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THE CENTRAL AFRICAN JOURNAL OF MEDICINE

ORIGINAL ARTICLES

Bilateral HIV related ocular surface squamous neoplasia: A paradigm shift

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Abstract

Four patients with bilateral ocular surface squamous neoplasia attended to at Sekuru Kaguvi Hospital Eye Unit are being presented to alert practitioners that OSSN is potentially a bilateral disease and its prevalence is likely to increase as the life expectancy of HIV infected patients is being positively affected by antiretroviral therapy. Reports on ocular diseases should be clear on laterality to avoid confusion between number of patients affected and number of eyes involved since the two cannot be used interchangeably.

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Introduction

Ocular surface squamous neoplasias (OSSN) range from dysplasias, carcinoma in-situ to invasive squamous cell carcinoma of the conjunctiva.[1-2] The geographical distribution of OSSN world over has not been spared by the HIV / AIDS pandemic, with countries like Zimbabwe reporting its first cases from 1990 ten years after the pandemic and Uganda, Malawi and Tanzania noticing dramatic increases in OSSN prevalence rates respectively.[3-5] The annual prevalence rate of the disease in Zimbabwe has been escalating with the National Cancer Registry rating it to be the fourth most frequently registered malignancy in the country.[6]

The disease is associated with high morbidity and mortality in Zimbabwe contrary to the traditionally reported similar tumours.[7,8] It is not clear whether the cause of these deaths in Zimbabwe is due to the malignancy alone or patients secumbing to the HIV / AIDS and its associated co-infections.

With the advent of highly active antiretroviral therapy (HAART), HIV / AIDS is now a treatable but chronic disease and patients live longer once effective treatment has been established for each individual.[9] The effect of HAART on HIV related malignancies like OSSN has not yet been studied. However, anecdotal evidence suggest that in patients who develop the malignancy prior to commencing treatment HAART does not interrupt tumour growth or even its recurrence.

There is very little published information on bilateral OSSN the world over today. Four patients with bilateral OSSN are being reported to illustrate that OSSN is potentially a bilateral condition and to encourage authors to be explicit on laterality when reporting eye problems. This report will alert practitioners of a possible increase in bilateral HIV related OSSN since HIV / AIDS has been transformed by HAART from being a very fatal disease to a chronic one.

Clinical records.

The table below summarises some important features of the four patients with bilateral OSSN who were attended to at Sekuru Kaguvi Hospital Eye Unit, Parirenyatwa Group of Hospitals in Zimbabwe between 2007 and 2010.

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Table I: Case summaries.

CASE	DIAGNOSIS	RISK FACTORS	MANAGEMENT	OUTCOME
1. 63 year old male who first presented in July 2007 with left conjunctival growth for six months.	1. Left invasive squamous cell carcinoma of conjunctiva. 2. Right eye was normal and did not have signs of OSSN.	1. HIV positive. 2. CD4 cell count was 150. 3. Peasant farmer. post exenteration to left	1. Enucleation of left eye. 2. Patient started on HAART. 3. Radiotherapy was given Orbit.	1. Left socket healed well within three months time
2. 27 year old male who first presented in Sept 2007 with right conjunctival growth for eight months.	1. Right invasive squamous cell carcinoma of conjunctiva. 2. Left eye was normal and did not have signs of OSSN.	1. HIV positive. 2. CD4 cell count was 200.	1. Enclueation of right eye. 2. Patient started on HAART.	1. Right socket healed well 1. Right socket healed well within four months time. 2. One and half years later patient presented with advanced OSSN left orbit.
3. 32 year old female who first presented in April 2008 with left conjunctival growth.	1. Left invasive squamous cell carcinoma of conjunctiva. 2. Right eye was free of tumour.	1. HIV positive. 2. CD4 cell count was 175.	1. Enucleation of right eye 2. Patient was started on HAART.	1. Left socket healed well within four months time. 2. One year later patient presented with advanced right OSSN.
4. 30 year old female who first presented in May 2008 with bilateral conjunctival growths.	1. Right invasive squamous cell carcinoma of conjuctiva 2. Left carcinoma in situ.	1. HIV positive. 2. CD$ cell count was 150.	1. Enucleation of right eye. 2. Excision of conjunctival growth left eye 3. Patient started on HAART.	1. Right socket healed well within three months time 2. Left eye no tumour recurrence as yet.

All the patients were black indigenous Zimbabweans, who did not smoke. They had no history of allergic eye problems. They all were heterosexual with multiple partners. The last patient lived in an urban setting while the others came from rural settings. Patients two and four were self-employed as informal traders, while the other two were peasant farmers. None of the patients had instilled traditional eye medicines in their eyes.

None of the patients had been tested for HIV when they presented to us initially. Extended enucleations had to be performed in all patients because the tumours were extensively involving the globes but had not spread into the orbits or beyond.

Histologically all four neoplasms showed figures of epithelial cells with focal keratinisation in keeping with squamous cell carcinomas. All the tumours were classical epidermoid carcinomas with no evidence of mucoid differentiation.

Although efforts had been made to commence all patients on HAART prior to their discharge from hospital, monitoring compliance to HAART was left to the local opportunistic infections clinics. Our contact with the last patient has been regular since she is living in Harare. The other three patients came from districts out of Harare and regular follow-up was technically difficult for patients to comply with because of transport costs.

All patients were alive and doing well with no clinical evidence of recurrent disease three months post surgery. Three patients who had presented with uni-ocular disease were lost to quarterly follow-up visits and only returned with advanced OSSN affecting the second eye approximately two years after removal of the first eye. Reasons given for defaulting follow-up were financial in all three. Fear of loosing the only eye was given as the reason for delaying coming back despite the counseling sessions received before the initial discharge from the ward and knowledge of their conditions. The three patients underwent orbital exenteration with the hope of clearing the tumours. Unfortunately this was not feasible since the tumours had eroded the orbital walls in all three patients and they all demised within three to six months of orbital exenteration surgery.

Figure 1: Patient 1 three weeks post exenteration.

The fourth patient had presented with bilateral disease. The eye with advanced disease involving the globe was

enucleated while the other lesion was completely excised. This patient has managed to maintain regular follow up with us and there is no clinical evidence of tumour recurrence in the socket and on the remaining eye. The patient continues to take HAART without fail and her general well being is impressive although she has to battle with the cosmetic problem of having lost one eye.

Discussion

The aetiology of OSSN is a subject of much debate and a lot still has to be done in terms of research to establish the cause of this disease.[10,11] Its association with HIV infection in some regions of the world is unquestionable.[12-14] Traditionally accepted risk factors for OSSN include advanced age, male gender, exposure to solar ultraviolet light, cigarette smoking and human papilloma virus infection.[15-17] Clinico-pathological diagnosis of OSSN has largely been based on histological reports of surgically excised tumour tissue while the standard treatment was surgical excision of tumour plus or minus cryotherapy. However of late, clinicians are moving towards less invasive investigative and treatment modalities for these cancers, hence the increasing use of impression cytology and the use of chemotherapeutic agents like mitomycin C, 5-flourouracil and interferon alpha 2b respectively.[18,19]

Increasing incidence of OSSN, emergency of OSSN epidemics in countries where the tumour had not been previously reported on before, lack of gender predilection, increased mortality and morbidity rates associated with OSSN and the identification of new risk factors like HIV infection have been much publicized during the last decade although very little has been reported on regarding bilateral cases of OSSN world wide.[20,21]

Gerick et al reported on a patient with atopic dermatitis who presented to them with bilateral OSSN[22], while Grueb and colleagues reported on a 75 year old patient who presented with bilateral OSSN following 30 years of chronic exposure to wood dust[23]. Lam and colleagues reported on two bilateral cases of conjunctival epidermoid carcinoma which is a rare familial type tumour seen among teenagers.[24]

The emergence of bilateral cases of OSSN the world over is a cause of concern for two reasons: whether the currently reported rates of OSSN refer to patients or eyes and whether increased longevity of HIV / AIDS patients with uni-ocular OSSN may be associated with increased likelihood of developing OSSN in the previously unaffected eyes.

Many publications on ocular diseases do not make a distinction on whether the quoted frequency rates of a condition refer to affected patients or eyes. Under normal circumstances patients have two eyes and disease severity is graded differently when one has bilateral disease as opposed to unilateral disease. Treatment options for each eye may be tailored according to laterality, location and severity of disease as has been the experience with retinoblastomas and choroidal melanomas.[25,26]

Three (75%) of our patients expressed fear of loosing the second eye contributed to delayed presentation. This should alert practitioners to look out for such cases and counsel patients reminding them of the importance of regular follow up and early presentation to the ophthalmologists once they notice symptoms of the disease.

The increased longevity of HIV / AIDS patients on HAART has been one of the greatest medical achievements World wide to date. The effect of HAART on OSSN growth and recurrence has not been studied. Experience gained on these four cases on the effect of HAART on OSSN is not conclusive since our center could not monitor these patients closely. It is our hope that the universal access to HAART being advocated for today is an achievable goal and HAART may be looked at as a tool to prevent HIV transmission and occurrence of HIV related malignancies.[9]

Conclusion

HIV related OSSN has a high potential of becoming bilateral disease. Clinicians should be on the look out for this in view of the drive towards universal access to HAART being advocated for to date.

References

1. Lee GA, Hirst LW. Retrospective study of ocular surface squamous neoplasias. *Austr and NZJ Ophthalmol* 1997;25: 269-76.
2. Lee GA, Williams G, Hirst LW, Green AC. Risk factors in the development of ocular surface squamous epithelial dysplasia. *Ophthalmol* 1994;101: 360-4.
3. Masanganise R, Rusakaniko S, Makunike R, Hove M, Chokunonga E, Borok MZ, Mauchaza BG, Chirenje MZ, Masanganise VN, Magure T. A historical perspective of registered cases of malignant ocular tumours in Zimbabwe (1990 to 1999). Is HIV infection a factor? *Cent Afr J Med* 2008;54: 28-32.
4. Waddell KM, Lewallen S, Lucas S, Ateenyi-Agaba C, Harrington CS, Liomba G. Carcinoma of conjunctiva and HIV infection in Uganda and Malawi. *Br J Ophthalmol* 1996;80: 503-8.
5. Poole TRG. Conjunctival squamous cell carcinomas in Tanzania. *Br J Ophthalmol* 1999;83: 177-9.
6. Zimbabwe National Cancer Registry Annual Report 2006.
7. Zimmerman LE. The cancerous, precancerous and pseudocancerous lesions of the cornea and conjunctiva. In Rycroft PV (ed): Corneo-Plastic Surgery. ELMS Ford, NY. Permason Press, 1969.
8. Ash JE, Wilder HC. Epithelial tumours of the limbus. *Am J Ophthalmol* 1942;25: 926.

9. Montaner JSG, Lima VD, Barrios R, Yip B, Wood E *et al. Lancet* 2010;376: 1-8.
10. Ateenyi-Agaba C, Franceschi S, Wabwire-Mangen F, Arsian A, Othieno E, Binta-Kahwa J, van Doorn L-J, Kleter B, Quint W, Weiderpass E. Human papillomavirus infection and squamous cell carcinoma of the conjunctiva. *Br J Cancer* 2010;102: 262-267.
11. Yu JJ, Fu P, Pink JJ, Dawson D, Wasman J, Orem J, Mwanda WO, Zhu H, Liang X, Guo Y, Petros WP, Mitsuyasu RT, Wabinga H, Remick SC. HPV infection and EGFR activation/alteration in HIV -infected East African patients with conjunctival carcinoma. *Brit J Cancer* 2010;104: 77
12. Ateenyi-Agaba C. Conjunctival squamous cell carcinoma associated with HIV infections in Kampala Uganda. *Lancet* 1995;345: 695-6.
13. Chinogurei TS, Masanganise R, Rusakaniko S, Sibanda E. Ocular surface squamous neoplasia\ (OSSN) and Human Immunodeficiency Virus at Sekuru Kaguvi Eye Unit in Zimbabwe. *Cent Afr J Med* 2006;52: 56-8.
14. Guech-Ongey M, Engels EA, Goedert JJ, Mbulaiteye SM. Evaluated risk for squamous cell carcinoma of the conjunctiva among adults with AIDS in the United States. *Int J Cancer* 2008;122: 2590-3.
15. Lee GA, Hirst LW. Incidence of Ocular Surface Epithelial Dysplasia in Metropolitan Brisbane. *Arch Ophthalmol* 1992;110:525-7.
16. Furahini G, Lewallen S. Epidemiology and management of ocular surface squamous neoplasia in Tanzania. *Ophthalmic Epidemiol* 2010;17:171 -6.
17. Lauer SA, Malter JS, Meier JR. Human papillomavirus type 8 in conjunctival intraepithelial neoplasia. *Am J Ophthalmol* 1990;110:23-7.
18. McKelvie P. Review Ocular Surface Impression Cytology. Adv Anat. Pathol 2003;10:328-37.
19. Poothullil AM, Colby KA. Review Topical Medical Therapies for ocular surface tumours. *Semin Ophthalmol* 2006;21:161-9.
20. Basti S, Macsai MS. Ocular surface squamous neoplasia: a review. *Cornea* 2003;22:687-704.
21. Odricch MG, Jakobeic FA, Lancaster WD, Kenyon KR, Kelly LD, Kommehl EW, et al. A spectrum of bilateral squamous conjunctival tumours associated with human papillomavirus type 16. *Ophthalmology* 1991;98: 628-35.
22. Gericke A, Pitz S, Strempel I, Sekundo W. Bilateral conjunctival squamous neurodermatitis. Two cases with different course. *Ophthalmologe* 2008;105: 1142-5.
23. Grueb M, Rohrbach JM, Kroeber SM. Bilateral ocular surface squamous neoplasia after wood dust exposure. *Acta Oncologica* 2006;45: 218-19.
24. Lam A, Borzeix A, Selk CM, Faye M, Saccaharin C. Two bilateral cases of conunctival epidermoid carcinoma. *J Fr Ophthalmol* 1996;19: 143-8.
25. Abramson DH, Schefler AC. Update on retinoblastoma. *Retina* 2004;24: 828-848.
26. Shields JA, Shields CL. Current management of posterior uveal melanoma. *Mayo Clin. Proc.* 1993;68: 1196-1200.