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A Young Woman with High-Grade Rectosigmoid Adenocarcinoma, no Other Specified, T2n2aM0: A Case Report and Literature Review

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Abstract

BACKGROUND: Colorectal cancer (CRC) is the fourth most common cancer in which the majority of CRCs are diagnosed between the ages of 50 and 70 years. Based on current trends, the incidence of colon and rectal cancers can increase by 124% in people aged 35–49 years and at the age of 20–34 will increase by 28% and 46%.

OBJECTIVES: To report a case of a 24-year-old female patient with CRC.

CASE REPORT: A 24-year-old female patient came to the Emergency Room at Bendan Hospital, Pekalongan City, with complaints of bleeding since 1 year ago. There are complaints in the past 6 months; the patient's weight has decreased by up to 20 kg. Rectal toucher examination revealed normal (+) anal sphincter tone, a palpable mass in the anal canal, and was fragile; there were feces and blood in gloves. Abdominal ultrasonography found a solid tumor mass in the rectum area with a volume of 181 cc, suggesting a malignancy of the rectum. During a colonoscopy, a circular, fragile, and easily bleeding tumor was found, approximately 1 cm from the anal verge, and then biopsy was performed. Histopathological examination of the colon biopsy suggests a well-differentiated, rectosigmoid, NOS adenocarcinoma. The patient then underwent surgery using the Miles procedure technique. The patient's condition after the operation improved, so after a week of treatment, the patient was able to undergo outpatient treatment.

CONCLUSION: A complete history, physical examination, and supporting investigation are very useful in early detection of colorectal carcinoma, especially in young patients.

Introduction

Colorectal cancer (CRC) is the fourth most common cancer and the second leading cause of cancer-related death worldwide. The majority of CRC patients are diagnosed between the ages of 50 and 70 years [1]. Many recent studies provide a clearer picture that as many as 7% of patients who develop CRC are often under 40 years of age and this incidence is steadily increasing [2].

Based on current trends, many scientists predict that by 2030, the incidence of colon and rectal cancers will increase by 124% in people aged 35–49 years, and in people aged 20–34 will increase by 28% and 46%, respectively. In several studies documenting that the low 5-year survival in colon cancer patients at a young age is equal to 23%, this shows that colon cancer mortality at a young age is still very high. Therefore, young adults aged <50 years are included in the economically active population, where the increasing prevalence of CRC in this demographic will cause a future socioeconomic burden [3]. The mechanisms underlying the increased incidence of CRC among young patients are currently unknown. This increasing trend is well understood, but this increasing trend is a population health problem [4]. Knowledge of the high incidence of CRC in young populations in some developing countries has led to increased rates of early diagnosis and improved early clinical management of CRC [5].

The findings of CRC in adolescents or young adults always receive attention because there has been a shift of CRC incidence in young adults coupled with the low 5-year survival rate of colon cancer at a young age [6], so it is necessary to emphasize the importance of early detection of CRC in this population. In this case report, we report the case of a young adult woman who was diagnosed with colorectal adenocarcinoma.

Case Report

A 24-year-old female patient came to the emergency room at Bendan Hospital, Pekalongan

City, with complaints of bloody diarrhea 1 year ago. Previously, the patient had received treatment at another hospital for diarrhea, but there was no improvement. The patient's bowel movements are usually soft but are getting softer and waterier every day; the patient can go to the bathroom 3 times a day and is accompanied by fresh blood. The patient also complained of a lump in the anal, but the doctors said that it was hemorrhoids. There are complaints in the past 6 months; the patient's weight has decreased by up to 20 kg. Complaints of vomiting blood and abdominal pain were denied. Previous similar complaints in the patient were denied. From the patient's family history, the patient's aunt had a tumor removed from the stomach, and was said to be benign (Figure 1).

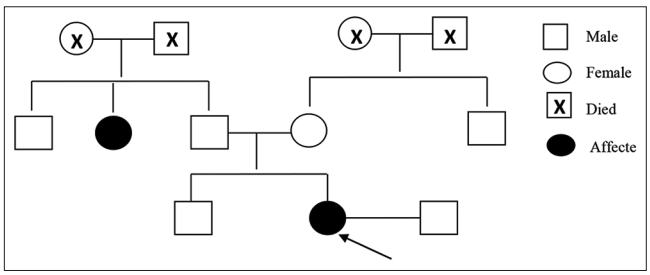

Figure 1: Family pedigree
Source: Personal document

Physical examination showed the good general condition, blood pressure 110/70 mmHg, pulse 82 ×/min, respiratory rate 20 ×/min, temperature 36.5°C, and oxygen saturation 98%. Physical examination of the eyes revealed anemic conjunctiva in both eyes. Other physical examinations were within normal limits. Rectal toucher examination revealed normal (+) anal sphincter tone, a palpable mass with a hump in the anal canal, and was fragile; there were feces and blood in gloves.

The patient underwent laboratory investigations for hemoglobin 10 g/dL, hematocrit 34.7%, leukocytes 35,790/uL, platelets 734,000/uL, MCV 75.9fL, MCH 21.9 pg, and MCHC 28.8 g/dL. Abdominal ultrasonography found a solid tumor mass in the rectum area with a volume of 181 cc, suggesting a malignancy of the rectum (Figure 2). The patient then underwent a colonoscopy and biopsy. When the scope of the camera was entered the anal, a circular, fragile, and easily bleeding tumor was found, approximately 1 cm from the anal verge, and then biopsy was performed. (Figure 3). Histopathological examination of the colon biopsy suggests a well-differentiated adenocarcinoma NOS, rectosigmoid.

History, physical examination, and supporting examinations showed that the patient had a suspected malignant rectosigmoid tumor of the abdomen. When the operation was performed, a large mass measuring 9 × 6 × 6 cm was seen from the sigmoid colon to almost the tip of the anus, then it was decided to undergo the Miles procedure technique (abdominoperineal rectosigmoidectomy, end colostomy, and total mesorectal excision). After surgery, the patient was admitted to the intensive care unit for observation for 1 × 24 h. During a week of treatment at the hospital, the patient's surgical wound was good, no seepage was found, and the stoma was vital (Figure 4). Then, the patient was asked for outpatient control.

Histopathological examination showed macroscopically a piece of intestinal tissue 30 cm long with a diameter of the first end of approximately 3 cm, and a diameter of the second end of approximately 2 cm. On cutting, it appears a mass growing exophilic into the lumen and endophilic in the lumen reddish-white, lumpy-like broccoli 9 × 6 × 6 cm in size. The distance from tip I is approximately 1 cm and from tip II is approximately 20 cm. From the exploration of the mesentery, five interconnected nodules with a diameter of 1–2 cm were found (Figure 5).

Examination using a microscope showed that the mucosa was found covered with complex columnar epithelium, with goblet. There was hyperplastic growth, with oval anaplastic shapes, pleiomorphic to odd shapes, then accompanied by cells that were hyperchromatic, coarse chromatin, and prominent nucleoli. Atypical mitoses may be found, consisting of 50% villous glands, which infiltrate the muscularis propria with an infiltration of lymphocytes, histiocytes, and neutrophils. Lymphangio-invasion is seen. No perineural invasion was found. Microscopic examination of the nodules showed anaplastic cells identical to the tumor mass cells infiltrating into the fibrous connective tissue stroma with large areas of mucin and pushing the lymphoid cells to the margins (Figure 6).

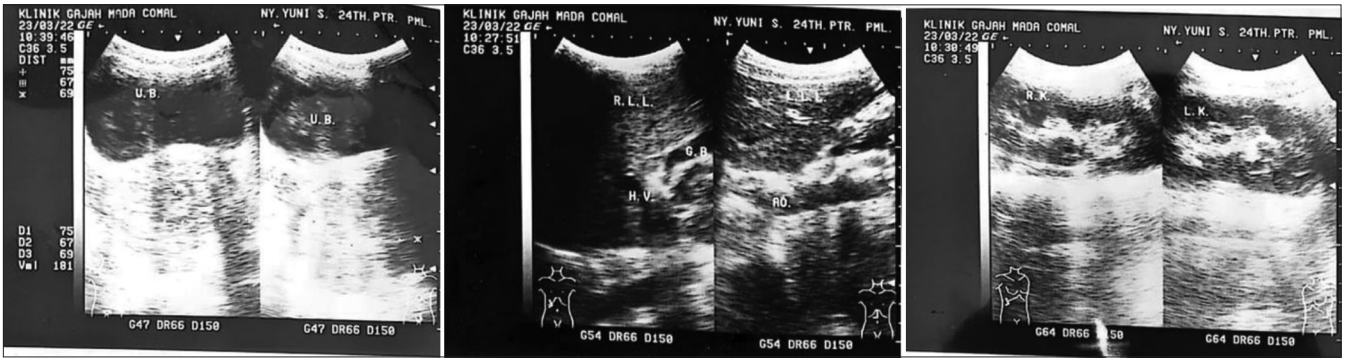

Figure 2: Ultrasonography result
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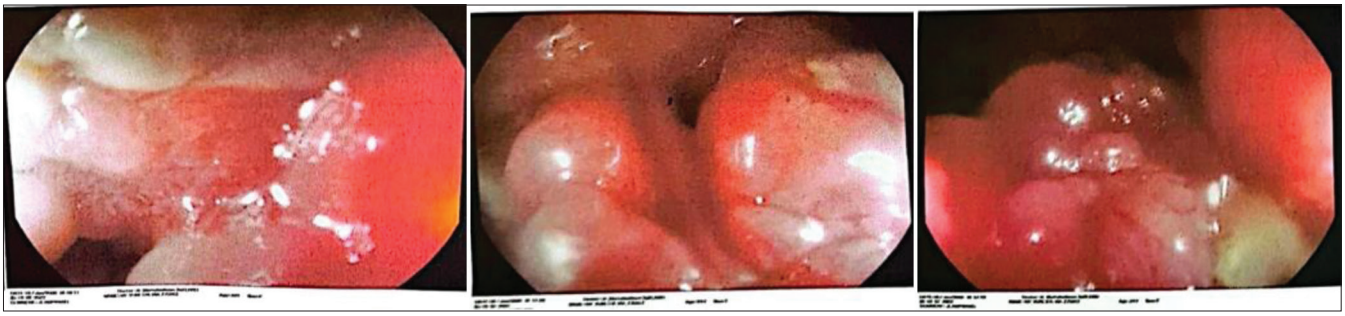

Figure 3: Colonoscopy result
Source: Personal document

Histopathological examination showed a malignant tumor in the form of high-grade adenocarcinoma, NOS, rectosigmoid. There was infiltration up to the muscularis propria layer, lymphangial invasion was found, perineural invasion was not seen, and metastases were found into 5 nodules found, both ends of the incision margin: tumor-free, stage IIIB (pT2n2aM0).

Discussion

Colorectal malignancy (CRC) is the most common malignancy of the gastrointestinal tract and the third leading cause of cancer death in the world. Adenocarcinoma of the colon and rectum is a type of cancer that is often found in patients with CRC [7]. Adenocarcinoma of the colon and rectum occurs due to the progression of colorectal cells from normal tissue to dysplastic epithelium which then develops into a malignancy, so it is often referred to as adenoma-carcinoma accompanied by several changes. Genetics include oncogenicity, activation, and inactivation of tumor suppressor genes, and gene incompatibility in repairing genes [8].

The incidence of CRC in young individuals has increased by 2–8% annually over the past two decades. CRC is now one of the 10 most common causes of death among individuals between the ages of 20 and 49 years [9]. The incidence of CRC diagnosed before age 40 varies from 0.8% to 15% [10].

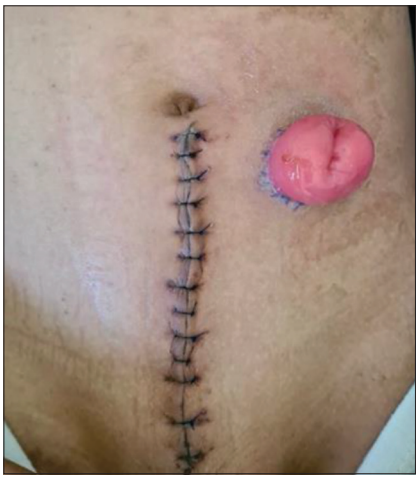

Figure 4: Postoperative wound
Source: Personal document

CRC arises in some cases as a result of the development of inherited cancer syndromes, such as Lynch syndrome (the most common syndrome), hamartomatous, hyperplastic, autosomal recessive associated with MYH, and polyposis. However, it represents only about 2–5% of all colon and rectal cancers. Inflammatory diseases, such as ulcerative colitis and Crohn's disease, have been associated with an increased risk of colon and rectal cancers but account for only 1–2% of all cases [8].

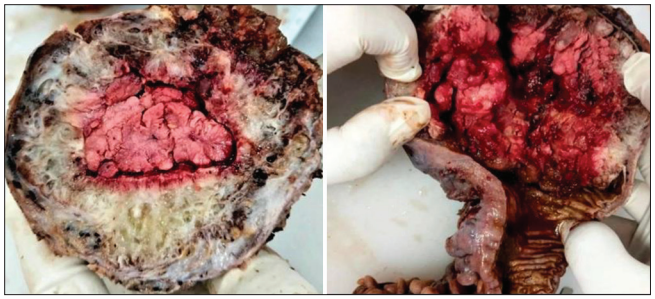

Figure 5: Macroscopic view
Source: Personal document

Three main pathways of CRC carcinogenesis have been described for their pathogenesis, namely chromosomal instability, microsatellite instability (MSI), and CpG island methylation phenotype. Approximately 70% of sporadic CRCs arise via chromosomal instability, which is characterized by somatic mutations in the APC tumor suppressor gene, an early driver mutation in the adenoma-carcinoma sequence. Tumors with stable microsatellite lack the CpG islet methylation phenotype, and harbor deactivating mutations in the tumor suppressor genes APC and TP53 and activating mutations in the proto-oncogenes KRAS and MYC. Young-onset CRCs exhibiting chromosomal instability appear primarily in the proximal colon, in contrast to CRCs associated with late-onset chromosomal instability, which tend to be located in the distal colon [11]. Although MSI is the hallmark of Lynch syndrome, a specific subset of young-onset CRCs is characterized as stable microsatellite CRCs and The chromosomes are stable and have an anatomical predisposition to the distal colon and rectum. Microsatellite-stable and chromosomally stable tumors

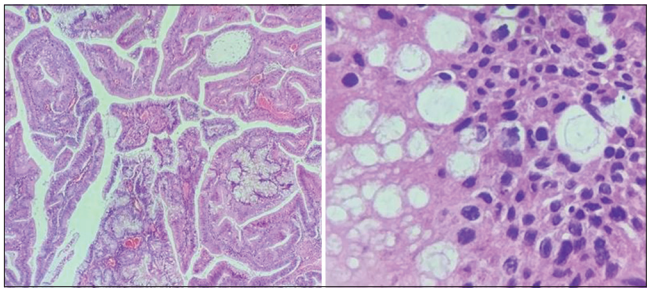

Figure 6: Microscopic overview
Source: Personal document

are biologically aggressive, with a tendency toward early metastasis and recurrence. They were further characterized by LINE-1 hypomethylation, low-status CpG methylator island phenotype, and absence of BRAF mutations. Another subset of young-onset CRCs is associated with a low-status CpG islet phenotype [12].

Early diagnosis in young adults is often detected late because the incidence rate of neoplasms is less in this age group and symptoms are more likely to be associated with benign pathological changes [7]. In addition, for young patients who have CRC but do not know the predisposing risk factors, the diagnosis is delayed and poor prognostic results can occur due to the failure of doctors to consider the differential diagnosis of several possible malignant diseases [2].

The finding of CRC in young patients is not only a challenge in establishing the diagnosis but also in the best management options for such patients. When treating young patients, it is better to separate true CRC from hereditary syndromes such as Lynch syndrome or familial adenomatous polyposis. However, even for CRC patients under 40 years of age, the prevalence of a positive family history of cancer is low, below 27%. Thus, in this age group, genetic testing is recommended [7].

Guidelines from the National Comprehensive Cancer Network (NCCN) state that it is necessary to test genetic material that related to colorectal cancer, if it is found that there is more than one family member who has colon cancer syndromes (e.g Lynch syndrome, adenomatous polyposis syndromes and hamartomatous polyposis syndromes). In this testing process it is necessary to consider testing from the youngest family members first or family members who have the closest relationship with the patient. If no family member is living with the disease described above, then consider testing a first- or second-degree relative with another cancer suspected to be linked in this gene (e.g, colorectal, endometrial, or urothelial with the pathogen). If no genetically linked variant is found, it is necessary to consider referral for evaluation to a geneticist [13].

In addition, the NCCN explains that in children <18 years, genetic testing is generally not recommended unless the results will impact medical management, such as initiation of early surveillance colonoscopy. Obvious exceptions include when FAP, JPS, PJS, or constitutional mismatch repair (MMR) deficiency syndrome is suspected or known to run in the family, in which case testing before the age of 18 years is recommended to guide medical management. Patients over the age of 18 years universal MSI or MMR testing is recommended for all patients with a personal history of colon or rectal cancer if a reimbursement policy allows and/or is required by clinical request, but this test is highly recommended and strongly recommended. However, in this case, neither genetic examination nor MSI/MMR examination was carried out considering that the hospital in this patient is a primary-level hospital where there are all limitations in costs and facilities, even though based on the guidelines, this patient is required for genetic examination [13].

MSI is a key biomarker in CRC, with important diagnostic, prognostic, and predictive implications. Testing for MMR deficiency (MMR-D)/MSI is recommended during screening for Lynch syndrome, an autosomal dominant hereditary disease characterized by germline mutations in the MMR gene and associated with an increased risk of some cancers. In addition, high MSI-H status (MSI-H) is associated with a better prognosis in early-stage CRC and a lack of benefit from adjuvant treatment with 5-fluorouracil in stage II disease. Recently, MSI has emerged as a predictor of sensitivity to immunotherapy-based treatments. The breakthrough success of checkpoint inhibitors in MMR-D metastatic CRC has opened up new therapeutic scenarios for patients with these tumors [14].

Detecting CRC at an early stage is important for patient recovery and survival, especially in young patients. Young patients with signs of bowel changes, recurrent rectal bleeding, anorexia, and significant weight loss should be considered to have worrisome symptoms suggestive of cancer and to have a relatively high risk of CRC. The factors that make clinicians late in diagnosing CRC in young adult patients are the assumption that the above symptoms are caused by a lack of a thorough history and physical examination [12].

A previous prevalence study with young patients showed that the most common symptoms were rectal bleeding (57%), abdominal pain (31%), changes in bowel habits (21%), weight loss (11%), and anemia (11%). Any symptoms suggestive of CRC may be an indication for further imaging tests. Once CRC is suspected, barium enema, abdominal ultrasonography, colonoscopy, abdominal CT, and therapeutic surgical resection may be performed [15].

In this patients, it is necessary to think about the diagnosis of CRC because these patients have symptoms such as rectal bleeding, changes in bowel habits, and weight loss, where these symptoms are common symptoms of CRC. This suspicion was confirmed by ultrasonography and clarified by colonoscopy which showed that there was a large, bleeding mass from the sigmoid colon to the rectum. Pathological examination results showed malignancy in

the form of high-grade adenocarcinoma, rectosigmoid NOS.

Tumor markers can also be used to suspect CRC. Many serum markers are associated with CRC, especially CEA. However, serum markers, including CEA, have poor diagnostic ability when compared to radiological studies because of their low sensitivity (only 46%) and the possibility of false positives, including in other benign tumors. However, a CEA level of more than 5 ng/mL predicts a poorer prognosis than lower levels [15].

When talking about a malignancy, a stage system will be known. The most commonly used staging system for CRC is the American Joint Committee on Cancer where T describes how far the cancer has grown into the wall of the colon or rectum which includes: The inner lining (mucosa), which is the lining where almost all CRCs started. These include a thin layer of muscle (mucosa muscularis), fibrous tissue beneath this layer of muscle (submucosa), a thick layer of muscle (muscularis propria), and an outer thin layer of connective tissue (subserosa and serosa) that covers most of the large intestine but does not cover the rectum. Next, N describes whether the cancer has spread to nearby lymph nodes, and finally M, which indicates whether the cancer has spread to distant organs, such as the liver or lungs. In this patient, pathologically, CRC has reached T2n2aM0 [16].

In stage I, this cancer is at its earliest stage. This stage is also known as carcinoma *in situ* or intramucosal carcinoma (Tis). Stage II cancer has grown through the muscularis mucosa into the submucosa (T1), and may even grow through the wall of the colon or rectum and adhere to or have grown into other nearby tissues or organs (T4b), but at this stage, the cancer has not spread to the lymph nodes nearest node (N0) or a distant place (M0). In stage III, it may grow through the mucosa into the submucosa (T1) and may even grow into the outermost layer of the colon or rectum (T3) or through the visceral peritoneum (T4a). At this stage, the cancer has spread to nearby lymph nodes but has not spread to distant sites (M0). In stage IV, cancer may or may not have grown through the wall of the colon or rectum (Any T) and may or may not have spread to nearby lymph nodes (Any N), but in this stage, it has spread to distant parts of the peritoneum (lining of the abdominal cavity), and may or may not spread to distant organs or lymph nodes (M1c). In the case of this patient, the patient has been diagnosed at stage IIIB, where the cancer has spread to nearby lymph nodes, but has not reached distant places [16].

Regarding the anatomical distribution, it has been documented that CRC in young people is limited to the topography of the distal spleen-colon angle in more than 80% of cases, which is why they usually present with rectal bleeding, abdominal pain, stool changes, and mucorrhea. The anatomical distribution of the CRC, in this case, showed that the mass was found in the sigmoid colon to the rectum [6].

Management procedures from CRC management are usually adjusted to colonoscopy results, biopsy results, and TNM stage results. Abdominoperineal resection or known as the Miles procedure is one of the techniques that are often used in therapy for low-lying rectal carcinoma by removing the sigmoid colon, rectum, and anus, leaving behind a permanent colostomy. Abdominoperineal resection, also known as the Miles procedure, is a technique often used in the treatment of low-lying rectal carcinoma by removing the sigmoid colon, rectum, and anus, and creating a permanent colostomy in the abdomen. Abdominoperineal resection is indicated for patients with low-lying rectal carcinoma who can be operated on by meeting several criteria, namely the distance between the tumor and the edge of the anus is less than 5 cm, it is impossible to get a tumor-free area (5 cm from proximal and 2 cm from distal), and/or the tumor has invade the surrounding tissue (external sphincter). After the surgical procedure, the management procedure of CRC can be accompanied by chemotherapy and/or radiotherapy but adjusted to the TNM stage results. In this case, the patient underwent surgery using the Miles procedure, and the patient was scheduled to undergo adjuvant chemotherapy [17].

(Note: Standard operating procedures can be added from the hospital where the patient is being operated on, based on standard operating procedures in Indonesia).

Although screening for CRC in average-risk populations is recommended starting at age 50 years, there are no data on optimal modalities for health screening programs. Colonoscopy is undoubtedly the most sensitive and specific screening test, combining diagnostic and therapeutic procedures. However, the primary role of colonoscopy as an early screening strategy for the general population remains a matter of debate [17].

In this case report, we found many limitations in our management of this patient. This patient was treated at a primary-level hospital where this patient could not undergo some of the examinations that should have been carried out due to limited funds and facilities, such as genetic testing to analyze the risk factors in this patient. In addition, we did not follow the treatment process to completion, where this patient required chemotherapy because the chemotherapy treatment had to be referred to a secondary hospital that has chemotherapy services.

Conclusion

A greater degree of suspicion and early screening is required when evaluating the examination of a young patient with complaints of abdominal pain,

changes in bowel habits, bloody stools, and weight loss. Early detection of CRC in young patients with extensive and careful evaluation will prevent late diagnosis and poor prognosis. In addition, the government needs to pay special attention to this issue, so that genetic testing for individuals with high risk of cancer is easier to obtain with affordable price.

The Author's Contribution

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