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Clinical Study on Porokeratosis in Tertiary Care Hospital

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Abstract
Introduction
porokeratosis (PK) is a genetic or acquired dermatosis characterized by disordered keratinization, manifesting clinically with annular or linear,keratotic plaques with central atrophy and the elevated border with histologically showing a column of parakeratotic keratinocytes (coronoid lamella). The etiology of porokeratosis is still unclear.
Aims and objectives
To study clinical, histopathological features and variants of porokeratosis
Methodology
A prospective observational study was conducted in S.V.R.R.G.G.H., Tirupati, for one year. We selected 12 patients of porokeratosis, and detailed clinical and histopathological evaluation was done in all the patients.
Results: A total of 12 cases of porokeratosis were reviewed between 2019 and 2020 from S.V.R.R.G.G.H. Tirupati. Out of 12 cases, there were 4 cases of porokeratosis of Mibelli(PM), 3cases of disseminated superficial actinic porokeratosis (DSAP), 3 cases of disseminated superficial porokeratosis(DSP), and one case each of isolated genital porokeratosis (IGP) and porokeratosisptychotropica .age of onset of lesions were variable in each variant. The ratio of males to females was 8:4. Among them, 4 cases had a family history of porokeratosis. .33% patients suffered from pruritus, and the remaining are asymptomatic.initial site of presentation of lesions are limbs(41%), body(25%), face(16%), genitalia(8.3%), and buttocks(8.3%) .75%patients showed obvious keratotic border and only 25%patients showed verrucous hyperplasia of skin lesions. Histopathological features are seen were coronoid lamella (100%) in all cases. no malignant changes were observed in any our cases
Conclusion: Most of the cases in our study showed classical clinical and histopathological features described in literature. Regular follow-up is required, as long-standing lesions may undergo a malignant transformation in porokeratosis.

Key words:*PorokeratosisMibelli, Disseminated superficial porokeratosis, Porokeratosisptychotropica.*

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I. Introduction

a hundred years ago, Vittorio Mibelli described a new keratotic disorder, called porokeratosis of Mibelli(1) They affect both sexes with small differences depending on the specific clinical form. PK of Mibelli seems to be more common in males, whereas disseminated superficial actinic PK is more often seen in women. The age of onset also varies depending on the form; it is lower in PK of Mibelli than the actinic form. no obvious ethnic predilection as PK has been observed worldwide in Caucasian, Asian, and black patients. (2,3)

the primary lesion of PK is a brown keratotic asymptomatic papule 1-3 mm in size that expands outwards and forms, after several weeks or months, a sharply-circumscribed plaque of various sizes and forms. Its border comprises a depression containing a keratotic lamella pointing towards the center of the plaque. (4) The center of the plaque is slightly atrophic and depressed, more rarely hyperkeratotic, often hyperpigmented.

According to the size, the arrangement, the number, and the location of the lesions, several clinical forms of PK have been described(1) PK of Mibelli consists of a single or several annular or scalloped, large plaques that are usually unilateral, less frequently bilateral and symmetric(2) PKM predominates on the limbs (hands/feet), and may also be located on the face, the lips, the palms and soles, the genitalia, the scalp, and the oral mucosa. PKM shows a male predominance. It can be sporadic or familial, transmitted as an autosomal dominant trait; in the latter case, the lesions usually appear during childhood. It is the most common form, usually seen in countries with high sun-exposure.

DSAP usually appears during the 3rd or 4th life decade, occasionally later in life. The transmission pattern is consistent with autosomal dominant inheritance. DSAP manifests with several (occasionally hundreds of) small (about 1 cm) annular lesions that are distributed in a bilateral and symmetric pattern on

sunexposedsites, namely the legs and forearms, the shoulders and the back, more rarely the face (cheeks)(5,6) They are pruritic in one-third cases.

Disseminated Superficial PK (DSP) Disseminated Superficial PK is clinically similar to DSAP except for younger age at onset (5-10 years, occasionally). The fact that UV rays are not a triggering factor. The lesions are therefore localized both on sun-exposed and non-exposed body zones (trunk, genitalia, palmoplantar zones). Oral localisations exist DSP lesions are pruritic in one-third of cases. Some cases are transmitted as an autosomal dominant trait.(7)

Linear PK is a rarer form, manifesting with linear, unilateral, hyperkeratotic plaques on the limbs, rarely the face, following Blaschko's lines;. LPK of the limbs may be associated with lesions of the nails (pterygium, longitudinal fissures)(8) LPK appears early in life and may even be congenital. It may be sporadic and shows a slight female predilection. It is likely due to a phenomenon of mosaicism of the gene responsible for the generalized form of PK(9)

Punctate Palmoplantarpk It manifests with multiple punctate lesions 1-2 mm in size, occasionally tender to pressure; they appear initially on the palms and soles (10)PK Palmaris, Plantaris, and Disseminata It is characterized by bilateral, symmetric red-brown keratotic papules measuring 1-2 mm, that develop in adolescence or adulthood, initially on the palms and soles. They may later spread to other body zones, sun-exposed or covered (limbs, trunk. PKPPD predominates in males. Even though sporadic forms exist, the majority of cases are familial(11)

Other rarer clinical variants of PK that have been described include: PK ptychotropica, manifesting with symmetric verrucous, hyperkeratotic red-brown plaques of the buttocks and the genitalia (12); reticulate pk,(13), isolated genital pk ulcerative PK; bullous PK; pustular PK follicular PK; and seborrhoeic keratosis-like PK . "porokeratoma" (or porokeratoticacanthoma(14)

The characteristic microscopic feature of PK is found at the periphery of the lesions within the keratotic rim. The thick orthokeratotic horny layer contains a narrow vertical column of parakeratoticcorneocytes reminiscent of a "stack-of-plates," the coronoid lamella. This rests on a shallow depression of the underlying epidermis and its top is oriented toward the center of the plaque. Under the coronoid lamella, the granular layer is reduced or absent, and the spinous layer contains dyskeratotic or vacuolated keratinocytes. The basal keratinocytes often show vacuolization. The upper dermis contains inflammatory infiltrate of variable density, made mainly of CD4+ lymphocytes (15)

The aetiopathogenesis of PK appears to be complex and multifactorial but is not well known. The classic hypothesis stipulates that PK lesions are due to the peripheral expansion of a clone of mutant epidermal keratinocytes located at the base of the coronoid lamella (16). This hypothesis is supported by the finding of aneuploid DNA (17). These are suggested by the existence of several familial cases of PKM, LPK, and PKPPD. Autosomal dominant inheritance with reduced penetrance. Sporadic cases would be due to somatic mutations (18). Several susceptibility loci of DSAP have been identified on Chr. 1, 12, 15, 16, and 18. Recently, mutations in the mevalonate kinase gene (MVK) detected inpatients with familial and sporadic DSAP. Functional in vitro studies suggested that MVK could protect keratinocytes from UVA-induced apoptosis(19)

Sun aggravates DSAP is suggested by clinical and demographic data (location of lesions on sun-exposed body zones, worsening in summer, increased incidence of DSAP in areas with high sun-exposure, onset in adulthood) (20)

Several cases of PK have been reported in the setting of various immunodeficiencies, like organ transplantation, leukemias/lymphomas, HIV infection, and various inflammatory or autoimmune diseases treated with immunosuppressive drugs (21)

CAP syndrome, autosomal recessive inheritance, associates craniosynostosis, anal and genitourinary abnormalities, and skin eruptions, most often PK. Infantile onset. The responsible gene maps on chromosome 22q12- q13(22)

on average, in 7.5% of cases, PK lesions may undergo malignant transformation into Bowen's disease, invasive squamous-cell carcinoma, more rarely into basal-cell carcinoma (23)long-standing lesions, lesions of large size, those located on the limbs and LPK are at higher risk; conversely, the risk of DSAP seems lower(24)

II. Aim And Objectives

To study clinical, histopathological features and variants of porokeratosis.

III. Material And Methods

Study design-prospective observational study
Place of study- S.V.R.R.G.G.H.,Tirupati,Andhra Pradesh
Duration of the study-1 year(March 2019 to Feb 2020)
Twelve patients of clinically diagnosed cases of porokeratosis were selected after taking valid written consent .prior to study, institutional ethical committee permission is taken .a general and cutaneous examination were

done. Histopathological examination was done in all patients .routine blood investigations like CBC, RBS, LFT, RFT, Serological status, and routine urine examination were done. .clinical and histopathological features of patients are collected in proforma .results are tabulated and analyzed.

IV. Results

A total of 12 cases of porokeratosis diagnosed by histopathology between 2019 and 2020 from S.V.R.R.G.G.H Tirupati were reviewed retrospectively. The present study enrolled seven males and five females, with an average age of 8-60 years. Among them, three individuals had a family history of porokeratosis, with ≥1 first-degree relative suffering from porokeratosis; however, the pattern of inheritance was not determined. The mean age of onset was ten years in inherited cases and 35 years in uninherited cases.

Clinical manifestations. In the present study, patients were classified into five clinical variants: i) 4 cases of PorokeratosisMibelli; ii) 3 cases of Disseminated Superficial Actinic Porokeratosis (with the main part of the lesions developed in sun-exposed areas); iii) 3 cases of Disseminated Superficial Porokeratosis, and iv) one case of Isolated Genital porokeratosis and 5)one case of Porokeratosisptychotropica. LP, PP, and DPP were not detected in the present study.

. In the analysis of the age of onset and clinical variant, no significant difference was identified. The number of cases of PM and DSP was higher in males, while the number of cases of DSAP was higher in females. The lesions were initiated on the face in 2cases, on the body in 3 cases, on the limbs in 5 cases, on the buttock in 1 case, and in the genital area in 1 case.

In total, four patients investigated in the present study suffered from pruritus, with no significant difference observed between the clinical variants. Patients, including one patient with PM, two patients with DSAP, 1 with isolated genital porokeratosis, and 1 with porokeratosisptychotropica, suffered from conspicuous pruritus.

Table 1

Clinical variants	Age of onset(in yrs)
PM	20-55
DSP	10-60
DSAP	8-45
IGP	15-50
Porokeratosisptychotropica	20-50

PM-porokeratosismibelli, DSP-disseminated superficial porokeratosis, DSAP-disseminated superficial actinic porokeratosis, IGP-isolated genital porokeratosis.

Chart 1 Sex ratio

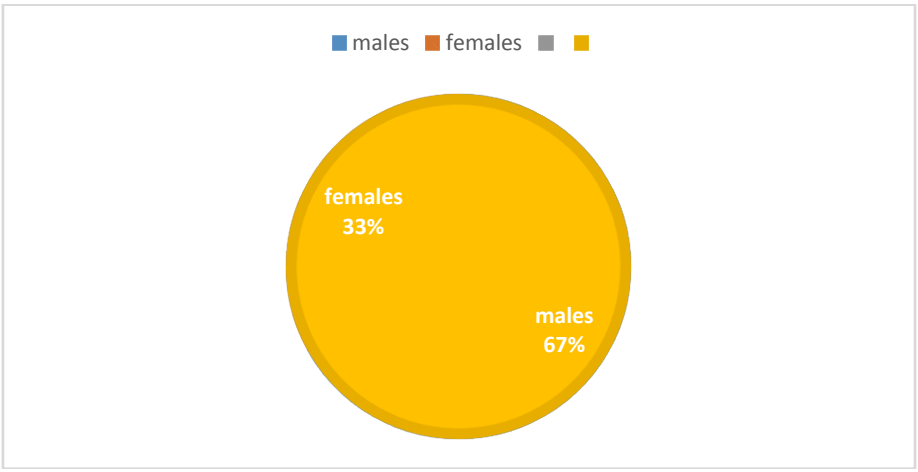


Chart 2 showing family history in patients

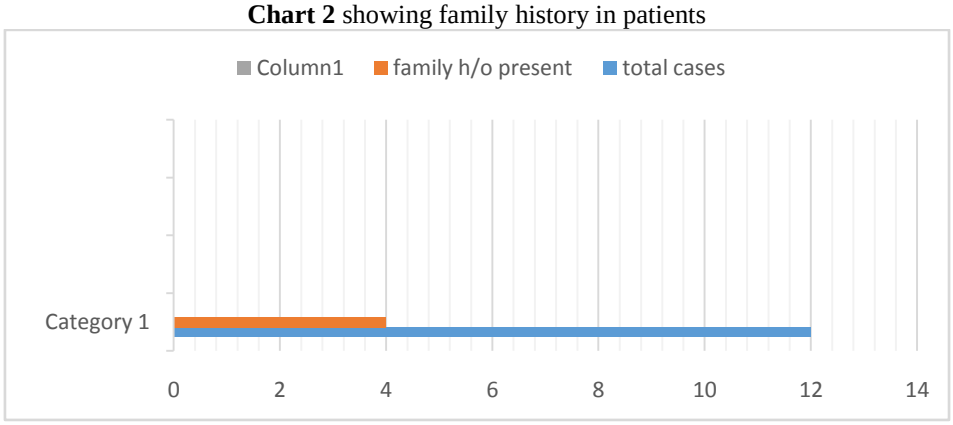


Chart 3

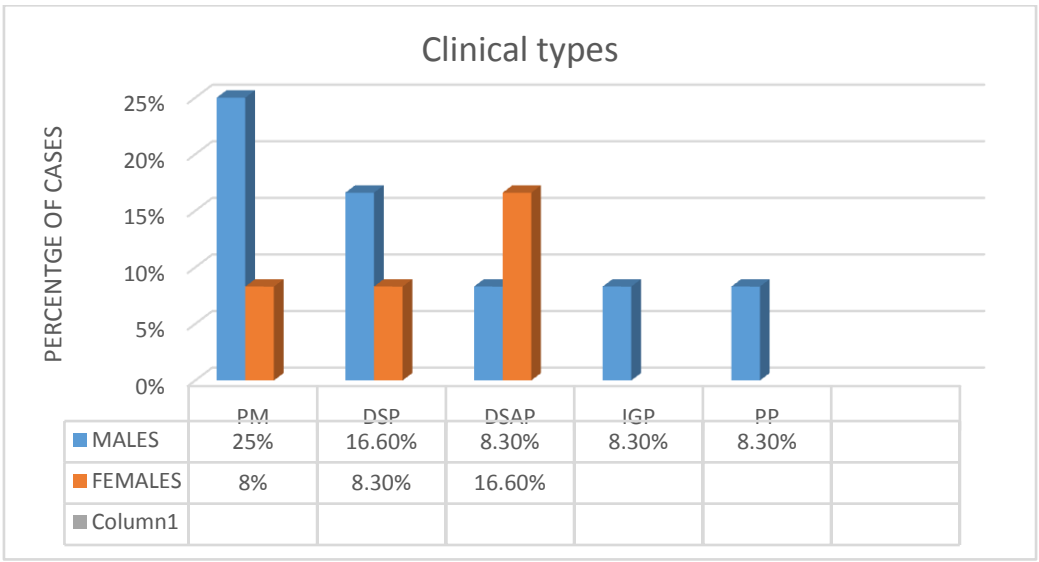


Table 2

Clinical types	Total	Males	Females
PM	33%	25%	8.3%
DSP	25%	16.6%	8.3%
DSAP	25%	8.3%	16.6%
IGP	8.3%	8.3%	0%
Porokeratosisptychotropica	8.3%	8.3%	0%

PM-porokeratosismibelli, DSP-disseminated superficial porokeratosis, DSAP-disseminated superficial actinic porokeratosis, IGP-isolated genital porokeratosis.

Table 3

Clinical variant	Obvious Keratotic border(%cases)	Verrucoushyerplasia
PM	75%	25%
DSP	100%	0%
DSAP	100%	0%
IGP	0%	100%
Porokeratosisptychoropica	0%	100%

PM-porokeratosismibelli, DSP-disseminated superficial porokeratosis, DSAP-disseminated superficial actinic porokeratosis, IGP-isolated genital porokeratosis.

Table 4
The initial onset of lesions

Clinical variant	Face %cases	Body	Limbs	Buttocks	Genitalia
PM	0%	25%	75%	0%	0%
DSP	0%	67%	33%	0%	0%
DSAP	67%	0%	33%	0%	0%
IGP	0%	0%	0%	0%	100%
Porokeratosisptychoropica	0%	0%	0%	100%	0%

PM-porokeratosismibelli, DSP-disseminated superficial porokeratosis, DSAP-disseminated superficial actinic porokeratosis, IGP-isolated genital porokeratosis.

Table 5

Clinical type	Pruritis	Asymptomatic
Porokertosismibelli	75%	25%
DSP	33%	66%
DSAP	66%	33%
IGP	100%	0%
Porokeratosisptychotropica	100%	0%

PM-porokeratosismibelli, DSP-disseminated superficial porokeratosis, DSAP-disseminated superficial actinic porokeratosis, IGP-isolated genital porokeratosis.

Demographic data are shown in tables one and chart 1,2&3. Clinical features are shown in tables 2,3,4 and 5.in our study, five variants of porokeratosis are seen; they are classic porokeratosismibelli, DSP, DSAP, porokeratosisptychotropica, and genital porokeratosis.

Figure 1 Porokeratosismibelli

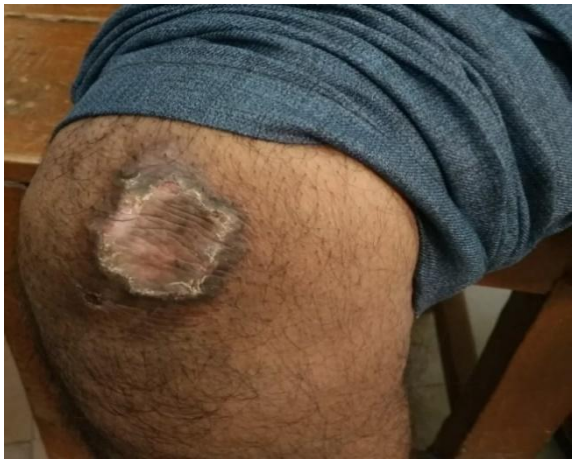


Figure 2-Disseminated superficialporokeratosis showing lesion on both neck and the inner side of the thigh

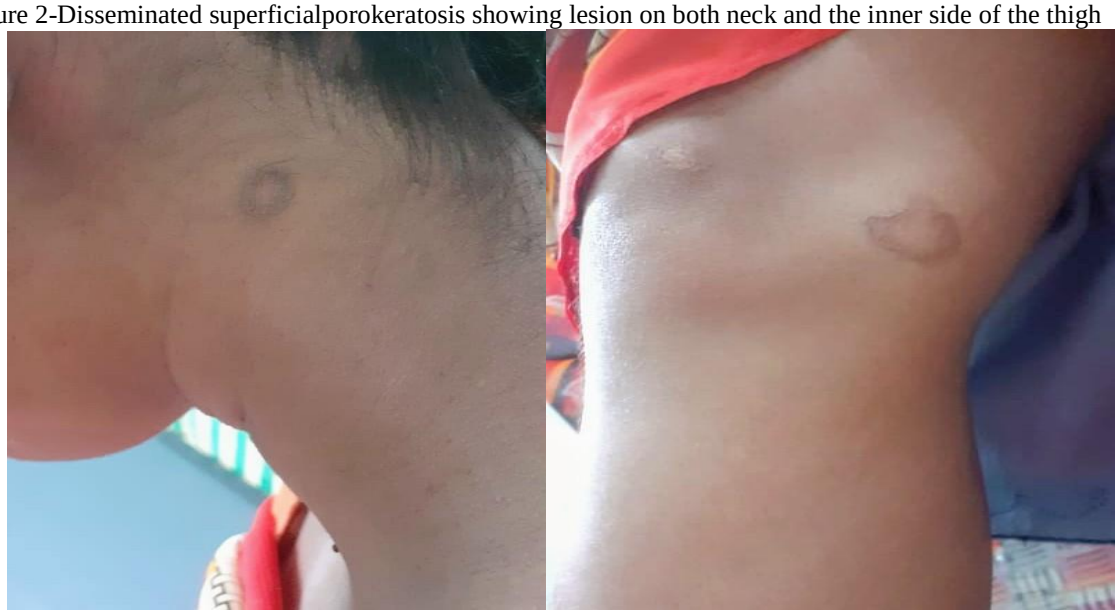


Figure 3 -DSAP showing lesions on sun-exposed sites face, upper back

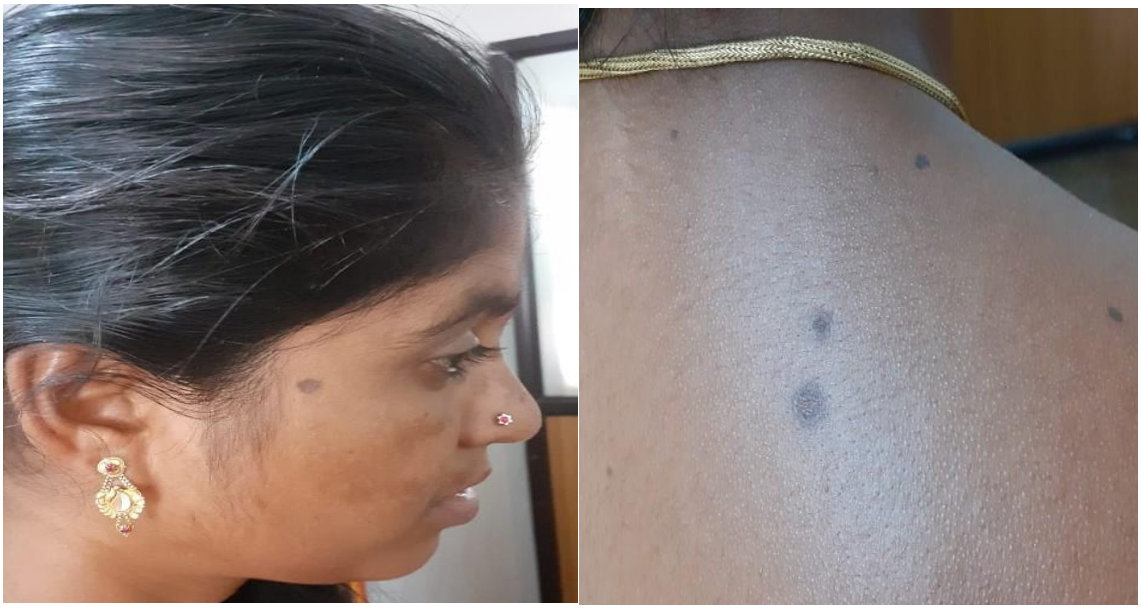


Figure 4 -Genital porokeratosis

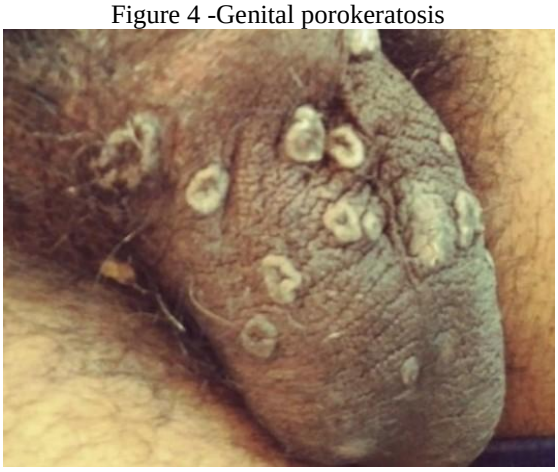


Figure 5- Porokeratosisptychotropica

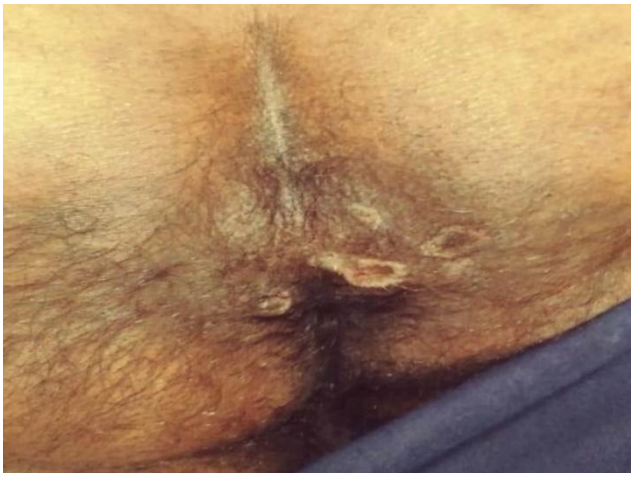
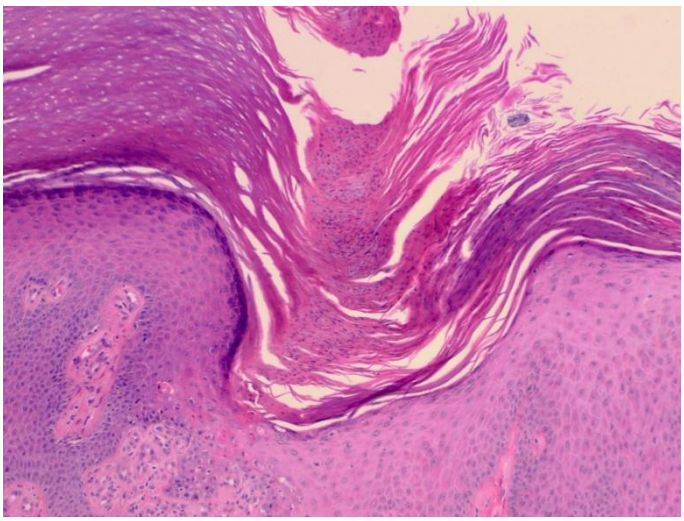


Figure 6- histopathology showing coronoid lamella, parakeratotic column within the crater, and few dyskeratotic cells are seen below it



V. Discussion

In our study, the usual age of onset is between 8-15 years in inherited cases and 35-55 years in acquired cases, which is similar to previous studies

Table 6

	Our study	Gu et al(3)
Male:Female ratio	2:1	2.4:1
Family h/o present	33%	21%

In our study, clinical features recorded are annular plaques with raised margins. These findings almost similar to other studies (3)

Histopathological examination of skin biopsy specimens in our study show specific changes like the presence of coronoid lamella, which is characterized by a column of parakeratotic cells extending through the surrounding orthokeratotic stratum corneum, and a dermal perivascular lymphocytic infiltrate, which is almost similar to previous studies (15)

porokeratosis (PK) is a group of acquired or genetic dermatoses, characterized by a keratinization disorders; skin lesions often begin as is brown keratotic asymptomatic papule 1-3 mm in size that expands outwards and forms a sharply-circumscribed plaque of various sizes and forms. Its border comprises a depression containing a keratotic lamella pointing towards the center of the plaque. The center of the plaque is atrophic and depressed.

According to the size, the arrangement, the number, and the location of the lesions, several clinical forms of PK have been described. These include besides classic porokeratosis of Mibelli (PM), disseminated superficial actinic porokeratosis (DSAP), 'linear porokeratosis' ('LP'), porokeratosispalmarisetplantaris disseminate (PPPD), disseminated superficial porokeratosis (DSP), and porokeratosispalmarisetplantarispunctata (PPPP). Rare variants like reticulate type (13) isolated genital porokeratosisptychotropica(12) and porokeratosis(14). in our study PM, DSAP,DSP, genital porokeratosis, and porokeratosisptychotropica are seen.

Differential diagnosis of the classical form includes psoriasis, lichen simplex chronicus, hypertrophic lichen planus, cutaneous tuberculosis, actinic keratosis, and contact dermatitis.

PK lesions may undergo malignant transformation into Bowen's disease, invasive squamous-cell carcinoma, more rarely into basal-cell carcinoma .long-standing lesions, lesions of large size, those located on the limbs and LPK are at higher risk; in our study of 12 patients, none of them showed malignant features.

Treatment for disseminated lesions is unsatisfactory.topical modalities like retinoids, imiquimod,5 FU ointment give symptomatic relief. If the lesions spread rapidly, surgery, laser treatment, and cryotherapy are suggested.

VI. Conclusion

Most of the cases in our study show classical clinical and histopathological features described in literature. Regular follow-up is required, as long-standing lesions may undergo a malignant transformation in porokeratosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate consent forms .in these form, the patient(s) has/have given his/her/ their consent for his/her/ their images and other clinical information to be reported in the journal .the patients understand that their names and initials will not be published. Due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil

Conflicts of interest

No conflicts of interest

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