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Oral Verruca Vulgaris in a Bone Marrow Transplant Patient: A Case Report and Review of Literature

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Viral infections can cause severe morbidity in immunosuppressed cancer patients. A case of rapidly enlarging, biopsy-documented oral verruca vulgaris in a patient undergoing conditioning chemotherapy prior to bone marrow transplantation (BMT) is described. Human papillomavirus infections in immunosuppressed patients are discussed. Copyright © 1996 Elsevier Science Ltd

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INTRODUCTION

The human papillomavirus (HPV) is a relatively common inhabitant of the oral mucosa; the virus may, but does not necessarily produce clinical oral lesions [1, 2]. A number of oral mucosal pathoses, including verruca vulgaris, condiloma accuminatum, lichen planus, tobacco-induced hyperkeratosis and cancer have been reported to contain HPV. The actual role of the virus in the aetiopathogenesis of these lesions remains unclear [1–3].

Increased rates of HPV-induced clinical lesions have been reported in immunosuppressed patient populations [4–7]. Oral verrucas and papillomas in BMT patients have been noted 1–3 years status/post-transplantation [6, 7]; however, there appear to be no published reports of HPV-related oral lesions developing during cytoreductive conditioning. This report describes a BMT patient who developed rapidly growing oral verruca vulgaris during conditioning therapy prior to transplantation.

CASE REPORT

A 57-year-old male with stage IV B-cell lymphoma was admitted to the BMT Unit for conditioning prior to autologous BMT. His lymphoma had been diagnosed 9 months prior to admission. The patient achieved remission after five cycles of cyclophosphamide, pednisone and adriamycin; however, subsequent progression of disease was noted. The patient's medical history was otherwise unremarkable.

A comprehensive oral examination was performed 5 days prior to admission. The patient had no oral complaints and denied a past history of oral mucosal lesions. He had worn the same complete maxillary and mandibular dentures for the past 15 years. Intra-oral examination revealed complete edentulism with intact alveolar ridges, and no mucosal lesions.

The patient was admitted to the BMT unit and a conditioning regimen consisting of busulfan 60 mg/kg, cyclophosphamide 90 mg/kg, and etoposide 60 mg/kg (ideal body weight) was initiated. The patient was advised not to wear his dentures during hospitalisation. However, he did not initially comply with this recommendation.

Two days before transplantation (day −2), the patient complained of mild discomfort affecting his right lower labial mucosa. Examination revealed multiple papillomatous exophytic lesions on a 0.5 cm^2 area of the right labial mucosa; the lesions were sessile, pliable, non-indurated, and mildy tender to palpation; other oral findings were within normal limits. The patient had a white blood cell count of 5000/mm^3 and 238 000 platelets/mm^3 at this time. Differential diagnosis of the oral lesions included verruca vulgaris, squamous papilloma, condyloma accuminatum, verrucous carcinoma and hyperplastic candidiasis. Viral and fungal cultures of the lesion were performed and were subsequently reported to be negative.

On day −1, the papillary masses covered approximately 5.0 cm^2 of the right labial/buccal mucosa and attached gingiva (Fig. 1). The patient complained of increased discomfort exacerbated by mastication. A biopsy was performed in view of the rapid growth of this lesion; the patient was again advised to remove his dentures and complied. On day +1 there was no change in the lesion's size, texture, colour or consistency. The patient continued to be evaluated biweekly until his discharge from the hospital; no further changes in the lesion were noted.

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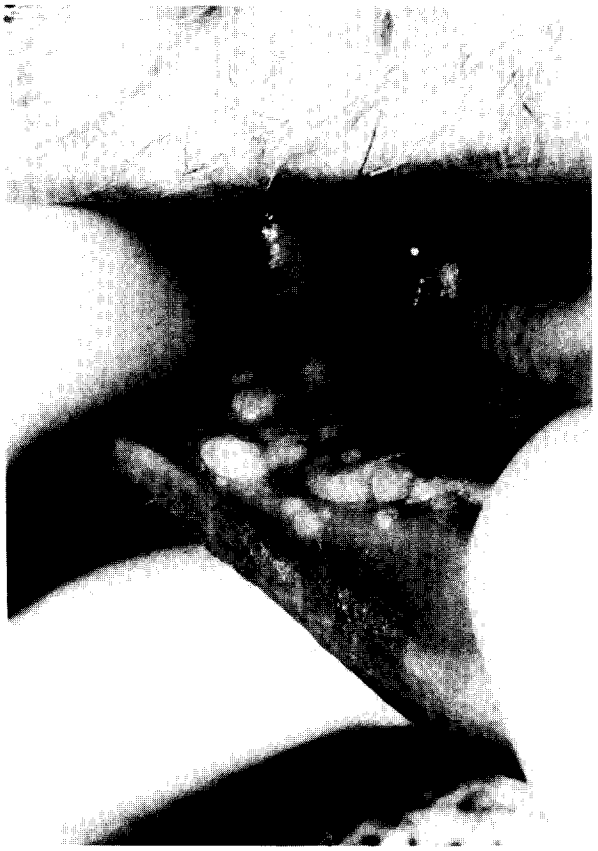

Fig. 1. Clinical appearance of lesion, day −1.

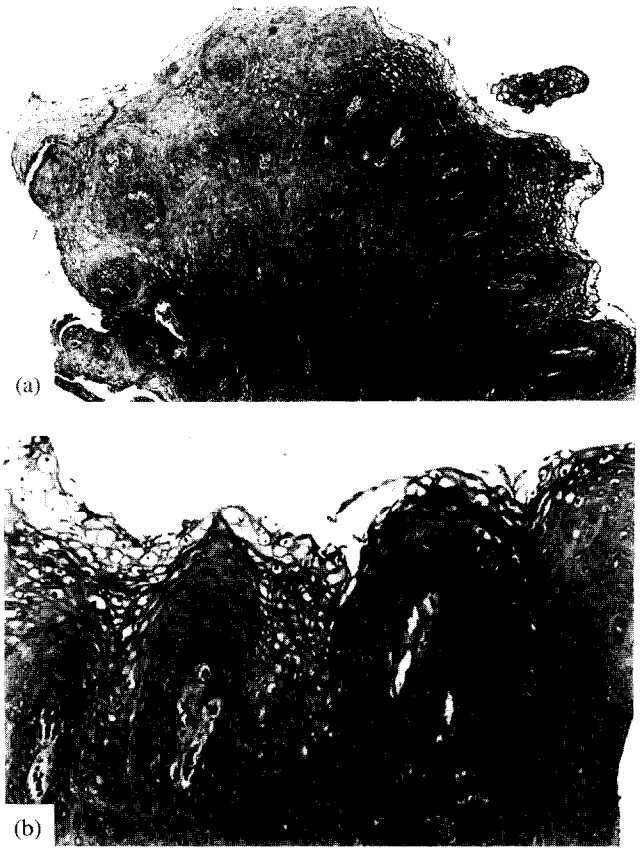

Fig. 2. (a) Papillary exophytic mass with koilocytic cells adjacent to cap-like parakeratotic surface (hematoxylin and eosin ×100); (b) higher magnification of verrucous surface and koilocytes. Findings strongly suggest HPV-related changes (haematoxylin and eosin ×400)

PATHOLOGICAL ASSESSMENT

Gross specimen

The gross specimen consisted of a single, firm, grey–white wedge of mucosa with an exophytic cauliflower-like mass measuring $0.3 \times 0.2 \times 0.1$ cm projecting above the surface.

Microscopic features

Paraffin-embedded, haematoxylin and eosin-stained sections demonstrated a polypoid mucosal nodule with a delicate, papillary surface configuration (Fig. 2a, b). The overlying epithelium was hyperparakeratotic with koilocytic-appearing subcorneal cells. Findings were consistent with papillomavirus-related modifications suggestive of verruca vulgaris. Streptavidin immunoperoxidase for HPV was performed on formalin-fixed, paraffin-embedded tissue, using a standard "screening" composite antibody of multiple HPV strains from bovine sources. Immunoreactivity confirmed the presence of HPV (Fig. 3) and a diagnosis of verruca vulgaris was established. DNA studies were not performed.

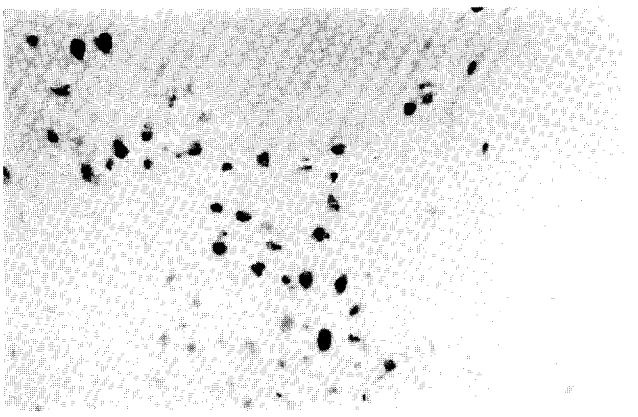

Fig. 3. Immunoperoxidase is positive for HPV (peroxidase with streptavidin ×600).

DISCUSSION

This report describes a case of oral verruca vulgaris in a lymphoma patient undergoing chemotherapy conditioning prior to autologous BMT. The lesion expanded over 4 days to involve a surface area of approximately 5.0 cm^2. This rapid expansion created concerns for potential upper respiratory involvement and/or regional growth during the patient's expected profound immune suppression. However, the lesion's growth arrested prior to WBC nadir (absolute neutrophil count <500 cells/m^3).

This patient's HPV infection most likely occurred prior to admission since: (1) risk for HPV contagion is minimal in the setting of the BMT unit where isolation and protection regulations are strictly observed; and (2) viral DNA is

commonly identified in intact oral mucosa [1, 3]. A direct effect of conditioning therapy such as mucosal oedema, combined with irritation from denture wearing, could have contributed to this patient's development and rapid growth of clinical lesions. A previous report of denture irritation-induced oral papillomatosis also supports this hypothesis [8]. The relationship between this lesion's onset and growth and the patient's immune status is unclear. However, a review of pertinent literature suggested a possible link between HPV-related mucosal lesions and immunosuppression.

An increased prevalence of HPV-related lesions has been reported in HIV-infected individuals [4, 5], but no conclusive association with subjects' immune status has been noted. A recent study showed significantly lower CD4+ lymphocyte counts in HIV patients infected with oncogenic versus non-oncogenic HPV strains [9]. However, this study did not analyse a corresponding non-HIV infected group. A separate report identified low CD4+ counts as well as impaired T-lymphocyte function in a non-HIV infected subject with persistent multiple refractory warts [10].

Renal transplant patients have also been reported to have an increased incidence of HPV-associated lesions [11, 12]. A humoral immune deficiency has been suggested as a possible explanation. However, the relationship between cellular immunity and lesion development/progression has not been documented. The prevalence of HPV and cervical abnormalities in renal transplant versus non-immunosuppressed females was also reported. Detection of HPV genome did not differ significantly between the two groups; the frequency of detection of HPV-associated clinical lesions in the respective groups was not reported [13]. Zaia noted an increased occurrence of warts in immunosuppressed cancer patients [7], although no prevalence data or references to other studies were presented. Similarly, Schubert described oral HPV infections occurring "occasionally" in BMT patients [6]. Both authors placed onset of these lesions between 1 and 3 years status/post BMT. The relation of these lesions to patients' immune status was not documented.

Further study of HPV-associated lesions in immunocompromised patients is necessary. However, the high prevalence of HPV viral genome in the population at large compared to the low occurrence of lesions in cancer patients suggests that immune dysfunction alone is not sufficient for HPV-related lesion development. This is consistent with the course of the presented case.

CONCLUSIONS

Oral HPV infections have been reported to occur more frequently in immunosuppressed than immunocompetent patients. However, few controlled studies document the relationship between immune function and clinical lesion onset; mechanisms of viral activation and the role of immunosuppression in lesion development remain unclear. This report documents the case of a BMT patient who developed a rapidly growing oral verruca vulgaris prior to his WBC nadir. The lesion did not demonstrate any growth during aplasia and no further changes were noted during or after engraftment. This pattern suggests that development of this oral lesion was not primarily related to the patient's immune function. Current methods of treatment for oral verruca vulgaris have not been sufficiently studied for use in immunosuppressed BMT patients. This case suggests that identification and removal of a possible source of local mucosal irritation is important and may produce lesional growth arrest.

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