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Original Article

Clinical and histopathological analysis of porokeratosis in series of fifty three patients

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Abstract

Background Porokeratosis is consisting of different group of diseases with autosomal dominant inheritance with wide types of presentations. While solar facial porokeratosis is a well distinguished non- inherited disease that triggered by sunlight exposure and was only reported in Iraq.

Objectives To evaluate all types of porokeratosis that had been seen during specific period of time and tries to analyze them into characteristic groups.

Methods This is descriptive case series study where fifty three patients with porokeratosis were seen during the period from April 2014-October 2022. Full history and clinical examination were carried out for all patients and biopsies from lesions for histopathological evaluation was done.

Results Fifty three patients with porokeratosis were evaluated into two groups: group one with 35 cases of different types of porokeratosis, with age range from 3-58 years with mean and SD of 30.1±11.7 . The duration of the disease was ranged from 1-34 years while the mean and SD of 6.2±5.6 year, and the mean age of onset was 23.3±10.2 years, 24 (68.5%)males and 11(31.4%) females. There were wide range of presentation, common among males with M: F 6.5:1 and the clinical picture could be divided into localized and generalized manifestations and porokeratosis of Mibelli constituting the commonest type in 15(42.85%) cases. While the second group included 18 patients with solar facial porokeratosis , 10(55.5%) cases were females and 8 (44.4%)males, with age range from 19–30 years while the mean and SD were 27± 4.4 year . The disease duration ranged from 2–12 years with a mean and SD of 4.1± 2.9 year, with negative family history in all patients. It was disease of young people with slightly more among females with F: M 1.14:1.This variant was triggered by sunlight exposure and mainly manifested in summer time. The location of lesions was only on the face and commonly around nose.

Conclusion The Porokeratosis is comprising of a heterogeneous group of diseases that could be classified into autosomal dominant inheritance fashion and consisted of localized and generalized diseases. While solar facial porokeratosis is non-inherited acquired variant with well distinguished clinical features that induced by sunlight exposure that could be considered as specific variant of porokeratosis.

Key words
Porokeratosis; Variants; Solar facial porokeratosis; Histopathology; Cornoid lamalla.

Introduction

They are a heterogeneous group of keratinization[1] disorders which is an enigmatic dermatological problems in terms of its etiopathogenesis, clinical findings, histopathological findings and therapies. It appeared to be as a clonal keratinizing diseases of ill -defined etiology.[2] They have distinguished clinical manifestations of a keratotic ridge with a central groove that corresponds to the cornoid lamella on histopathology.[1] Porokeratoses have a wide range of findings[1] which includes plaque type porokeratosis of Mibelli[3] giant

porokeratosis,[4] hyperkeratotic porokeratosis,[5] linear porokeratosis,[1] disseminated superficial porokeratosis; disseminated superficial actinic porokeratosis; porokeratosis palmaris et plantaris disseminate (PPPD), and punctate porokeratosis.[3] Porokeratosis of Mibelli (PM), disseminated superficial porokeratosis (DSP) and disseminated superficial actinic porokeratosis (DSAP) are more common variants of porokeratosis, from which an increasing number of patients having the disease.[3]

Porokeratosis is characterized by an autosomal dominant inheritance.[1] They include Porokeratosis palmaris et plantaris disseminativa (PPPD) and disseminated superficial actinic porokeratosis (DSAP) but many patients appear to be sporadic.[7] PPPD and Porokeratosis of Mibelli affect males twice as often as females. While DSAP is three times more common in females in comparison with males and LP is noticed with equal incidence in males and females.[8] PPPD and LP may be observed at any age, from birth to adult age. While PM usually appears in childhood, DSAP generally seen in the third or fourth decade of life.[9,10] Given its relationship to sun exposure, DSAP is more common in Caucasian race and while it is rare in black population.[7] Although porokeratosis is considered to be a disease of keratinization, the definitive etiopathogenesis stays ill-defined.[7] Heterozygosity loss at 12q and sequence variations in genes at this locus have been reported, but the significance of these findings is ill-defined.[3] More recently, heterozygous mutations in the *MVK* gene have been reported to cause porokeratosis of Mibelli and in DSAP,[11] Triggering factors such as UVR exposure[12] or immunosuppression due to AIDS,[13] transplant operations,[14] immunodeficiency syndromes have been incriminated in the porokeratosis pathogenesis. Also chronic failure of kidneys,[15] chronic hepatic disease,[15] infections, blood malignancies ,hepatitis C virus infection[16] have been incriminated in the pathogenesis of porokeratosis. Drugs like adalimumab and etanercept had also been incriminated in disease pathogenesis.[11]

So on summary, porokeratosis is consisting of generalized and localized variants.[6] The most common localized types are classical porokeratosis of Mibelli,[17] linear porokeratosis, punctate porokeratosis, sun induced facial porokeratosis and genital porokeratosis.[18,19] While the generalized forms are disseminated superficial actinic porokeratosis, disseminated superficial porokeratosis and disseminated palmoplantar porokeratosis. While the unusual forms including, pruritic papular porokeratosis, hyperkeratotic porokeratosis and verrucous porokeratosis (localized) to buttocks[20] and reticulate porokeratosis.

The aim of present work is to collect all cases of porokeratosis and to do full clinical analysis of the different types and try classify them into well-defined variants

Patients and Methods

This is descriptive case series clinical and histopathological study that conducted at the Dermatology center, Medical City Hospital. Fifty three cases of different varieties of porokeratosis were enrolled in this study during the period from April 2014- October 2022. All demographic features were recorded including personal information, disease history, onset, duration and family history. All patients were photographed with a mobile camera (iPhone x

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max 12 MP) in the same position and illumination .Clinical examination was done to confirm the diagnosis of porokeratosis and solar facial porokeratosis and trying to exclude other differential diseases.Skin biopsies of lesions were carried out and processed for H & E stain for histopathological evaluation. For the purpose of statistical analysis, Microsoft Excel program was used to describe quantitative data, the mean±standard deviation and median were applied. For the description of qualitative data, absolute numbers, frequency and percentage were included. This present work was approved by the ethical committee of the Iraqi Board for Medical Specializationn.

Results

Fifty three patients with porokeratosis with different types and variants were included and were subtyped into two groups **(Table 1).**

Group one including 35 (66%) cases with different types of porokeratosis, 24 males (68.57%) and 11 females (31.4%), with male to female ratio: F 2.18:1. The ages ranged from 3-58 years with mean and SD of 30.1±11.7 while the mean age of onset was 23.3±10.2 years. The duration of the disease ranged from 1-34 years with mean and SD of 6.2±5.6 year. Among them, 4 (11.4%) individuals have had a family history of porokeratosis. This group had a Wide range of presentation and could be divided into localized and generalized. The patients with localised variant were seen in 21 (60%) patients, while 14 (40%) patient had generalised variant.

Table 1 Patients demographic features for patients in group one porokeratosis.

Patient dermographic features			*%age*
Age	Range	2-58 y	
	mean±SD	30.1 ± 11.7	
Age at onset	Range	1-55 y	
	mean±SD	23±10.2	
Sex	Male	24	68.5
	Female	11	31.4
Duration	Range	1-34 y	
	mean±SD	6.2± 5.6 y	

The localized form

The localized variants included porokeratosis of Mibelli in 15 (42.8%) patients, genital porokeratosis 4 (11.4%), linear porokeratosis 1 (2.8%), giant porokeratosis 1 (2.8%). While punctate porokeratosis and reticulate porokeratosisi had not been detected in the present work.

Porokeratosis of Mibelli Fifteen patients were observed, the ages ranged ranged from 3-58 years with mean and SD of 30.1± 11.7, with 11 males, 4 females with male to female ratio 2.7:1. These patients presented with variable clinical presentations, 11 (73.3%) patients had classical picture which was distinguished by single plaques with a thread-like hyperkeratotic margin (**Figure 1**), most commonly cited on the limbs in 6 (37.3%), while on face in 6 (37.3%), and face and extremities in 4 (25%) patients. Other clinical findings were erythematous-hyperchromic plaques with slightly elevated edge and atrophic centeres in 1 (6.25%) case,

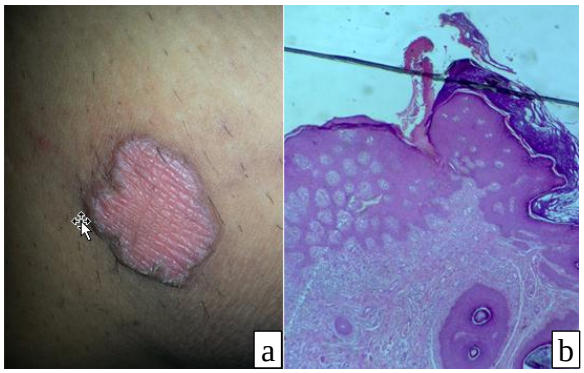

Figure 1 28 year old female showing: a-porokeratosis of mibelli solitary plaques with a hyperkeratotic margin; b- histopathology showing coronoid lamella overlying focal hypogranulosis with acanthotic epidermis.

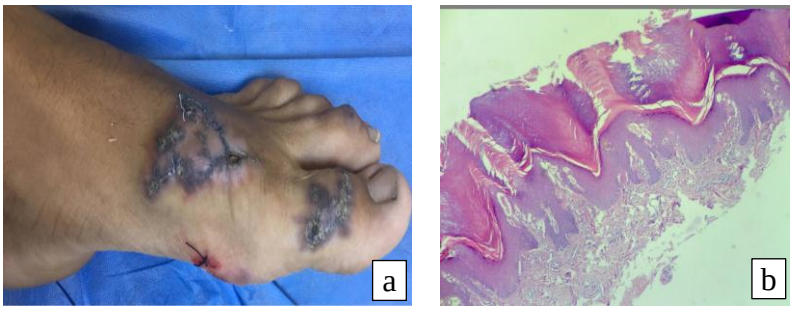

Figure 2 a) Porokeratosis of mibelli showing erythematous- hyperchromic plaques with slightly elevated edges and atrophic center.
b) Histopathology of Porokeratosis of mibelli showing coronoid lamellae.

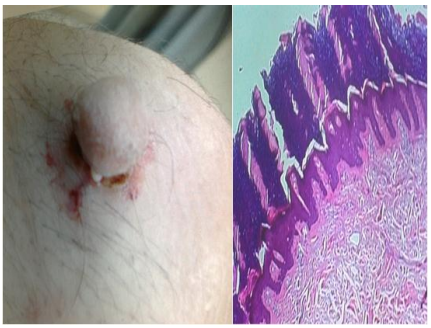

Figure 3 Nodular porokeratosis showing: a- dome- shaped skin coloured nodule on extremities b- multiple coronoid lamellae with underlying hypogranulosis.

(**Figure 2**), nodular 1 (6.25%) patient (**Figure 3**) and atrophic in 2 (18.7%) cases (**Figure 4**). No symptomatic complaints were noticed in all patients.

Linear porokeratosis This was seen in one (2.8%) patient and presented as unilateral, linear array of plaques and papules with well distinguished raised peripheral ridge are seen unilaterally on the trunk, limbs, and the heads (**Figure 5**).

Giant porokeratosis of mibelli One patient was reported (2.8%) and seen as solitary plaque attain 15 cm diameter, and with the surrounding margin being elevated about 1 cm (**Figure 6**).

Genital porokeratosis

It was detected in 4 patients (11.4%), all of them were males and all lesions were seen in the genital area only .They were characterised by multiple red papules with red keratotic plaques in 2 patient whilst porokeratosis of mebilli –like lesions seen in 1 patient and hyperkeratotic in 1 patient (**Figure 7**). While no family history of porokeratosis was observed.

The generalized variants

They included 14 patients with the disseminated porokeratosis that accounted for 14 (40%) of porokeratosis, 9 (64%) males, 5(35%) females,

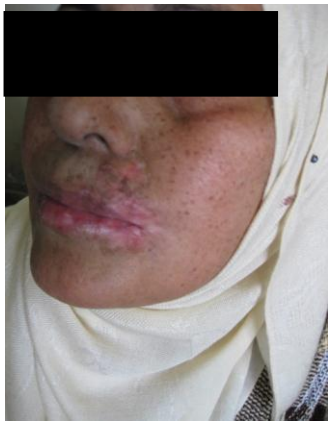

Figure 4 45 years old females showing multiple atrophic palques of lips simulating discoid lupus erythematosus.

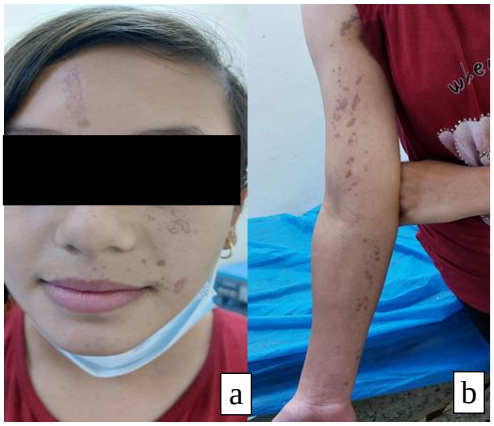

Figure 5 (a,b) 12 year old child with linear arrangement of keratotic papules and plaques with elevated peripheral ridge, some of them form annular plaques unilaterally distributed on the face (a) and limbs (b).

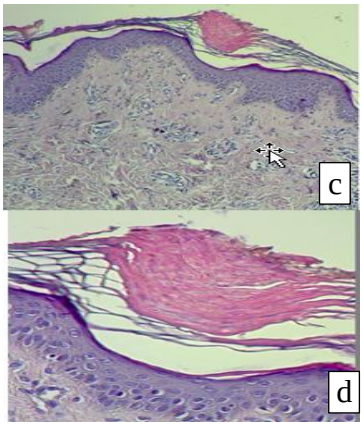

Figure 5 (c,d) Histopathology of linear porokeratosis showing coronoid lamella, basket weave hyperkeratosis,underlying hypogranulosis and dermal perivascular infiltrate.

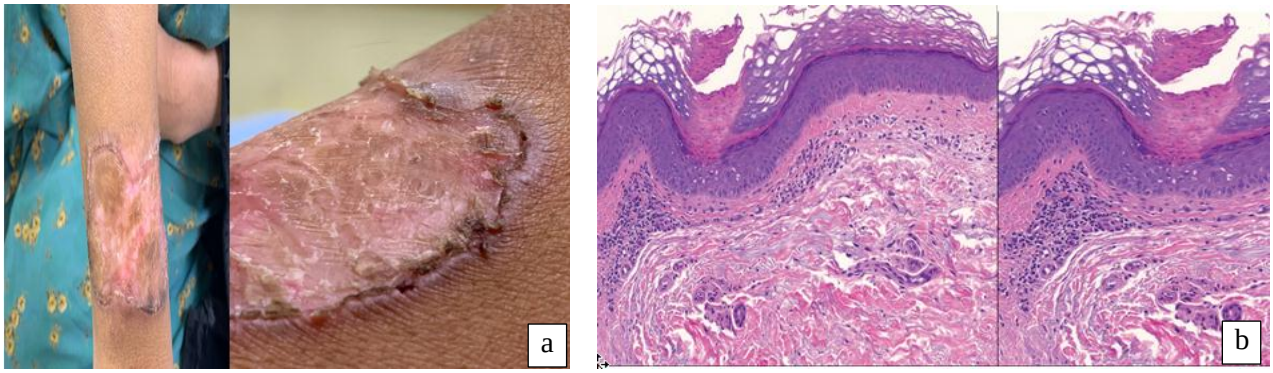

Figure 6 a) Giant porokeratosis of mibelli in 42 y old female characterised by well demarcated solitary plaque on forearm with keratotic border and atrophic border. b) Histopathology of giant porokeratosis of mibelli showing coronoid lamella.

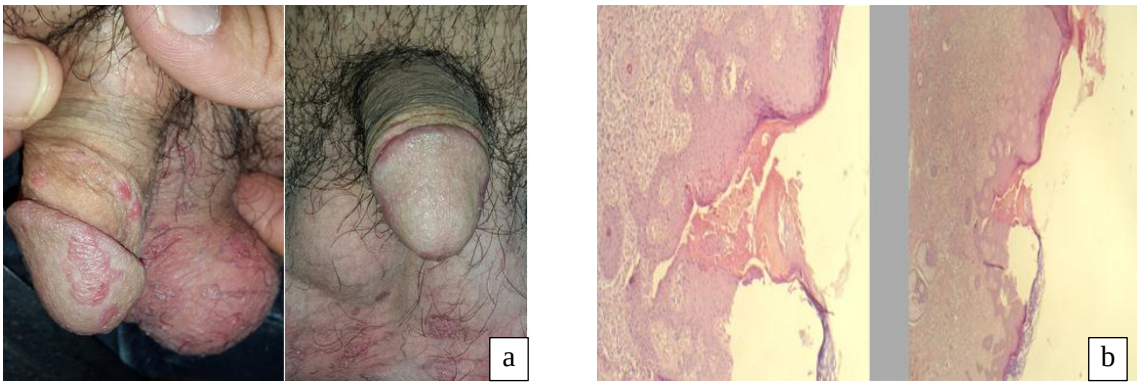

Figure 7 a) Genital porokeratosis in 27 year old male with multiple small and large red thickened papules and plaques involving the penis and scrotum. b) Histopathology of genital porokeratosis showing coronoid lamella with underlying hypogranulosis

with male to female ratio 1.8:1. While family history was found in 4 (11.4%). These patients presented with scaly papules or plaques with a fine, elevated keratotic border. These cases were either bilateral symmetrical generalized (DSP) or on sun-exposed sites (DSAP) (**Figure 8**).

Histopathology of group one porokeratosis

Out of 35 patients, biopsy done for 15 patients and the histopathology of the disease was as follow: the epidermis was acanthotic with basket weave hyperkeratosis or normal thickness, or atrophic. The epidermis invagination by column of keratin reaching epidermal basal layer was observed. There was absence of granular layer at site of invagination. These columns were made of parakeratotic cells, forming a typical picture of cornoid lamella. Many single dyskeratotic cells were observed under the base of lamella reaching almost the basal layer of epidermis. While the dermis containing many dilated blood vessels with marked inflammatory reaction at the base of cornoid lamella that consisted of many lymphoid cellular infiltrate **(Table 2)**.

Group two: Solar facial porokeratosis Eighteen (34%) patients with solar facial porokeratosis

Table 2 Histopathological findings in patients with group one porokeratosis.

Histopathological changes	*frequency*	*%*
Coronoid lamella	18	100
Underlying hypogranulosis	16	88
Dyskeratotic keratinocytes	6	20
Epidermis		
Normal thickness	11	61
Thick	2	11
Thin	6	27
Lymphocytic infiltrate	16	88

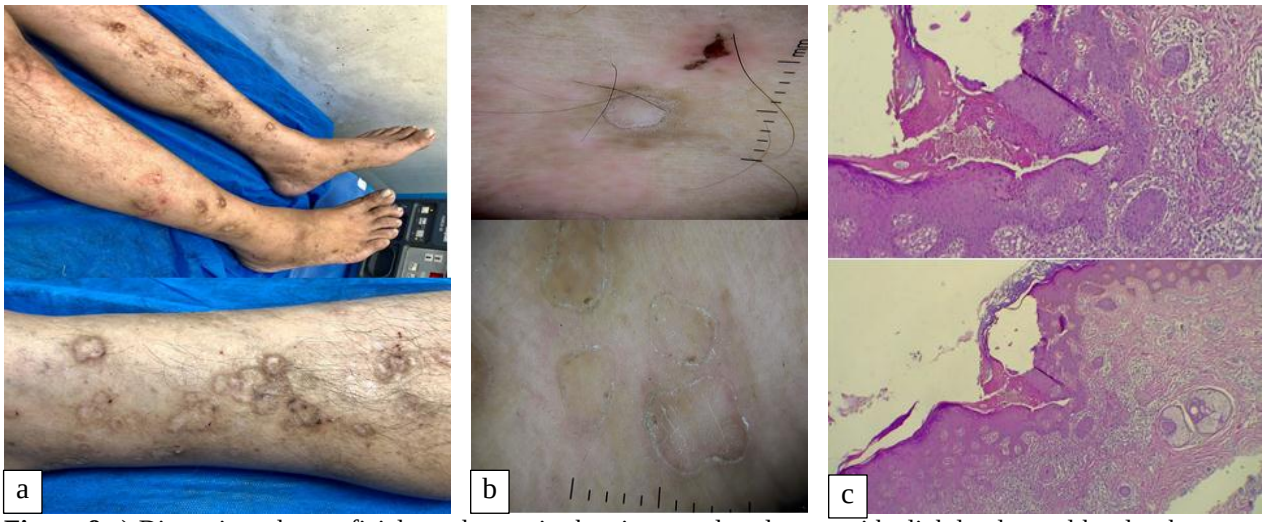

Figure 8 a) Disseminated superficial porokeratosis showing annular plaques with slightly elevated border that was distributed over the trunk and limbs. b) Dermoscopy of disseminated superficial porokeratosis(DSP) showing Peripheral white to brownish scaly rim (*white track") with double white track at some sites of the peripheral rim and homogeneous white-yellowish center. c) Histopathology of DSP Showing coronoid lamella ,hypogranulosis and dermal perivascular infiltrate.

Table 3 Demographic features of patients with solar facial porokeratosis.

Patient dermographic features			*%age*
Age	Range	19–30 y	
	mean±SD	27± 4.4 y	
Sex	Male	10	55.5
	Female	8	44.4
Duration	Range	2–12 y	
	mean±SD	4.1± 2.9 y	

were included, 10 (55.5%) females and 8 (44.4%) male with female to male ratio 1.25:1. The age range was from 19-30 years with a mean and SD of 27±4.4 year. The disease duration ranged from 2–12 year with a mean and SD of 4.1±2.9 year. While history of family was not positive in any patient **(Table 3)**. The patients showed single to multiple, skin colored scaly papules with centrifugal extension forming plaques ranged from 0.1 cm to a few centimeters in size and surrounded by a keratotic rim. The rash was present on the face only, especially on the distal site of the nose and the sites surrounding the nose **(Figure 9)**. The rash number in each patient ranged from 1–18, with a mean±SD of 4.73±4.35. The rash gradually increased in size over time. These porokeratotic lesions were persistent with marked relapse in the summer time while incomplete remission in winter and new rashes were only detected in the season of summer.

Dermoscopic assessment of solar facial porokeratosis revealed yellowish-whitish annular structures surrounding a white –pink scar-like area in the centers of lesions.

Histopathology of solar facial porokeratosis

The histopathological assessment of lesions of solar facial porokeratosis showed characteristic findings of cornoid lamellae, that consisted of epidermal invaginations that filled with parakeratotic columns. The collar of cornoid lamellae of the porokeratosis seen as two parakeratotic horns, that simulate two gazelle horns **(Figure10)**. The parakeratosis often ran over the epidermis that was located between the two orthokeratotic horns that was observed in all patients. The granulosa layers were not detected under the cornoid lamella except in some patients. Perivascular lymphoid infiltrate was observed in the dermis while no other remarkable changes were observed **(Table 4)**.

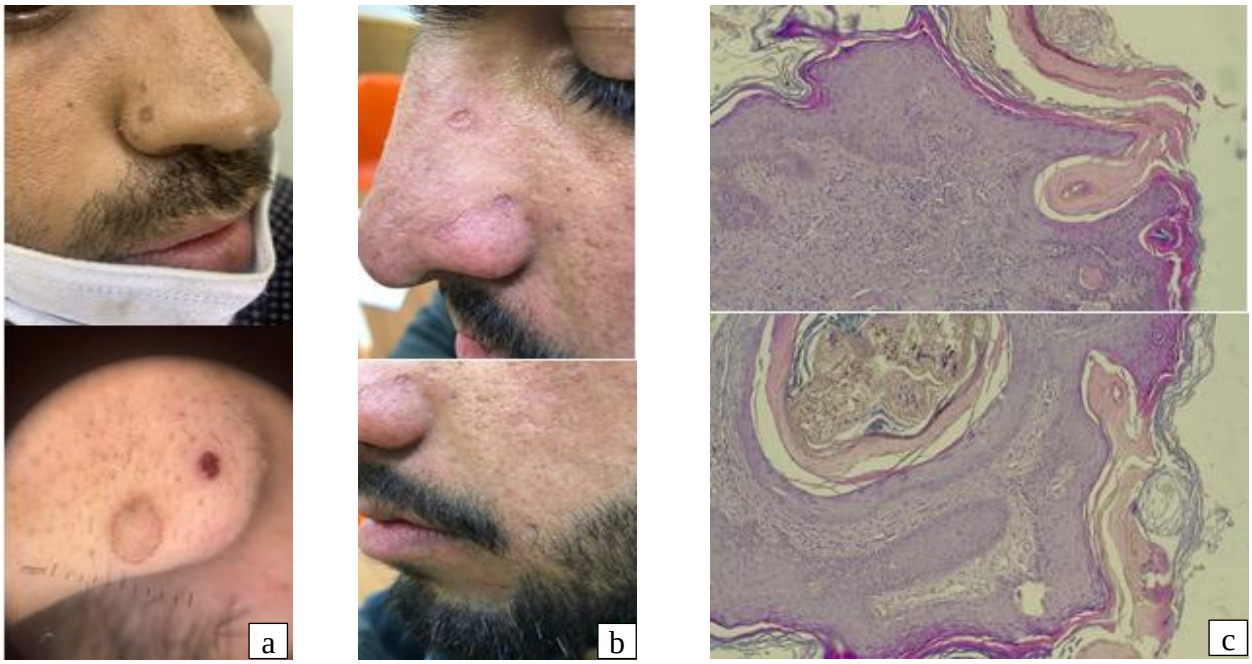

Figure 8 a) Solar facial porokeratosis showing lesions with keratotic collar on the nose and surrounding area in a male patient; Dermoscopy showing keratotic border. b) Solar facial porokeratosis showing lesions with keratotic collar on the nose and surrounding area in a male patient. c) Histopathology of solar facial porokeratosis showing parakeratotic horn-like column simulating the two gazelle horns.

Table 4 Histopathological findings in patients with solar facial porokeratosis.

Histopathological features	*Frequency*	*%*
Coronoid lamella	10	100
Underlying hypogranulosis	8	80
Dermal perivascular Infiltrate	8	80
Follicular distribution of the cornoid lamella	1	10

Discussion

Porokeratosis is a primary disorder of epidermal keratinization of ill-defined etiology and could be classified into generalized and localized forms. The localized forms consisted of porokeratosis of Mibelli, and punctate porokeratosis and linear porokeratosis. The generalized variants consisted of disseminated superficial actinic porokeratosis, disseminated superficial porokeratosis,and disseminated palmoplantar porokeratosis.[1] These forms or variants are more common subtypes of porokeratosis, from which an increasing number of individuals are suffering.[6]

While Porokeratosis seems to be rare problem in Iraqi population and was not documented before although Sharquie *et al.* had reported localized porokeratosis.[18,19]

The present work showed that the commonest type of porokeratosis was porokeratosis of Mibelli (45.7%), followed by disseminated superficial actinic porokeratosis (DSAP) and disseminated superficial porokeratosis (DSP) (40%), genital porokeratosis (21.4%), linear porokeratosis (2.8%), giant porokeratossis (2.8%). while other reported studies had shown that the commonest variants were disseminated superficial actinic porokeratosis; followed by Mibelli, disseminated superficial, linear, palmoplantaris punctata and palmaris, plantaris et disseminata.[21] While porokeratosis palmoplantaris disseminata and Porokeratosis palmaris et plantaris disseminata (PPPD), punctate porokeratosis were not documented in

present study.

Also the old studies have revealed that male patients more commonly suffer from porokeratosis, compared with female patients, and the results from these studies had also shown that Porokeratosis of Mebili is more common in male patients than in female and this may also be true for DSP.[6] These findings are corresponding to our study which showed that porokeratosis frequently seen among males, as out of 35 patients enrolled in the study, 68.5% were males and 11 (31.4%) were females .In addition the result from this study also showed porokeratosis of Mibelli was more common in male (73.3%) than female (26.6%). This is also applicable for DSP as out of 14 patient with DSP 9 (64%) were males while 5 (35.7%) females.

Many familial reports for porokeratosis had been previously published and a large portion of the reports described DSAP in families.[30-32] In addition, it was detected that among the inherited patients of porokeratosis, 66.7% of them was DSAP. Therefore, this does suggest that inheritance may potentially be important in DSAP.[6] This similarly was also seen in present work as all inherited cases was DSP. While porokeratosis of Mibelli, linear porokeratosis, genital porokeratsis may arise in an autosomal dominant form, but more commonly in a random sporadic form.[6,7]

In present work, Porokeratosis of Mibelli was the most common variant account for 42.8% of all cases of porokeratosis, being more prevalent in males, commonly located on the limbs,face followed by trunk and buttocks and the lesions are asymptomatic and persistent. Also the clinical manifestations of porokeratosis of Mibelli generally expanding to include variety of clinical manifestations.[22] The most common presentation that was observed in the, present study, were the classic solitary plaques with a thread-like hyperkeratotic margin as recorded in 73.3% of cases, less common presentations were observed, as 2% cases presented with multiple hypopigmented atrophic facial lesions resembling discoid lupus erythematosus lesions, this was also similarly reported.[22] Another less common presentation was nodular porokeratosis which was confirmed histologically by the presence of multiple coronoid lamellae. Also erythematous hyperchromic plaques with slightly elevated edges and atrophic center located on the hands and feet were seen in the present study and this was similarly reported but involving the face.[22]

In addition, the present work showed linear porokeratosis as unilateral presentation which is identical with Mibelli morphology and these lesions presented as keratotic papules, annular plaques with atrophic canter and hyperkeratotic ridge in a linear distribution and this is similarly reported.[22]

Genital Porokeratosis is a rare condition and commonly seen among Asian poeple.[3-5] Recently, Sharquie *et al.* documented a patient of scrotal porokeratosis, presented with nnumerous papules and plaques and nodules that were distributed over the scrotum but no penile involvement. Some of the lesions were keratotic plaques misdiagnosed as lichen simplex chronicus for years with positive close family history, and associated with itching while the diagnosis was confirmed by histopathologic examination which showed coronoid lamellae.[19] An analysis of all the documented patients of genital porokeratosis (29 cases were seen in Asian population), 26 of them was males,[24] 3 were females.[25-27] While in the present work,4 cases with genital porokeratosis were seen, all of them were males that associated with itching but with negative family history.

In addition, the present work showed that giant porokeratosis is a rare entity and many considered it as a variant of porokeratosis of Mibelli, while other researchers considered it as a separate variant which presents as solitary irregular plaque around 18-20cm in size located on the distal extremities.[28]

Furthermore, Sharquie *et al.* in 2003,[18] described a new entity of porokeratosis so called solar facial porokeratosis among 15 cases with rash exclusively located on the face, mainly nose and adjacent areas around the nose, that induced and exacerbated by exposure to sunlight and observed mainly among young females. Facial solar porokeratosis was considered as a new relatively common variant of porokeratosis that has well distinguished clinical and histopathological features and could be easily separated clinically from other types of porokeratosis.[18] The present work showed similar results as facial solar porokeratosis is a common type of porokeratosis as accounted for 34% of all cases of porokeratosis. Also this present work revealed that this variant of porokeratosis is commonly among young age group, more in females. The lesions are only localized to face and triggered by sunlight exposure. The histopathology was in general similar to other types of porokeratosis. Positive family history was similarly negative. Solar facial porokeratosis was only reported among Iraqi population while no other reports appeared from surrounding middle east countries especially Arabian countries. The reasons behind that could not be established but we can speculate that these cases either not diagnosed or confused with other facial dermatoses. Although facial lesions might be seen in 15% of cases with disseminated superficial actinic porokeratosis, but exclusive face involvement is rarely documented.[29]

Conclusion

Porokeratosis is comprising of a different group of disorders that could be classified into autosomal dominant inheritance fashion and consisted of localized and generalized diseases. While solar facial porokeratosis is non-inherited acquired variant with well distinguished clinical pictures that induced by sunlight exposure and mostly observed in summer time that could be considered as specific variant of porokeratosis. This variant has been only described in Iraq while no reports were appeared from the surrounding and Middle East Countries. The reason behind that either was not recognized or mixed up with other variants of porokeratosis.

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