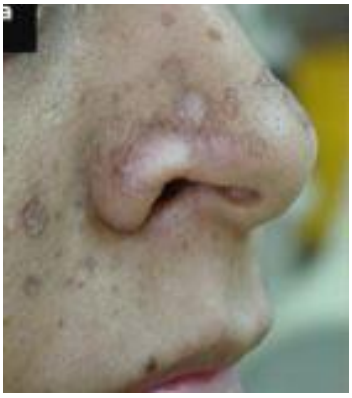

Fig. 5: Showing DSAP lesions over the face.

6.5 Disseminated Superficial Porokeratosis (Dsp)

DSP is a rare variant. It commonly presents in the age of 5 to 10 years, but also develop in adult life particularly in immunodeficient patients. However, DSP lesions are also found to occur in elderly patients with no immuno-deficencies.[18] Palmoplantar lesions may be associated. The distribution of lesions is similar to DSAP. DSP differs from DSAP by its involvement of both sun protected and sun exposed areas.

Figure 6

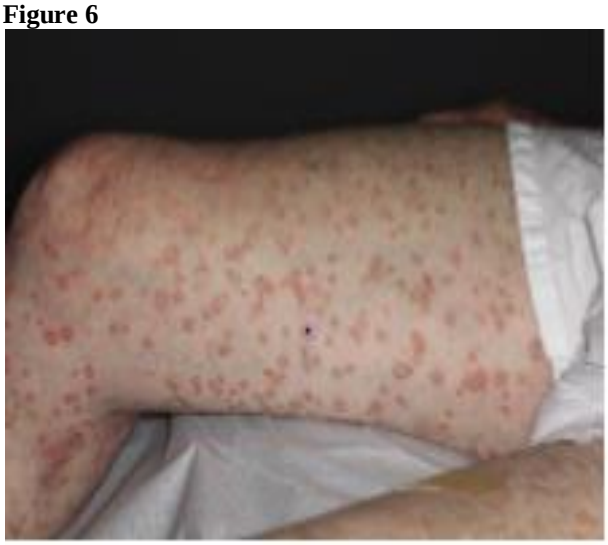

Fig. 6: Image showing DSP Lesions over the thighs and legs.

6.6 Palmo Plantar Porokeratosis Disseminate

It commonly occurs in the adolescent or in adulthood. It appears to be more frequent in men. Majority of the cases are familial, but sporadic forms also exist. It is characterized by bilateral, symmetric, red-brown keratotic papules initially seen on palms and soles and later spreads.[1]

Figure 7

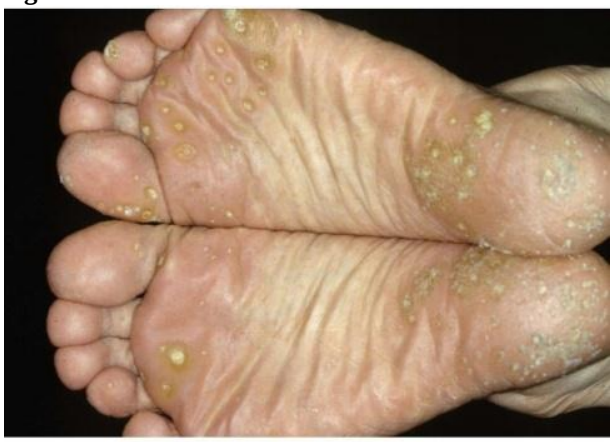

Fig. 7: Image showing keratotic papules over the soles.

7. Rare Variants

Rare variants of PK include PK ptychotropica, follicular porokeratosis, prurigo nodularis like PK, bullous PK, pustular PK, genital PK, seborrheic keratosis like PK, ulcerative PK, eruptive pruritic PK, porokeratoma or porokeratotic acanthoma.[38,47]

7.1 Porokeratosis Ptychotropica

Porokeratosis ptychotropica is a rare variant described in 1995 by Lucker et al. It is usually confined to body folds. It appears to be more frequent in men. It most commonly presents as symmetrical brownish to reddish macules or plaques with a hyperkeratotic ridge like border in the gluteal cleft, perianal region and as reported in one patient on the scrotum. The lesion is highly pruritic. It can also be designated as verrucous or hypertrophic porokeratosis.[38] Linear porokeratoses or DSAP may also coexist in some patients. The characteristic histopathological feature is the presence of multiple cornoid lamellae which serves as a gold standard for the diagnosis of porokeratosis ptychotrophica. No evidence of malignancies have been reported, but neoplastic transformation cannot be ruled out.[39]

7.2 Follicular Porokeratosis

Follicular porokeratosis is a rare pathological variant of porokeratosis. It is characterized by the presence of cornoid lamellae located exclusively in the follicle. Follicular porokeratosis have distinctive clinical and histopathological presentation. Porokeratosis with follicular involvement presents with asymptomatic, erythematous, brownish or skin-color, less than 1 cm in the areas excluding palm and plantar, which is commonly seen in middle-age patients.[40]

7.3 Pustular Porokeratosis

It is an unusual variant of DSAP characterized clinically by pustules along the elevated rim. On histopathological examination, neutrophilic pustules can be seen within the cornoid lamellae.[41]

7.4 Ulcerative Porokeratosis

It is a rare variant of porokeratosis characterized by eruptive and ulcerative changes over pre-existing skin lesions. Histological examination reveals a band like infiltration beneath the epidermis, liquefactive degeneration of basal cell layer and coagulative necrosis of keratinocytes.[42]

7.5 Porokeratoma

Porokeratoma is usually manifested as a single verrucous plaque or nodule and histologically by multiple cornoid lamellae.[43]

7.6 Porokeratotic Adnexal Ostial Nevus (Paon)

PAON is a rare congenital disorder of keratinization involving eccrine glands and hair follicle. Clinical features and a new name proposal which unified porokeratotic eccrine ostial and dermal duct nevus and porokeratotic eccrine and hair follicle nevus has been reported in the literature.[44]

7.7 Pruritic Papular Porokeratosis

It is a rare variant of porokeratosis which presents with intensely pruritic papules and plaques. It can occur in cases with or without pre-existing DSP.[45,46]

7.8 Pigmented Porokeratosis

A case of pigmented porokeratosis, a distinct variant of porokeratosis has been reported in the literature.[47]

7.9 Punctate Follicular Porokeratosis

It is a unique form of porokeratosis in which cornoid lamellae originate exclusively from hair follicles.[48]

8. Complications

The main complication that develops on a porokeratotic lesion is the development of malignancy. Large, long-standing, linear lesions have a greater risk for malignant transformation.[49] Porokeratosis involving the digits circumferentially can cause pseudo ainhum and amputation.[50]

9. Diagnosis

Diagnosis is mainly based on the characteristic histopathological feature which is seen on the edge of the lesion when cut at right angles. It is characterized by a narrow stack of parakeratotic corneocytes (cornoid lamella) embedded in the horny layer. This rests on a shallow depression of the epidermis where the granular layer is reduced or absent. The spinous layer contains apoptotic keratinocyte. Occasionally cornoid lamella is found in a hair follicle ostium. The upper dermis contains inflammatory infiltrate mainly CD4+ lymphocytes. The papillary dermis occasionally contains eosinophils, colloid bodies, or amyloid deposits. The central area of the lesion is usually atrophic, but may occasionally show gross hyperkeratosis. Dermoscopy shows an atrophic center surrounded by a thick hyperkeratotic rim. Rare findings include focal epidermal necrosis, sub-epidermal clefts, and ulceration. Electron microscopy shows pyknotic nuclei, disrupted organelles and lipid droplets in the corneocytes of cornoid lamella. Under the cornoid lamella, keratohyalin granules and lamellar bodies are reduced.[1] Differential diagnosis includes actinic keratoses, seborrheic keratosis, stucco keratosis, lichen planus, psoriasis, epidermal naevi, Darier's disease, basal cell-naevus syndrome.

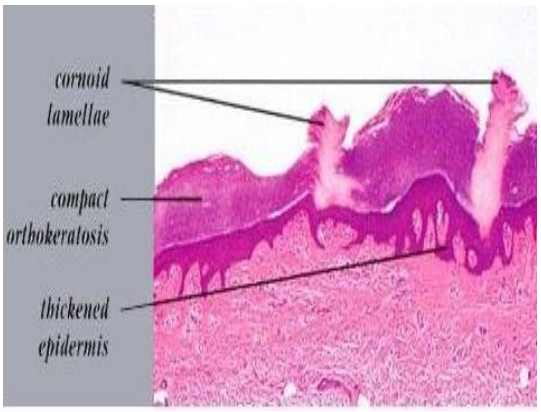

Fig.8

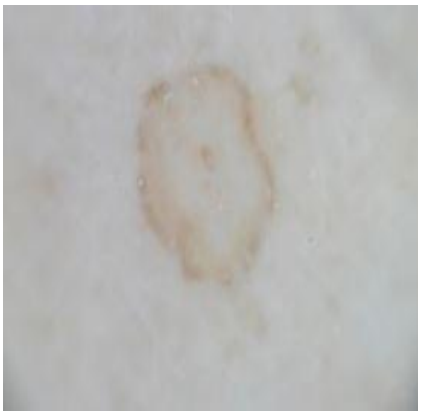

Fig.9

Fig. 8: Histopathology of porokeratosis showing cornoid lamellae, compact orthokeratosis, and thickened epidermis.

Fig.9 –Dermoscopy showing an atrophic center surrounded by a hyperkeratotic rim.

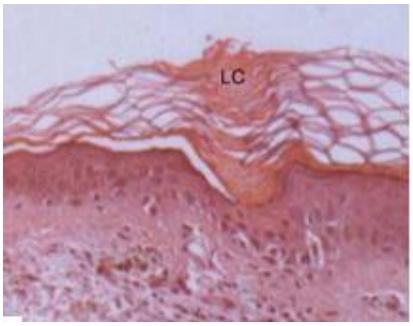

Fig.10

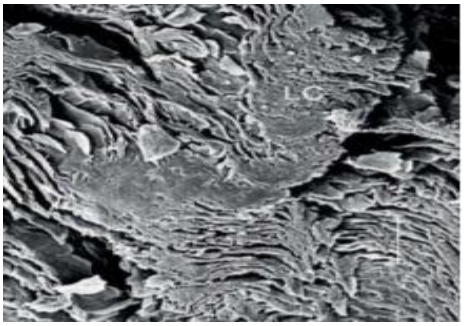

Fig.11

Fig. 10: Light microscopic features of porokeratosis showing cornoid lamellae (LC).
Fig. 11: Scanning electron microscopy showing cornoid lamellae (LC).

10. Management

The approach to treatment should be based on the size of the lesion, the location, duration of lesion, the risk of malignancy and patient's preference. General measures like protection from sun exposure, use of emollients, symptomatic treatment and observation for signs of malignancy should be done. Management of porokeratoses includes local and systemic treatment which are used alone or in combination.

10.1 Topical Therapy

10.1.1 Topical 5-fluorouracil

Topical treatment with 5-fluorouracil can induce remission in almost all forms of porokeratoses.[51,52] Better response can occur by the addition of topical tretinoin, tazarotene, or salicylic acid.[53] It can also be used in combination with 70% glycolic acid peel.[54] 5-FU is also found to be very effective in combination with photo dynamic therapy.[55]

10.1.2 Topical vitamin D-3 analogues

Calcipotriol and tacalcitol are the vitamin –D3 analogues which have been shown to be effective in the treatment of DSAP.[56,57,58] Calcipotriol and adapalene therapy were also found to be effective in the treatment of DSAP.[59] Topical vitamin D acid derivatives were found to be very effective in the treatment of disseminated porokeratosis.[60] Significant improvement of DSAP after local administration of calcipotriol and betamethasone combination gel has also been reported in the literature.[61]

10.1.3 Immunomodulators

Topical imiquimod 5% cream is proved to be a useful treatment option for DSAP. It may suppress the abnormal mutant genes on both adaptive and innate immunity. This topical therapy treated the plaques effectively. There was also an improvement in color and texture over the central scars.[62] A case of facial sporadic DSAP treated effectively with topical imiquimod has been reported in the literature. The patient underwent a once weekly application and there was no relapse for 2 years.[10] It has also been found to be effective in the treatment of classic porokeratosis of mibelli (PM).[62,63] Treatment of porokeratosis of mibelli with Ingenol mebutate is a newer therapeutic approach which is also found to be effective.[64] It has also been used successfully in linear porokeratosis and PKPD.[65,66]

10.1.4 Calcineurin inhibitors

Tacrolimus, a calcineurin inhibitor was found to be effective in the treatment of linear porokeratosis.[67] Calcineurin inhibition leads to amplify the innate immune response in keratinocytes and prevent the proliferation of abnormal keratinocyte, and leading to improvement in lesions. Another calcineurin inhibitor, pimecrolimus in low concentrations showed minimal efficacy in the treatment of facial porokeratosis in a woman has been reported in the literature.[68]

10.1.5 Diclofenac gel

Diclofenac 3% gel is found to be effective for DSAP.[69,70] It has also succeeded in achieving symptomatic relief in a patient with disseminated porokeratosis restricted to genitalia.[71]

10.1.6 Topical retinoids

Topically applied retinoids like tretinoin, tazarotene reduce the hyperkeratosis over the edge of lesions. It is reported to be effective in the treatment of porokeratosis, particularly DSAP.[72,73] But in some cases, it was found to be ineffective.[74,75] The combination of topical retinoids and 5-FU has been reported to be very effective in the treatment of porokeratosis.[51] Linear porokeratosis responds well to topical or systemic retinoids.[92]

10.1.7 Keratolytic agents

Keratolytic agents like salicylic acid and urea can also be used in the treatment of porokeratosis. It reduces the hyperkeratotic surface of the lesions.[6]

10.1.8 Emollients

Emolients is also found to be useful in achieving symptomatic improvement and also reduces pruritus in porokeratosis.[12]

10.2 Cryo Therapy

Cryotherapy is a minimally invasive method that can be used for the resolution of lesions. It was found to be successful in the treatment of porokeratosis particularly porokeratosis of mibelli linear porokeratosis, PPPD.[76,77] But several years of treatment was needed in a case of

linear porokeratosis for the complete clearance of lesions.[77]

10.3 Photodynamic Therapy

Photodynamic therapy (PDT) is relatively a new treatment modality useful in the treatment of porokeratosis which includes the sequential administration of a photosensitizer drug and light. PDT using 5-amino levulinic acid has been successfully used in some cases of PKM and LP.[78,79] Combined use of 5-FU and PDT is found to be very effective in the treatment of PKM.[55] PDT is potentially a useful treatment modality for DSAP as it can selectively target highly active, atypical cells and cause the destruction of these cells. Methyl amino levulinate (MAL)- PDT was found to be a better choice than aminolevulinic acid (ALA). MAL-PDT was found to be successful only in some cases of DSAP.[80] Topical PDT with no satisfactory results has been reported in the literature.[81]

10.4Laser Therapy

Various types of laser therapy have been used which includes CO2, Erbium, Q-switched ruby, Nd:YAG laser. CO2 laser vaporization gave satisfactory results in cases of PKM.[82] CO2 laser vaporization is a treatment option for DSAP also, but it is not sufficient by itself for removing the rims.[83] Adverse reactions of CO2 laser include scars and hypopigmentation. A rapid recurrence has also been reported after C02 laser ablation.[84] Nd:YAG laser was found to be effective in a patient with DSP. DSP lesions showed significant improvement after treatment with 1927-nm thulium fiber fractional laser.[85] Fractional photothermolysis with erbium which is a novel therapy in the treatment of DSAP also showed significant improvement of lesions.[86,87] Ruby laser therapy was found to be moderately successful in treating DSAP and can be used as a good alternative to other available treatments.[88]

10.5 Electro Chemotherapy (Ect)

It is a form of intra lesional chemotherapy. Linear porokeratosis is most frequently associated with malignant transformation into squamous cell carcinoma. LP with multiple SCC was found to be successfully treated with bleomycin intralesional chemotherapy.[89]

10.6 Diamond Fraise Dermabrasion

It was found to be effective in improving the appearance of linear porokeratosis. Recurrence after treatment has been reported in the literature.[90]

10.7 Systemic Treatments

10.7.1 Retinoids

The use of oral retinoids reduces the risk of carcinoma in porokeratotic lesions in immunosuppressed patients and those who are at higher risk of malignancy. Oral isotretinoin combined with topical 5-FU gave satisfactory results in DSAP and PPPD. Oral Etretinate was shown to be helpful in linear porokeratosis and PKM. But higher doses were found to exacerbate the lesions of DSAP.[91] Acitretin also gave good results in the treatment of linear porokeratosis.[92]

10.7.2 Antihistamines

Oral antihistamines in combination with topical corticosteroid gave symptomatic relief in a case of inflammatory DSP with severe pruritus.[93]

10.8 Surgery

Surgery is a elective treatment, which is useful in cases of multiple and larger lesions. Excision is appropriate if malignant degeneration develops.[94]

CONCLUSION

Porokeratoses are a group of keratinization disorders .Apart from the six clinical variants of porokeratosis, rare variants like PK ptychotropica, follicular porokeratosis, prurigo nodularis like PK, bullous PK, pustular PK, genital PK, seborrheic keratosis like PK, ulcerative PK, eruptive pruritic PK, porokeratoma or porokeratotic acanthoma also exist and we should consider these rare variants also in the diagnosis of porokeratotic lesions. Since the lesions are more commonly seen in sun-exposed areas, sun protection should be advised. We reviewed several treatment approaches.Topical therapies were found to be effective in the symptomatic improvement and clearance of lesions in almost all types of porokeratosis, but none of them showed complete cure of lesions. Newer therapeutic approaches like Cryotherapy, photodynamic therapy, electrochemotherapy were found to give rapid and satisfactory results in cases of PKM, DSAP, and in PPPD. But recurrences can occur. Also, combination therapy were found to be more effective than monotherapy. Porokeratotic lesions should be closely monitored for any malignant transformation.

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