High Risk HPV Induced Subungual/Periungual In Situ Squamous Cell Carcinoma

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Background

- Squamous cell carcinoma (SCC) of the nail bed, also known as subungual or periungual squamous cell carcinoma, is a rare malignancy.
- Nail SCC is often misdiagnosed in its early stages because of clinical resemblance to benign conditions such as fungal infections, warts, or trauma-induced nail deformities.
- Incidence age ranges between 50 to 69 years but is reported in younger patients with risk factors such as high-risk HPV infection or immunosuppression.

Case Presentation

- Described is a 79-year-old male with an unusual filiform plaque on the distal aspect of the left middle finger with extension under the nail plate (Figure 1).
- Biopsies showed in situ squamous cell carcinoma involving the nail matrix, nail bed and fold, with prominent verrucoid architecture to the nail bed lesion (Figures 2, 3 & 4).
- Of note, p16 by immunohistochemistry (IHC) was positive in a blocky pattern typically seen in high-risk HPV infections (Figures 5 & 6).
- In particular, Ki-67 (IHC) helped in the evaluation of the matrix biopsy (Figure 7).
- In situ hybridization ancillary studies demonstrated positivity for one of the high-risk HPV subtypes (16, 18, 31, 33, & 51) validating high-risk HPV induced in situ squamous cell carcinoma of the distal fingernail matrix, bed and fold.

Fig. 1
Clinical photograph of distal left middle finger.
Physical examination revealed 0.6cm x 1.3cm filiform plaque on the distal aspect of the left middle finger with extension under the nail plate (Figure 1).

Histologic Findings

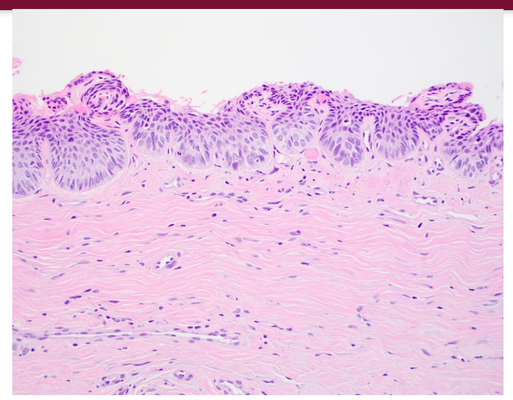

Fig. 2
Biopsy histopathology from left middle finger nail matrix, with nearly full thickness keratinocytic atypia (H&E 20X)

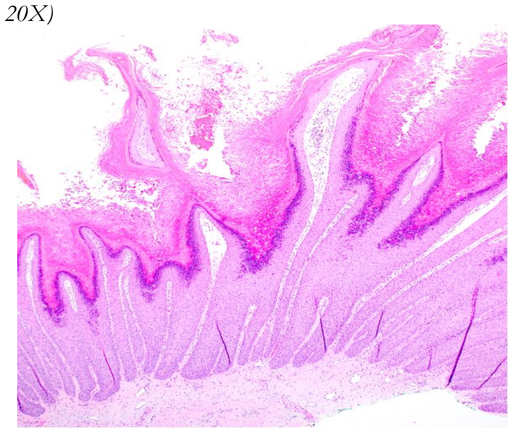

Fig. 3
Biopsy histopathology from left middle finger nail matrix, with nearly full thickness keratinocytic atypia (H&E 20X)

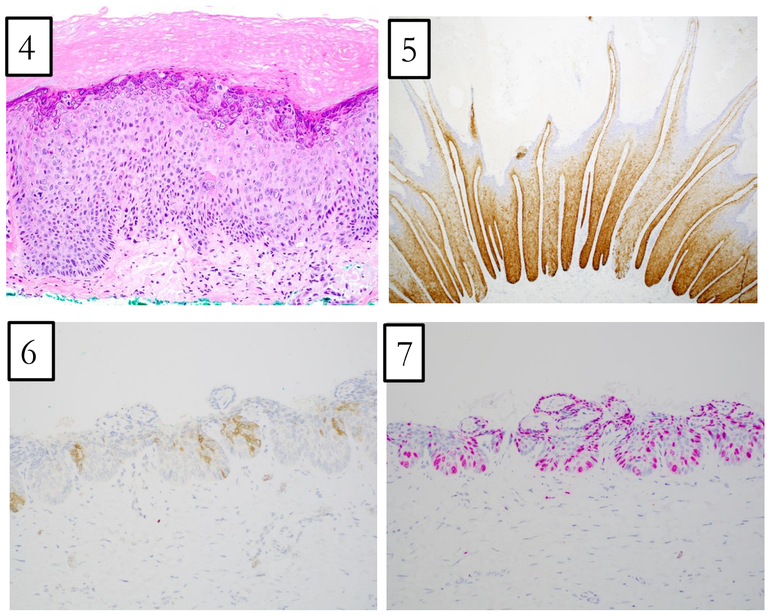

Fig. 4 *Biopsy histopathology from left middle finger nail fold with full thickness keratinocytic atypia and viral cytopathic changes (H&E 20X)*
Fig. 5 *Biopsy from left middle finger nailbed showing blocky pattern of p16 immunohistochemical positivity typically seen in high-risk HPV infections (4X)*
Fig. 6 *Biopsy showing blocky pattern p16 immunohistochemical positivity typically seen in high-risk HPV infections, left middle finger nail matrix (20X)*
Fig. 7 *Biopsy utilizing Ki-67 immunohistochemistry showing nuclear positivity that is focally full thickness, supporting in situ squamous cell carcinoma, left middle finger nail matrix (20X)*

Clinical Course

- A 79-year-old male presented to dermatology office in consultation for a lesion of the distal aspect of the left third finger
- Patient noted the lesion had been present for at least a year, but believed it was secondary to a traumatic injury. Lesion continued to grow under the distal nail plate and became mildly painful.
- At initial visit biopsy of the 1.3 cm x 0.6 cm filiform plaque on the distal aspect of the left middle finger with extension under the nail plate (Figure 1). Initial biopsy was not diagnostic as the lesion extended to the biopsy base.
- Pathology report noted "Atypical verrucoid squamous proliferation: An inflamed verruca vulgaris with squamous atypia is favored. However, the squamous proliferation does extend to the biopsy base and a verrucoid squamous cell carcinoma is in the histologic differential diagnosis."
- Repeat biopsies showed in situ squamous cell carcinoma involving the nail matrix, nail bed and fold, with full thickness atypical keratinocytes and prominent verrucoid architecture of the nail bed lesion (Figures 2, 3 & 4).

Discussion

- SCC of the nail bed, also known as subungual or periungual SCC, is a rare malignancy. It is often misdiagnosed in its early stages due to its clinical resemblance to benign conditions such as fungal infections, warts, or trauma-induced nail deformities.
- There are several treatment options for SCC including: surgical excision, Mohs micrographic surgery, therapeutic radiation, and potential topical chemotherapy.
- HPV-driven SCC of the nail poses unique diagnostic and management challenges, and clinicians should maintain a high index of suspicion for malignancy in persistent nail lesions.
- This case underlines the importance of clinical acumen leading to, appropriate biopsy, and surgical management to achieve optimal outcomes.

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