Giant Ulcerating Squamous Cell Carcinoma Arising From Linear Porokeratosis: A Case Study

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Abstract
Linear porokeratosis is one of the infrequent variants of porokeratosis, a rare disorder of keratinization that may develop into several epidermal malignancies, among them squamous cell carcinoma. Clinical surveillance for malignancy is imperative, but in cases when large or many lesions are present, surgical removal of porokeratosis lesions would result in an unfavorable amount of scarring. A case of a large, nonhealing full-thickness ulcer caused by a giant ulcerating squamous cell carcinoma occurring within lesions of long-standing linear porokeratosis is reported in a 43-year-old woman with a recent diagnosis of ulcerative colitis (UC). Wide excision of the ulcer and plastic surgical reconstruction of the area were performed. PET scans did not show metastases, so her prognosis is good based on definitive excision of the tumor. Physicians should be aware of this cutaneous disease and the importance of annual follow-up for these patients to monitor for any lesion that exhibits clinical features concerning for malignancy.

Keywords: case study, porokeratosis, squamous cell carcinoma, skin ulcer, treatment

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Porokeratosis (PK) is a group of disorders of keratinization that usually present early in life as well-defined hyperpigmented macules or patches with a distinctive, typically raised, ridge-like hyperkeratotic border histologically characterized by a cornoid lamella. Linear PK is a rare form of porokeratosis that usually presents unilaterally with grouped characteristic lesions following the lines of Blaschko (see Figure 1). The condition affects fewer than 20,000 people in the US population and accounts for 13% of cases of PK. Other variants of PK include disseminated superficial actinic (the most common type, accounting for 42% of cases, most commonly seen in women in their third to fourth decade of life and involving sun-exposed areas such as arms, legs, shoulders, and back; it spares palms and soles); the classic plaque form of Mibelli (the second most common type, accounting for 35.5% of cases, presenting typically in young boys with a large lesion on an extremity and associated with immunosuppression); and plantaris palmaris et disseminata and puncutuate PK (less common type occurring in 9.7% of cases and presenting on palms and soles). Simultaneous presentation of several types of PK can occur but is seldom reported.

Although progression to malignancy is rare, it can occur in all types of PK; linear PK is the most common subtype susceptible to malignant degeneration. The role of heredity. Inherited or sporadic genetic defects likely play an important role in the pathogenesis of PK. The mutations causing the inherited form of linear PK are either postzygotic novel heterozygous mutation or loss of heterozygosity for the same allele. The later mutation carries a more severe clinical presentation. Particularly, linear PK is usually sporadic with no definitive pattern of inheritance, but because linear PK has been reported concomitantly with disseminated superficial and disseminated superficial actinic PK, which are inherited in an autosomal dominant fashion types, it has been hypothesized that linear PK may be a mosaic form of these conditions.

Diagnosis. The diagnosis of all types of PK is typically
PoroKeratosis and CarCinoma

based on clinical examination. The presence of a flat, discolored, discrete lesion with a well-defined, elevated border suggests this disorder. Histopathologically, PK is characterized by a column of tightly fitted parakeratotic cells with pyknotic basophilic nuclei. This histopathologic feature (cornoid lamella), which correlates to the raised hyperkeratotic border, is observed at the periphery of the lesion.

Differential diagnosis of linear PK includes linear verrucous epidermal nevus, lichen striatus, incontinentia pigmenti, linear lichen planus, linear Darier disease, and warts.11

Malignancy. A review9 of cases and case series in the literature show linear PK has approximately 19% chance of malignant transformation compared to approximately 7% to 11%5 in other types of PK. The most common malignancy is squamous cell carcinoma (SCC) (in situ and invasive), followed by basal cell carcinoma (BCC). The exact mechanism by which malignant degeneration develops in PK is not yet completely understood, but a genetic mechanism of allelic losses at an early stage of embryonic development has been suggested.5 Moreover, experimental research has proposed a role of the tumor suppressor gene p53 in the pathogenesis of all types of PK, because an overexpression of this gene has been demonstrated in these conditions through immunohistochemical studies12,13 using immunoperoxidase-stained antibody directed against the P53 protein. Malignancy can occur following p53 gene inactivation resulting from mutation and/or loss of function. Interestingly in PK, gene alterations have not yet been detected; thus, it is hypothesized the alteration might be at the protein level.14

Unrepaired ultraviolet (UV)-induced DNA lesions are directly responsible for p53 mutations in human BCCs and SCCs in a case review.14 However PK-derived malignant lesions seem to have an increased occurrence in nonexposed skin, correlating with the results of a study in which no relation was found between UV exposure and the increased expression pattern of p53.14 Despite this, one of the consistently described risk factors for malignancy in PK is sun exposure. Other predisposing factors include exposure to ionizing radiation, the presence of extensive lesions, long duration of the lesion, and immunosuppression.2,14

Microscopically, keratinocytes from the center of the lesions display the same staining patterns as those observed in other premalignant lesions, such as actinic keratoses and SCCs.9 Furthermore, keratinocytes with abnormal DNA are noted under the cornoid lamella, which is a sensitive marker of premalignant conditions. This correlates with the stronger expression of p53 in this location.

Treatment. Treatment of malignancies associated with PK may require micrographic surgery in addition to standard surgical and plastic surgery procedures in order to disconnect the tumor from its porokeratotic source.7 Similar to cutaneous SCC unrelated to PK, the majority of SCCs that develop within lesions of PK are successfully treated with local therapy. However, several cases of metastatic SCC arising in the setting of PK have been reported.15 Prognosis and recurrence depend on the success of initial treatment.

Case Report
Ms. P, a 43-year-old woman, presented to the authors’
wound care clinic with a painful, burning, and progressively worsening nonhealing wound on her left buttock of 4 years’ duration. Her past medical history included a lifelong history of linear PK and a more recent (2 years before presentation) diagnosis of ulcerative colitis (UC). Initially believing the chronic, nonhealing wound was of benign etiology, Ms. P’s clinicians treated her with multiple (unsuccessful) topical therapies, including antimicrobial silver-containing foams and creams and absorbent polymer gel pads, among others. She also received a 2-year course of prednisone (10 mg daily) for the treatment of her UC that seemed to improve the appearance and symptoms of the ulcer. She was not taking any other medications at the time.

Physical examination of the left buttock abutting the gluteal cleft showed a 9 cm x 4.5 cm ulcer with red, exuberant granulation tissue (see Figure 2). Below the ulcer, in a linear pattern reaching the foot, clinicians found well-demarcated, slightly atrophic, rough, brown confluent macules delineated by a distinct raised erythematous to brown border (see Figure 3). Four years prior, a biopsy from the center of the acute ulceration at that time reported characteristic features of PK, leading to the clinical assumption it was an ulcerating form of this condition. A new biopsy of the ulcer bed, performed at the time the patient was seen in the authors’ clinic, found ulcerating SCC. Work-up for malignancy included a CT scan of the chest that was negative and a positron emission tomography, which detected a suspected focus of activity in the ipsilateral inguinal lymph nodes; subsequent biopsy did not demonstrate metastatic disease. Ms. P was referred to plastic surgery and shortly after underwent complete excision of the ulcer with preservation of the muscle and reconstructive surgery of the left gluteal area. She then had an uneventful postsurgical recovery with complete healing of surgical wounds and successful cosmetic results. No recurrence has occurred to date.

Discussion
This case depicts a classic presentation of linear PK with malignant transformation that went undiagnosed and became an extensive malignant ulceration that required major surgical repair. Physicians and other clinicians including wound care specialists should be aware of the malignant potential of this condition.

Conclusion
Linear PK presents an increased oncogenic potential. Its characteristic cornoid lamella appears to occur from a mutant group of anomalous keratinocytes, and the frequency of p53 mutations increases with the severity of the atypia. Linear PK is diagnosed clinically, due to the characteristic features of the lesions; however, histology can guide the diagnosis when equivocal. Linear PK should be considered a pre-malignant condition that requires continuous observation for early detection of malignant transformation and therefore avoidance of progression of the malignancy or development of metastatic disease.

References
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