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Signet Ring Cell Colorectal Cancer in a 26-Year-Old Young Adult Woman: A Case Report

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ABSTRACT

Background: Colorectal cancer (CRC) remains the third most common cancer worldwide and the fourth most common cause of death related to cancer. One of them is signet ring cell carcinomas, which is represented as one of the rarest, characterized by histologic differentiation. Signet ring cell carcinoma of the colon is a rare subtype of mucinous adenocarcinoma, making up less than 1%. This low rate is mainly because it is generally diagnosed at advanced stages, thus giving a poor prognosis at presentation. In this report, our objective was to highlight the risk factors, diagnostic challenge, and the significance of early detection in this case. ***Case:*** A 26-year-old female was admitted to the ER with abdominal pain and a change of bowel habit. A contrast CT abdomen showed a 4cmx3.3cm lobulated mass in the wall of the descending colon, which causes a total obstruction. Left-sided hemicolectomy and end-to-end anastomoses between the transverse colon and sigmoid were then performed. Pathology reports revealed neoplastic cells with morphology of intracytoplasmic mucin that presses the nucleus to the edge, forming a signet ring cell appearance (>90%), confirming a Signet Ring Cell (SRCC) of colorectal cancer. ***Conclusion:*** Signet Ring Cell Carcinoma (SRCC) of colorectal cancer represents a challenge; further research is needed to fully understand the causes and risk factors specific to SRCC. Early detection and genetic profiling may help identify individuals at higher risk for improving survival rates and quality of life for individuals afflicted with this rare malignancy.

Keywords: signet ring cell carcinoma; colorectal cancer; causes and risk factors; Lynch Syndrome.

INTRODUCTION

Colorectal cancer (CRC) remains the third most common cancer worldwide and the fourth most common cause of death related to cancer. In Indonesia, the absence of population-based data leads to an unclear overview of the incidence of CRC specifically. Various reports show increases in the number of cases of CRC as one of the ten most common cancers [1,2]. The World Health Organization (WHO) developed a histological classification of colorectal cancers. One of them is signet ring cell carcinomas, which represents one of the rarest, characterized by histologic differentiation, whose cells typically contain a high quantity of mucin that pushes the nucleus to the periphery, giving the distinctive signet ring morphology [3].

Signet ring cell carcinoma (SRCC) of the colon is a rare subtype of mucinous adenocarcinoma, making up less than 1% of all tumors of the colon and rectum [3,4]. This low rate is mainly because it is generally diagnosed at advanced stages. The most common stage at which it is diagnosed for the first time is III or IV, thus giving a poor prognosis and the lower median survival rates than other histological subtypes [5]. At the time of primary diagnosis, the patients have already demonstrated more advanced clinical stages, typically lymph node metastases, as in our patient case described below.

CASE PRESENTATION

A 26-year-old female was admitted to the ER with chief complaints of abdominal pain for 2 weeks before being admitted to the hospital. She also had constipation and couldn't pass gas for the past days.

No complaints of fever. Physical examination showed abdominal distention and increased bowel sound on the right side of her abdomen and diminished in the other. Family history shows a second-degree relative with endometrial cancer. The patient had no history of smoking and alcohol consumption, but she was a passive smoker from her environment, and she had low-fiber eating habits. No significant findings in her laboratory result, with 7.01x10'3/ul leukocyte counts and 12.4 gr/L hemoglobin counts. A contrast CT abdomen showed a 4cmx3.3cm lobulated mass in the wall of the descending colon, which causes a total obstruction (Figure 1).

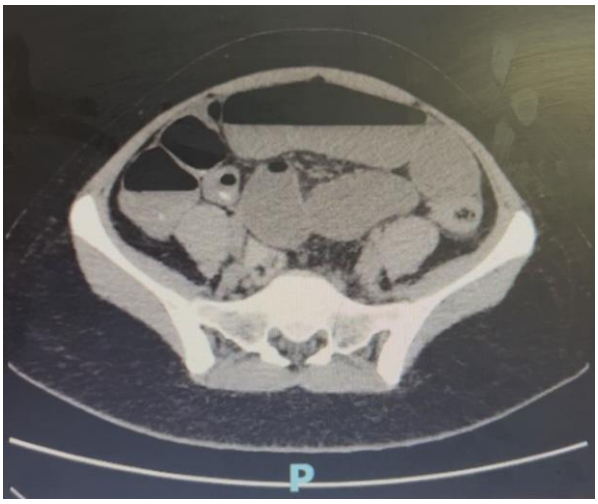

FIGURE 1: A contrast CT abdomen shows a 4cmx3.3cm lobulated mass in the wall of the descending colon, which causes a total obstruction.

The patient then underwent left-sided hemicolectomy, and an end-to-end anastomosis between the transverse colon and sigmoid was performed. Postoperative condition shows improvement in bowel movements. She was then discharged from the hospital and was scheduled to be referred to Prof. Ngoerah Hospital for chemotherapy via the policlinic.

Pathology reports revealed neoplastic cells with morphology of intracytoplasmic mucin that presses the nucleus to the edge, forming a signet ring cell appearance (>90%), irregular nuclear membrane, hyperchromatic, vesicular with prominent nucleus (Figure 2). The neoplastic cells form single cell structures, small clusters, and anastomosing cords, infiltrating into the serosal fat layer of the descending colon, therefore a T4 tumor (Figure 3). The patient was also checked for Carcinoembryonic Antigen (CEA) marker test, which resulted in a 0.98 ng/mL, and then continued to get Chemotherapy in a referred hospital.

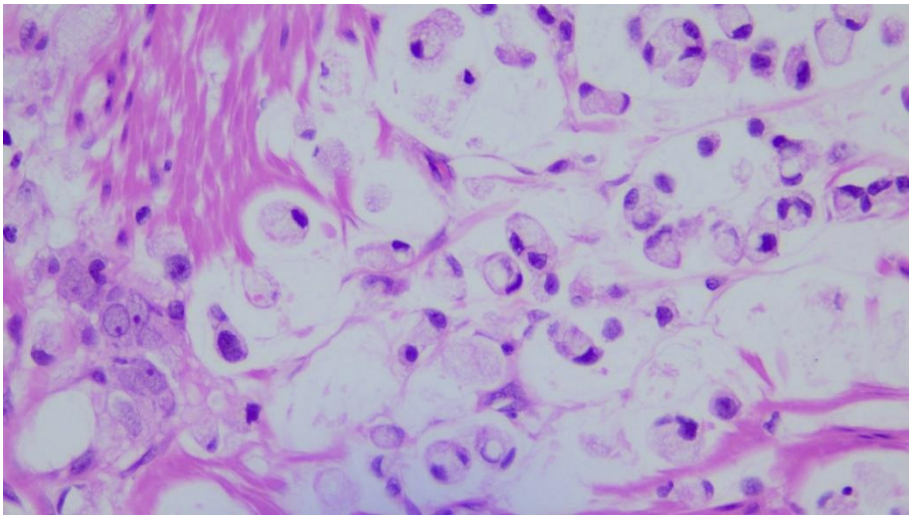

FIGURE 2: Pathology reports revealed neoplastic cells with morphology of intracytoplasmic mucin that presses the nucleus to the edge, forming a signet ring cell appearance (>90%), irregular nuclear membrane, hyperchromatic, vesicular with prominent nucleus.

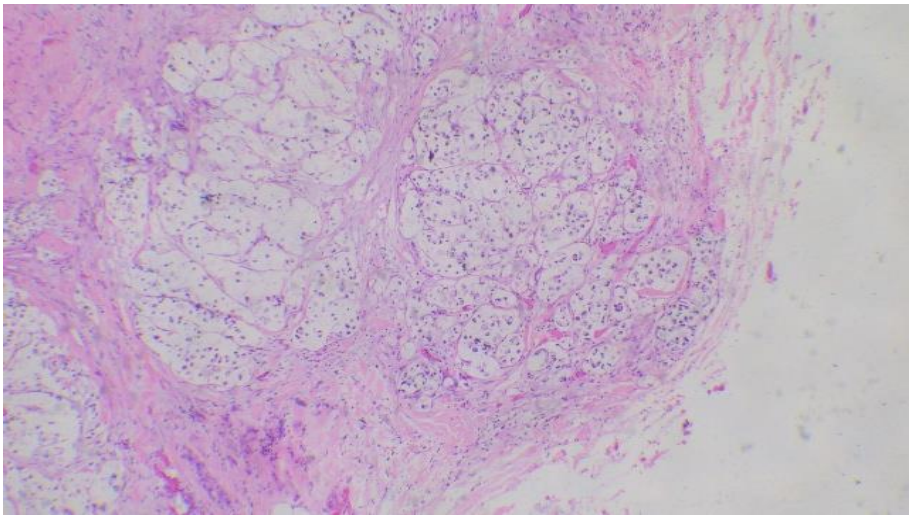

FIGURE 3: Pathologic report showing single cell structures, small clusters, and anastomosing cords, infiltrating into the serosal fat layer of the descending colon, therefore a T4 tumor.

DISCUSSION

Signet-ring cell carcinoma (SRCC) of the colorectal is an aggressive malignancy of the glandular lining of the digestive tract with distinct histological features. This type of tumor consists of >50% of 'signet-ring' cells, which contain mucin that pushes the nucleus to the periphery [4]. In one study reported by Wang et al, among other subtypes of colorectal cancer, SRCC among the young (ages 20-40 years) is four times more prevalent than among older adults (>40 years). They analyzed 279,623 CRC patients from SEER data and concluded that the patients aged 20 to 40 years had more mucinous carcinoma or signet ring-cell carcinoma, higher grade, and later stage examined compared with CRC patients aged 41 to 50 years and >50 years [6].

Colorectal SRCC patients had a higher risk of lymph-vascular invasion, poorly differentiated carcinoma, visceral peritoneum invasion, lymph node, and distant metastasis. This also indicated that the behavior of SRCC was more aggressive compared to non-SRCC patients. This is also the case in our patients, whose histologic findings show the neoplastic cells infiltrating into the serosal fat layer of the descending colon.

The exact causes for SRCC are yet to be fully understood, but some literature has described several factors that contributed to its development. For one, it is associated with mutations in genes such as CDH1, BRAF, KRAS, PIK3CA, TP53, and APC [4,7]. These mutations can drive colorectal carcinogenesis through pathways like microsatellite instability. Other factors that contribute to the Signet ring cell of colorectal cancer include chronic inflammatory conditions (inflammatory bowel disease). Some study findings from the present study add support to the concept that the frequency of mucinous/signet-ring cell colorectal adenocarcinoma is higher in IBD [8]. Environmental and lifestyle factors like alcohol consumption and smoking might not have been the direct cause of SRCC, but these were known to increase the risk of colorectal cancer in general [9].

We found similar risk factors in our patient's case; she admitted to having high red meat consumption and low fiber in her diet, also her environment is often exposed to an active smoker. Although we hadn't explored whether she had any history of IBD. One of the highlights was, we found out her aunt from her mother's side had a history of endometrial cancer. This is consistent with the Bethesda criteria, which are associated with Lynch Syndrome.

The Bethesda criteria are a standardized set of guidelines designed to identify individuals who may have Lynch Syndrome, also known as hereditary nonpolyposis colorectal cancer (HNPCC) [10]. The criteria were as follows :

(1) Colorectal cancer diagnosed before age fifty
(2) Presence of synchronous or metachronous HNPCC-associated tumors
(3) High microsatellite instability (MSI-H) histology diagnosed before age sixty
(4) One or more first-degree relatives diagnosed with an HNPCC-related tumor before age fifty
(5) Colorectal cancer diagnosed in two or more first- or second-degree relatives

We could conclude that our patient fell into category number (1), and we also suspected she was included in category number (5). However, in our case, genetic testing has not been explored, due to the nature of its non-availability in our hospital and urgency. We expected, through genetic testing, that we might get an insight into how to help determine the appropriate age to start screening and the frequency of screening procedures.

Patients with an increased risk of Lynch syndrome should undergo frequent screening. It was recommended that family members who have tested positive for the mutation, or for those who have not been tested, should start colonoscopy screening during their early 20s, or 2 to 5 years younger than the youngest person in the family with related diagnosis. Testing should be done every 1 or 2 years, so that any polyps and any cancers found at the earliest possible stage shall be removed [11].

Other methods of screening include the Fecal immunohistochemistry test (FIT) and Fecal Occult Blood Test (FOBT). In one meta-analysis comparing the two, FIT was significant in positivity rate and had fewer false-negative numbers compared to FOBT. It was also considered easier to take for the participants due to short sampling times and no food restrictions [12].

Understanding a patient's genetic profile can help guide treatment decisions, such as choosing specific medications. This posed a challenge for medical professionals, especially in Indonesia, because not every medical facility and professional could do so. The lack of data and research in our country contributed to the challenge as well. There were very few Indonesian-specific studies on the epidemiology, genetic profiles, or treatment of colorectal SRCC, so it was very difficult to develop tailored diagnostic or therapeutic protocols.

Immunohistochemistry (IHC) is also a valuable tool for diagnosing SRCC and distinguishing it from other cancers, such as CK20 and CDX2, CK7, MUC2, MUC5AC, and Ki-67, which helps in determining SRCC of colorectal origin and potentially aids in prognosis [13]. But, unfortunately, in Indonesia, our national health insurance didn't fully cover many of the diagnostic tests. In dealing with this matter, our medical professionals normally choose a tumor marker test, namely CEA.

While CEA is not typically used for initial diagnosis, it is related to the presentation of colorectal cancer and recommended for surveillance before and after curative resection, often indicating a poorer prognosis and higher risk of mortality with a threshold of ≥5 ng/mL [14]. Although in our case the CEA levels were normal (i.e., 0.98 ng/mL), it didn't entirely confirm good outcomes due to the nature of poorly-differentiated tumor cells in SRCC contributed to lower expression of CEA [15]. But this tumor marker remained essential in monitoring because in most recurrent cases, regardless of baseline CEA levels, it shows elevated CEA, highlighting its importance in surveillance, especially when combined with other tests [16].

Other than just diagnostic tools, one should always have basic knowledge about SRCC to encourage them to get these procedures. Our patients didn't have enough knowledge related to her condition, thus she never had herself checked or examined before having the symptoms, which were then found in a later stage. This shows that the lack of knowledge contributed to the delay of diagnosis.

CONCLUSION

Signet ring cell carcinoma of the colorectal represents a challenge due to its aggressive nature and diagnostic complexities. Further research, especially in Indonesia, is needed to fully understand the causes and risk factors specific to SRCC, and the importance of screening and early detection.

We also concluded that public knowledge had significant roles in increasing patients' awareness regarding a disease, which helped in thoroughly diagnosing cases like SRCC. Thus, it is important to improve vigilance of cancers like SRCC in society and to expand the accessibility of pathology services in regional hospitals, such as genetic profiling, tumor markers, and early detection, to help identify individuals with higher risks.

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