Pigmented Squamous Cell Carcinoma Presenting as Longitudinal Melanonychia in a Transplant Recipient

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PRACTICE **POINTS**

- Risk factors for the development of pigmented squamous cell carcinoma (pSCC) include older age, male sex, and use of immunosuppressant medications.
- Subungual pSCC can present as longitudinal melanonychia and should be considered in the differential diagnosis for melanonychia in patients with skin of color or those who are immunosuppressed.

We report the case of a 62-year-old black man who was on a maintenance immunosuppressive regimen that included mycophenolate mofetil and cyclosporine following renal transplantation 9 years prior. He presented to the dermatology department for evaluation of a pigmented longitudinal streak on the left third finger adjacent to the lateral nail fold that had been present for several months. He noted that the streak was increasing in size, and his fingertip had recently become tender. The pigmented band was biopsied, and histopathology showed atypia of the epidermis consistent with pigmented squamous cell carcinoma (pSCC).

Although subungual melanoma is the most concerning cause for longitudinal melanonychia, there are a number of other potential causes, including fungal infection, trauma, benign melanocytic lesions, or other cutaneous malignancies. Pigmented squamous cell carcinoma is another potential cause of longitudinal melanonychia and should be included in the differential diagnosis, particularly in individuals with skin of color or those who are immunosuppressed. This article highlights features of the clinical presentation of pSCC presenting as longitudinal melanonychia that mimicked the clinical appearance of subungual malignant melanoma in a renal transplant recipient. A review of pSCC and its associated risk factors also is provided.

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Case Report

A 62-year-old black man presented for examination of a dark longitudinal streak located adjacent to the lateral nail fold on the third finger of the left hand. The lesion had been present for several months, during which time it had slowly expanded in size. The fingertip had recently become tender, which interfered with the patient's ability to work. His past medical history was remarkable for end-stage renal disease secondary to glomerulonephritis with nephrotic syndrome of unclear etiology. He initially was treated by an outside physician using peritoneal dialysis for 3 years until he underwent renal transplantation in 2004 with a cadaveric organ. Other remarkable medical conditions included posttransplantation diabetes, hyperlipidemia, and gout. His multidrug regimen included 2 immunosuppressive medications: oral cyclosporine 125 mg twice daily and oral mycophenolate mofetil 250 mg twice daily.

A broad, irregular, black, pigmented, subungual band was noted on the left third finger. The lesion appeared to emanate from below the nail cuticle and traveled along the nail longitudinally toward the distal tip. The band appeared darker at the edge adjacent to the lateral nail fold and grew lighter near the middle of the nail where its free edge was noted to be irregular. A slightly thickened lateral nail fold with an irregular, small, sawtoothlike hyperkeratosis and hyperpigmentation also was noted (Figure 1).

Subungual melanoma, onychomycosis, squamous cell carcinoma (SCC), and a verruca copresenting with onychomycosis were considered in the differential diagnosis. The patient underwent nail avulsion and biopsy of the nail bed as well as the nail matrix. Histopathology was notable for malignant dyskeratosis with a lack of nuclear

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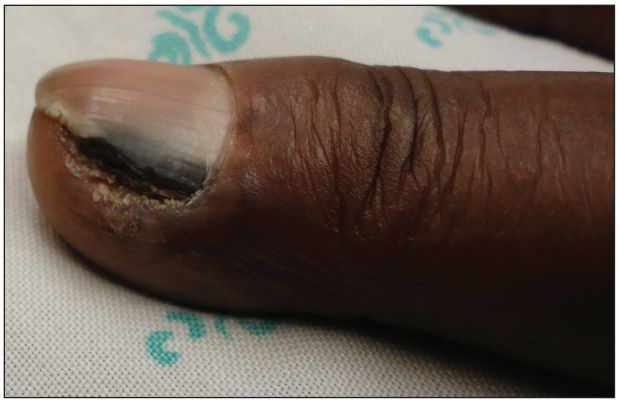

FIGURE 1. Pigmented squamous cell carcinoma presenting as a broad, black, pigmented, subungual band emanating longitudinally from the nail bed toward the distal tip of the left third finger.

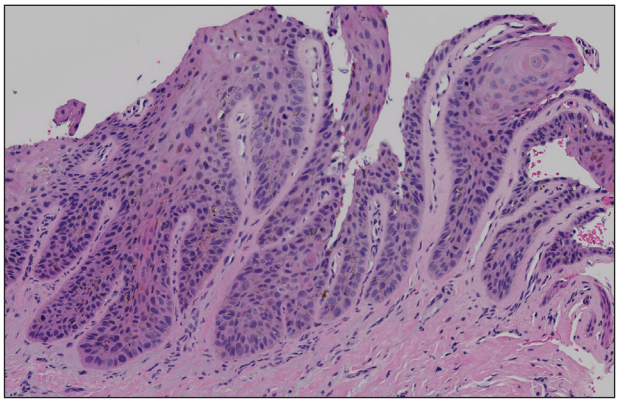

FIGURE 2. Nail matrix biopsy showed characteristic papillary architecture, malignant dyskeratosis with a lack of nuclear maturation, occasional mitosis, individual cell keratinization, and prominent pigmentation (H&E, original magnification ×160).

maturation, occasional mitoses, multinucleation, and individual cell keratinization (Figure 2). Immunostaining for S100 was negative, while staining for cytokeratins AE1/AE3 was positive. Deposition of melanin pigment in the malignant dyskeratotic cells was noted. Periodic acid–Schiff staining identified pseudohyphae without invasion of the nail plate. A diagnosis of pigmented SCC (pSCC) was made. The patient's nail also was sent for fungal cultures that later grew *Candida glabrata* and *Candida parapsilosis.*

The patient underwent Mohs micrographic surgery for removal of the pSCC, which was found to be more extensive than originally suspected and required en bloc excision of the nail repaired with a full-thickness skin graft from the left forearm. The area healed well with some hyperpigmentation (Figure 3).

Comment

Among the various types of skin cancer, an estimated 700,000 patients are diagnosed with SCC annually, making it the second most common form of skin cancer in the United States.[1] Basal cell carcinoma (BCC) is the most common skin cancer among whites in the United States, while in contrast SCC is the most common skin cancer in patients with skin of color.[2] Only an estimated 2% to 5% of all SCCs are pigmented, and this variant is more commonly seen in patients with skin of color.[3-5] One analysis of 52 cases of pSCC showed that common features included a flat or slightly raised appearance and hyperpigmentation with varying levels of scaling.[6] Studies have shown an altered presentation of pSCC in black skin with increased melanin production and thickness of the stratum corneum in contrast with cases seen in white patients.[7] Other potential features include scaling, erosive changes, and sharply demarcated borders. Squamous cell carcinoma typically occurs in sun-exposed areas, reflecting its association with UV light damage; however, SCC in skin of color patients has been noted to occur in sun-protected areas and in areas of chronic scarring.[8] Pigmented SCC also appears to follow this distribution, as affected areas are not necessarily in direct exposure to the sun. Pigmented SCCs have been associated with pruritus and/or burning pain, which also was seen in our case when our patient complained of tenderness at the site.

We describe the case of a subungual pSCC clinically presenting as longitudinal melanonychia. Pigmented SCC presenting as longitudinal melanonychia was first described by Baran and Simon in 1988.[9] Since that time, it has been reported that approximately 10% of subungual pSCCs clinically present as longitudinal melanonychia.[10,11] A retrospective study reviewing 35 cases of SCC of the nail apparatus found that 5 (14.3%) cases presented as longitudinal melanonychia.[10] Another retrospective study found that 6 of 51 (11.8%) cases of SCCs affecting the nail unit presented as the warty type of SCC in association with longitudinal melanonychia.[12] Cases of pSCC in situ appearing as longitudinal melanonychia also have been reported.[13,14]

Risk factors for the development of pSCC include advanced age, male sex, presence of human papilloma virus, and use of immunosuppressants.[15] Male predominance and advanced age at the time of diagnosis (mean age, 67 years) have been observed in pSCC cases.[16] It is now well established that renal transplant recipients have an increased risk of SCC, with a reported incidence rate of 5% to 6%.[16] When these patients develop an SCC, they typically follow a more aggressive course. Renal transplantation has a higher ratio than cardiac transplantation for SCC development (2.37:1), whereas cardiac transplantation is associated with a higher risk of BCC development.[17] A study of 384 transplant recipients found that 96 (25.0%) had a postsurgical nonmelanoma skin cancer (NMSC), with a ratio of SCC to BCC of 1.2:1.[16] The calculated incidence of NMSC at 10 and 20 years posttransplantation was 24.2% and 54.4%, respectively. Another study also determined that SCC rates (50.0%) in postrenal transplant recipients were approximately twice that of BCC (27.0%).[18]

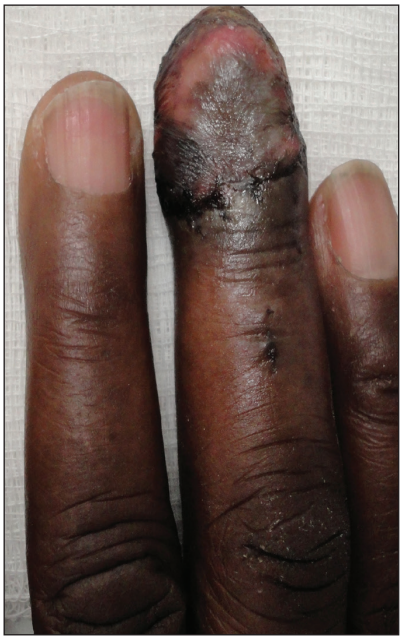

FIGURE 3. Well-healed site of a pigmented squamous cell carcinoma with hyperpigmentation following Mohs micrographic surgery and a full-thickness skin graft.

A daily regimen of immunosuppressive medications such as cyclosporine and mycophenolate mofetil showed an increased risk for development of NMSC.[15] Immunosuppressive medications play an important role in the pathogenesis of SCC due to a direct oncogenic effect as well as impairment of the immune system's ability to fight precancerous developments.[15] A 4-year study of 100 renal transplant recipients using mycophenolate mofetil as part of an immunosuppressive regimen reported 22% NMSC findings among 9 patients.[19] On average, patients developed an NMSC approximately 61 months posttransplantation, with a wide range from 2 to 120 months.

Advanced age was another important risk factor, with each decade of life producing a 60% increase in instantaneous risk of SCC development for transplant recipients.[15] A steady increase in risk was related to the length of time adhering to an immunosuppressive regimen, especially from 2 to 6 years, and then remaining constant in subsequent years. For older patients on immunosuppressant regimens for more than 8 years, the calculated relative risk was noted to be over 200 times greater than the normal population's development of skin cancers.[18]

Conclusion

Although cases of pSCC presenting as longitudinal melanonychia have previously been reported,[9-14,20] our case is unique in that it describes pSCC in a renal transplant recipient. Our patient had many of the known risk factors for the development of pSCC including male sex, advanced age, skin of color, history of renal transplantation, and immunosuppressive therapy. Although regular full-body skin examinations are an accepted part of renal transplantation follow-up due to SCC risk, our case emphasizes the need to remain vigilant due to possible atypical presentations among the immunosuppressed. The nail unit should not be overlooked during the clinical examination of renal transplant recipients as demonstrated by our patient's rare presentation of pSCC in the nail.

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