Int J Clin Exp Pathol 2022;15(2):56-62
www.ijcep.com /ISSN:1936-2625/IJCEP0137713

Original Article

Porokeratosis: a differential diagnosis to consider in benign lichenoid keratosis

Charlotte Foster[1], Ben Tallon[2]

[1]Histopathology Department, Middlemore Hospital, Auckland, New Zealand; [2]Dermatology Division, Department of Anatomical Pathology, Pathlab, 829 Cameron Road, Tauranga 3112, New Zealand

Received July 26, 2021; Accepted October 30, 2021; Epub February 15, 2022; Published February 28, 2022

Abstract: Porokeratosis is a disorder of keratinization with many clinical variants. The histological hallmark feature of porokeratosis is a cornoid lamella. Other accompanying features include lichenoid inflammation, atrophy towards the centre of the lesion, dermal cytoid bodies, and adjacent lichenoid changes. Lichenoid keratosis is a benign cutaneous condition, thought to largely represent a degenerating seborrheic keratosis or solar lentigo. The classical histologic appearances are characterized by parakeratosis, epidermal acanthosis, and a dense band of lichenoid lymphocytic infiltrate. Since a lichenoid inflammatory reaction pattern can be seen in porokeratosis it has the potential to be misdiagnosed as a lichenoid keratosis if the cornoid lamella is not identified or missed due to sampling selection. We critically review 104 cases of benign lichenoid keratosis to establish whether any of these cases had features to support a diagnosis of porokeratosis. With 9.6% of cases considered for re-classification, we review clues to reaching this histologic diagnosis.

Keywords: Anatomy & histology, diagnosis, pathology, dermatopathology, porokeratosis, benign lichenoid keratosis

Introduction

Porokeratosis is a well-described disorder of keratinization. This condition most commonly affects sun-exposed skin of patients in their fifth decade [1]. The male to female ratio is approximately equal [2, 3]. There are numerous clinical types of porokeratosis [2]. Well described variants include disseminated superficial actinic porokeratosis, classical porokeratosis of Mibelli, porokeratosis palmaris plantaris et disseminatum, and linear porokeratosis [2, 4]. There are many additional described variants of porokeratosis, all of which have overlapping features [1]. Porokeratosis can be familial or sporadic, depending on the clinical variant. Disseminated superficial actinic porokeratosis is an inherited autosomal dominant condition and causal genes in the Mevalonate pathway have been identified [5]. Since porokeratosis carries a small risk of transformation to squamous cell carcinoma [2, 6], it is important to diagnose this condition correctly so that appropriate clinical follow up can be arranged.

Porokeratosis has a broad spectrum of clinical presentations. However, the classic clinical presentation of porokeratosis is one or multiple keratotic papules or circular plaques which have an elevated border, typically with a central atrophic area [1, 2]. The lesions may also be pruritic [2].

The histologic hallmark feature of porokeratosis is a cornoid lamella which is present in all variants of porokeratosis [7]. The cornoid lamella consists of a dense column of parakeratosis, an absent or attenuated granular layer, and dyskeratotic keratinocytes [1, 2, 8, 9]. The lamella is angulated so the inferior aspect points away from centre of lesion and the tip is angulated toward centre [9]. The porokeratosis of Mibelli variant of this condition shows epidermal invagination [9]. The cornoid lamella corresponds to the macroscopically seen raised keratotic circular area and is present at the elevated border of the lesion. Although a cornoid lamella is the hallmark feature, it is not pathognomonic of porokeratosis and is present in other conditions [1]. Additionally, the cornoid

lamella may be missed if the peripheral ridge of abnormal keratosis is not sampled [1, 9].

The cornoid lamella may also be accompanied by the following features: atrophy towards the centre of the lesion, lichenoid inflammation, dermal cytoid bodies and adjacent lichenoid changes [1, 2, 8, 9]. Additionally, in sun-damaged skin melanocytic hyperplasia has been reported [10].

Since a lichenoid inflammatory reaction pattern can be seen in porokeratosis it has the potential to be misdiagnosed as lichenoid keratosis if the cornoid lamella is not identified or missed due to sampling selection [1, 8, 9, 11].

Lichenoid keratosis is a benign cutaneous condition, thought to largely represent a degenerating seborrheic keratosis or solar lentigo [12]. Clinically it presents as a single papule or plaque which can be erythematous, and pruritic [13]. The classical histologic appearances are characterized by parakeratosis, epidermal acanthosis, a dense band of lichenoid lymphocytic infiltrate with variable plasma cells, eosinophils, and neutrophils [14].

Recognizing benign lichenoid keratosis and porokeratosis can be difficult clinically and histologically [15-17]. Their differentiation is important, given the small risk of malignant transformation in porokeratosis, and different treatment pathways [18, 19].

The aims of this study were to critically review cases with a diagnosis of 'benign lichenoid keratosis' to establish whether any of these cases had features to support a diagnosis of porokeratosis. To this end, we re-examined 104 surgical skin biopsies within a single general pathology laboratory.

Methods

A search for 'Lichenoid keratosis' on Delphic AP IBM notes was conducted. The authors had consent for data access. This search brought up a list of all the cases which contained the text 'Lichenoid keratosis' within the report. The reports were then reviewed in order of most recent sign out. Any case which had the diagnosis of 'lichenoid keratosis' and was stored on site was chosen for review. 104 cases were selected for review. Four of these cases were from two patients who had two biopsies from different sites.

These 104 cases were reviewed twice using microscopy: initially, by an experienced dermatopathologist. The cases were then reviewed again at a multi-header with a team of four consultant pathologists.

Neither lichenoid keratosis nor porokeratsis have a definitive diagnostic 'gold standard', although the presence of a cornoid lamella is typically considered definitive for porokeratosis. We set diagnostic features for reviewing slides which were as follows:

The presence or absence of a parakeratotic column, underlying dyskeratosis, underlying lichenoid inflammation, atrophy towards the centre of the lesion, dermal cytoid bodies, adjacent lichenoid changes.

A case was initially selected if it contained a parakeratotic column in a pattern suggestive of porokeratosis, with or without the presence of the other supportive features as listed above. These slides were then reviewed again with a team of four pathologists, using the same criteria. Cases designated as eligible for reclassification must have been decided upon unanimously.

Results

Upon initial microscopic ex-amination, 17 cases were thought to show features consistent with porokeratosis. On second review with the team of four consultant pathologists, 10 of the 17 identified cases were regarded as having enough features to be eligible for the re-diagnosis of porokeratosis. Based upon the clinical information obtained from the request form, only one of these 10 cases stated 'porokeratosis' as a possible differential diagnosis. We summarise our results in **Table 1**.

In summary, 10 out of 104 (9.6%) cases on critical review were considered eligible for reclassification from benign lichenoid keratosis to porokeratosis.

Discussion

This study demonstrates that porokeratosis may be overlooked and can go undetected under the diagnosis of 'benign lichenoid keratosis'. It is evident that porokeratosis has the potential to be misdiagnosed as lichenoid keratosis if the cornoid lamella is not identified

Table 1. Diagnostic features present and absent in the 10 cases of revised diagnosis

Number	Sex	Site and nature of excision	Clinical details	Age	Parakeratosis	Dyskeratosis	Lichenoid inflammation	Dermal Cytoid Bodies	Adjacent lichenoid changes
1	M	Excision left thigh	'Atypical nevus/pupuric lesion. Present for 6 months and darkening over time. To exclude malignancy'	35	Y	N	Y	N	Y
2	M	Punch biopsy right supraclavicular fossa	No clinical details supplied	57	Y	Y	Y	Y	N
3	F	Punch biopsy from the left forehead	'Lichenoid keratosis'	38	Y	Y	Y	N	Y
4	M	Punch biopsy lower mid back	'Raised red lesion'	67	Y	Y	Y	Y	Y
5	M	Punch biopsy from left lower arm	'? BCC Lesion'	62	Y	Y	Y	Y	Y
6	F	Skin excision left scapular	'Lesion for analysis'	67	Y	Y	Y	N	Y
7	F	Skin excision left upper arm	No clinical details supplied	61	Y	Y	Y	N	Y
8	F	Punch biopsy distal left forearm (medial)	'flat tan lesions with areas of vascularity'	67	Y	Y	Y	Y	Y
9	F	Shave biopsy left shin	'?porokeratosis/SCC in situ'	66	y	Y	Y	N	Y
10	F	Punch biopsy right anterior thigh	'FHX melanoma-brother. Pink papule, no structures? amelanotic melanoma? compound naevus? dermatofibroma'	56	Y	Y	Y	Y	Y
Total					10/10	9/10	10/10	5/10	9/10

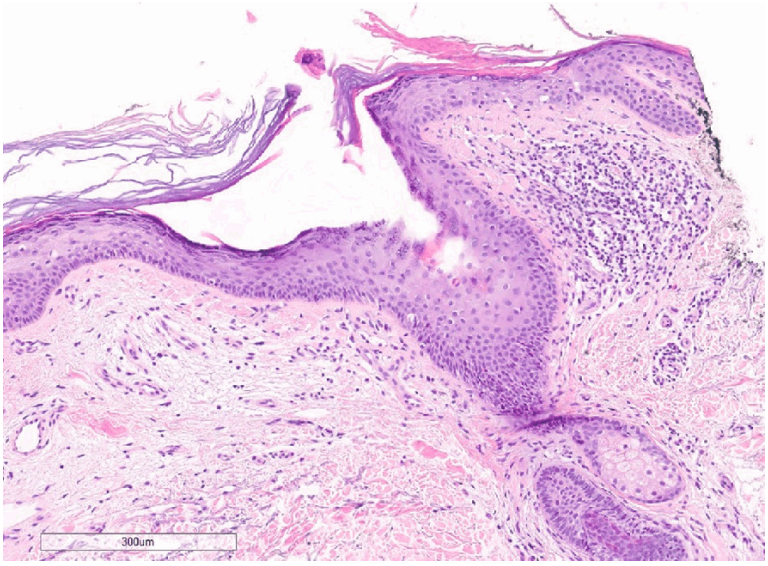

Figure 1. Cornoid lamella. This figure demonstrates a cornoid lamella appearing on the edge of the specimen. This came into view with additional levels. H&E with scale bar 300 μm magnification.

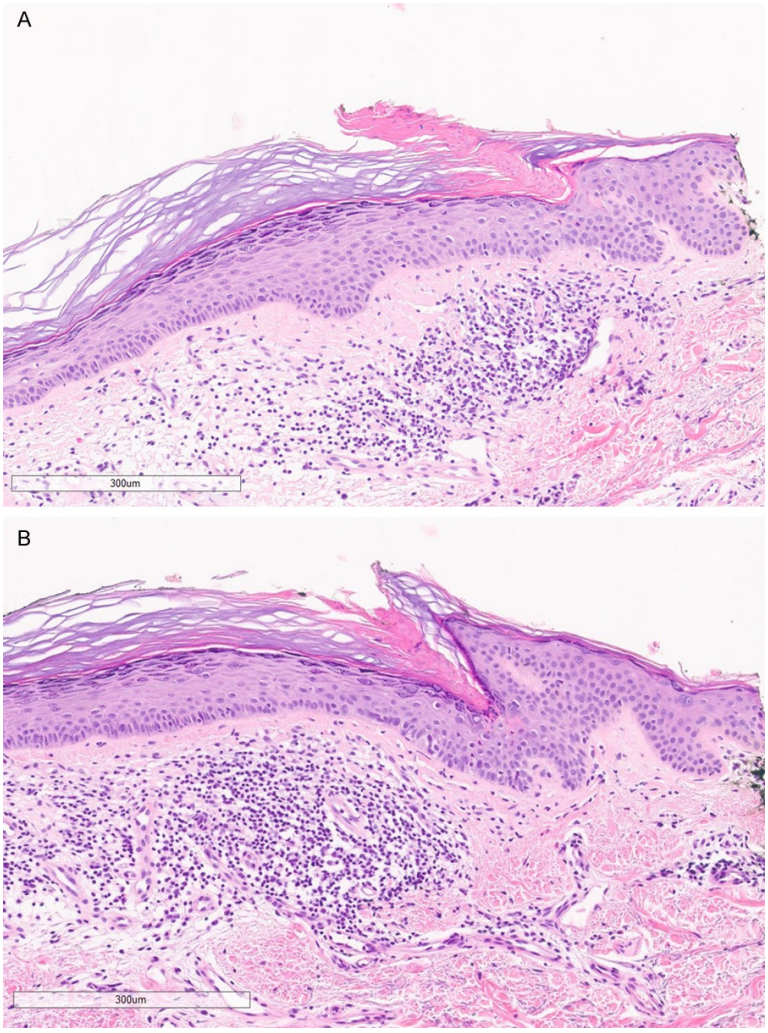

Figure 2. Cornoid lamella migrating across the specimen with deeper levels. A shows a subtle cornoid lamella within the specimen. B shows a deeper level which demonstrates the cornoid lamella cutting into clearer view and migrating across the specimen. H&E with scale bars 300 μm.

or missed due to selective histologic sampling [8, 9]. Additional studies support this conclusion. The *Australian Journal of General Practice* outlines how disseminated superficial actinic porokeratosis is often misdiagnosed as a rash at the clinical level [20]. Joshi and Mesquita [21] outline how histologically it is easy to misdiagnose porokeratosis as interface dermatitis. Their report describes three cases of what appeared to be interface dermatitis without evident cornoid lamellae. The initial diagnoses were: atrophic lichen planus, focal interface-lichenoid dermatitis, and vacuolar interface dermatitis. Deeper sections were performed for all these cases. The deeper levels demonstrated a cornoid lamella and the diagnosis of porkeratosis was then able to be made [21]. Furthermore, Kim et al. [12] report a case of porokeratosis which presented clinically with the appearance of a benign lichenoid keratosis. This further adds to the diagnostic confusion.

As discussed previously, porokeratosis has varied clinical appearances, making the diagnosis difficult. The failure to include porokeratosis in the clinical differential diagnosis can lead to a failure to look for this possibility upon histologic examination. Here we show that the diagnosis of poroker-

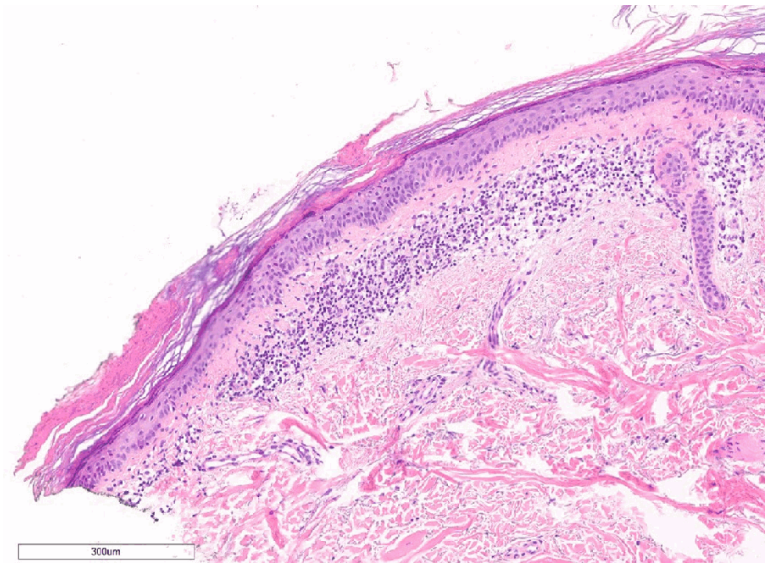

Figure 3. Flattening of the cornoid lamella. A subtle cornoid lamella can be identified in this figure. It is noticeable by the parakeratosis and thinning of the adjacent epidermis. H&E with scale bar 300 μm.

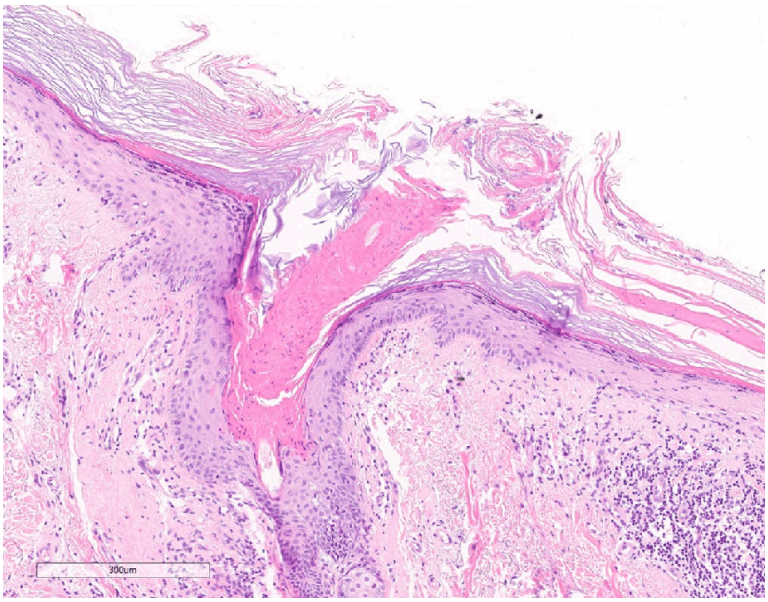

Figure 4. A follicle involved by cornoid lamella. This figure demonstrates how follicular involvement can hide the cornoid lamella. H&E with scale bar 300 μm.

atosis can be overlooked when biopsies are only partially represented on slides. For example, when there is only a subtle or absent cornoid lamella due to incomplete sampling. Such considerations are important factors for making an accurate diagnosis.

On re-review of the cases examined in this study, specific features were identified that helped define porokeratosis. These were as follows:

1. Careful inspection of consecutive levels was helpful in seeing the cornoid lamella cut into view. (**Figure 1**) shows a cornoid lamella appearing on the edge of the specimen.

2. There may be a narrowing or widened gap between possible cornoid lamellae on consecutive sections (**Figure 2**).

3. Areas of thinned epidermis with lichenoid inflammation adjacent to a possible cornoid lamella are a helpful diagnostic clue.

4. The cornoid lamella may also be inconspicuous when significantly flattened (**Figure 3**).

5. Carefully assessing for the presence of dysplasia under a parakeratotic column may also allow a more confident diagnosis of a cornoid lamella.

6. Apoptotic bodies may be present in the superficial dermis.

7. The cornoid lamella may also involve and appear hidden within a follicle. Of interest, this has also been documented in recent literature as a case of porokeratosis with predominant follicular involvement [22]. A cornoid lamella involving a follicle was identified in one of our cases eligible for reclassification (**Figure 4**).

8. The stratum corneum may also be compressed within the lesion or inside the cornoid lamella (**Figure 5**).

In summary, our study of benign lichenoid keratosis showed that when reviewed critically 9.6% of the cases examined had features to support a diagnosis of porokeratosis. This highlights the difficulties in discriminating be-

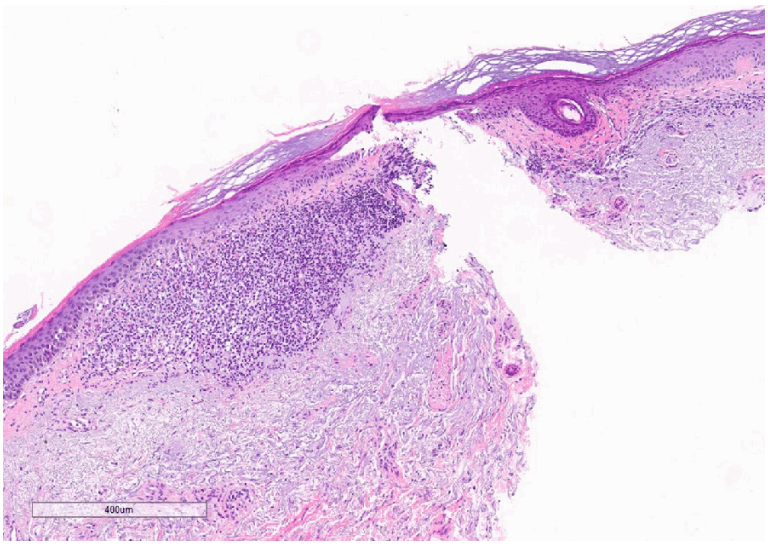

Figure 5. Altered stratum corneum. This figure shows an area of thinned epidermis with lichenoid inflammation adjacent to a potential cornoid lamella. The stratum corneum is compressed inside the cornoid lamella. H&E with scale bar 400 μm.

tween lichenoid keratosis and porokeratosis. We recommend that when making the diagnosis of benign lichenoid keratosis the possibility of porokeratosis should also be considered, and the features listed above taken into account. Specifically; the cornoid lamella may cut in on levels with concentric narrowing or widening. The cornoid lamella may be flattened. Dyskeratosis may be present underlying a parakeratotic column. There is usually intervening lichenoid inflammation and a thinned atrophic epidermis at the centre of the lesion.

Disclosure of conflict of interest

None.

Address correspondence to: Charlotte Foster, Histopathology Department, Middlemore Hospital, Auckland, New Zealand. Tel: +64-7-578-7073; E-mail: charlotte.foster@doctors. org.uk

References

[1] Patterson JW. Weedon's skin pathology. Forth edition. Elsevier; 2016.
[2] Kanitakis J. Porokeratoses: an update of clinical, aetiopathogenic and therapeutic features. Eur J Dermatol 2014; 24: 533-544.
[3] Williams GM and Fillman EP. Porokeratosis. StatPearls [internet]. Treasure Island (FL): StatPearls Publishing; 2021.
[4] McKee PH, Calone E and Granter SR. Pathology of the skin (Third edition). Elsevier; 2005.
[5] Zhang Z, Li C, Wu F, Ma R, Luan J, Yang F, Liu W, Wang L, Zhang S, Liu Y, Gu J, Hua W, Fan M, Peng H, Meng X, Song N, Bi X, Gu C, Zhang Z, Huang Q, Chen L, Xiang L, Xu J, Zheng Z and Jiang Z. Genomic variations of the mevalonate pathway in porokeratosis. Elife 2015; 4: e06322.
[6] Sasson M and Krain AD. Porokeratosis and cutaneous malignancy. A review. Dermatol Surg 1996; 22: 339-342.
[7] Elston DM and Ferringer T. Pathology of the skin (3rd edition, 2005). Elsevier; 2005.
[8] Hamodat M. Porokeratosis. Pathologoutlines.com Website 2011; https://www.pathologyoutlines.com/topic/skinnontumorporokeratosis.html.
[9] Collins GR, Susa J and Cockerell CJ. Porokeratosis. ExpertPath App 2021; [https://app.expertpath.com/document/porokeratosis/8fca42b42-45a44b-482f-a118-486a666daee745?searchTerm=porokeratosis].
[10] Tan TS and Tallon B. Pigmented porokeratosis. A further variant? Am J Dermatopathol 2016; 38: 218-221.
[11] Tumminello K, Cochran CA and T BR. Online pearls: the appearance or disappearance of the cornoid lamella due to level and direction of sectioning in porokeratosis. J Am Acad Dermatol 2020; [Epub ahead of print].
[12] Kim MS, Ha KM, Cho EB, Park EJ, Kim KH and Kim KJ. Porokeratosis presenting with a benign lichenoid keratosis-like appearance. Ann Dermatol 2015; 27: 778-779.
[13] Berger TG, Graham JH and Goette DK. Lichenoid benign keratosis J Am Acad Dermatol 1984; 11: 635-638.
[14] Morgan MB, Stevens GL and Switlyk S. Benign lichenoid keratosis: a clinical and pathologic reappraisal of 1040 cases. Am J Dermatopathol 2005; 27: 387-392.
[15] Mazzilli S, Cosio T, Campione E, Gonzalez S, Lanna L, Di Prete M, Velasco V and Bianchi L. Lichenoid keratosis: a clinical trap without secrets for reflectance confocal microscopy. Case Rep Dermatol 2020; 12: 47-51.

[16] Liopyris K, Navarrete-Dechent C, Dusza SW, Marghoob AA, Deng L, Wilson BB and Marchetti MA. Clinical and dermoscopic features associated with lichen planus-like keratoses that undergo skin biopsy: a single-center, observational study. Australas J Dermatol 2019; 60: e119-e126.
[17] Zaar O, Polesie S, Navarrete-Dechent C, Errichetti E, Akay BN, Jaimes J, Cabo H, Cohen Sabban E and Paoli J. Dermoscopy of porokeratosis: results from a multicentre study of the International Dermoscopy Society. J Eur Acad Dermatol Venereol 2021; 35: 2091-2096.
[18] Weidner T, Illing T, Miguel D and Elsner P. Treatment of porokeratosis: a systematic review. Am J Clin Dermatol 2017; 18: 435-449.
[19] BinJadeed H, Aljomah N, Alsubait N, Alsaif F and AlHumidi A. Lichenoid keratosis successfully treated with topical imiquimod. JAAD Case Rep 2020; 6: 1353-1355.
[20] Ng D and Brand R. A precancerous skin lesion that is often misdiagnosed. Aust J Gen Pract 2019; 48: 765-768.
[21] Joshi R and Mesquita L. Interface dermatitis without cornoid lamellae is a pitfall in the diagnosis of porokeratosis: a report of three cases. Indian J Dermatol Venereol Leprol 2016; 82: 70-72.
[22] Geat D, Tonin B, Colato C and Girolomoni G. A case of porokeratosis with predominant follicular involvement. G Ital Dermatol Venereol 2020; 156: 619-620.