EFFECT OF RADIATION THERAPY ON IMMUNOLOGICAL AND VIROLOGICAL STATUS IN HIV/AIDS CANCER PATIENTS

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Abstract

A multicenter observational study was conducted among HIV-positive cancer patients who received radiation therapy to determine effects of radiation therapy (RT) on immunological (percentage of CD4) and virological status.Blood samplings were taken for CD4% and plasma HIV-RNA viral load (HIV-VL) assays before the last week of RT. Only CD4% was determined in 3-month follow-up. 92 HIV-positive cancer patients were included from August 22, 2009 to December 30, 2011. 78 patients (84.8%) were currently on antiretroviral treatment(ART). The mean CD4% in patients receiving ART at baseline, post-RT and 3-month follow-up were 17.5%, 19.6%, and 16.8%, respectively. The values for the non-ART group were 25.6%, 22.4%, and 16.8%, respectively. The changes of CD4% in non-ART patients was significantly more than in the ART group (p 0.000). Only one out of 78 ART patients had increased HIV-VL more than 1 log compared with three out of 14 non-ART patients. Radiation therapy has more effect on the immunological status in HIV-positive cancer patients who did not receive ART, than those who were currently on ART. The time for initiation of ART during radiotherapy should be considered for future study.

1. INTRODUCTION

Due to the increased survival and decreased opportunistic infections from the effects of anti-retroviral therapy (ART), the incidence of malignancies in HIV-infected patients appears to be increased [1]. HIV status does not affect cancer treatment plan in the current standard guidelines. Radiation therapy is usually administered for HIV-positive cancer patients. The use of conventional fraction of RT always causes haematological side effects through bone marrow suppression; white blood cell and percentage of lymphocyte were decreased in all HIV-positive patients. RT significantly reduced total lymphocyte count on higher radiation dose among HIV-positive patients [2].Total lymphocytes include T-lymphocyte, B-lymphocyte, and natural killer cells. CD4 T-cell count, which is a component of T-cell lymphocyte, is used to determine the immunological status whether in initiate antiretroviral drug or failure of treatment of HIV positive patients [3,4]. In the setting of patients who have been receiving RT, the absolute CD4 count seemed not to be a useful immunological predictor. Immunological status is more appropriately predicted by CD4% [2].

This study aimed to describe immunological status through the CD4% and virological status in HIV/AIDS-cancer patients.

2. MATERIALS AND METHODS

This prospective observational study has been conducted in Therapeutic Radiology and Oncology Unit of seven hospitals: Rajavithi Hospital, Siriraj Hospital, Maha Vajiralongkorn Cancer Center, Chonburi Cancer Center, Maharaj Nakorn Chiang Mai Hospital, Lopburi Cancer Center and Ramathibodi Hospital. This report presents the results of patients studied from August 22, 2009 to December 30, 2011 and 3-month follow-up post RT.

เสนอโดยนางปฐมพร ศิรประภาศิริ นายแพทย์เชี่ยวชาญ โรงพยาบาลราชวิถี
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To be eligible for the study, patients had to be serologically positive for HIV antibodies and histologically confirmed malignancies with ages between 18 and 65 years. All patients must not have had previous malignancy or RT before being enrolled in the study. All RT treatment plans were using external photon beam in conventional fraction (fx); 1.8-2 Gy/fx and 5 fx /week, at least 40 Gy. The external electron beam, brachytherapyand concurrent chemoradiation were applied according to standard guidelines. The exclusion criteria were patients who had CD4 count less than 200 cells/μL at baseline without antiretroviral treatment, or patients with metastasis stage, or patients with two primary cancers, and who received RT for palliative intention.

The CD4% and HIV-RNA viral load (HIV-VL) were assessed at baseline (within 7 days before RT), at the last week of RT. Only CD4% was determined at 3-months after completing RT. The CD4 test was performed using flow cytometrytechnique in the standard pathological laboratory of each center. HIV-VL was assayed by using the standard pathological laboratory of each center.This report compared mean CD4% between baseline, the last week of RT and 3-month follow up. Statistical analysis was carried out using repeated measure ANOVA.

3. RESULTS

This study reports data from August 22, 2009 to December 30, 2011, ninety two patients were included in this analysis. The patients' median age was 40 years (range 19-61). Seventy eight patients were on ART before starting radiation treatment. Fourteen non-ART HIV-positive patients were evaluated by infection physicians and ART was not initiated at the time of RT. The median RT dose was 5400 cGy (range 4000-7000cGy) by conventional fraction. All invasive cervical cancer patients received intracavitary brachytherapy, and 42 patients received concurrent chemoradiation with platinum-based chemotherapy according to standard guidelines. The characteristics of patients are shown in Table1.

TABLE 1. CHARACTERISTICS OF HIV-CANCER PATIENTS

Patient characteristics		Received ART	Non-ART	Total (%)
Sex	Female	64	14	78 (84.8)
	Male	14	0	14 (15.2)
Cancer site	Uterine cervix	53	12	65 (70.7)
	Others	25	2	27 (29.3)
Radiation dose	Less than 56 Gy	41	7	48 (52.2)
	56 Gy and over	37	7	44 (47.8)
Baseline percentage of CD4	Less than 15%	25	2	27 (29.3)
	15% and over	53	12	65 (70.7)
Baseline HIV-RNA viral load (copies/mL)	< 50	59	0	59 (64.1)
	50-999	11	3	14 (15.2)
	1000 – 100,000	8	11	19 (20.7)

The mean CD4% of HIV infected cancer patients decreased from baseline to post-RT and 3-month follow up at 18.7%, 17.1%, and 16.9%, respectively. The respective values for the ART group are: 17.5%, 19.6%, and 16.8%. For the non-ART group the respective values are: 25.6%, 22.4%, and 16.8%. Figure 1 compares the decrease of mean CD4% in the non-ART and ART group (p 0.000). The decreased CD4% in both groups was clearly observed at 3 months after radiation therapy. Proportion of decreased CD4% more than 3% at 3 month follow-up after RT treatment was found significantly difference in non-ART (80.0%) more than ART group (40.3%), (p 0.037).

Of the 14 in the non-ART group, four patients missed follow up at 3 months after RT,and of these, one patient had HIV-VL increased 1.55 log. Eight non-ART patients had decreased percentage of CD4 of more than 3% three months after radiation, 2 out of 8 immunological suppressed patients also had HIV-VL increase 1.04 log and 3.40 log. Only two non-ART patients had stable CD4% and HIV-VL values pre-RT and post-RT.

Of the seventy-eight ART patients, 6 patients missed the 3-month follow-up, 43 patients had no effect from radiation to CD4% and HIV-VL, 29 patients had percentage of CD4 decrease of more than 3%. One out of 29 immunological failure patients had HIV-VL increased 2.18 log after complete radiation treatment, which diagnosed HIV disease progression.

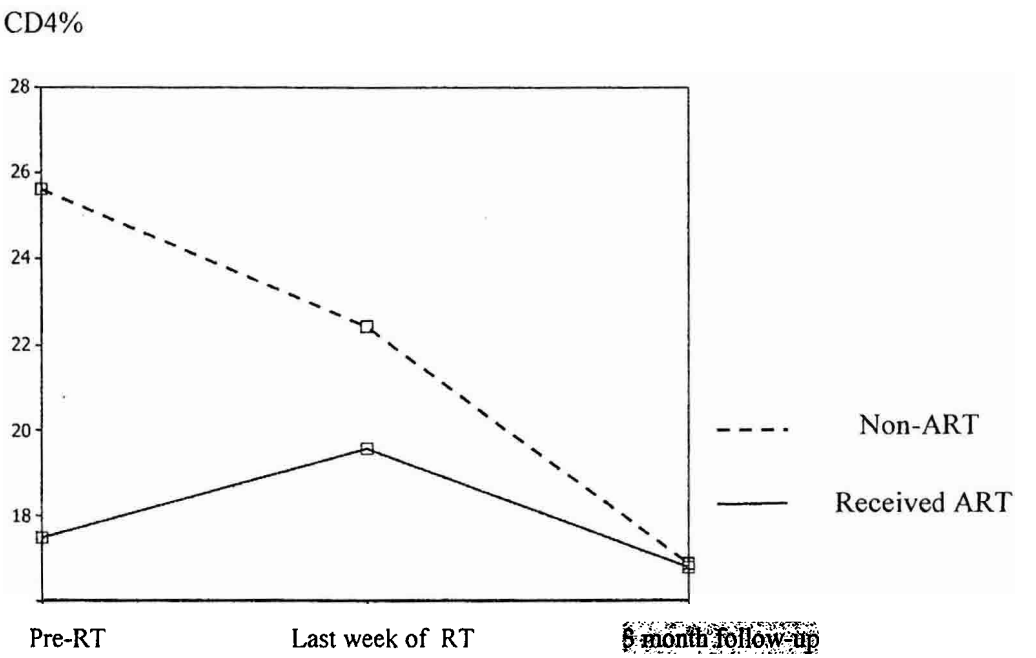

FIG. 1. Estimated marginal means of percentage of CD4 by ART, using repeated measure ANOVA

4. DISCUSSION

The CD4% is more an appropriate immunologic marker than absolute CD4 and lymphocyte count during radiation [2]. We found the maximum suppression of CD4% was at 3 months after radiation. Non-ART patients had immunological changes more than ART patients (p 0.000). Although mean baseline CD4% in non-ART patients was higher (25.6%)at baseline, the mean CD4% at 3 month follow up were the same (16.8%) in both groups.

The decreased CD4% as indicated for immunological suppression may not be well described about HIV disease progression during radiation therapy without the virological status. This study did not have information of VL at 3 month follow up, which is the maximum period of immunological depression. One of 78 ART patients and 3 of 14 non-ART patients had HIV disease progression using virological status criteria. The optimal virologic control by administration of ART before RT may prevent the immunological failure and progression of HIV disease during RT, and for a short duration post RT.

5. CONCLUSION

Conventional radiation therapy more than 40 Gy affects the immunological status in HIV-positive cancer patients. The time for initiation of ART during radiotherapy should be considered for future study.

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REFERENCES

[1] PATEL, P., HANSON, D.L., SULLIVAN, P.S., et al., Incidence of types of cancer among HIV-infected persons compared with the general population in the United States, 1992-2003, Ann. Intern. Med.**148** 10 (2008)728-736.

[2] SIRAPRAPASIRI, P., THARAVICHITKUL, E., TOVANABUTRA, C., et al., Effect of radiation therapy to immunological and virological status in HIV/AIDS-cancer patients, preliminary report,J. Med. Assoc. Thai, **94** Suppl. 2(March 2011)S88-93

[3] SUNGKANUPARPH, S., ANEKTHANANON, T., HIRANSUTHIKUL, N., et al., Guidelines for antiretroviral therapy in HIV-1 infected adults and adolescents: the recommendations of the Thai AIDS Society (TAS) 2008, J. Med. Assoc. Thai, **91** 12(Dec. 2008) 1925-1935.

[4] HAMMER, S.M., ERON Jr., J.J., REISS, P., et.al. Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA Panel, J. Am. Med. Assn., **300** 5 (Aug. 2008) 555-570.