



Verrucous Carcinoma in a Diabetic Foot Ulcer: A Case Report

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Abstract

Verrucous Carcinoma (VC) is a rare malignant lesion that is often misdiagnosed as a simple wart. It is a variant of squamous cell carcinoma most commonly found in the foot and is locally destructive with frequent invasion to deep tissue and bone. Treatment is typically wide surgical excision, including amputation when clinically indicated. This study presents a case of Verrucous Carcinoma found in the distal toe after a chronic diabetic ulceration that required amputation and repeat surgical excision.

Keywords: Verrucous Carcinoma; Diabetic Foot Ulcer; Amputation

Abbreviations

VC: Verrucous Carcinoma; DFU: Diabetic Foot Ulcers

Introduction

Verrucous Carcinoma (VC) is a rare malignant lesion that is often misdiagnosed as a simple wart. It is a variant of a squamous cell carcinoma that typically arises in a long-standing verrucous lesion of the foot. It has been shown that these lesions often arise in areas of micro-trauma, surgical amputations, and previous ulceration [1].

Etiology

VC is a low-grade well-differentiated squamous cell carcinoma variant seen in oral and anogenital mucosa but rare in the skin. Although the exact etiology is not known, lesions have been associated with human papillomavirus (HPV) infection where HPV 6, 11, 16, and 18 are typically causative agents [2]. Studies have shown

the most common location of verrucous carcinoma in the skin occurs in the foot [3-4]. Metastasis is rare, although a study by Kao, et al. [4] showed 3 of 26 (12%) patients who were followed after initial treatment had metastasis to regional lymph nodes. In the same study, 5 of 46 (11%) lesions progressed with local invasion to muscle or bone. More recent studies have shown bone involvement in up to 19-28% of cases [5].

Differential diagnosis

Typically, patients with VC have a history of a wart that has undergone prior unsuccessful local treatment. Lesions suspicious for VC can appear as well-circumscribed fungating, polypoid masses with cauliflower-like protrusions. These lesions have been associated with chronic ulcerations and draining sinus tracts. Thus, superimposed infections should be ruled out as a source of regional lymphadenopathy. VCs are found most commonly on the plantar side of the foot, specifically the heel and forefoot, as well as on the digits [6]. Lesions may often be confused with chronic ulceration,

verruca plantaris, pseudoepitheliomatous hyperplasia, carcinoma cuniculatum [7] and actinomycosis. It is important to differentiate VC from pseudoepitheliomatous hyperplasia (PEH). Under microscopic examination, PEH shows digitate epidermal hyperplasia without invasive features, mitotic figures, or PCR positive for HPV [8].

Diagnostic modalities

The gold standard diagnostic measure is a soft tissue biopsy. Misdiagnosis secondary to superficial biopsies leads to progression of local invasion. Imaging studies are helpful in evaluating the extent of deep tissue involvement. MRI may be performed to examine depth of soft tissue involvement, whereas CT imaging is indicated to examine level of cortical invasion [9].

Treatment and prognosis

First-line therapy is surgical management with wide excision rather than marginal excision. Guidelines have varied for width of excisional margins (0.5cm - 3.0cm), with highly variable recurrence rates of VC (4.6-75%) [5]. Delayed treatment may lead to local spread to adjacent muscle or bone, necessitating a larger scale of amputation.

Case Report

A 67-year-old male with type 2 diabetes mellitus presented with a distal third digit ulceration due to hammertoe deformity. X-rays did not demonstrate osteomyelitis, and the ulceration healed with daily wound care. The patient subsequently developed a soft tissue lesion at the distal toe with pinpoint hemorrhage indicative of verruca. The verruca was treated for approximately three months with sharp debridement and application of Cathardin solution with eventual reduction in size of the lesion. The patient was then lost to follow up for 3 weeks. By the next follow up visit, the lesion had doubled in size and appeared to have a new protruding mass overlying the lateral border (Figure 1).

Due to the recurrence of the wound, suspicion for carcinoma, as well as a history of prior adjacent digital osteomyelitis with subsequent amputation, the patient declined attempt at salvage of the toe and opted for surgical amputation of the digit. A distal symes amputation of the third digit was performed (Figure 2), and pathology examination revealed verrucous carcinoma with clear margins >1mm at all borders. Sutures were removed two weeks

post-operatively, and the amputation site healed without complications (Figure 3).

Eight months after initial amputation, the patient returned for a new pinpoint lesion at the amputation site. An excisional biopsy was performed and returned positive for verruca vulgaris. Two weeks later, the site had healed with no signs of new lesions. After full discussion with the patient, the decision was made to monitor the site and plan for a revisional amputation if indicated in the future.



Figure 1: Initial presentation of Verrucous lesion.

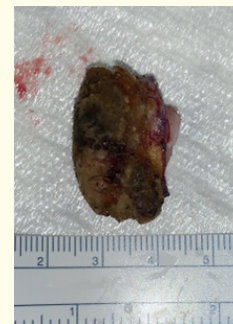


Figure 2: Amputated digit with visualization of margins.



Figure 3: Healed amputation site.

Discussion

Malignant lesions in the foot are rare. Typical malignancies include melanoma, squamous cell carcinoma, and chondrosarcoma, which is the most common malignant lesion in the foot [10]. Given the anatomy of the foot, typical surgical excisions of verrucous lesions lead to partial toe or ray amputations, and lesions involving the midfoot or rearfoot typically lead to below knee amputations. Thus, delayed diagnosis and delay in definitive treatment can lead to significant morbidity. Similarly, inadequate previous treatment has shown to have adverse effects on prognosis and limb salvage [11]. Additionally, while radiation therapy typically is pursued for treatment of other primary malignant lesions, radiation therapy for VC has been shown to increase the risk of anaplastic transformation and is not recommended [12].

Diagnosis should include a biopsy that most accurately evaluates the depth of the lesion. In this case, shave biopsies are highly likely to be non-diagnostic, and wedge or punch biopsies may not adequately encompass the total thickness and depth of the tumor [13]. Subsequently, excisional biopsies are more likely to lead to definitive diagnosis but are more difficult to perform at the level of the foot without leading to an amputation. In the case presented in this report, an excisional biopsy with clear margins of the soft tissue alone would have led to bone exposure without consideration of wound closure. A partial amputation of the digit provided both diagnostic and therapeutic value. In the case of a diabetic ulcer of the toe with simultaneous concern for VC, a partial amputation of the digit is more likely indicated.

VC has been shown to complicate wound healing in diabetic foot ulcers. Palma, *et al.* [15] discussed a case of delayed wound healing in a patient with bilateral diabetic foot ulcers (DFU). Due to the bilaterality of the patient's ulcerations, diagnosis of VC was delayed. Once incisional biopsies were performed, VC was diagnosed. There is increased risk of delay in diagnosis of VC in patients with DFUs due to similarities in the presentation of both pathologies. Both occur more often in weight-bearing areas, tissue irritated by chronic inflammation, dermatologic scars, or areas of trauma [4,14,16]. In cases of DFUs with delayed wound healing, the differential diagnosis should include a malignant process such as VC.

Conclusion

VC is a rare malignancy atypically found in the skin. When occurring in skin, VC is found most commonly in the foot. VC is often

misdiagnosed as verruca vulgaris, actinomycosis, and chronic ulceration. DFUs can be complicated by VC, and delay in diagnosis of VC can eventually lead to amputation. There should be a low threshold to biopsy lesions when indicated, and Mohs surgery should be strongly considered to avoid amputation.

The authors of this paper propose more frequent biopsies of atypical lesions and wounds with delayed healing or significant change in clinical appearance and size. The authors propose definitive treatment with surgical excision when there is high clinical suspicion of VC to prevent local invasion that may necessitate a more proximal amputation. Further research is needed to investigate the causative factors and etiology of VC, the association between HPV and VC, the possible etiology of malignant transformation of long-standing verruca vulgaris to VC, and the association between VC overlying areas of irritation secondary to repetitive microtrauma and chronic ulceration, such as toes, as seen in the case presented in this study.

Conflict of Interest

No funding or support was received for the collection, analysis, interpretation of data or preparation of the article.

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