Collision Tumor of the Thorax

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ABSTRACT

Cutaneous squamous cell carcinoma (SCC) is the second most common cancer in the United States, and high-risk SCC is associated with more aggressive tumor behavior and correlated with poorer outcomes. This case study illustrates a patient who was found to have a large, fungating mass that had been neglected for 20 years. An excisional biopsy was completed, and the mass was identified histologically with two distinct patterns of invasive carcinoma: SCC and adenoid basal cell carcinoma, thus a collision tumor. This case report discusses risk factors and possible treatment options for this rare presentation.

Key words: Adenoid basal cell carcinoma, collision tumor, cutaneous squamous cell carcinoma, skin cancer

INTRODUCTION

Cutaneous squamous cell carcinoma (SCC) is the second most common cancer in the United States. The development of SCC is dependent on environmental, genetic, and immunologic factors. SCC commonly develops on the skin under prolonged sun exposure and sites of chronic inflammation or radiation. Localized SCC generally has high cure rates due to its low propensity to recur or metastasize after local excision with 4-mm margins. Although localized SCC has a high cure rate post-excision, high-risk SCC has a propensity for recurrence and metastasis. High-risk SCC is associated with more aggressive tumor behavior and correlated with poorer outcomes. Some clinical characteristics of high-risk SCC are location on the ear and lip or sites of chronic inflammation, tumor diameter >2 cm, tumor recurrence, presence of multiple tumors, and presence of tumor encroachment on peripheral nerves.[1] Histological characteristics of high-risk SCC include poorly differentiated tumor, desmoplastic growth pattern, tumor invasion of reticular dermis (Clark IV or Breslow depth >2 mm), and tumor invasion of nerve sheath or vasculature. Patients with a history of immunosuppression (HIV and chronic lymphocytic leukemia), autoimmune disease, and epidermolysis bullosa are also at increased risk of developing high-risk SCC. Currently, there are no agreed-upon criteria for diagnosis or well-studied treatments for high-risk SCC, making this variant of SCC challenging. Giant non-melanoma skin cancer (NMSC), defined as basal or SCC >5 cm in diameter, develops commonly due to neglect. These lesions qualify as high-risk lesions due to their large size. Here, we present a case of giant SCC and adenoid basal cell carcinoma that had been neglected for over 20 years.

CASE REPORT

A 55-year-old chronically ill-appearing Caucasian male presented with over 20-year history of cutaneous mass on the left chest and neck region. The mass measured 20 cm in diameter and was found to have opened just before presentation with necrosis, ulceration, and maggots within the tissue. It was gangrenous and very foul smelling, concerning for secondary infection of the mass. The patient presented as a poor historian, alert, and responsive to name but unable to answer questions

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concerning his symptoms or medical history. Chart review and later discussion with partner revealed patient's past medical history of poorly controlled HIV and diabetes mellitus, both for which he had not received medical care in the past year along with a 20-pack year smoking history.

Initial laboratory studies were remarkable for anemia (hemoglobin 7.5), hypoalbuminemia, hypophosphatemia, and hypomagnesemia with other laboratories within normal limits. Due to the concern for secondary infection based on the appearance of the mass, infectious disease was consulted and the patient was started on vancomycin and zosyn, while blood cultures and CD4 count/HIV viral load were pending. The patient, however, remained afebrile, without leukocytosis and with stable vital signs. Computed tomography scan of the neck was obtained and showed large irregular soft tissue mass of skin surface on the left upper chest extending to anterior soft tissues of the left shoulder and left lower neck without invasion of musculature or chest wall. The mass was incompletely seen on this examination and measured approximately 12 cm × 3 cm with enlarged axillary node measuring approximately 4.9 cm × 2.8 cm. Additional enlarged left supraclavicular lymph nodes were noted.

The patient was referred to cardiothoracic surgery for excisional biopsy of the left chest wall and left axillary lymph node dissection. The mass was found to have a significant tumor burden and was highly vascular and friable requiring the use of pressure, Arista, clips, and bovie electrocautery for achievement of hemostasis. Lymph node dissection was performed, and the mass was wrapped in Kerlix and ACE wrap. The patient tolerated the procedure well, and the Betadine Prep helped to eradicate the maggots within the mass. Preliminary pathology revealed SCC.

Final pathology revealed hematoxylin and eosin sections of tissue sample showing two distinct patterns of invasive carcinoma. The first pattern was SCC that ranged from poorly differentiated type with nuclear atypia and multiple mitotic figures to well-differentiated keratinizing type, evidenced by whorls of keratin pearls and debris. The second pattern was that of an adenoid basal cell carcinoma. Immunochemistry of both variants showed diffuse strong positivity for pankeratin and cytokeratin 5/6 as well as nuclear strain p40 and p63. The SCC component tested positive for epithelial membrane antigen, whereas the basaloid component of the invasive carcinoma tested positive for BerEP4. Both components of invasive carcinoma were negative for S100 and polyclonal carcinoembryonic antigen (CEA). Shown in Figures [1-8]

The patient's laboratories returned showing CD4 count of 134, HIV viral load of 162,000, and positive blood cultures for *Staphylococcus aureus*, *Pseudomonas aeruginosa,* and Gram-negative bacillus. Due to cultural sensitivity, the patient was started on meropenem for 4 weeks.
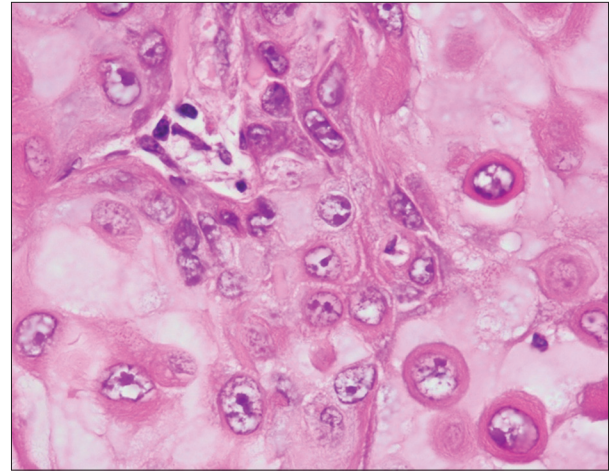
Figure 1: Poorly differentiated squamous cell carcinoma showing spiny projections
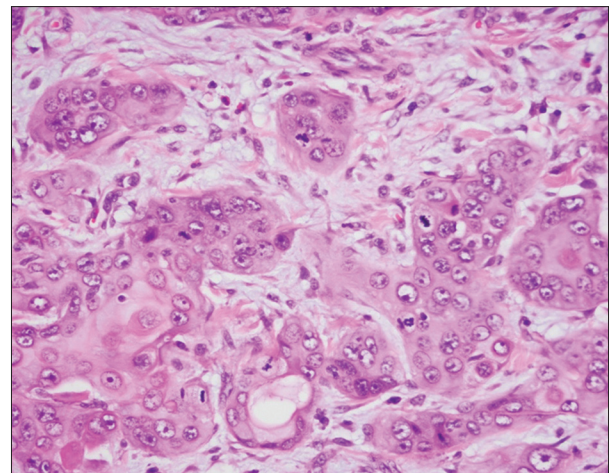
Figure 2: Poorly differentiated squamous cell carcinoma with prominent nucleoli and numerous mitotic figures seen
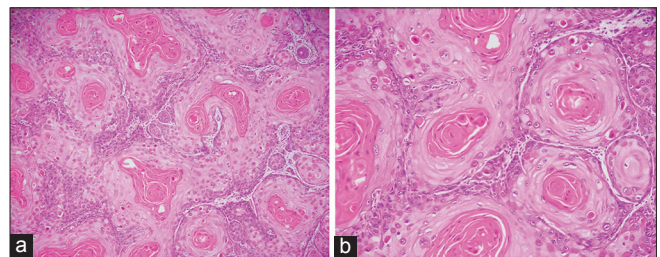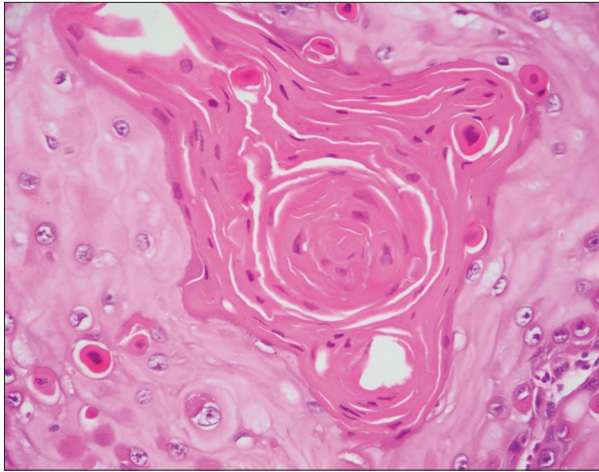

Figure 3: (a) Well-differentiated squamous cell carcinoma producing whorls of keratin. (b) Magnified view
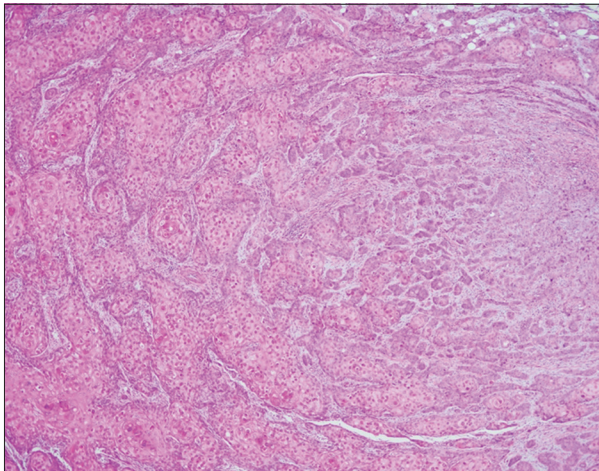
Transthoracic echocardiogram was performed which ruled out bacteremia and endocarditis.

Due to the extent of tumor burden, the patient was referred to surgical oncology for tumor resection and hematology/oncology for possible radiation/chemotherapy post-resection. Plastic surgery was also consulted who would
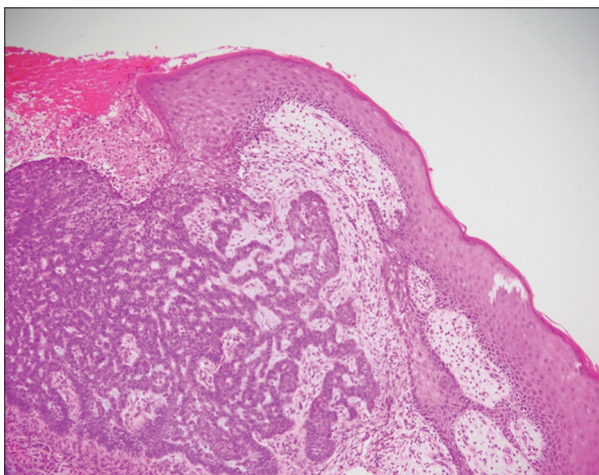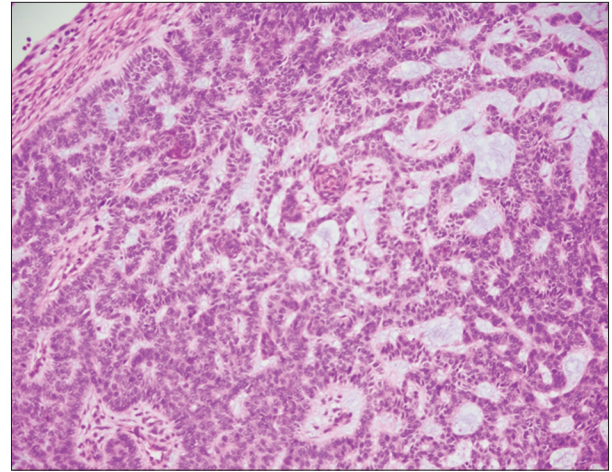
Figure 4: Keratin Pearl

Figure 5: Well-differentiated squamous cell carcinoma (left) with keratin pearls and kertain debris slowly transitioning to undifferentiated squamous cell carcinoma (left)

Figure 6: Epidermis and underlying adenoid basal cell carcinoma. Left adjacent to epidermis layer is necrotic tissue and fibrin debris

Figure 7: Magnified adenoid basal cell carcinoma producing significant amounts of mucin (pale blue material) and forming tubules and cords (cribriform pattern)
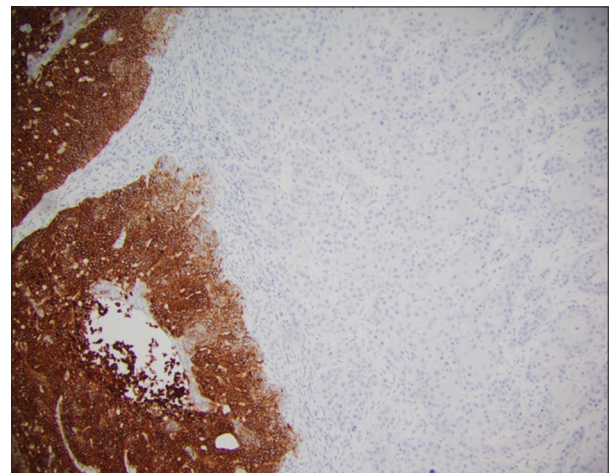
Figure 8: BerEP4 cytoplasmic immunostaining of adenoid basal cell carcinoma. BerEP4 is an epithelial cell adhesion molecule specific for adenoid basal cell carcinoma. S-100 and carcinoembryonic antigen are also markers for adenoid basal cell carcinoma but did not stain in this patient

plan for staged reconstruction after complete excision of the mass revealed negative margins. Further workup was done including computed tomography angiography to inspect the vascular supply of the mass which appeared to be from proximal branches of the internal thoracic artery along with branches of the cost-cervical and an unnamed small branch arising from the left subclavian artery distal to the takeoff of the dorsal scapular artery. Medical optimization was sought with the enhancement of nutritional status. Ultimately, however, due to the large size of the mass, it was deemed unlikely to be able to achieve clear margins and surgical resection was not attempted. Due to the patient's poor performance status, he was referred to hospice care.

DISCUSSION

Our report describes a patient who presented with giant SCC due to neglect for over 20 years. The patient's SCC displayed several high-risk features including tumor diameter >2 cm, presence of poorly differentiated histologic variants, and tumor invasion of reticular dermis. His untreated HIV status also played an important role in the development of a high-risk variant of cutaneous SCC and ultimate poor outcome of his disease. This discussion will cover the pathogenesis of HIV as a risk factor to the development of SCC and management of SCC.

The patient's immunodeficiency is very relevant to the pathogenesis of this disease because it is well established that skin cancer is the most common type of cancer in organ transplant patients.[2-4] The US Military HIV Natural History study found that, in those with HIV, NMSC also appears to be the most common type of cancer developed and incidence was inversely related to the use of HAART.[5] Several studies have shown that HIV is uniquely associated with cutaneous SCC.[6,7] A large cohort study consisting of 6560 HIV-positive and 36, 821 HIV-negative non-Hispanic Caucasian adults in Kaiser Permanente Northern California and found that HIV patients compared to HIV-negative patients had 2.1 times more diagnosis of BCC and 2.6 times more diagnoses of SCC. Furthermore, the risk of developing SCC in HIV-positive individuals was proportional to viral load and inversely proportional to CD4 count.[7] The association of immune dysfunction in HIV-positive patients and the development of SCC suggest that the pathogenesis may be infectious. Several studies have shown an association between β-papillomavirus species 2 and SCC. In organ transplant patients, infection with an increased number of viral strains and greater viral load of β-papillomavirus was associated with 2 fold increased risk of developing SCC.[8] Furthermore, beta-papillomavirus species 2 was found to predominate in SCC.[9]

Treatment for high-risk SCC consists of excision, radiation therapy, and chemotherapy. The mainstay of treatment is surgical excision. Two different methods of excision are standard surgical excision with operative margin assessment and microscopically controlled surgery. Both options have proven to have similar rates of recurrence (at least 95% cure rate) after 5 years for primary SCC and BCC. [10] However, according to the National Cancer Network, Mohs surgery is preferred in high-risk lesions.[11] A small study of 10 HIV-positive patients diagnosed with SCC with aggressive features, "diameter larger than 1.5 cm, rapid growth rate, local recurrence, and/or evidence of metastasis," found that mortality from SCC was dependent on early initiation of aggressive surgical excision for localized disease and radiotherapy for metastasis than degree of immunosuppression. HIV patients treated with Mohs surgery had lower rates of recurrence than those treated with non-Mohs surgery.[12] Therefore, due to the aggressive nature of high-risk SCC in HIV-positive patients, they should be treated aggressively with Mohs surgery, radiation for metastatic disease, and local radiation, and sentinel lymph node biopsy should also be considered.

Radiation therapy as a primary mode of treatment is warranted in small SCC lesions or lesions located on cosmetically sensitive areas. However, in high-risk SCC, radiation therapy cannot be used as the primary mode of treatment due to decreased ability to control local disease in tumors with high rate of recurrence and metastasis.[13] Therefore, a combination of surgical excision and adjuvant radiation therapy is recommended for SCC with perineural involvement and positive tumor margins after resection. Radiation therapy can also be used in palliative care to reduce pain and hemorrhage in patients who are not candidates for surgery.

Electrochemical therapy is also indicated in locally advanced tumors such as melanoma, Kaposi's, and NMSC. It uses electrical current to increase the permeability of the cell membrane, thereby allowing cytotoxic drugs, commonly bleomycin, and cisplatin in SCC, to enter the tumor cell. Electro cancer therapy (ECT) also reduces tumor hemorrhage by causing vasoconstriction and destruction of endothelial cells which delays tumor angiogenesis and growth. Ricci, Paradisi, Fossati, Mancini, Curatolo, Guerriero, and Capizzi described a case of giant metastatic SCC to the lungs and right pectoral and infraspinatus muscles. The patient was treated with palliative ECT which reduced pain and partial cutaneous metastasis.[14] ECT has also been shown to have few reported adverse effects due to its ability to spare healthy tissue and minimally scar.[15]

Chemotherapeutic agents are commonly used for SCC that is not excisable; however, there have been few conclusive studies to develop a standard treatment regime. Cisplatin and carboplatin have been studied in non-excisable SCC receiving radiation therapy with overall complete response rate of 63%.[16] Several epidermal growth factor inhibitors, such as cetuximab and panitumumab, are in phase II clinical trials for the treatment of unresectable or metastatic disease. Dacomitinib, an epidermal growth factor inhibitor, has also been shown to control metastatic or locally advanced unresectable disease by 86%.[17]

This case report highlights the importance of patient education on prevention and recognition of skin cancer. Although most NMSCs are detected early, giant NMSCs still occur which poses a significant difficulty in treatment. Giant NMSC is more common in those with low socioeconomic status and infrequent physician visits.[18] These patients were also less concerned about their general health.[18] Therefore, education about skin cancer should be especially targeted toward these populations. Barriers to seeking medical care should be analyzed and resolved to prevent future incidences of giant NMSC.

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