

A Case Report of Verrucous Squamous Cell Carcinoma of the Scalp Treated with Docetaxel and Carboplatin at the Divine Word Hospital, A Tertiary Hospital in Tacloban City, Philippines

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Background. Verrucous squamous cell carcinoma is a rare form of squamous cell carcinoma characterized by slow growing exophytic tumors, verrucoid papule or plaque that develop at sites of chronic irritation. It is usually seen in the oral cavity, larynx, esophagus and skin, however it may also present elsewhere in the body. It was defined by Ackerman in 1948 as a diagnostically problematic squamous cell carcinoma. The standard of care for squamous cell carcinoma is a combination of surgery, systemic chemotherapy and radiation therapy, however radiation therapy is not available in our region.

Objective. The objective of this study is to present a rare case of verrucous squamous cell carcinoma presenting as a non-healing wound on the scalp managed with chemotherapy using docetaxel and carboplatin.

Case Summary. This is a case of a 61-year-old Filipino male from Daram, Samar, presenting with non-healing wound on the scalp. The patient had a hyperpigmented palpable nodule approximately <1cm on the scalp which he constantly scratched and peeled off. The lesion progressed into a 2x2cm hyperpigmented plaque. After a few weeks, hyperpigmented plaques on other parts of the scalp were noted and on the posterior right auricular area. Hyperpigmentation on the right side of the face was manifested, for which antibiotics and antifungals were given however, lesions persisted. Diagnostic workup was done in our institution and he underwent wide excision of the hyperpigmented plaque on the scalp. Biopsy report revealed a well-differentiated verrucous squamous cell carcinoma of the scalp. He underwent three cycles of chemotherapy with docetaxel and carboplatin and had significant reduction of the lesions.

Learning Points. The case was not immediately identified as a malignant entity; hence it was initially managed as skin and soft tissue infection. Therefore, a high index of malignancy suspicion should be taken on lesions that manifest with broadening and non-healing characteristics particularly in sun-exposed cutaneous regions.

Conclusion. Despite being in a resource limited setting, a trial of surgery and chemotherapy with docetaxel and carboplatin was able to reduce the size of lesions of verrucous squamous cell carcinoma on the scalp.

Keywords. verrucous squamous cell carcinoma, scalp, scalp tumors, docetaxel, carboplatin

Introduction

Verrucous carcinoma also called Ackerman's tumor is a distinct form of squamous cell carcinoma. The vast majority of tumors are identified in the oral cavity, with the remaining tumors identified in the larynx, sinonasal tract and pharynx. Patients are usually in the sixth and seventh decades of life (1).

The etiopathogenesis of verrucous squamous cell carcinoma is unclear however, the leading theories

include chemical carcinogenesis due to oral tobacco, betel nut, alcohol consumption, and chronic inflammation. The initial link of Human papilloma virus (HPV) infection to the development of cutaneous malignancies like epidermodysplasia verruciformis is established (1,2,3).

The gross appearance is usually of a broad-based, warty, exophytic or fungating, bulky, firm to hard, tan or white mass measuring up to 10cm in greatest dimension. The papillary-exophytic structure may show surface ulceration. Microscopically, it has filiform projections which are thickened and club-shaped and lined by well differentiated squamous epithelium. The advancing margins of the tumor are usually broad or bulbous rete

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pegs with a pushing appearance and a dense inflammatory response in the subjacent tissues. The cells are arranged in an orderly maturation towards the surface, with abundant surface keratosis (1,2,3,4).

The management involves wide surgical excision, radiotherapy or chemotherapy. Surgical resection remains the choice of treatment for this neoplasm (2,5). There is a controversy regarding the role and effect of radiation therapy on verrucous carcinoma (2,3). There are some reports of radiation-induced anaplastic transformation manifesting two to eight months following the therapeutic cycle (4). Chemotherapy in verrucous carcinoma is scarce and limited to small case series and case reports. The chemotherapeutics effective in differentiated squamous cell carcinoma were used more frequently in drug combinations or as a single-agent therapy for verrucous carcinoma (e.g. methotrexate, bleomycin, vinblastine, 5-fluorouracil, and cisplatin). The choice of chemotherapy was mainly empirical and derived from treating squamous cell carcinoma (6,7).

Case Presentation

This is a case of a 61-year-old Filipino male from Daram, Samar presenting with non-healing wound on the scalp. He had pruritus on the scalp and was able to palpate a nodule which he constantly scratched. He noted bleeding from the site but still continued to scratch and peeled off the scab. On his first consult three months prior to admission, he was just given tetanus toxoid however, noted hyperpigmented plaques on the scalp. Two months prior to admission, he sought consult and was prescribed with Co-amoxiclav 625 mg one tablet thrice daily for 10 days and mupirocin ointment and had good compliance but still with persistence of lesions. One month prior to admission, he noted the lesions to be necrotic and painful. He also had onset of an irregularly shaped, raised plaque on the right posterior auricular area which also bled upon scratching. He sought another consult and was prescribed with ciprofloxacin 500mg one tablet twice daily and fluconazole 100mg one capsule once daily for seven days. Two weeks prior to admission, he also developed a hyperpigmented plaque around the right eye extending to the right side of the face accompanied by edema but no visual acuity problems. He was given sultamicillin 750mg one tablet twice daily and clindamycin 300mg one capsule four times a day and was compliant for one week. However, worsening of skin lesions was noted. Further evaluation and management were advised, and was referred to our institution.

The patient is a known hypertensive and with history of gouty arthritis. He is currently unemployed but previously a fisherman and fish vendor. He has a family history of hypertension. He is a previous smoker with 20 pack years smoking history, and an alcoholic beverage drinker, consuming 1 liter of beer two times weekly. His habits coupled with constant exposure to sunlight, could have been the risk factors for developing skin malignancy.

On admission, the patient was noted to have hyperpigmented elevated plaques of various sizes on the scalp and on the posterior right auricular area (Figure 1A). His right side of the face was also hyperpigmented and had periorbital edema on the right eye (Figure 1B). Other physical examination findings were unremarkable. Laboratory tests were done including blood culture. He was managed for Necrotizing fasciitis of the scalp and was started with ticarcillin- clavulanic acid and doxycycline for infection control. He was referred to the Surgery Department and underwent wide excision of the hyperpigmented plaques. He had no febrile episodes while admitted. He was discharged stable and advised for follow up once biopsy result is obtained.



Figure 1. A. Hyperpigmented plaques on the scalp and right posterior auricular area noted upon admission (November 16, 2020) 1. 5x5cm 2. 2x2cm 3. 4cmx1.5cm 4. 1.5x 1.5 cm **B.** Periorbital edema and hyperpigmentation on the right side of the face upon admission (November 16, 2020)

On follow up, 1 week after discharge, he was noted to have increased periorbital edema and hyperpigmentation on the right eye and on the right side of the face respectively. The exophytic mass on the posterior right auricular area was also increased and with hemorrhagic portions. He had no febrile episodes but had pain on the lesions.

Biopsy report revealed an ulcerated verrucous papillomatous lesion composed of keratinized columns and lobules of squamous epithelial cells. In the underlying stroma, preserved lobules of keratinized pleomorphic neoplastic squamous epithelial cells could be identified. Bacterial colonies were present on the ulcerated surface. The lesion extended all the way to the basal plane of resection. Thus, histopathologic diagnosis of a well differentiated verrucous squamous cell carcinoma (Figure 2).

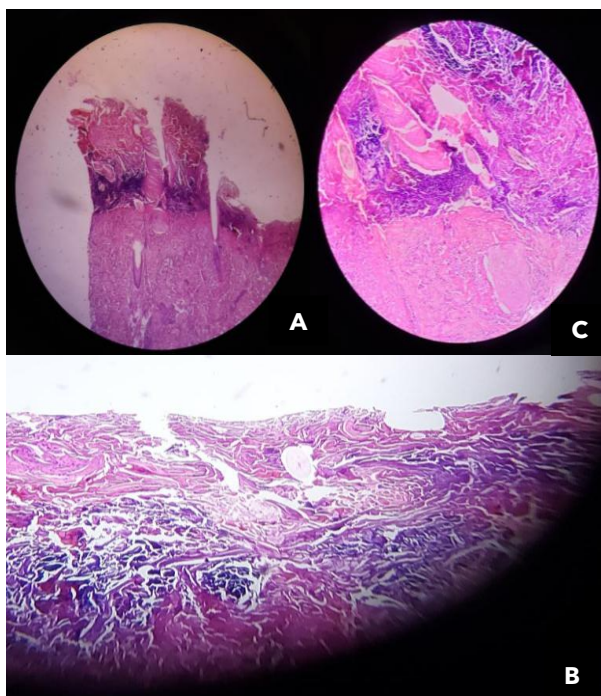


Figure 2. Histopathologic finding of a well differentiated verrucous squamous cell carcinoma A. Scanner view B. Low power objective view C. High Power Objective view

* Images courtesy of Divine Word Hospital Department of Pathology (S-20-1758)

Radiation therapy is the treatment of choice for areas where extensive surgical resection would result in poor cosmetic outcome such as near eyelids, ear lobes, or the tip of the nose (8). The patient was referred for radiotherapy at a tertiary hospital in Manila, but the COVID-19 pandemic was an obstacle on top of financial difficulties. He underwent chemotherapy with docetaxel 100mg and carboplatin 450mg every 21 days for three cycles at our institution. Lesions had favorable response to the chemotherapeutic regimen (Figure 3 and Figure 4). Adverse events such as nausea and vomiting were tolerated well. Renal and hepatic function post chemotherapy were tolerable. After the third cycle, family opted to transfer to a hospital in Luzon for further management.



Figure 3. Changes of the periorbital edema and hyperpigmentation on the right side of the face A. Prior to initiation of chemotherapy (December 9, 2020) B. Immediately one day after the 1st chemotherapy (December 12, 2020) C. After 1st cycle of chemotherapy (January 8, 2021) D. After 2nd cycle chemotherapy (January 29, 2021)



Figure 4. Changes of the lesions in the scalp A. Prior to initiation of chemotherapy (December 9, 2020) B. Immediately one day after the 1st chemotherapy (December 12, 2020) C. After 1st cycle of chemotherapy (January 8, 2021) D. After 2nd cycle chemotherapy (January 29, 2021)

Discussion

In this patient who presented with a non-healing wound on the scalp the differential diagnosis included infectious and non-infectious causes. The patient was first thought to have an infectious cause such as a carbuncle and necrotizing fasciitis due to the initial lesion which seemingly just started as palpable nodules that progressed to hyperpigmented plaques. However, this was ruled out since the patient was immunocompetent and the skin lesion did not respond to antimicrobial therapy. Malignancy was considered as a non-infectious cause since the lesion was evolving in terms of color, size

and shape and there was progression of lesions to contiguous scalp regions. There was also a significant history of sun exposure. Melanoma and non-melanoma skin cancers were considered and the diagnosis was supported by the histopathological finding of a verrucous squamous cell carcinoma.

Non-melanoma skin cancers, mainly basal cell carcinoma and squamous cell carcinoma are the most common type of skin malignancies. Basal cell carcinoma (BCC) originates in the basal layer of the epidermis. Distant metastases are extremely rare. Squamous cell carcinoma (SCC) usually presents as a hyperkeratotic papule, plaque or nodule. Hyperkeratosis is an important feature of SCC. Both are seen predominantly in the elderly. Risk factors include age greater than 60 years, prior heavy sun exposure, fair complexion and light colored eyes or hair. Other etiologic factors include prior irradiation to the skin for benign disorders, chronic inflammation, scarring or burns, and arsenic exposure (8-11).

Verrucous carcinoma is a subtype of low-grade squamous cell carcinoma and not simply SCC with a verrucous clinical presentation. It has a benign histology and cytology with aggressive potential (2,5). However, it has an indolent clinical behavior with negligible metastatic potential. Its apparent clinical benignity may lead to a period of misdiagnosis.

Diagnosis of verrucous carcinoma involves both examination of the lesion in the patient and vigilant histologic study. The pathological diagnosis is extremely difficult and it has been reported that multiple biopsies are often required before diagnostic histological features supporting an appropriate interpretation of verrucous carcinoma is identified (4). A suitable biopsy must show not only a well-differentiated hyperkeratotic warty superficial surface but also an equally well-differentiated bulbous rete-ridge pattern at the bottom of the lesion (5,6).

Treatment for squamous cell carcinoma is based on tumor characteristics, histopathology, and the nature or location of the skin lesion from which the tumor arises. Surgical excision to attain margins of at least 3 to 10mm is the preferred treatment in squamous cell carcinoma because of the higher metastatic potential (7-11). For this patient, wide excision was done both for therapeutic and diagnostic purposes. Chemotherapy used in combination with surgery allows for less extensive resections and improved functional and cosmetic results.

Moh's micrographic surgery is a cost-effective procedure that affords the highest cure rate, maximal tissue preservation, and superior cosmetic outcomes. Nonsurgical methods may be used as a primary treatment for low-risk squamous cell carcinomas, but the cure rates are lower (12,13).

Several new chemotherapeutic agents with activity against head and neck squamous cell carcinoma have enabled the development of combination regimens that provide excellent response rates and improved toxicity profiles. A combination chemotherapy with docetaxel

with carboplatin is an effective therapy for locally advanced, recurrent or metastatic squamous cell carcinoma of the head and neck. (14-18).

Taxanes, particularly docetaxel has been widely used for combination therapy of head and neck squamous cell carcinoma. In addition to stabilizing b-tubulin polymerization to suppress microtubule dynamics and impair mitosis, taxanes are involved in many oncogenic signaling pathways such as angiogenesis, inflammatory response, reactive oxygen species production and apoptosis induction (19-22.)

This patient underwent chemotherapy with docetaxel and carboplatin and showed significant improvement. Adverse reactions or toxicity such as emesis, myelosuppression, renal function and hepatic function were tolerable.

When combined with radiation, chemotherapy compensates for deficient effectiveness of radiotherapy and allow safe reduction in radiotherapy dose to alleviate its toxicity (23). Patients with head and neck cancer benefit from radiation therapy whether primary or adjunct therapy after surgical resection. The major goal of radiotherapy is to achieve local control of the tumor while minimizing damage to the critical organs. The combination of chemotherapy and radiotherapy has been introduced to increase tumor control and preserve organ integrity (24). Unfortunately radiation therapy is still not available in our locality hence only surgery and chemotherapy was done.

In a study by Wang et al. (2020), the cancer-related survival rate and overall survival rate of head and neck squamous cell carcinoma were better than other malignant tumors of the head and neck. Patients who had surgery alone had a better prognosis than patients with chemotherapy alone, but patients who received chemotherapy alone had a little difference in prognosis with patients who had undergone both surgery and chemotherapy. Patients with surgery alone had a higher cancer-specific survival rate than patients with both surgery and radiotherapy, and chemotherapy but had a little difference in overall survival.

Prognosis for verrucous carcinoma is generally favorable when detected early and managed appropriately. Prognostic factors influencing outcomes include tumor size, depth of invasion, anatomical location and Human Papilloma Virus status. Overexpression of molecular markers such as p53 and high Ki-67 proliferation indices has been linked to aggressive disease behavior. Host-related factors such as age, immune competence, and the presence of comorbidities play crucial roles in determining prognosis (25).

Conclusion

Verrucous squamous cell carcinoma is a rare form of squamous cell carcinoma. It usually presents as a slow growing exophytic tumor. Histologically, it shows a verrucous surface and downward growth seeming to compress the underlying connective tissue and typically

has minimal or absent cytological atypia. A high index of suspicion of malignancy in broadening or non-healing lesion, particularly on sun exposed areas warrants immediate diagnosis in order to appropriately manage and prevent further spread of the lesion. Treatment options for verrucous squamous cell carcinoma are typically based on individual factors including location of institution, available treatment facilities, and the physician's clinical skill.

In this case, radiation facility is not available in Region VIII (Leyte and Samar) and financial constraints barred immediate referral to other hospitals. These obstacles to the therapeutic approach of this case were hindrances to combat this carcinoma. Hence, wide surgical excision coupled with combination chemotherapy with docetaxel and carboplatin were the options done. The two treatment modalities offered encouraging results by the visible decrease in the size of the lesions on the scalp and face as shown in the patient. Since the physical appearance of the lesions greatly affected the patient's self-esteem and his social activities, he was truly grateful to receive all of the treatments given to him and was willing to share his case for learning purposes.

Patient Consent

Informed consent was obtained from the patient and the service case consultants for the presentation of this case and for the images presented.

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