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Clinicopathological Profile of Colorectal Cancer Patients in Anatomical Pathology Department of Hasanuddin University Makassar

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Abstract

Colorectal cancer (CRC) is the third most common cancer in men, the second in women, and it's the second for leading cause of cancer death worldwide, with more than 1.2 million new cancer cases and 608,700 deaths. The World Health Organization (WHO) in 2018, explained that globally there were 1.80 million new cases of colorectal cancer diagnosed and 862,000 patients died of colorectal cancer. This study aims to define the epidemiological and clinicopathological characteristics of CRC with metastasize in Makassar. Retrospective study was performed used cross-sectional design included all patients diagnosed with colorectal adenocarcinoma with metastasize at Anatomical Pathology Laboratory Dr. Wahidin Sudirohusodo, Faculty of Medicine Hasanuddin University and Makassar Pathology Diagnostic Center, from January 2016 to December 2021. A total of 60 patients were included in this study, 45% were females and 55% were males. Samples with the age category <50 years were 13 samples (21.7%) and the age category > 50 years were 47 samples (78.3%). Based on the location of the tumor, the location of tumor in the right colon were 24 samples (40.0%), in the left colon were 14 samples (23.3%), and in the rectum were 22 (36.7%) samples. The low-grade colorectal adenocarcinoma group were consisted of 31 samples (51.7%) and 29 samples (48.3%) of the high-grade. Samples with positive lymphovascular invasion were 17 samples (51.7%) and 43 samples (71.7%) were negative.

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The depth of invasion were 28 samples (46.7%) at muscularis externa and 32 samples (53.3%) at serosa. Colorectal adenocarcinoma is more frequent at the age more than 50 years old and right colon is the most affected sub site. The mean age at diagnosis was 57.2 years with male predominance. Most patients had low grade tumor, no lymphovascular invasion findings at microscopic and the depth of invasion reach the serosa. Lymph nodes is the most common metastatic site.

Keyword: colorectal adenocarcinoma; clinicopathological profile; makassar.

1. Introduction

Colorectal cancer is the third most common cancer in men, the second in women, and it's the second for leading cause of cancer death worldwide, with more than 1.2 million new cancer cases and 608,700 deaths [1,2]. The World Health Organization (WHO) in 2018, explained that globally there were 1.80 million new cases of colorectal cancer diagnosed and 862,000 patients died of colorectal cancer. In the US, approximately 145,600 cases of colorectal cancer are diagnosed each year of 1,014,200 cases of colon cancer. In general, 71% of colorectal cancers occur in the colon and 29% in the rectum. About 50,000 patients die with colorectal cancer each year in the US [3]. GLOBOCAN data in 2012, the incidence of colorectal cancer in Indonesia is 12.8 per 100,000 adult population, with a mortality of 9.5% of all cancer cases. The overall risk of getting colorectal cancer is 1 in 20 people (5%). In Indonesia, this cancer ranks 3rd, which is caused by changes in the diet of Indonesians which contains high fat but low fiber [4]. Based on the data of GLOBOCAN 2020, the incidence of new colorectal cancer in Indonesia was 33,427 cases or about 8.4% of the total 396,914 cancer cases [5]. Although therapeutic methods have developed well, colorectal cancer remains the leading cause of cancer death. Some patients can experience recurrence and tumor cells are resistant to treatment [6], besides that invasion and metastasis are the major cause of cancer morbidity and mortality [7]. Colon cancer represents a significant health challenge worldwide. Prognosis actually varies widely according to combination of risk factors. The aim of this study was to review the clincopathological features of colorectal cancer in Anatomical Pathology Laboratory Dr. Wahidin Sudirohusodo, Faculty of Medicine Hasanuddin University and Makassar Pathology Diagnostic Center, Makassar.

2. Matherial and Methods

2.1 Collection of samples

This retrospective study was included 60 patients diagnosed with colorectal adenocarcinoma with metastasize at Anatomical Pathology Laboratory Dr. Wahidin Sudirohusodo, Faculty of Medicine Hasanuddin University and Makassar Pathology Diagnostic Center, from January 2016 to December 2021. Data were collected from patients' files and pathology records. Parameters studied were age, sex, location, microscopic feature includes histopathological grade, lymphovascular invasion and the depth of tumor invasion.

2.2 Data Processing

The data in this study were processed using SPSS 18 for Windows software. Descriptive statistical techniques used to describe the characteristic of the basic data obtained in the form of frequency age includes average of

age, sex, location, histopathological grade, lymphovascular invasion and the depth of tumor invasion.

3. Results

Of the 60 samples, distribution of colorectal adenocarcinoma with metastisize based on age, gender, tumor location, histopathological grade, lymphovascular invasion and the depth of tumor invasion are shown in Table 1.

Table 1: Sample Characteristics in Metastatic Colorectal Adenocarcinoma

Sample Characteristics	Total	
	n	**%**
Age		
Mean ± SD	57,28 ± 11,19	
<50 years old	13	21.7
≥50 years old	47	78.3
Gender		
Male	33	55.0
Female	27	45.0
Tumor Location		
Right colon	24	40.0
Left colon	14	23.3
Rectum	22	36.7
Histopathological Grade		
Low grade	31	51.7
High grade	29	48.3
Lymphovascular invasion		
Positive	17	28.3
Negative	43	71.7
Depth of Invasion		
Muscularis externa	28	46.7
Serosa	32	53.3
Total	**60**	**100**

Based on table 1, it can be seen that this study used a total of 60 samples, which the mean of age was 57.28 years old with a standard deviation of 11.19 years old. Twenty seven samples (45%) were females and 33 samples (55%) were males. Samples with the age category <50 years were 13 samples (21.7%) and the age category > 50 years were 47 samples (78.3%). Based on the location of the tumor, the location of tumor in the right colon were 24 samples (40.0%), in the left colon were 14 samples (23.3%), and in the rectum were 22 (36.7%) samples. The low-grade colorectal adenocarcinoma group were consisted of 31 samples (51.7%) and 29 samples (48.3%) of the high-grade. Samples with positive lymphovascular invasion were 17 samples (51.7%) and 43 samples (71.7%) were negative. The depth of invasion were 28 samples (46.7%) at muscularis externa and 32 samples (53.3%) at serosa.

The histopathological findings of low grade and high grade colorectal adenocarcinoma are shown in Figure 1.

Low grade tumors composed of glandular, tubular and cribriform infiltrative pattern. Tumor cells with round/oval nuclei, pleomorphic, hyperchromatic, vesicular and eosinophilic cytoplasm.While high grade tumors arranged in solid pattern.

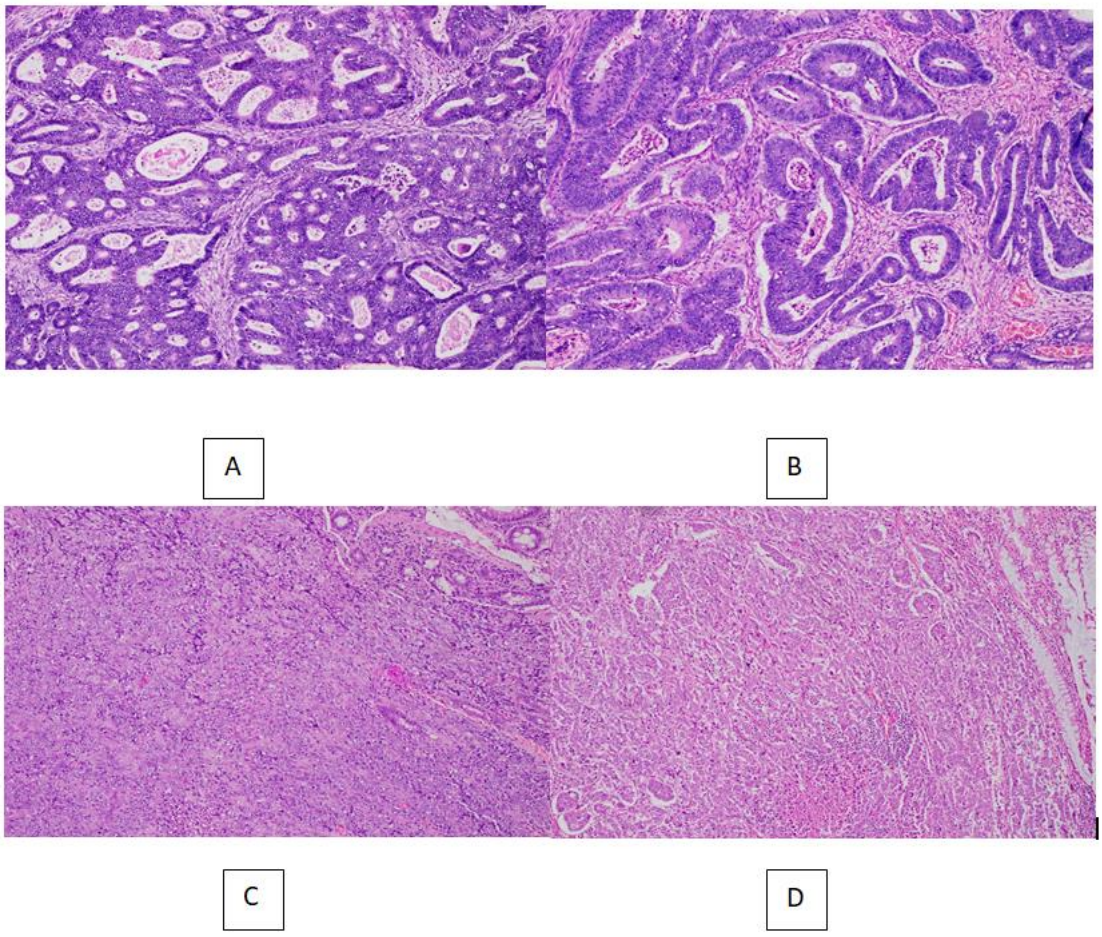

Figure 1: Low grade and high grade colorectal adenocarcinoma. A-B. Low grade adenocarcinoma arranged in glandular, tubular and cribriform pattern. C-D. High grade adenocarcinoma arranged in solid pattern with pleomorphic tumor cells. Hematoxilin and Eosin, Magnification 100x

4. Discussion

This study used a total of 60 colorectal adenocarcinoma samples with an age range of patients ranging from 26-78 years where the most of age was above 50 years with a mean of age was 57.28 years (table 1). This is in line with epidemiological studies which state that more cases of colorectal cancer (more than 90%) occur in people aged 50 years or older [8,9]. The main risk factors of colorectal cancer in old age are being overweight, smoking, heavy alcohol consumption, high intake of red or processed meat, and lack of physical activity [10].

In our study, some patients were under 50 years old and there was even one patient who was 26 years old. The reason for the increasing colorectal cancer among people that younger than 50 years remains unclear [8]. There may be a combination of risk factors, including increasing of obesity's prevalence, inactivity, alcohol intake and

smoking [11].

The strongest risk factor of colorectal cancer is a family history of the disease. People with a first-degree relative (FDR) who have been diagnosed with colorectal cancer have two to four times the risk than someone without a family history of this, with a higher risk before 50 years old. More than a quarter of patients are under 50 years old have FDR with history of colorectal cancer or adenoma, and an additional 16% had hereditary syndromes, half of whom had Lynch Syndrome. Another high-risk group that should be considered for initial screening are those who have received pelvic radiation in adolescence or early adulthood [10]. Currently with the increasing modality of colonoscopy for diagnostic and screening purposes it may also be responsible for the proportion of colorectal cancers detected in young adults [11].

In the table 1, it can be seen that the most colorectal adenocarcinoma occurred in the male (33 cases) compared to female (27 cases). These data are consistent with previous studies which stated that the incidence rate of colorectal cancer was higher in male than female [4,8,12]. The incidence of colorectal cancer is higher in male than female, possibly reflecting differences in exposure to risk factors (eg, smoking) and sex hormones [8]. In female, the steroid hormone estrogen has a protective role in the development of colorectal cancer [12]. This effect is not limited to endogenous hormones only, but the use of oral contraceptives and postmenopausal hormone replacement therapy also appears to protect female from colorectal cancer [13]. A key of proliferative pathway in colorectal cancer tumorigenesis suggests that better survival in female occurs through estrogen-regulated genes and cell signaling. Estrogen regulates the activity of genes that control ion transport function in the colon and epithelial mesenchymal transition through bidirectional interactions with the Wnt/β-catenin signaling pathway. Estrogen also regulates the proliferative response of colorectal cancer in hypoxic conditions through membrane estrogen receptors GPER (G protein coupled estrogen receptor) and HIF1A as well as VEGF signaling [12].

Overall, in our study, the most tumor locations of colorectal adenocarcinoma were on the right side and the majority of high grade colorectal adenocarcinoma also occurred in the right side colon. This is not accordance with the literature which states that most colorectal cancers are left or rectal [14]. Meanwhile, right-sided cancer is more often found in advanced and high-grade stages [15]. Tumors in the proximal colon (right side) and distal colon (left side) show different molecular and histological characteristics. In right-sided tumors, mutations in the DNA mismatch repair pathway are usually observed and these tumors generally have a flat morphological appearance. In left-sided tumors, associated with pathways of chromosomal instability mutations, such as KRAS, APC, PIK3CA, p53 mutations, and these tumors usually exhibit polypoid-like morphology [16]. Colonoscopy screening is easier to detect tumors on the left side because it can detect small adenomas at an early stage. Right-sided tumors can still be detected at an early stage, but are much more difficult than left-sided tumors because they have a flat morphology. Thus, right-sided tumors are generally detected at more advanced stage than left-sided tumors [16]. The survival of colorectal cancer is adjusted according to a history of screening which by early screening the diagnosis of cancer can be made [15].

Our study showed that 43 samples (71.7%) with no lymphovascular invasion. It is higher than samples with lymphovascular invasion. This is not accordance with the other literatures that state lymphovascular invasion

commonly found in metastatic colorectal adenocarcinoma. Our study in line with Hui Hong Jang and his colleagues which state that lymphovascular invasion is suggested to be an early and important step in tumor progression toward metastasis but its prognostic value and genetic mechanisms in colorectal cancer CRC have not been well investigated [17]. In this study we do not examine the expression of CRC-associated genes and could be caused by an unsampled portion of the tumor that contains lymphovascular invasion macroscopically.

In agreement with a previous study, the rate of vascular invasion was observed to be significantly higher in rectal than colon carcinomas. Differences in vascular invasion may have resulted from differences between the anatomical features of the rectum and colon [18].

Our study also showed that the most common of tumor invasion was reached the serosa. This is in line with the findings of other studies showed a relationship between depth of invasion and metastasis. Some studies showed that the depth of tumor invasion as the factor to predict the risk of local recurrence and nodal metastasis [19]. Thus, colorectal cancers limited to the mucosa (pT1) are unlikely to metastasize, whereas those invading the submukosa and deeper structure are more likely to metastasize to the lymph nodes and adjacent organs. In this study, we found that the most common metastatic site is in the lymph node. Lymph node metastasis is an important prognostic factor in patients with rectal and colon carcinoma and affects disease management. Nodal involvement is associated with an increased risk of local recurrence and shorter overall and disease-free survival time. [18,19].

5. Conclusion

In this study, we conclude that colorectal adenocarcinoma is more frequent at the age more than 50 years old and right colon is the most affected sub site. The mean age at diagnosis was 57.2 years with male predominance. Most patients had low grade tumor, no lymphovascular invasion findings at microscopic and the depth of invasion reach the serosa. Lymph nodes is the most common metastatic site.

6. Suggestions

Additional studies are needed to analyze the CRC associated-gene marker that may be involved in the CRC prognostic factors especially to predict metastasis of colorectal adenocarcinoma.

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