

CHEMORADIOTHERAPY OF SQUAMOUS CELL CARCINOMA OF LEFT CONJUNCTIVA IN A HIV POSITIVE MAN

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ABSTRACT

Intra ocular and orbital tumors, although rare, represent an important entity in the field of oncology. Worldwide, conjunctiva squamous cell carcinoma is an uncommon diseases, the incidence of which varies geographically from 0.02 to 3.5 per 100, 000. The American cancer society estimated approximately 2, 360 new diagnoses of ocular and orbital tumors in the United States during the year 2006.

Macroscopic patterns of squamous cell carcinoma have been described as gelatinous, velvety or papilliform, leukoplakia, nodular and diffuse. In general, squamous cell carcinoma of the conjunctiva is reported as a low grade malignancy. Recurrence rates are generally higher for more severe grades (ocular surface squamous neoplasm).

Squamous cell carcinoma of the conjunctiva typically presents with ocular surface epithelial dysplasia, most frequently on the nasal aspect of the eye. Metastases are very rare and the prognosis with local excision is good.

These tumors occur more frequently in sub-Saharan African, where the incidence is up to 12/10⁶ per year and have been thought to be related to exposure to UV light. In a cattle model for squamous carcinoma of the conjunctiva, an association has been found with bovine papilloma virus, suggesting that Human Papilloma Virus (HPV) might have a role in the pathogenesis of this malignancy in humans.

We present a 35 year old man who was referred to Radiotherapy Clinic, University College Hospital, Ibadan with 6 years history of painful left eye swelling, progressively increasing in size with associated headache. He was also a known Retroviral positive patient on anti-viral medication.

He received 3 weekly combination chemotherapy with vincristine 1.5mg/m², methotrexate 50mg/m² and Bleomycin 50mg/m² X 6 courses and Radiotherapy total of 45Gy in 22 fractions over 4.5 weeks from a cobalt-60 machine to the left eye. Anterior field was used with the eye lids open. He was placed on Retroviral Drugs (Zidovudine, Didanosine and Nevirapine).

Patient has been seen on follow up for 3 years now, during which there was no evidence of local recurrence. The disease has been well controlled and the HIV infection also well controlled, with CD4 count of 855cell/mls. Last visit was November 2012.

Keywords: Chemo-radiotherapy, Conjunctiva carcinoma, HIV patient

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Introduction

Intra ocular and orbital tumors, although rare, represent an important entity in the field of oncology⁽¹⁾. Worldwide, conjunctiva squamous cell carcinoma is an uncommon diseases, the incidence of which varies geographically from 0.02 to 3.5 per 100, 000⁽²⁾. The American cancer society estimated approximately 2, 360 new diagnoses of ocular and orbital tumors in the United States during the year 2006.⁽¹⁾

Macroscopic patterns of squamous cell carcinoma have been described as gelatinous, velvety or papilliform, leucoplakia^(3, 4) nodular and diffuse⁽⁵⁾. In general, squamous cell carcinoma of the conjunctiva is reported as a low grade malignancy. Recurrence rates are generally higher for more severe grades (ocular surface squamous neoplasm).

Squamous cell carcinoma of the conjunctiva typically presents with ocular surface epithelial dysplasia, most frequently on the nasal aspect of the eye⁽⁶⁾. Metastases are very rare and the prognosis with local excision is good.

These tumors occur more frequently in sub-Saharan African, where the incidence is up to 12/10⁽⁶⁾ per year and have been thought to relate to exposure to UV light⁽⁶⁾. A number of case – control studies have been conducted in Africa, demonstrating an increased incidence of these tumours in HIV-positive people, with a relative risk of around 10.

In a cattle model for squamous carcinoma of the conjunctiva, an association has been found with bovine papilloma virus, suggesting that Human Papilloma Virus (HPV) might have a role in the pathogenesis of this malignancy in humans⁽⁶⁾

Radiation, either as external beam or brachytherapy, remains an effective therapeutic option⁽¹⁾. Satisfactory results have been observed in the management of both intraocular and orbital tumors when radiotherapy was used as primary or adjuvant therapy along with surgery. Chemotherapy, Thermotherapy, Immunotherapy, Cryotherapy, photocoagulation and other treatments are still under investigation.

Case Reporting

A 35 year old man who was referred to Radiotherapy Clinic, University College Hospital, Ibadan with 6 years history of left eye painful swelling, progressively increasing in size with associated headache. He was also a known Retroviral positive patient on Anti-Retroviral medication.

Examination revealed a young man, not pale, anicteric afebrile. Direct examination revealed protruding left eye, invasion of the corneal and anterior part of the eye with loss of vision and no light perception. There was purulent conjunctiva hypereamia, there were also palpable discrete lymph nodes in the left upper cervical not attached to overlying skin. Right eye was normal and other systems were within normal limit.

Heamatological, Biochemical and Radiological work up such as FBC, E&U, Cr, LFT, clothing profile, Retroviral screening skull X-ray all were reported normal, except Retroviral screening that was reactive. The CD4 count on 3/3/12 was 550 cells/mls. He had biopsy and histology came as squamous cell carcinoma of the left conjunctiva. He received 3 weekly combination chemotherapy with vincristine $1.5\text{mg}/\text{m}^2$, methotrexate $50\text{mg}/\text{m}^2$ and Bleomycin $50\text{mg}/\text{m}^2$ X 6 courses and Radiotherapy total of 45Gy in 22 fractions over 4.5 weeks from a cobalt-60 machine to the left eye. Anterior field was used with the eye lids open. He was placed on Retroviral Drugs (Zidovudine, Didanocine and Nevirapine).

Patient was seen on follow up for 3 years now, during which there was no evidence of local recurrence. The disease has been well controlled and the HIV was also well controlled, with CD4 count of 855 cell/mls. Last visit was November 2012 with normal FBC + diff, CRT, C – XRAY and Abdominal pelvic ultrasound.

Discussion

Human Immunodeficiency Virus (HIV) infection is strongly associated with an apparent increase in the incidence of conjunctiva carcinoma in Africa. ⁽⁷⁾

Conjunctival squamous cell carcinoma can occur in immunosuppressed patients and can be more aggressive and invasive, requiring enucleation or exenteration. Surgical resection plus topical interferon alpha-2B might reduce the risk for recurrence or new tumor. ⁽⁸⁾

Squamous cell carcinoma can be multi focal and aggressive in HIV infected patients. Rapid progression to intraocular penetration can be observed ⁽⁹⁾

Since the 1980s the number of patient presenting with squamous cell carcinoma of the conjunctival has been increasing exponentially. Seen in age from 18-60 years with the majority between 20 and 40 years. Both male and female are equally affected. Often the squamous cell carcinoma of the conjunctival may be the only manifestation in otherwise healthy looking adults. ⁽¹⁰⁾

The exact cause of squamous cell carcinoma is not known but the human papilloma virus has been implicated. Polymerase chain reaction tests have turned positive in patients with squamous cell

carcinoma. It is suggested that the immune-suppression caused by Human Papilloma virus promote the growth of the tumor.⁽¹⁰⁾

Earlier report have suggested 90% response to radiotherapy when diagnosed early. A dose between 45-60Gy was found to be adequate⁽¹¹⁾, this patient received 45Gy and was combined with chemotherapy in view of the advanced stage of the disease to take advantage of the synergistic effect of the two modalities. Patient tolerated the regimen with very minimal side effects.

The disease is an advanced type of ocular surface squamous neoplasia (OSSN). OSSN is the most common ocular surface tumor in HIV infected individuals in Africa. The spectrum varies from noninvasive (CIN) to invasive forms. It is associated with HPV and HIV infections. Incidence of squamous cell carcinoma of conjunctiva (SCCC) is increasing because of the spread of HIV infection.^{(12), (13), (14)}

In a case control study, Ateenyi Agaba *et al.* have shown that out of 94 patients of SCCC, 79 suffered from HIV, and cutaneous HPV was detected in 45% of cases. Most common types of HPV were 5 and 8.⁽¹⁵⁾ Apart from these two, other HPV types like 19-25 and 36-38 are associated with SCCC, but not 16 and 18.⁽¹⁶⁾ In another study Ateenyi Agaba and colleagues observed that 75% of patients with conjunctival tumours seen at Mulago Hospital Uganda were HIV seropositive compared with 19% of cases with non-malignant eye conditions⁽¹⁷⁾

Primary management of SCCC is surgical resection.⁽¹⁸⁾ Adjuvant radiation therapy has shown some benefit. Radiotherapy using beta rays (strontium applicator), brachytherapy or superficial X-rays have shown good response.^{(19), (20), (21)}

In an adjuvant setting, 25-40 Gy dose is delivered. Usually, this superficial therapy is well tolerated and the control rate is around 97%.⁽²⁰⁾ In poor resource like ours only cobalt -60 therapy machine was available and equally good response was obtained. In view of the advanced stage at presentation surgical resection was not considered. He was considered for chemo-radiotherapy, the disease was controlled and good cosmetic was achieved.

Conclusion

Chemo – Radiation therapy achieved a long disease free period in this patient with back ground of HIV disease. The control of the HIV infection by the antiretroviral drugs also contributed to this good response. Hence Chemo-radiotherapy could be considered in advanced conjunctiva cancer.

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