An unusual case of generalized hyperkeratotic and verrucous porokeratosis

Johann de Wet, MBChB, MMed(Derm), MMed(Skin Cancer), FCDerm, CCFP,[a]
Minette Swart, MBChB, FCDerm,[a] H. Francois Jordaan, MBChB, MMed(Derm), M Acad SA,[a]
Johann W. Schneider, MBChB, MMed(Anat Path), FCPath(SA) Anat,[b] Suzanne Mulder, MBChB,[a] and
Willem I. Visser, MBChB, MFamMed, MMed(Derm)[a]
Cape Town, South Africa

Key words: acitretin; generalized; hyperkeratotic; porokeratosis; verrucous.

INTRODUCTION

Porokeratosis represents a heterogeneous group of hereditary and acquired disorders of clonal hyperproliferation of keratinocytes.[1] Numerous clinical variants of porokeratosis have been described, including a rare hyperkeratotic variant.[1,2] We report an unusual case of generalized hyperkeratotic and verrucous porokeratosis associated with immunosuppression.

CASE REPORT

A 40-year-old man with Fitzpatrick skin type 2 presented with an 8-year history of pruritic, debilitating skin lesions affecting most of his body. The lesions started out as small wart-like papules on his chest that progressed into verrucous plaques and gradually spread to the rest of his trunk, extremities, and face. Because of the restrictive nature of the lesions, he lost function of his hands and was unable to work.

His medical history was significant for HIV disease, which was diagnosed at the age of 28. He was started on antiretroviral therapy (ART) 4 years after diagnosis but defaulted treatment after only 1 year.

The patient reported a history of intravenous drug abuse as well as significant occupational and recreational ultraviolet radiation exposure. He reported no constitutional symptoms, and his family history was noncontributory.

Physical examination found widespread, symmetrical, hyperkeratotic, verrucous plaques (Fig 1). He had universal scarring alopecia (Fig 2, *A* to *C*), ocular ectropion, and numerous filiform hyperkeratotic lesions on his chin (Fig 2, *G*). Additional features included onychogryphosis and palmar keratoderma (Fig 2, *D*). His feet were the only areas with normal skin, displaying primary lesions comprising erythematous plaques with raised thread-like scaling borders (Fig 2, *E*). His mucous membranes were spared.

Abbreviations used:

ART: antiretroviral therapy
HPV: human papilloma virus

Laboratory investigations found an iron deficiency anemia. Hepatitis B and C and autoimmune screens were negative, and a comprehensive metabolic screening was normal. An age-appropriate cancer screen did not find an underlying malignancy. His CD4 count was 198 cells/mm^3.

Histologic examination of biopsies taken from the hyperkeratotic border of lesions on his chest and thigh found irregular acanthosis and papillomatosis as well as several large broad cornoid lamella characterized by vertical columns of parakeratosis with underlying marked diminution of the granular layer and dyskeratosis and vacuolisation of keratinocytes in the stratum spinosum. The epidermis between cornoid lamella showed a relatively normal granular layer and basket weave and lamellar orthokeratosis. The papillary dermis displayed perivascular lymphocytes and the reticular dermis showed variable fibrosis (Fig 3).

From the Division of Dermatology, Department of Medicine[a] and the Division of Anatomical Pathology,[b] Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Academic Hospital.

Funding sources: None.
Conflicts of interest: None disclosed.

Correspondence to: Johann de Wet, MBChB, MMed(Derm), MMed(Skin Cancer), FCDerm, CCFP, Division of Dermatology, Department of Medicine, University of Stellenbosch and Tygerberg Academic Hospital, PO Box 19063, Tygerberg 7505, Cape Town, South Africa. E-mail: dewetjohann@yahoo.com.

JAAD Case Reports 2020;6:925-30.
2352-5126

https://doi.org/10.1016/j.jdcr.2020.07.017

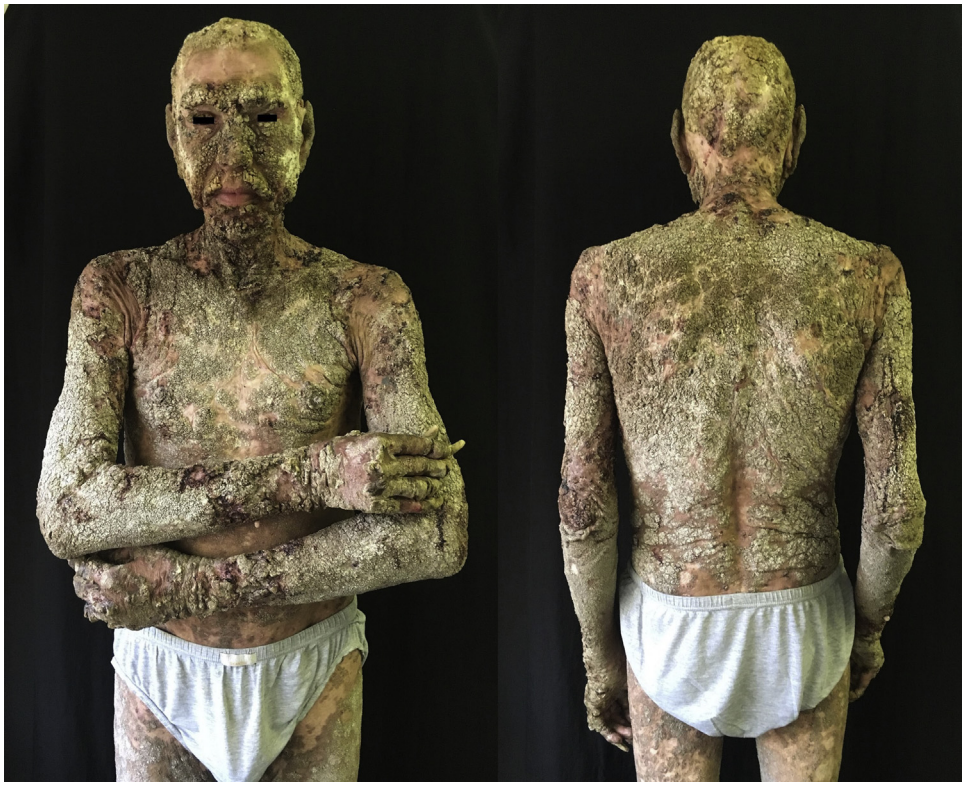

Fig 1. Generalized hyperkeratotic plaques affecting more than 90% body surface area.

A biopsy of a chronic ulcer on his right calf found organizing chronic inflammation with fibrosis and scarring of the underlying dermis. Malignancy was absent.

Immunohistochemical stains for human papilloma virus (HPV) and polymerase chain reaction HPV genotyping, performed on sections from the skin biopsy, were negative. A clinicopathologic diagnosis of generalized hyperkeratotic and verrucous porokeratosis was made.

The patient started on oral acitretin, 25 mg/d and received counselling about sun protection. Local-first line ART (efavirenz/tenofovir/emtricitabine) was reintroduced together with trimethoprim/sulfamethoxazole. After 16 weeks of treatment, the skin lesions showed marked improvement with clearing of a large area of body surface but with underlying scarring. New lesions were absent, and the pruritus resolved. The patient regained function of his hands (Fig 4). After 1 year of treatment, the patient's skin was clear of any hyperkeratotic and verrucous lesions and the acitretin was discontinued. His CD4 count remained low at 185 cells/mm^3 despite his compliance with ART. At his most recent assessment (18 months since his first presentation), his skin showed no signs of recurring lesions (Fig 5).

DISCUSSION

Since Degos' description of the hyperkeratotic variant of porokeratosis in 1953,[3] various case reports documented significant variation in the clinicopathologic features of hyperkeratotic porokeratosis.[4-7] The current case is unusual compared with previous reports, given the generalized verrucous hyperkeratotic lesions affecting more than 90% of the body surface area.

The classic lesions of porokeratosis comprise keratotic papules, which spread centrifugal to form annular plaques with raised keratotic borders. The history of lesion progression and the morphology of the primary lesions on the patient's feet led to the diagnosis of porokeratosis. A biopsy taken from the lesions showed a cornoid lamella, the histologic hallmark of the disorder, confirming the diagnosis.

A cornoid lamella is a morphologic reaction pattern that may rarely be associated with a variety of conditions such as viral warts, actinic keratosis, some ichthyoses, epidermodysplasia verruciformis and nevoid hyperkeratosis.[1,2,8] These conditions were ruled out on clinical and histologic grounds. In particular, the absence of hypergranulosis, koilocytes and parakeratosis in conjunction with the absence of demonstrable HPV by immunohistochemistry and

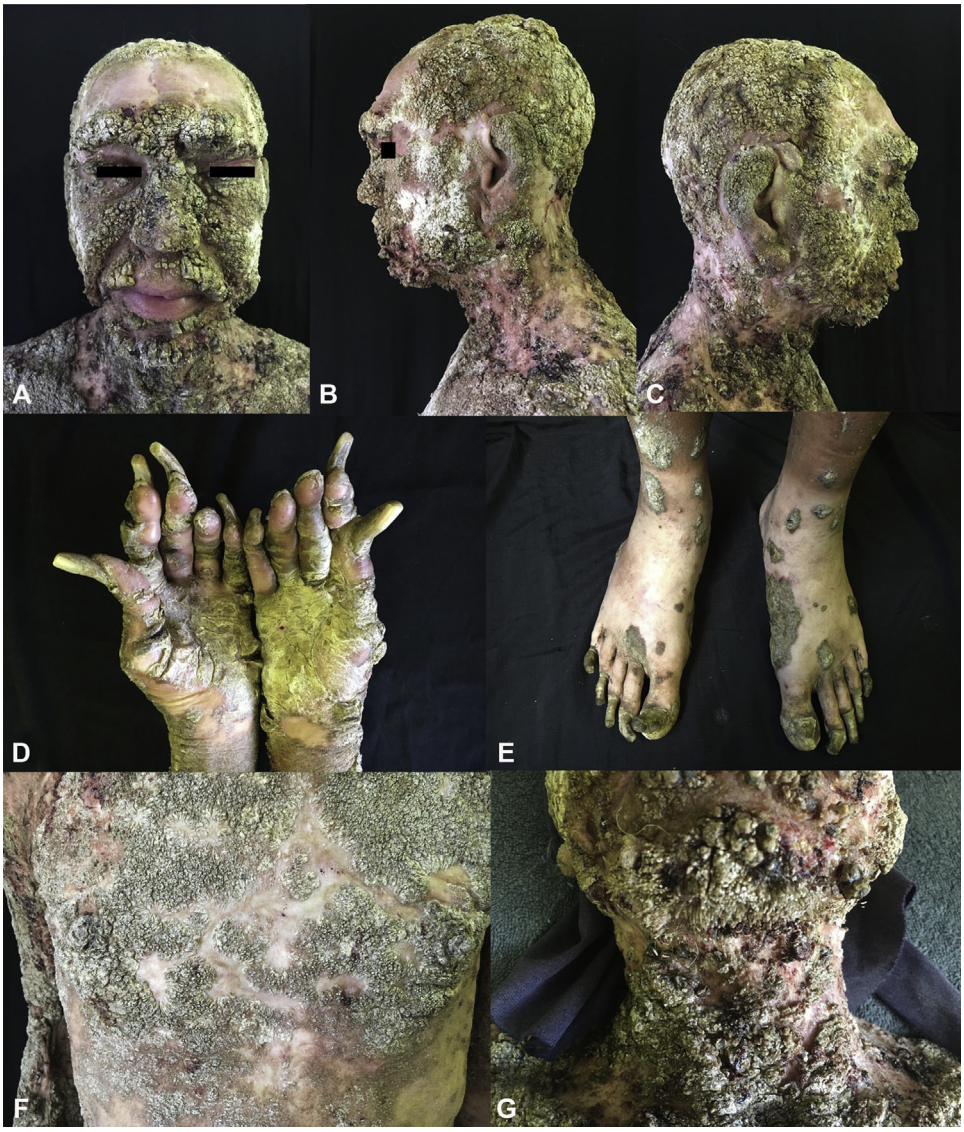

Fig 2. **A** to **C**, Hyperkeratotic and verrucous plaques affecting the head and neck area with associated universal scarring alopecia and ocular ectropion. **D**, Onychogryphosis and palmar keratoderma. **E**, His feet displayed primary lesions comprising erythematous plaques with raised thread-like scaling borders. **F**, Hyperkeratotic plaques first appeared on his chest and then spread to the rest of his body. **G**, Numerous filiform hyperkeratotic lesions on his chin.

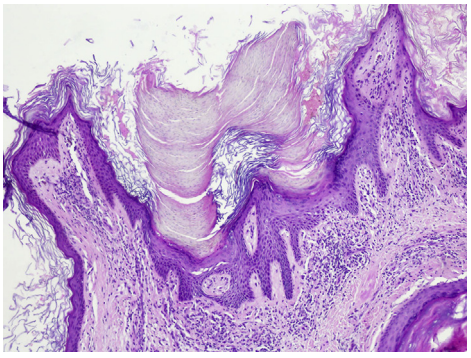

Fig 3. Biopsies taken from the hyperkeratotic border of lesions on his chest and thigh show irregular acanthosis and papillomatosis and several large broad cornoid lamella, characterized by vertical columns of parakeratosis, marked diminution of the granular layer, and dyskeratosis and vacuolisation of keratinocytes in the stratum spinosum.

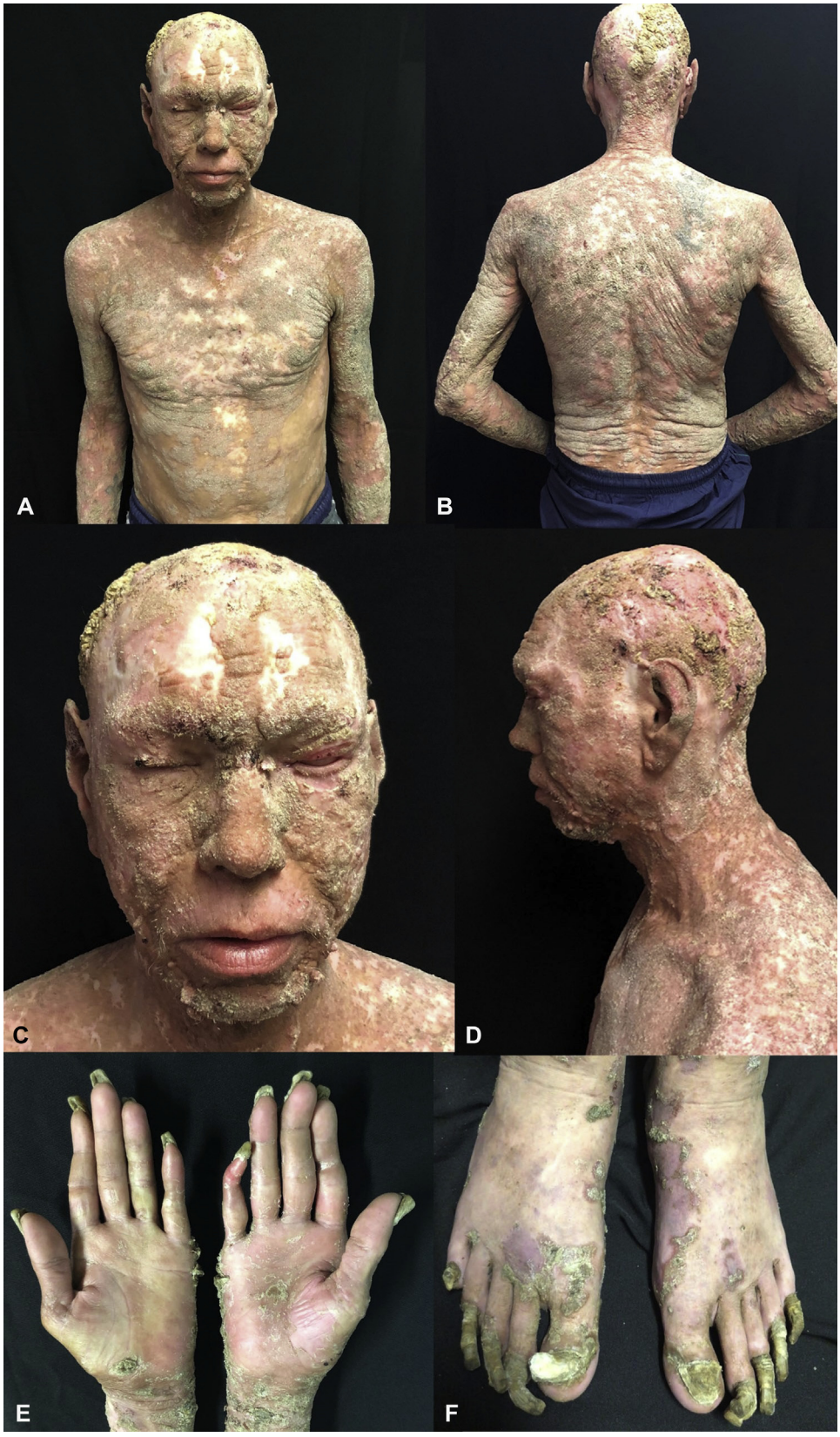

Fig 4. The patient showed a dramatic response to oral acitretin after 16 weeks of treatment.

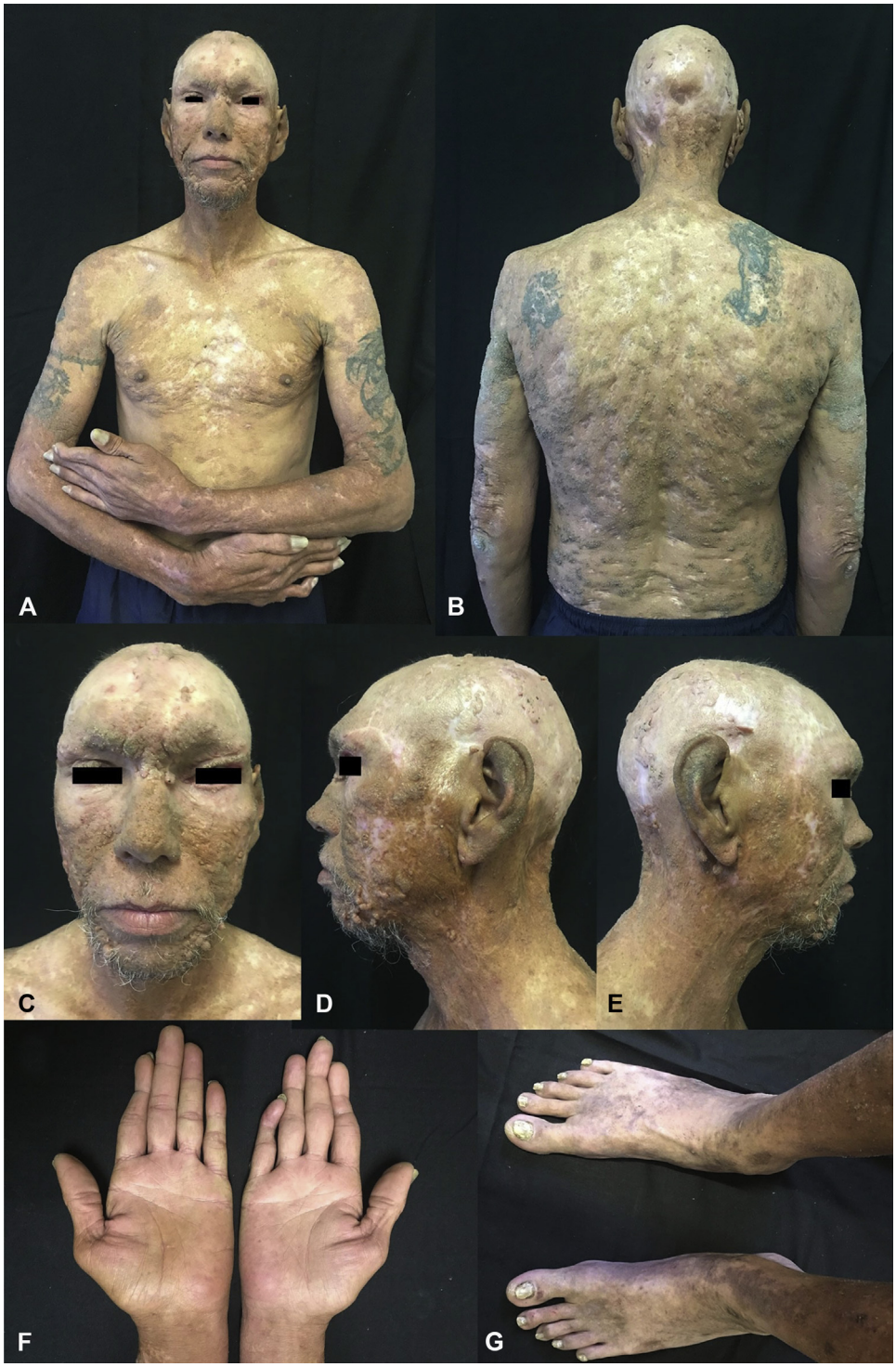

Fig 5. After 18 months, the patient's skin showed signs of scarring but no recurring hyperkeratotic or verrucous lesions.

polymerase chain reaction militates against an associated HPV infection.

The pathogenesis of porokeratosis is not fully elucidated, but a clonal proliferation of abnormal epidermal keratinocytes is believed to account for the clinical manifestations of the disease. A variety of factors may be potential contributors, including genetic susceptibility, ultraviolet radiation and immunosuppression.[1,6,9]

Inherited or sporadic genetic defects play an important role in porokeratosis with mutations in

the mevalonate pathway genes reported in most cases.[9] Genetic testing was unfortunately not undertaken in our patient because of resource constraints.

Acquired immune deficiency is a well-established risk factor for porokeratosis development and accounts for up to 50% of new cases.[1] The combination of hyperkeratotic porokeratosis and HIV infection has been described in 1 other case report in the literature. This patient was also positive for hepatitis C that was excluded in the current case.[6]

Exposure to ultraviolet radiation is a well-described trigger for the development of porokeratosis and significantly contributed to the pathogenesis of the current patient's skin lesions, given his history of occupational sun exposure for most of his life without the necessary sun protection.[1]

A review on disseminated eruptive porokeratosis by Shoimer et al[10] reported that 30% of patients had an underlying malignancy. Age-appropriate cancer screening in our patient ruled out underlying malignancy.

Porokeratosis can be a premalignant condition. Malignant transformation to Bowen disease, squamous cell carcinoma, and basal cell carcinoma has been reported in up to 7.5% of cases.[11] Our patient did have significant risk factors for malignancy including chronic ultraviolet radiation exposure, immunosuppression, long history of the lesions, and significant size and distribution of the porokeratosis. Biopsies of areas suspicious for malignancy excluded neoplastic transformation.

The patient significantly improved on oral Acitretin, ART and, trimethoprim/sulfamethoxazole. The rationale for using systemic aromatic retinoids was based on previous case reports and the postulation that it seems to ameliorate keratinization and hinder proliferation of the mutant parakeratotic cells at the cornoid lamella. This agent may also inhibit tumour angiogenesis.[7,12]

The patient's CD4 count did not increase over the course of 1 year; therefore, we cannot conclude that an improvement in the patient's immune function was responsible for the improvement in skin lesions.

At the time of writing this report, the patient was compliant with his ART and he had no recurring hyperkeratotic and verrucous skin lesions. The patient will continue regular follow-up for cancer surveillance. This case report emphasises the importance of clinical awareness and early diagnosis of rare variants of porokeratosis, the value of skin biopsies to support the diagnosis, and the therapeutic value of acitretin.

REFERENCES

1. Sertznig P, von Felbert V, Megahed M. Porokeratosis: present concepts. *J Eur Acad Dermatol Venereol*. 2012;26(4):404-412.
2. Biswas A. Cornoid lamellation revisited: apropos of porokeratosis with emphasis on unusual clinicopathological variants. *Am J Dermatopathol*. 2015;37(2):145-155.
3. Degos R, ed. *Dermatologie*. Paris: Flammarion; 1953;669a-669l.
4. Yu HJ, Park KT, Oh DH, et al. A case of the hyperkeratotic variant of porokeratosis of Mibelli. *J Dermatol*. 2006;33:291-294.
5. Inazawa M, Satoh T, Yokozeki H. Hyperkeratotic variant of inflammatory disseminated superficial porokeratosis with lichenoid reaction and extensive amyloid deposition. *Int J Dermatol*. 2013;53(2):e94-e95.
6. Parekh V, Kabihting FD, Junkins-Hopkins JM. Hyperkeratotic variant of porokeratosis in a patient with Hepatitis C virus infection and a concomitant immunosuppressed state. *Dermatol Online J*. 2015;21(11):13030/qt2sc54934.
7. Uusküla A, Erm T. Disseminated giant hyperkeratotic porokeratosis and treatment with acitretin: a case report. *Acta Derm Venereol*. 2015;95(2):241-242.
8. Champagne C1, Moore L, Reule R, et al. Cornoid lamella-like structures in HIV-associated epidermodysplasia verruciformis: a unique histopathologic finding. *Am J Dermatopathol*. 2015;37(12):929-932.
9. Leng Y, Yan L, Feng H, et al. Mutations in mevalonate pathway genes in patients with familial or sporadic porokeratosis. *J Dermatol*. 2018;45(7):862-866.
10. Shoimer I, Robertson LH, Storwick G, Haber RM. Eruptive disseminated porokeratosis: a new classification system. *J Am Acad Dermatol*. 2014;71(2):398-400.
11. Vence L, Thompson CB, Callen JP, Brown TS. Giant porokeratosis with malignant transformation to squamous cell carcinoma. *Dermatol Surg*. 2018;44(4):580-581.
12. Weidner T, Illing T, Miguel D, Elsner P. Treatment of porokeratosis: a systematic review. *Am J Clin Dermatol*. 2017;18(4):435-449.