Squamous Cell Carcinoma Arising in Epidermodysplasia Verruciformis: Case Report and Literature Review

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OBJECTIVES: Epidermodysplasia verruciformis (EDV) is a rare autosomal recessive skin condition that predisposes patients to HPV infection and are at high risk for squamous cell carcinoma (SCC). We report a case of forehead SCC in a 24 year old patient with EDV and review the literature regarding the diagnosis, management and outcomes.

STUDY DESIGN: Retrospective chart review and review of the literature via a PUBMED search.

METHODS: The patient’s medical record was reviewed and photographs were taken. The PUBMED search was performed using “epidermodysplasia verruciformis.”

RESULTS: The patient had a two year history of a right forehead lesion which slowly grew and became ulcerated. Physical exam showed a 5 x 7 cm deep ulcerated plaque with a pink base and focis of necrosis. Frontals was immobile on the right. There was a history of rash since infancy consisting of hypopigmented macules scattered over the torso, and raised flat warts on the dorsum of hands and feet. The patient underwent wide local excision, right superficial parotidectomy, selective neck dissection with radial forearm flap reconstruction. Tumor board discussed post-operative radiation due to grafted vessel involvement. Literature review suggests avoiding radiation as this increases recurrence and malignant transformation of other lesions.

CONCLUSION: Treatment of cutaneous squamous cell carcinoma is wide local excision with lymph node dissection based upon imaging studies. Radiation is recommended for patients with high risk features which contradicts the recent literature which does not recommend radiation for patients with EDV.

INTRODUCTION

Epidermodysplasia verruciformis (EDV) is a rare autosomal recessive skin condition characterized by susceptibility to chronic β HPV infections, specifically types 3, 5, 8. It is immunocompromised hosts, these viruses are non-virulent because they do not possess the E5 protein. In contrast, patient’s with EDV, and other immunocompromised patient’s, can become infected with these common viruses. Specifically, EDV patient’s harbor an inactivating mutation in TM6 (EVER1) and TMCI (EVER2), a complex which associates with a zinc transporter. This zinc transporter complex usually blocks infection of β-HPV but with its patient’s becomes chronically infected with β-HPV. The infection manifests as ptyriasis versicolor-like macules and flat wart-like papules with onset starting between the ages of 1-20 years. Development of non-melanoma skin cancers and other benign skin lesions occurs over time.

In the literature, development of squamous cell carcinoma (SCC) in this patient subset has been described and the treatment has been controversial. The national comprehensive cancer network (NCCN) has defined guidelines for treatment of high risk cutaneous SCC. In these guidelines, radiation therapy is recommended for patients with high risk features. In contrast, radiation therapy in these patients has been associated with aggressive tumor recurrence and the malignant degeneration of current benign lesions.

METHODS AND MATERIALS

A PUBMED literature search was performed using the terms “epidermodysplasia verruciformis”, “radiation”, “squamous cell carcinoma.” The current literature was reviewed regarding the pathogenesis of EDV and squamous cell carcinoma. All cases of patients with EDV and SCC were reviewed. Clinical information such as age, presenting symptoms, progression of disease, all treatment modalities and outcomes were extracted. Our study included patients with EDV and SCC from the literature.

CASE PRESENTATION

A 24-year-old male presented to the emergency department with a lesion on the right forehead that had slowly grown over the past 2 years. The patient was previously healthy and had no significant past medical history. No other family members had a similar condition. The patient denied any recent travel and had no history of immunosuppression.

On physical examination, there was a 5 x 7 cm deep ulcerated plaque with a pink base and foci of necrosis centrally and along the border. Overlying portions of the ulcer were areas of serous crust. There was no movement of the forehead on the right side. The patient also had innumerable ptyriasis versicolor-like lesions and flat verrucular-like lesions on his extremities and posterior back. The patient’s hair was thin and normal skin color. Biopsy of the frontals ulcer showed a thick dermis with hyperkeratotic, parakeratotic, acanthotic epidermis, consistent with verruca plana of epidermodysplasia verruciformis. The patient underwent local excision, right superficial parotidectomy with facial nerve monitoring, right selective lymph node dissection levels 1 through 3 and reconstruction with left radial forearm free flap and left thigh latissimus dorsi free flap.

The patient was not a candidate for radiation therapy due to high risk features such as age, location of the lesion, and histologic features. The patient presented 1 year after initial treatment with multiple recurrences in the same location. The patient underwent local excision and radiotherapy to the forehead and parotid. The patient is alive and free of disease 10 years after initial treatment. The patient is being followed closely by dermatology for skin cancer surveillance. Several punch and shave biopsies have been performed and are positive for squamous cell carcinoma in situ arising in a background of EDV.

Additional cases have been reported in the literature.4 Other therapies have been described for EDV, such as acitretin.5 It is important to identify which therapies may accelerate the condition and should thus be avoided. Patients with EDV develop malignant skin lesions in sun exposed areas. Just as in healthy skin, ultraviolet radiation induces malignant transformation of epithelial skin cells. With HPV associated abnormally suppressed, this transformation occurs more quickly. Therefore, these patients are highly encouraged to avoid sun and photoprotection (i.e., wear sun screens and sun protective clothing).

CONCLUSIONS

A therapeutic dilemma exists in the management of EDV patients with a high risk squamous cell carcinoma. Per the NCCN guidelines, adjuvant radiation therapy is indicated in the treatment of EDV. However, anecdotal evidence and the known HPV associated predisposition to malignant transformation, suggests that radiation therapy may induce tumor progression of other EDV lesions in the radiation field. In our patient, there were positive margins on the orbital peristemum as well as facial nerve involvement. As such, radiation therapy was administered to the patient. He has completed his course and his operative site is well healed. There have been no new lesions observed in the post radiation period though it is likely too soon to make any final statements from this radiation. Previously, the reported mean time from completion of therapy to recurrence was 1.5 years.8, 9

The patient will continue close skin cancer surveillance with dermatology and ophthalmology.

REFERENCES