Absolute Neutrophil Count Levels among Degree of Differentiation and Tumor Location in Colorectal Cancer Patients in Medan

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Abstract

BACKGROUND: Absolute Neutrophil Count (ANC) recently a derived score composed of white blood cell and has been evaluated in a large number of malignancy.

AIM: The aim of this study was to investigate ANC levels among degree of differentiation and tumor location in Colorectal Cancer (CRC) in Medan.

METHODS: This study was a cross-sectional analytical study on eighty consecutive patients with CRC. Data collection was obtained from the medical record of the patient at Adam Malik General Hospital, Medan, Indonesia. Inclusion criteria were included male or female aged ≥ 18 years old, the patient with CRC, blood test especially ANC, and the patient with histopathology test. The exclusion criteria were defined as a patient with chemotherapy, HIV, and the patient with sepsis. Data were analyzed with SPSS for window version 21.

RESULTS: here were Rectal cancer 49.4%, Left side colon cancer 43.2%, and Right-side colon cancer 6.2%. Histopathological findings well differentiated 40.7%, moderate differentiated 32.1%, and poorly differentiated 25.9%. This study showed that no significant differences between ANC and location of the tumor (p = 0.951), but ANC level was significant in histopathological findings (p = 0.0001).

CONCLUSION: ANC increased in poorly differentiated, and location of the tumor is left side colon cancer.

Introduction

Colorectal Carcinoma (CRC) is a malignant tumor from colon and rectum [1]. CRC is the human tumor which equally affects both men and women. It belongs to common, solid tumors and is the third most common in men. By mortality, it ranks as fourth after lung, stomach, and liver. The highest frequency is recorded in the highly industrialized countries, such as countries of North America, Australia, and New Zealand. The incidence of CRC is rapidly increased including in Indonesia, making it the second most common of malignancies [2].

The population in Indonesia is more than 235,000,000 and the age-incidence rates per 100,000 for CRC by gender was 19.1 for male and 15.6 for female [3]. As one of the leading causes of cancer death in developed countries, much interest has grown in research in the development of biomarkers to improve the diagnostic process.

The tumor microenvironment is very important about the preservation and promotion of tumor development and progression; inflammation has been identified as the seventh hallmark of cancer [4], [5]. It is widely accepted that inflammation has a critical role
in the pathogenesis and progression of cancer [6]. On the other hand, systemic inflammatory response to tumors causes changes in the hematological components like white blood cells, specifically the neutrophils. Human neutrophils, initially recognized as effectors in the first line host defense against invading pathogens, are the most abundant subpopulation of leukocyte [6]. In addition to direct bactericidal activities, neutrophils can regulate angiogenesis and tissue remodeling by releasing multiple proteases. Recently, a derived score composed of white cell and neutrophil counts has been evaluated in a large number of cancer patient. Increased level absolute neutrophil count (ANC) have been found in various human tumors, and tumor is infiltrating neutrophils are capable of being pro-tumor effect [4]. Thus, the examination of ANC could be used as an additional effective marker in identifying those CRC patients at increased risk of tumor metastasis and/or progression.

The aim of this study was to investigate ANC levels among degree of differentiation and tumor location in Colorectal Cancer (CRC) in Medan.

Material and Methods

Data collection

This study was a cross sectional analytical study on eighty consecutive patients with Colorectal Carcinoma (CRC). Data collection was obtained from medical record of patient at Adam Malik General Hospital and Permata Bunda Hospital, Medan, Indonesia from January to December 2016. Inclusion criteria are stated as followings: male or female aged ≥18 years old, patients with CRC, patient with blood test especially ANC, and patient with histopathology test. While the exclusion criteria were defined as patient with positive chemotherapy, patient with HIV, and patient with SEPSIS.

All data were analyzed with SPSS for window version 21. If data with normal distribution using ANOVA test, but data with abnormal distribution using KRUSKAL WALLIS test.

Results

Total of 80 patients, consisted of 48 males (60%), and 32 females (40%). Demographic characteristics of patient are shown in Table 1. The median age of these patients was 53 (25-80) years old. The majority of patient's education level was senior high school (43.2%), elementary school (25.9%), undergraduate (16%) and junior high school (13.6%).

The most common of tumor location were rectal cancer 49.4%, left side colon cancer 43.2%, and right-side colon cancer 6.2%. The data of histopathology from patient were well differentiated 40.7%, moderate differentiated 32.1%, and poorly differentiated 25.9%.

The majority of histopathology was well differentiated (41.3%)

Table 1. Demographic and clinical characteristics of patient

| Variables       | N = 80 (100%) |
|-----------------|---------------|
| Gender          |               |
| Male            | 48 (60%)      |
| Female          | 32 (40%)      |
| Age             | 53 (25-80)    |
| Education Level |               |
| Elementary School| 21 (26.3%)  |
| Junior High School | 11 (13.8%)  |
| Senior High School | 35 (43.8%)  |
| University      | 13 (16.3%)    |
| Tumor Location  |               |
| Rectal cancer   | 40 (50%)      |
| Left side colon | 35 (43.8%)    |
| Right side colon| 5 (6.3%)      |
| Histopathology  |               |
| Well differentiated| 33 (41.3%)   |
| Moderately differentiated| 26 (32.5%) |
| Poorly differentiated| 21 (26.3%) |
| Hemoglobin      |               |
| White blood cells| 8850 (1650-25750) |
| Platelet        |               |
| 325178.75 ± 135551.146 |
| ANC             | 11.86 (6.38-27.55) |

The correlation between routine blood count with ANC is shown Table 2. Hb, WBC and Platelet, there was no significant difference between them (p > 0.05).

Table 2. Correlation routine blood test with ANC

| Variables     | ANC Correlation Coefficient | P   |
|---------------|-----------------------------|-----|
| Hb            | -0.01                       | 0.99|
| WBC           | -0.102                      | 0.36|
| Platelet      | 0.093                       | 0.44|

Table 3 shows a comparison ANC to location of tumor and Histopathology. Mean of ANC to location of tumor Rectal cancer 12.83, Left side colon 13.01, and right-side colon 12.3, there was no significant difference (p = 0.951). Differentiated histopathology, well differentiated 9.48, moderate differentiated 11.89 and poorly differentiated 19.45, there was significant difference (p = 0.0001).

Table 3. Comparison of Absolute Neutrophil Count (ANC) levels among degree of differentiation and tumor location in Colorectal Cancer

| ANC            | Tumor location | Mean ± SD | P   | P   |
|----------------|---------------|-----------|-----|-----|
| Tumor location |               |           |     |     |
| Rectal cancer  | 12.83 ± 4.63  | 0.47      | 0.951|
| Left side colon| 13.02 ± 5.98  |           |     |     |
| Right side colon| 12.3 ± 4.24  |           |     |     |
| Histopathology | Mean ± SD     |           |     |     |
| Well           | 9.48 ± 2.14   | 77.23     | 0.0001|
| Moderate       | 11.89 ± 2.92  |           |     |     |
| Poorly         | 19.45 ± 3.58  |           |     |     |
Discussion

Total of 80 patients are mostly male gender 60% than female 40% this is according to research of American cancer society 2012 obtained majority of gender is male than female. The localization the large number of patients had colorectal cancer 50% and Left side colon cancer 43.8%. Study of Bin Jin et al., [7] show that they have found 44 cancers in the rectal region and 68 cancers in the other regions of the colon.

In our study differentiated histopathology findings the mostly well differentiated 41.3%, this is similarly from study of Sudoyo et al., [8] where most colorectal carcinoma was well differentiated [8].

In CRC patients, tumor infiltrating have been shown to be independent prognostic factors of survival in all clinical stages. Elevated neutrophil count, however, may reflect tumor progression by providing an adequate environment or its growth [6]. Previous study showed that infiltration of neutrophils was increased in colorectal adenomas compared to normal mucosa and correlated with size of adenoma, suggesting that the presence of neutrophils is involved in the early stage of colorectal tumor [9]. In our study show that mean of ANC increased in poorly differentiated 19.45, there were significant differences between them (p = 0.0001). Similarly, the study from Eileen and carlos show that ANC was increased in poorly differentiated compared to well differentiated [10]. Mean of ANC to location tumor, ANC was increased in left side colon cancer 13.01. Rao et al., show that ANC was increased in colon than rectum [4].

In conclusion, in our study found that Absolute Neutrophil Count (ANC) increased in poorly differentiated and location of tumor is left side colon cancer.

References

1. American cancer. Cancer Facts & Figures 2012. Atlanta: American Cancer Society, 2012: 1.
2. International Agency for Research on Cancer. GLOBOCAN 2012: estimated cancer incidence, mortality and prevalence worldwide in 2012.
3. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010; 127(12):2893-917. https://doi.org/10.1002/ijc.25516 PMid:21351269
4. Rao HL, Chen JW, Li M, Xiao YB, Fu J, Zeng YX, Cai MY, Xie D. Increased intratumoral neutrophil in colorectal carcinomas correlates closely with malignant phenotype and predicts patients’ adverse prognosis. PloS one. 2012; 7(1):1-2. https://doi.org/10.1371/journal.pone.0030806 PMid:22295111 PMCid:PMC3266280
5. Walsh SR, Cook EJ, Goulder F, Justin TA, Keeling NJ. Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer. J Surg Oncol. 2005; 91(3):181-4. https://doi.org/10.1002/jso.20329 PMid:16118772
6. Absenger G, Szokandera J, Pichler M, Stotz M, Arming F, Weissmueller M, Schaberl-Moser R, Samonigg H, Stojakovic T, Gerger A. A derived neutrophil to lymphocyte ratio predicts clinical outcome in stage II and III colon cancer patients. British journal of cancer. 2013; 109(2):396-399. https://doi.org/10.1038/bjc.2013.346 PMid:23820252 PMCid:PMC3721404
7. Bin J, Xin W, Yan J, Wensen X, Bel C, Lin L, Zheng C, Liu H, Damping F. Detection of serum gastric cancer Associated MG7-Ag from gastric cancer patients using a sensitive and convenient ELISA Method. Cancer Investigation. 2009; 27:223-227. https://doi.org/10.1080/07357900802175609 PMid:19235597
8. Sudoyo AW, Hernowo B, Krishunohi E, Reksodiputro AH, Hardjisaidastro D. Colorectal cancer among young native Indonesians: a clinicopathological and molecular assessment on microsatellite instability. Med J Indonesia. 2010; 19(4):245-51. https://doi.org/10.13181/mji.v19i4.411
9. McLean MH, Murray GI, Steward KN, Norrie G, Mayer C, et al. the inflammatory microenvironment in colorectal neoplasia. PLoS One. 2011; 6:e15366. https://doi.org/10.1371/journal.pone.0015366 PMid:21249124 PMCid:PMC3017541
10. Uribe-Querol E, Rosales C. Neutrophils in cancer: two sides of the same coin. Journal of immunology research. 2015; 2015. https://doi.org/10.1155/2015/983698 PMid:26819959 PMCid:PMC4706937
11. Mantovani A. Cancer: Inflamming metastasis. Nature. 2009; 457:36-37. https://doi.org/10.1038/457036b PMid:19122629