International Journal of Clinical Research

Case Report

Diagnosis and Progression of Rectal Signet Ring Cell Carcinoma in a 15 Year Old Lebanese Boy: A Case Report

Mohammad Rida Farhat, MD[1], Houssam Khodor Abtar, MD[2], Abbass Shibli, MD[1], Youssef Hamdan, MD[1], Zakaria Dika, MD[1], Moustafa Wahib Diab, MD[3], Alaa Abdulnasser Taha, MD[3], Mariam Hijazi, MD[4], Zahraa H. Moussawi, MD[1]

[1]Department of General Surgery, Faculty of Medical Sciences, Lebanese University, Beirut, Lebanon
[2]Department of General Surgery, Military Central Hospital, Beirut, Lebanon
[3]Department of Gastroenterology, Military Central Hospital, Beirut, Lebanon
[4]Department of Radiology, Faculty of Medical Sciences, Lebanese University, Beirut, Lebanon

Corresponding Author: Mohammad Rida Farhat, Beirut, Lebanon, farhat.mhd@outlook.com

doi: https://doi.org/10.38179/ijcr.v3i1.162

Received: 2021.10.26
Accepted: 2022.02.25
Published: 2023.01.28

Financial support: None
Conflict of interest: None
Patient Consent: Written consent was obtained from the patient's parents for the publication of this case and accompanying images

Abstract

Introduction: Colorectal cancer (CRC) is a rare entity in children and adolescents compared to adults. In the young, it is mostly detected in the right and transverse parts of the colon. Among the variants of CRC are the uncommon Signet Ring Cell Carcinoma (SRCC) which has a late presentation and pessimistic prognosis. Patients are asymptomatic for a long time and suddenly develop changes in bowel habits or obstruction.

Case Report: A 15-year-old boy with no known health issues presented with recent rectorrhagia and weight loss. He was stable but pale with abdominal tenderness and no rectal mass on digital rectal examination (DRE). Colonoscopy unveiled a 13 centimeters segment of circumferential ulcerated blackish mucosa extending from the upper rectum to the rectosigmoid junction. Pathology studies revealed SRCC of the rectum and sigmoid. Metastatic workup showed rectosigmoid wall thickening and denoted the tumor a stage IV with ascites and intraperitoneal implants. Palliative treatment with chemotherapy was initiated, and a follow-up CT was done later to assess disease progression and response to treatment. The disease had worsened and the patient deteriorated.

Conclusion: In children, colorectal SRCC is scarce and usually presents at a late stage due to the lack of characteristic symptoms and findings. It is then usually missed by physicians and not considered in the differential thus delaying the diagnosis and rendering the prognosis poorer. To improve the outcome, pediatricians ought to keep CRC in mind when facing obstructive symptoms or refractory abdominal pain.

Keywords: Signet ring cell carcinoma, Rectum, Sigmoid, Chemotherapy, Carcinomatosis

Introduction

Of all pediatric cancers, about 2% are primary gastrointestinal tract malignancies with colorectal carcinoma (CRC) being the second most common neoplasm [1]. Approximately 1.3 cases per million children are diagnosed with colon cancer each year. On the other hand, rectal cancer is a very rare malignancy in early adolescence. In this age group, the right and transverse colon involvement are higher relative to adults while rectal involvement is significantly lower [1].

Colorectal signet ring cell carcinoma (SRCC) is a histological variant of the neoplasm that is not usual with an occurrence between 0.1% and 2.6% of all cases reported in the literature [2]. It is defined as the subtype of colorectal adenocarcinoma with prominent intra-cytoplasmic mucin in more than 50% of tumor cells, according to the World Health Organization (WHO) classification of tumors [3]. SRCC has higher malignant potential, is commonly diagnosed at a late stage, and is characterized by distant metastasis with an extremely poor prognosis [4,5].

While SRCC may be asymptomatic, most pediatric patients report signs of varying degrees of obstruction following changes in bowel habits. The final diagnosis is confirmed by histological biopsy [6]. We hereby present the case of a 15-year-old Lebanese child who was admitted for rectorrhagia and found to have rectal signet ring cell carcinoma on colonoscopy.

Case Presentation

A 15-year-old Lebanese boy without a significant medical or surgical history arrived at the Military Hospital due to 6-month history of recurrent pain and discomfort mostly in the left lower quadrant, intermittent rectorrhagia during defecation, melena, and weight loss of about 20 kg over the past 3 months. No family history of cancer was evident. Vital signs were within the normal range.

On physical exam, the patient looked pale with a poorly injected conjunctiva. The abdomen was soft and mildly tender, and there was no palpable rectal mass on the digital rectal examination.

Laboratory tests showed microcytic anemia (hemoglobin 10.6 g/dl, mean corpuscular volume (MCV) 67 fl), high calprotectin level 184 µg/mg, but normal creatinine, International Normalized Ratio (INR), and liver function tests.

A flexible colonoscopy was done and the scope was introduced up to the terminal ileum. It revealed, at 10 cm from the anal verge, a 13 cm segment of continuous, circumferential, severely inflamed, and ulcerated fragile blackish mucosa in the upper rectum and rectosigmoid junction, in the absence of a vascular pattern (Figures 1,2,3).

Endoscopic rectal and sigmoid biopsy showed infiltrating adenocarcinoma of signet ring cell type, however, the ileal biopsy was normal.

Chest and abdominopelvic computed tomography (CT) scans were done for the initial metastatic workup. They revealed an abundant amount of ascites that was occupying almost the entire peritoneal cavity. Ascites could be seen filling the perihepatic and peri-splenic regions and extending to the pelvis associated with multiple nodular peritoneal implants (Figure 4). In addition, the scans showed extensive thickening of the sigmoid wall and the rectum (Figures 5, 6).

For further investigation, magnetic resonance imaging (MRI) of the pelvis emphasized significant mucosal thickening of rectal and sigmoid walls (Figures 7, 8) and pointed out multiple enlarged metastatic mesorectal lymph nodes, the largest of which measuring 2 cm (Figure 7), accompanied by omental caking (Figure 9).

Given those findings, the decision was made to start chemotherapy, FOLFOX regimen (5 Fluorouracil, calcium folinate, oxaliplatin) as a palliative treatment. Each cycle given constituted of an intravenous injection of fluorouracil 400 mg/m2 bolus, then 600 mg/m2 over 22 hours days 1 and 2, calcium

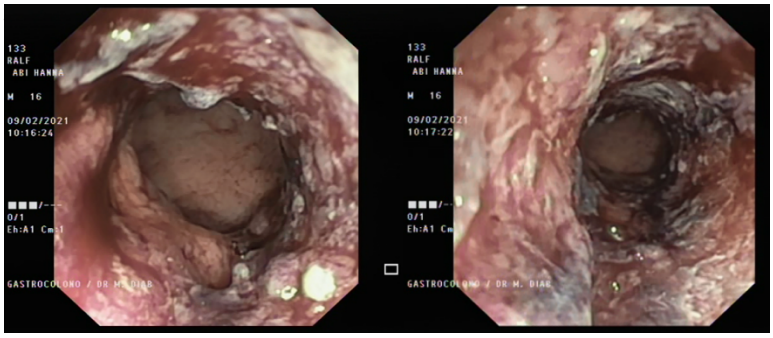

Figure 1: Colonoscopy of a Lebanese 15-years-old child demonstrating ulceration and severe inflammation of the mucosa in the rectosigmoid junction.

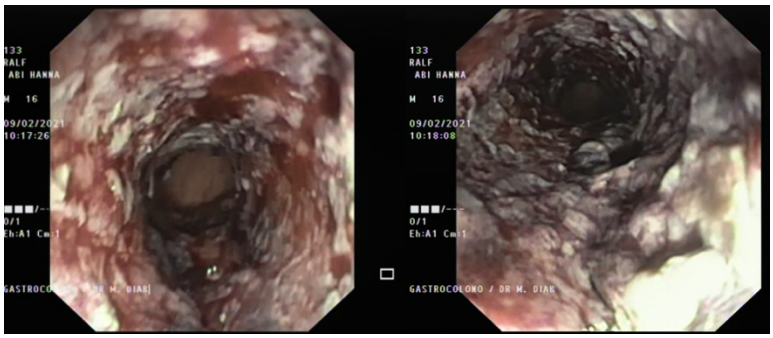

Figure 2: Colonoscopy revealing continuous circumferential inflamed mucosa of the rectum associated with necrotic black mucosa and absence of vascular pattern.

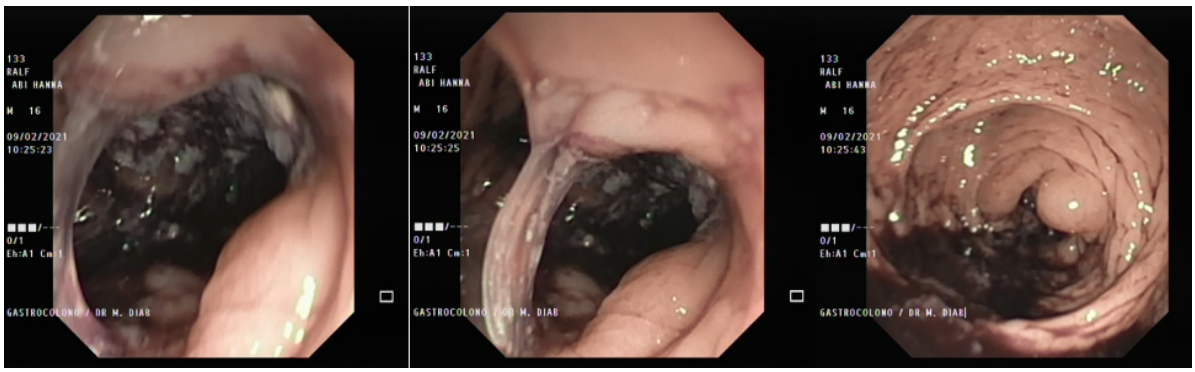

Figure 3: Inflamed and necrotic mucosa appearing 13cm from the anal verge.

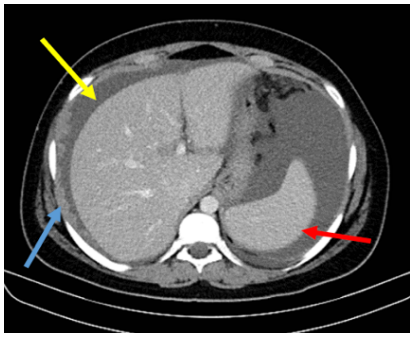

Figure 4: Axial intravenous contrast-enhanced portal phase CT scan of the abdomen done after colonoscopy demonstrating ascites in the perihepatic (yellow arrow), peri-splenic (red arrow) regions, and multiple nodular peritoneal implants (blue arrow).

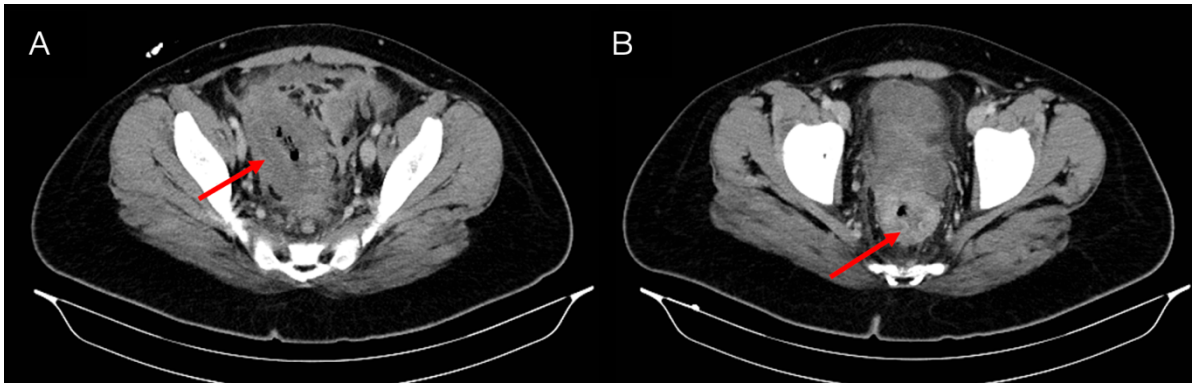

Figure 5. Axial reformatted image from abdominopelvic CT shows considerable mucosal thickening of the sigmoid wall (A) extending down to the upper rectum (B).

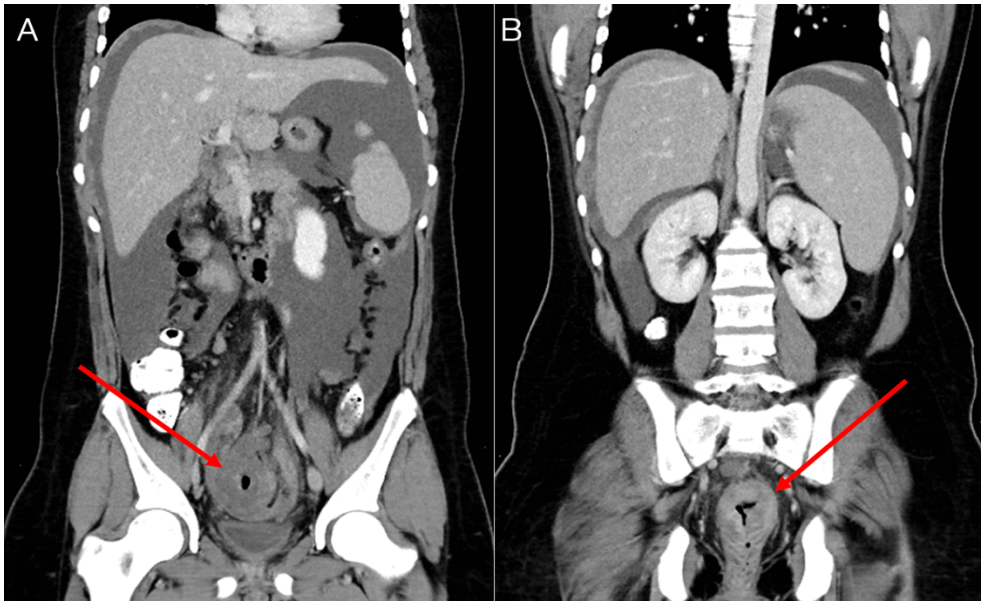

Figure 6. Coronal reformatted image from intravenous contrast-enhanced abdominopelvic CT demonstrates a circumferential thickening of the sigmoid wall (A) reaching the upper rectum (B) .

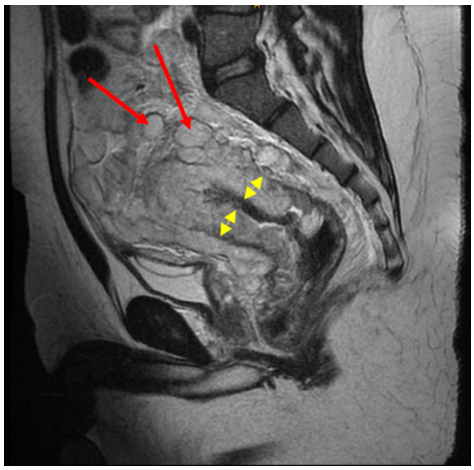

Figure 7: Sagittal T2 weighted MR image showing mucosal thickening of the upper rectum (yellow arrows) with infiltration of the surrounding fat and multiple enlarged metastatic mesorectal lymph nodes(red arrows).

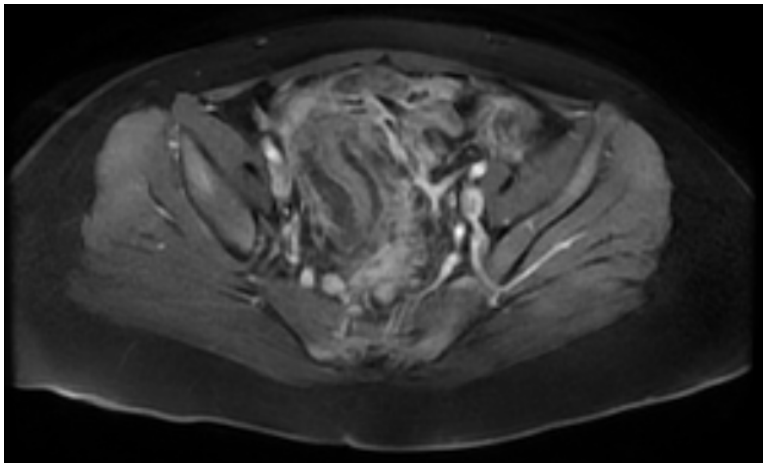

Figure 8: Axial contrast-enhanced MR image showing significant mucosal thickening of the sigmoid wall, with adjacent enhancing lymph nodes, and mild ascites.

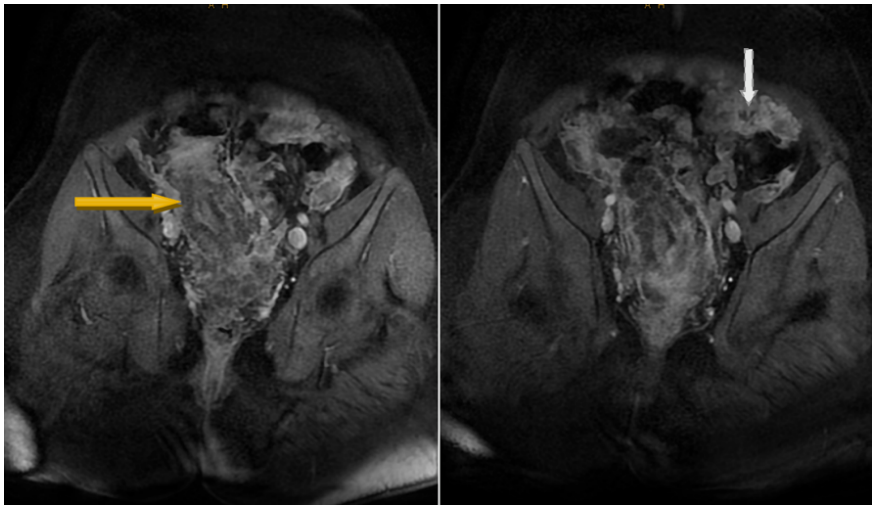

Figure 9: Coronal reformatted contrast-enhanced MR images showing significant mucosal thickening of the rectum and sigmoid wall (yellow arrow), with enhanced infiltration of the surrounding fat and mesorectum. In addition to anterior omental caking (white arrow).

Folinate 400 mg/m2 over two hours days 1 and 2, and oxaliplatin 85 mg/m2 day 1. This cycle was repeated every two weeks. Five months following chemotherapy, the patient underwent another injected abdominopelvic CT scan to assess disease progression and its response to treatment. It revealed prominent peritoneal carcinomatosis with omental caking, accompanied by a dramatic sudden increase in the rectal and sigmoid wall thickening (Figures 10, 11). Based on the poor response to the present chemotherapy, treatment was switched to another protocol, FOLFIRINOX (leucovorin calcium, fluorouracil, irinotecan hydrochloride, and oxaliplatin). This cycle consists of intravenous injection of oxaliplatin 85 mg/m2, leucovorin 400 mg/m2, irinotecan 180 mg/m2, and fluorouracil 400 mg/m2. All are given on day 1 and will be repeated every two weeks for up to 6 months.

Discussion

Colorectal adenocarcinoma is a rare malignancy in youngsters when compared to adults where it is the third most common malignancy. Its incidence in children is nearly one in a million and comprises about 1% of pediatric neoplasms [7]. Due to its low occurrence and index of suspicion, it is overlooked in the initial differential diagnosis, thus, its recognition is delayed, explaining why it is mostly at an advanced stage when diagnosed. The fact that it presents with nonspecific symptoms also contributes to this delay [8]. Colorectal adenocarcinoma has two very rare subtypes, the signet ring cell carcinoma, and the mucinous carcinoma [2]. SRCC primarily arises in the stomach and is only rarely found in the colon or rectum [9].

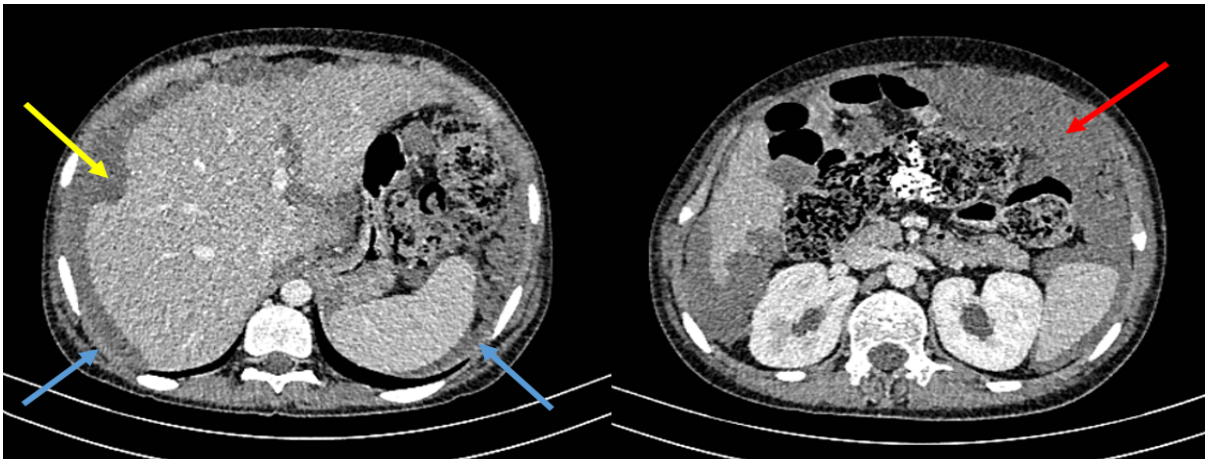

Figure 10: Peritoneal mucinous carcinomatosis from signet ring cell carcinoma. Axial intravenous contrast-enhanced abdominal CT scan performed 5 months after chemotherapy shows scalloping of the liver surface by mucinous ascites (yellow arrow). There is also an increase in the amount of low-attenuation mucinous ascites (blue arrows) and omental caking (red arrow).

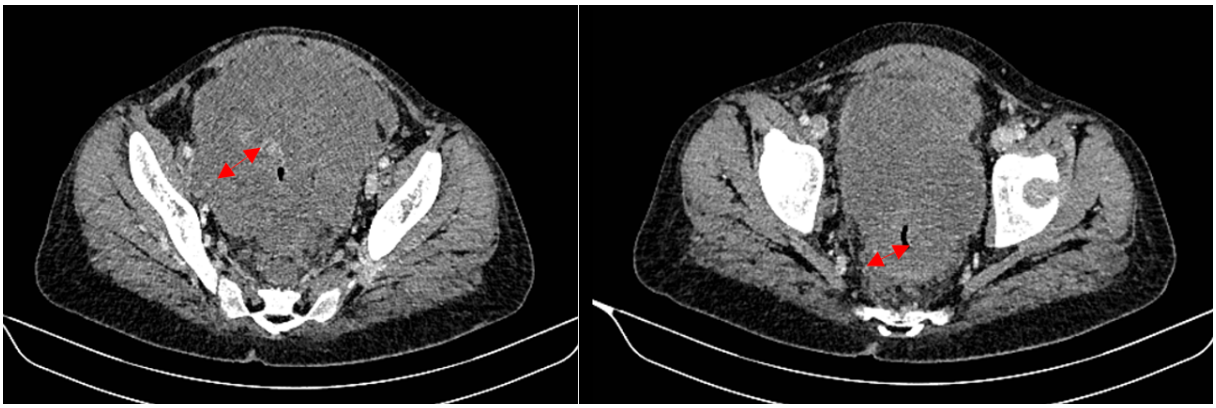

Figure 11: Axial intravenous contrast-enhanced abdominopelvic CT scan shows an impressive increase in sigmoid and rectal wall thickening 5 months after chemotherapy (compared to figure 5).

WHO defined it as a variant of colorectal adenocarcinoma having intracytoplasmic mucin in more than 50% of tumor cells. It represents about 1% of CRC [3]. It is usually sporadic in children or occurs in association with familial adenomatous polyposis, ulcerative colitis, Crohn's disease, or other syndromes. The peak age of colorectal carcinoma in children is 15 years without a preference in gender or race [8]. In this age group, SRCC arises in the colon in about 67% of cases whereas it appears in the rectum in only 23% of patients [7].

Concerning presentation, earlier stages of the disease are discreet, and symptoms are not evident until it has become advanced with about 75% of patients having stages III and IV upon diagnosis. Manifestations are nonspecific and include abdominal pain, signs of bowel obstruction, gastrointestinal bleeding, and changes in bowel habits [3,10]. The severity of symptoms is related to the location of the tumor, its TNM stage, penetration of adjacent organs, metastasis, and operability [9]. Note that the tumor may also be assigned a stage based on the Modified Dukes system or the Astle-Coller system besides the TNM classification [11].

Prognosis is generally dismal and unfavorable, with the median age of survival being approximately 17 months and the 5-year survival rate not reaching 10%. The invalid operation rate for patients with SRCC also appears to be higher [12]. A high TNM stage, infiltration of adjacent organs or peritoneum, and distant organ metastases, all predict a poor prognosis [9]. Our patient was assigned as stage IV/Dukes D at diagnosis. He had SRCC with peritoneal carcinomatosis.

Since SRCC is rapidly progressive, some patients who are fortunate enough to be diagnosed before metastasis and peritoneal carcinomatosis are selectively recommended to undergo cytoreductive surgery and hyperthermic intraperitoneal chemotherapy [13]. Hugen et al. proclaimed that adjuvant chemotherapy would still be of benefit to SRCC patients like it is in other CRC forms despite SRCC subtyping being an independent risk factor for worse prognosis [10]. In 2016, Fu et al. reviewed the cases of 3568 patients with metastatic CRC among whom 2.63% had SRCC and concluded that resecting primary and metastatic SRCC lesions would have minimal benefit [12]. However, patients who had possibly curative surgical procedures had a better prognosis than those in whom only palliative measures were taken [9]. In their study to evaluate how efficient perioperative adjuvant therapy is in cases where colonic SRCC is resected, Sun et al. found that for stage IV patients, the prognosis was not significantly different between patients in groups who received 5-FU, Bevacizumab, or FOLFOX/FOLIRI regimens but they all had significantly better prospects than the ones who didn't receive any treatment [14]. New evidence is emerging regarding the role of immunotherapy in revolutionizing treatment methods for gastrointestinal cancer patients when combined with radiotherapy in an effort to improve their anti-tumor immune response [15].

Our patient was classified as stage IV/Dukes D at diagnosis. He had SRCC with peritoneal carcinomatosis. Given the advanced condition, and in the absence of an indication for surgical intervention, it was decided that the patient's management would be palliative with chemotherapy. Five months later, the patient had a follow-up CT which showed rapid disease progression as his peritoneal carcinomatosis developed into caking, and he suffered a substantial increase in sigmoid and rectal wall thickness. In addition, he likely developed a pseudomyxoma, as highly suggested by the characteristic liver scalloping seen on the CT.

Due to the low incidence, reported cases of signet ring cell carcinoma are of a limited number and occur sporadically. Also when it occurs, it is more often at the right colon, as deduced by an analysis from the National Cancer Data Base [16]. Until 2014, metastatic primary SRCC in the rectum of patients below 21 years was reported by Singh et al. in six cases only [4]. Beyond that, there has not been any documented case

with similar conditions. To the best of our knowledge, this case would be the first.

Conclusion

In conclusion, the absence of typical clinical symptoms at presentation, along with the lack of specific radiological data for diagnosing signet-ring cell carcinoma of the rectum in children contribute to its gloomy prognosis. Occasionally, the clinical symptoms could go unnoticed by parents or be ruled irrelevant by physicians, thus leading to the diagnosis of advanced-stage tumors with a poor prognosis. To improve the outcome and chances of survival, pediatricians should consider malignancies in the differential diagnosis whenever a child presents with a change in bowel habits, signs and symptoms of intestinal obstruction, or incurable abdominal pain, and consult pediatric surgeons promptly, as early diagnosis and treatment decrease the rate of mortality.

References

1. Pandey A, Gangopadhyay A, Sharma S, Kumar V, Gupta D, Gopal S, Singh R. Pediatric carcinoma of rectum--Varanasi experience. Indian J Cancer. 2008 Jul-Sep;45(3):119-22. PMID: 19018116. https://doi.org/10.4103/0019-509x.44068
2. Morales-Cruz M, Salgado-Nesme N, Trolle-Silva AM, Rodríguez-Quintero JH. Signet ring cell carcinoma of the rectum: atypical metastatic presentation. BMJ Case Rep. 2019;12(4):e229135. Published 2019 Apr 30. PMID: 31040144. https://doi.org/10.1136/bcr-2018-229135
3. Arifi S, Elmesbahi O, Amarti Riffi A. Primary signet ring cell carcinoma of the colon and rectum. Bull Cancer. 2015;102(10):880-888. PMID: 26412710. https://doi.org/10.1016/j.bulcan.2015.07.005
4. Singh K, Singh A, Bhutra S, Pachori G, Jangir MK. Metastatic Primary Signet Ring Cell Carcinoma of Rectum: A Case Report of 10-Year-old Male Child. J Clin Diagn Res. 2014 Feb;8(2):177-8. PMID: 24701526. https://doi.org/10.7860%2FJCDR%2F2014%2F6988.4051
5. Marone J, Patel S, Page M, Cheriyath P. Signet cell carcinoma of the colon in a 17 year old child. J Surg Case Rep. 2012;2012(9):3. Published 2012 Sep 1. PMID: 24960789. https://doi.org/10.1093%2Fjscr%2F2012.9.3
6. Irene I, Ariawati K. Signet ring cell carcinoma of the colon in a 10 year-old boy. PI. 2011 Apr; 51(2):116-2. https://doi.org/10.14238/pi51.2.2011.116-22
7. Poles GC, Clark DE, Mayo SW, et al. Colorectal carcinoma in pediatric patients: A comparison with adult tumors, treatment and outcomes from the National Cancer Database. J Pediatr Surg. 2016;51(7):1061-1066. PMID: 26703433. https://doi.org/10.1016/j.jpedsurg.2015.11.005
8. Koh KJ, Lin LH, Huang SH, Wong JU. CARE--pediatric colon adenocarcinoma: a case report and literature review comparing differences in clinical features between children and adult patients. Medicine (Baltimore). 2015;94(6):e503. PMID: 25674743. https://doi.org/10.1097%2FMD.0000000000000503
9. Belli S, Aytac HO, Karagulle E, Yabanoglu H, Kayaselcuk F, Yildirim S. Outcomes of surgical treatment of primary signet ring cell carcinoma of the colon and rectum: 22 cases reviewed with literature. Int Surg. 2014;99(6):691-698. PMID: 25437572. https://doi.org/10.9738/intsurg-d-14-00067.1
10. Hugen N, Verhoeven RH, Lemmens VE, et al. Colorectal signet-ring cell carcinoma: benefit from adjuvant chemotherapy but a poor prognostic factor. Int J Cancer. 2015;136(2):333-339. PMID: 24841868. https://doi.org/10.1002/ijc.28981
11. Akkoca AN, Yanık S, Ozdemir ZT, et al. TNM and Modified Dukes staging along with the demographic characteristics of patients with colorectal carcinoma. Int J Clin Exp Med. 2014;7(9):2828-2835. PMID: 25356145.
12. Fu J, Wu L, Jiang M, et al. Signet ring cell carcinoma of resectable metastatic colorectal cancer has rare surgical value. J Surg Oncol. 2016;114(8):1004-1008. PMID: 27891617. https://doi.org/10.1002/jso.24437
13. Solomon D, DeNicola N, Feingold D, et al. Signet ring cell features with peritoneal carcinomatosis in patients undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy are associated with poor overall survival. J Surg Oncol. 2019;119(6):758-765. PMID: 30650185. https://doi.org/10.1002/jso.25379
14. Sun J, Wang X, Gao P, et al. Prognosis and

efficiency of adjuvant therapy in resected colon signet-ring cell carcinoma. Transl Cancer Res. 2018;7(4):1006-1025. https://tcr.amegroups.com/article/view/22906/html#:~:text=The%20SRCC%205%2Dyear%20survival,also%20shown%20in%20Table%202.

15. Badiyan S, Kaiser A, Eastman B, et al. Immunotherapy and radiation therapy for gastrointestinal malignancies: hope or hype?. Transl Gastroenterol Hepatol. 2020;5:21. PMID: 32258525. https://doi.org/10.21037%2Ftgh.2019.10.07

16. Hyngstrom JR, Hu CY, Xing Y, et al. Clinicopathology and outcomes for mucinous and signet ring colorectal adenocarcinoma: analysis from the National Cancer Data Base. Ann Surg Oncol. 2012;19(9):2814-2821. PMID: 22476818. https://doi.org/10.1245/s10434-012-2321-7