

RADIOTHERAPY EFFECT ON COMPLETE BLOOD COUNT PARAMETER IN PATIENTS WITH NASOPHARYNGEAL CARCINOMA

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Abstract

Introduction: Nasopharyngeal carcinoma (NPC) is the most common malignant tumor of the nasopharynx. Radiotherapy is a therapy of choice for NPC that has been recognized for a long time and used in various centers of the world. However, radiotherapy is known to still have an adverse effect. It is common practice to evaluate Complete Blood Count (CBC) before, during, and after radiotherapy. However, there has been no study regarding the effect of radiotherapy on all CBC parameters. This study aims to analyze the effect of radiotherapy on CBC in NPC patients before and after radiotherapy treatment.

Method: This study was an observational study using secondary data from medical records at the radiotherapy outpatient clinic at Dr. Soetomo General Hospital Surabaya. The subject of this study was patients with NPC who underwent a full cycle of radiotherapy treatment on radiotherapy outpatient clinic in 2016. Patients with incomplete medical records and did not finish the radiotherapy treatment were excluded. A paired T-test and Wilcoxon signed-rank test were used for statistical analysis.

Result: There were 105 patients included in this study. Mean Corpuscular Hemoglobin Concentration (MCHC), total leucocyte, lymphocyte, and thrombocyte was significantly decreased after a full cycle of radiotherapy (all $P < 0.05$). Eosinophil, basophil, neutrophil, monocyte, Neutrophil to Lymphocyte ratio (NLR), and Platelet to Lymphocyte ratio (PLR) was significantly increased after a full cycle of radiotherapy (all $P < 0.05$).

Conclusion: Radiotherapy had a significant effect on the CBC parameter in NPC patients.

Article Info

Key words:

Nasopharyngeal carcinoma, complete blood count, radiotherapy

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1. INTRODUCTION

Nasopharyngeal carcinoma (NPC) is the most common malignant tumor of the nasopharynx. Globally, NPC is uncommon cancer with approximately 80,000 new cases reported per year and accounting 0.7% of all cancers [1]. In Indonesia, NPC is the most common malignancy in the head and neck, and, the 4th most common cancer after cervical, breast, and skin cancer. The estimated incidence of NPC nationwide is 5.66/100,000 population, and East Java region had the highest incidence (16.42/100,000 population). In Surabaya the estimated incidence of NPC is 7.23/100,000 population [2].

Radiotherapy is a therapy of choice for NPC that has been recognized for a long time and used in various centers in the world. It can be given as definitive and or palliative which can be followed by symptomatic chemotherapy according to symptoms to provide improving tumor control and survival rate in advanced stage NPC [3]. However, this procedure has adverse effects. In the acute phase, it can be mucositis, dermatitis, xerostomia and in the late phase, it can be soft tissue fibrosis, trismus, xerostomia, hearing loss, vasculopathy, osteoradionecrosis, temporal lobe necrosis, hypothyroidism, hypopituitarism [4]. For the systemic adverse effect, one of the most common symptoms experienced by patients is fatigue that considered as radiotherapy-related fatigue [5].

Studies about the evaluation of NPC patients' conditions that undergo radiotherapy in Indonesia are still minimal. Complete blood examination (CBC) is routinely measured to evaluate the condition of NPC patients who undergo radiotherapy. It is chosen because it is fast, inexpensive, and has a practical functional index. Moreover, the CBC could reflect the biological characteristics of tumor cells indirectly and combining it with the TNM stage is very useful for building a more accurate predicting system of NPC patients' individualized outcomes [6]. However, there has been no study regarding the effect of radiotherapy on the CBC parameter. This study aims to analyze the effect of radiotherapy on CBC in NPC patients before and after radiotherapy treatment.

2. MATERIAL AND METHODS

This study was an observational study using secondary data from medical records at the radiotherapy outpatient clinic at Dr. Soetomo General Hospital Surabaya, a tertiary referral hospital for the eastern part of Indonesia. Ethical approval from the Research Ethics Committee was received before the study begins (Ethical Approval Number: 639/panke.KKE/XI/2017). This study has been performed in accordance with the Declaration of Helsinki.

The subject of this study was patients with NPC who underwent radiotherapy treatment on radiotherapy outpatient clinic. Inclusion criteria were NPC patients who underwent radiotherapy in 2016 from the first cycle until the last cycle and had done laboratory evaluation before after radiotherapy treatment. Exclusion criteria were patients with incomplete medical records and did not finish the radiotherapy treatment. CBC evaluation was done at the same hospital. NPC staging was based on the 7th edition of the International Union against Cancer/American Joint Committee on Cancer (UICC/AJCC) staging system [7].

Acquired data were analyzed with SPSS 17.0.0 for Windows, 2007, SPSS Inc. Chicago, IL, USA. Data distribution was analyzed using the Kolmogorov-Smirnov test. Laboratory evaluation data was presented in mean \pm SD and analyzed using paired T-test or Wilcoxon signed-rank test. A P-value of < 0.05 was considered statistically significant.

3. RESULT

There were 260 patients underwent radiotherapy treatment in 2016 at radiotherapy outpatient clinic Dr. Soetomo General Hospital. From all patients, only 105 fulfill the inclusion criteria and did not fulfill the exclusion criteria. Based on gender, 68 patients were male and 37 patients were female. Patient's ages ranged from 8 to 69 year old, with a mean of 46.18 ± 12.25 year old. The majority of patients were already in the late stage, only 17 patients were in the early stage (table 1).

Table 1. Characteristic of the Study Subjects

Characteristic	N = 105 n (%)
Gender	
Male	68 (64.8)
Female	37 (35.2)
Age (mean ± SD)	46.18±12.25
< 18 years old	4 (3.8)
18 – 59 years old	92 (87.6)
≥ 60 years old	9 (8.6)
Staging	
1	1 (1)
2	16 (15.2)
3	19 (18.1)
4a	64 (61)
4b	5 (4.8)

The CBC parameter was evaluated for data distribution normality using the Kolmogorov-Smirnov test. Effect of radiotherapy on Hemoglobin and Mean Corpuscular Hemoglobin Concentration was analyzed using paired T-test, while other parameters were evaluated using the Wilcoxon signed-rank test. Mean Corpuscular Hemoglobin Concentration (MCHC), total leucocyte, lymphocyte, and thrombocyte was significantly decreased after a full cycle of radiotherapy (all $P < 0.05$). On the other hand, eosinophil, basophil, neutrophil, monocyte, Neutrophil to Lymphocyte ratio (NLR), and Platelet to Lymphocyte ratio (PLR) was significantly increased after a full cycle of radiotherapy (all $P < 0.05$). Hemoglobin, erythrocyte, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin and mean platelet volume did not change significantly after the treatment (table 2).

Table 2. Complete Blood Count Parameter Evaluation Before and After Full Cycle Radiotherapy

Complete Blood Count Parameter	Before radiotherapy	After radiotherapy	P
Hemoglobin (g/dL)	12.13±1.62	11.90±1.23	0.066 ^a
Erythrocyte	4.20±0.62	4.53±3.97	0.505 ⁺
Hematocrit	36.47±5.66	36.07±4.51	0.461 ⁺
MCV	87.23±10.70	88.57±6.15	0.366 ⁺
MCH	29.58±6.60	28.91±2.24	0.261 ⁺
MCHC	32.90±1.19	32.64±1.31	0.049 ^{a*}
Total Leucocyte	8.09±4.88	6.61±2.46	< 0.001 ⁺⁺
Eosinophil	3.26±3.73	5.39±5.93	< 0.001 ⁺⁺
Basophil	0.62±0.38	0.65±1.45	0.022 ⁺⁺
Neutrophil	61.94±13.03	74.53±9.21	< 0.001 ⁺⁺
Lymphocyte	25.61±11.05	11.04±5.11	0.139 ⁺⁺
Monocyte	8.27±3.89	8.57±2.41	< 0.001 ⁺⁺
Thrombocyte	318.01±120.17	275.17±86.67	< 0.001 ⁺⁺
MPV	13.59±46.98	8.44±1.58	0.367 ⁺
NLR	3.25±2.58	9.08±6.90	< 0.001 ⁺⁺
PLR	2.04±1.34	4.91±2.87	< 0.001 ⁺⁺

* $P < 0.05$ was considered statistically significant

#Paired T-test was used

+Wilcoxon signed rank test was used

MCV = Mean Corpuscular Volume; MCH = Mean Corpuscular Hemoglobin; MCHC = Mean Corpuscular Hemoglobin Concentration; MPV = Mean Platelet Volume; NLR = Neutrophil to Lymphocyte Ratio; PLR = Platelet to Lymphocyte Ratio

4. DISCUSSION

There was a significant difference in several laboratory parameters before and after radiotherapy treatment. MCHC, total leucocyte, lymphocyte, and thrombocyte were significantly reduced. On the other side, eosinophil, basophil, neutrophil, monocyte, NLR, and PLR were significantly increased after radiotherapy treatment. Similar to our findings, a recent study that evaluates the hematologic biomarker in patients with NPC treated with intensity-modulated radiotherapy found that neutrophil, platelet, and lymphocyte count were significantly decreased after treatment, while NLR and PLR were significantly increased after treatment. It is argued that decreased neutrophil, platelet, and lymphocyte count were most likely due to malnutrition as an impact of poor oral intake and increased protein catabolism. On the other hand, increased NLR and PLR were most likely because of systemic inflammation and critical lymphopenia due to the treatment [8].

The previous study that analyzes the leukocyte and neutrophil counts in NPC patients found that initial hyperleukocytosis and neutrophilia were independent poor prognostic factors. It is because the patients with initial hyperleukocytosis or neutrophilia were more likely to be at an advanced disease stage and, therefore, have poorer survival. Moreover, initial hyperleukocytosis or neutrophilia could also be a sign of aggressive cancer because of its roles in tumor progression by altering the tumor microenvironment [9]. In general, inflammatory cells could enhance the proliferating and metastatic abilities of tumor cells. Therefore, the elevated level of inflammatory cells might affect prognosis adversely [6, 10].

CBC evaluation was very useful to predict the prognosis of NPC patients. A combination of CBC with TNM staging has been used as prognosis prediction in NPC and it shows higher prediction efficiency on the 5-year disease-specific survival (DSS) compare to the TNM staging system alone. The CBC parameter that was included in the scoring system was hemoglobin, NLR, and thrombocyte [11]. Other than as an independent prognostic factor for DSS, thrombocyte count was also an independent predictor of metastasis-free survival in patients with NPC [12]. It has been suggested that lymphocyte should also be considered as a prognostic marker that may reflect the immunological status of patients during and after treatment [13]. PLR and NLR pretreatment were also found to be a reliable predictor factor for overall survival, progression-free survival, disease-specific survival, and distant metastasis-free survival [8, 14-17].

Other than systemic effect, radiotherapy also causes local side effects in the surrounding healthy tissue because oxidation of protein and lipids induced by the free radicals produced by exposure radiotherapy [18]. There are currently 2 scoring system for evaluating the late radiation toxicity, RTOG/EORTC and LENT/SOMA. These scores are specific for each organ tissue. However, there is no evaluation regarding the hematologic value [19, 20]. For acute radiation toxicity, there is only RTOG/EORTC scoring systems. This scoring system has evaluation regarding the hematologic value, where the lower the hematologic evaluation value, the higher the radiation toxicity score [19].

5. CONCLUSION

Radiotherapy had a significant effect on several CBC parameters in NPC patients. Future study needs to be done to determine whether the change is because of the regression or progression of the tumor or because of the radiotherapy effect solely. Moreover, there is also a need to evaluate the changes in all CBC parameters as prognostic factors for the 5-year survival rate in NPC patients.

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