Non-AIDS Defining Malignancies Become an Emerging Problem in HIV-Infected Patients: At a Glance on Oral Pathology Unit, University of Dental Medicine (Yangon)

Khin Soe* and Zaw Moe Thein**
***Department of Oral Medicine, University of Dental Medicine, Mandalay.**
****Department of Oral Medicine, University of Dental Medicine, Yangon.**

Abstract
The introduction of HAART (Highly Active Antiretroviral Therapy) caused significant decrease in the incidence of AIDS-defining illnesses among individuals undergoing antiretroviral therapy. In the resent years, the research observed a worrying increase in the incidence of non-AIDS-defining cancers (NADC) and increases mortality related to these cases. In this retrospective study, we observed surgical pathology cases with HIV infection those sent to Oral Pathology Unit, University of Dental Medicine, Yangon, from January 2013 to November 2015. Twelve cases were analyzed in relation with their request forms and biopsy results. In general, there were noticeably larger numbers of NADCs (for instance, oral squamous cell carcinoma). According to this study, NADC is found to be an emerging problem in HIV-infected patients. Further epidemiological and clinico-pathological studies as well as screening procedures should be warranted to solve this problem.
Key words: AIDS-defining cancers, HIV/AIDS, Oral squamous cell carcinoma.

Introduction

AIDS-defining cancers are a subset of HIV-associated malignancies that include Kaposi sarcoma, some forms of non-Hodgkin lymphoma (NHL), and invasive cervical cancer. Compared to non-AIDS-defining cancers (NADCs), Kaposi sarcoma and NHL demonstrated the highest incidence in the early acquired immunodeficiency syndrome (AIDS) epidemic.1 Advances in molecular biology, immunology, virology, and anti-viral therapy have combined to create unique research opportunities in HIV/AIDS patients. New antiretroviral therapies are able to substantially reverse or delay the profound immunosuppression of HIV infection. The changes in the epidemiology of malignancies, and understanding the mechanism of action of this new therapeutics provide research opportunities to understand the pathogenesis of these malignancies.2

There was a markedly increased risk of Kaposi's sarcoma, NHL and invasive cervical cancer during the course of infection with the human immunodeficiency virus (HIV).3 In the era of HAART (Highly Active Antiretroviral Therapy) there was significant decrease in the incidence of AIDS-defining illnesses. However, it was evident dramatic increase in the incidence of NADCs and increased mortality related to these cases. In the resent years, the research observed a worrying increase in the incidence of NADCs and increases mortality related to these cases. Changes in the incidence of cancers associated with HIV since antiretroviral therapy era were detected by many authors. The objective of this study was to find out the prevalence data of AIDS-defining malignancies and NADCs among the HIV-positive surgical pathological cases.

Material and method

In this retrospective study, we observed surgical pathology cases with HIV infection those sent to Oral Pathology Unit, University of Dental Medicine, Yangon, from January 2013 to November 2015. Archives of paraffin-embedded tissue blocks in relation with their request forms those were marked as HIV-positive were studied by using hematoxylin and eosin staining. Twelve cases of HIV-positive cases were analyzed and prevalence rate of oral squamous cell carcinoma (OSCC) cases without HIV infection were compared in this study.

Results

Among twelve HIV infected cases, only one patient was diagnosed as NHL which was AIDS-defining malignancy. The rest eleven cases were NADCs, five of which are benign lesions and six of which are oral malignancies. In oral malignancies, one case was fibrosarcoma and five cases were OSCCs. It was estimated that prevalence rate of OSCC in HIV-infected surgical pathology cases was 42%. In comparison to surgical pathology cases without HIV infection, prevalence rate of squamous cell carcinoma was 27.53%; that is 397 SCC cases in number among the total 1442 cases within three year period.

Case No.	Age in Years	Gender	Pathology Diagnoses
1	51	Male	Squamous cell papilloma
2	51	Male	Squamous cell papilloma
3	41	Male	Verrucous carcinoma
4	12	Female	Non-Hodgkin lymphoma
5	45	Male	Fibrosarcoma
6	37	Female	Pleomorphic adenoma
7	67	Male	Oral squamous cell carcinoma (well differentiated)
8	64	Male	Lipoma (forehead) and fibroepithelial hyperplasia (gingiva)
9	48	Male	Oral squamous cell carcinoma (well differentiated)
10	42	Male	Oral squamous cell carcinoma (well differentiated)
11	43	Male	Oral squamous cell carcinoma (well differentiated)
12	41	Female	Oral squamous cell carcinoma (well differentiated)

Table 1. Pathology diagnoses of HIV-positive cases. This table showed prevalence rate of squamous cell carcinoma in HIV-infected surgical pathology cases was 42%.

Years	Total Non-HIV patients	OSCC diagnosed cases	Prevalence rate
2013	505	135	26.73%
2014	565	127	22.48%
2015	472	135	28.6%
Total	1442	397	27.53%

Table 2. Prevalence rate of OSCC cases among the surgical pathology cases of non-HIV patients. This table showed prevalence rate of OSCC in non-HIV surgical pathology cases was 27.53%.

Discussion

In this study, prevalence rate of OSCC in HIV-positive patients was higher than that of HIV-negative patients. At the same time, NADCs showed more prominent results than AIDS-defining malignancies.

During the potent antiretroviral therapy era, the incidence of AIDS-defining cancers has decreased and the incidence of NADCs has increased, as has the proportion of mortality associated with NADC in HIV-infected patients. The increase in NADCs is partly associated with increased longevity of the HIV-infected population, but it may also reflect consequences of increased immune activation and decreased immune surveillance as well as direct effects of HIV. The NADCs appear to have earlier onset and worse prognosis in HIV-infected patients than in the general cancer population.5

A review of the literature on NADC published in 2003 (Chiao and Krown, Curr Opin Oncol, 2003) indicated increased incidence rates in the United States for anal cancer, Hodgkin disease (mixed cellularity and lymphocyte-depleted types), lung cancer (adenocarcinoma, tobacco-related), testicular cancer (mostly seminoma), skin cancers (basal and squamous cell and melanoma), multiple myeloma, leukemia, and pediatric leiomyosarcoma (affecting 1 in 5000 and accounting for 8%-14% of pediatric cancers), as well as for lip, head and neck, penile, and conjunctival cancers.6

The success of antiretroviral therapy has led some people to now ask whether the end of AIDS is possible. For patients who are motivated to take therapy and who have access to lifelong treatment, AIDS-related illnesses are no longer the primary threat, but a new set of HIV-associated complications have emerged, resulting in a novel chronic disease that for many will span several decades of life. Treatment does not fully restore immune health; as a result, several inflammation-associated or immunodeficiency complications such as cardiovascular disease

and cancer are increasing in importance.

HIV-infected individuals with access to modern antiretroviral regimens should be able to suppress viral replication for life, preserve immune function, and avoid most AIDS-related complications. Antiretroviral therapy does not fully restore health in all individuals; well treated HIV-infected adults have higher than expected risk of several non-AIDS disorders, including cardiovascular disease, kidney disease, liver disease, malignancy, and some neurological diseases. Although antiretroviral therapy often restores peripheral CD4+ T-cell counts, persistent immune dysfunction, inflammation, and coagulation abnormalities persist and strongly predict risk of non-AIDS morbidity and mortality. The growing burden of comorbidities in ageing adults will require well-resourced health-care delivery systems for chronic care, which are staffed by experts in both infectious and non-infectious complications.4

In conclusion, there were noticeably larger numbers of NADCs (for instance, OSCCs). According to this study, NADC is found to be an emerging problem in HIV-infected patients. Further epidemiological and clinico-pathological studies as well as screening procedures should be warranted to solve this problem.

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