Case Report

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Medullary carcinoma of the left colon in a 16-year-old male: an extremely rare case report from Syria

Lutfallah Raffoul, MD[a,b,*], Majd Mansour, MD[b], Ghina Majd Hussain, MD[b,c], Abdallah N. Mansour, MD[b], Soliman Mortada, MD[c], Aiman Mortada, MD, PhD[d], Zuheir Alshehabi, MD, PhD[b,e]

Introduction and importance: Medullary carcinoma (MC) is a rare type of colon carcinoma that accounts for less than 1% of colorectal neoplasms. Morphologically, MC resembles many colorectal cancer (CRC) subtypes, mainly Neuroendocrine Carcinoma (NEC) due to exhibiting neuroendocrine features. In consequence, MC is exceedingly challenging to detect; numerous immunohistochemistry tests are required in order to distinguish it from the other subtypes of CRC.

Case presentation: We report a case of a 16-year-old male who presented with severe abdominal pain and symptoms of bowel obstruction. Computed tomography scan showed a mass in the descending colon. The patient underwent an emergency colectomy. The left part of the transverse colon, the descending colon, and part of the sigmoid were removed, along with the regional lymph nodes. Microscopic examination suggested NEC, whereas immunohistochemical staining confirmed the diagnosis of MC of the left colon. After surgery, a course of chemotherapy was administered.

Clinical discussion: Medullary carcinoma usually presents in elderly Caucasian women, and is mainly observed in the right colon. Therefore, it is highly unusual to appear in a 16-year-old boy's left colon. The diagnosis is based on microscopic and immunohistochemical tests. The optimal management of MC is surgery, combined with chemotherapy, and in some cases a full colectomy is needed.

Conclusion: The purpose of this paper is to highlight the dilemma of diagnosing MC of the colon, as well as the successful management of MC through surgical intervention, and post-operative care.

Keywords: colectomy, colorectal cancer, immunohistochemistry, medullary carcinoma, poorly differentiated adenocarcinoma

Introduction

Medullary carcinoma (MC) is an extremely rare subtype of colon carcinoma, with an estimated 0.29% of CRC cases[1]. The recent finding that about 90% of MC is linked to microsatellite instability (MSI), may account for part of its biological behavior. MC is more common in elderly women, and it has a better prognosis than poorly differentiated (typical type) adenocarcinoma (AC). Comparing left-sided MC to right-sided MC, the former was linked to a lower survival rate[1,2]. The majority of patients exhibit symptoms like melena, diarrhea, or changed bowel habits, which are indicative of lower gastrointestinal cancer[2]. Treatment for MC is similar to that for colon AC. Advanced colon cancer is treated with chemotherapy, whereas localized disease is treated with surgical resection only[2,3]. In this study, we describe an unexpected case of MC in a 16-year-old male with unique characteristics that developed in the left colon. This case report has been reported in line with the SCARE Criteria[4].

HIGHLIGHTS

- Medullary carcinoma (MC) is a rare type of colon carcinoma that accounts for less than 1% of colorectal neoplasms.
- Due to resemblance between MC and other colorectal cancer subtypes especially neuroendocrine carcinoma (NEC), many microscopic and immunohistochemical tests are required in order to make the right Diagnosis.
- MC usually presents in elderly Caucasian women, and is mainly observed in the right colon. Therefore, it is highly unusual to appear in a 16-year-old boy's left colon.
- The optimal management of MC is surgery, combined with chemotherapy, and in some cases a full colectomy is needed.
- The purpose of this paper is to highlight the dilemma in diagnosing medullary carcinoma of the colon, as well as the successful management of MC through surgical intervention, and post-operative care.

[a]Faculty of Medicine, Al Andalus University for Medical Sciences, Tartous, Syrian Arab Republic, [b]Cancer Research Center, Tishreen University, Latakia, Syrian Arab Republic, [c]Faculty of Medicine, Tishreen University, Latakia, Syria, [d]Department of Surgery, Tishreen University Hospital, Latakia, Syria and [e]Department of Pathology, Tishreen University Hospital, Latakia, Syria

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*Corresponding author. Address: Faculty of Medicine, Al Andalus University for Medical Sciences, Tartous, Syrian Arab Republic; Cancer Research Center, Tishreen University, Latakia, Syrian Arab Republic. Tel.: +963 994 307 098. E-mail: lutfallahraffou1@gmail.com (L. Raffoul).

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Case presentation

A 16-year-old male presented to the emergency department with a 7-day history of abdominal pain. At the day of presentation, the pain had continuously increased in intensity and was described as colicky in nature, did not relieve in any position, and was unresponsive to painkillers. The patient also reported nausea and a 4-day cessation of passing stools and gas. There was no diarrhea, fever, or vomiting. The patient is a non-smoker and does not consume alcohol. The patient was admitted to the general surgery department. Computed tomography (CT) scan of the abdomen and pelvis showed a mass at the level of the descending colon with severe dilation that appeared on the level of the ascending and transverse colons (Fig. 1A + B + C + D). Additionally, the presence of the pseudokidney sign in the longitudinal section (Fig. 1C) and the target sign in the transverse section (Fig. 1D), points to colon intussusception as an initial diagnosis prior to surgery. CT scan showed no lymph nodes or liver metastases.

The patient was scheduled for a colectomy. The procedure was open surgery. Midline incision was performed above and below the umbilicus, and the abdomen was opened in layers. There was a firm mass obstructing the lumen, which could be palpated at the level of the descending colon. Upon opening the colon wall and examining the mass, a tumor was found (Fig. 2A). The left part of the transverse colon was removed, along with the descending colon and part of the sigmoid after tying and cutting the mesentery of the colon. The specimen was sent for pathological examination. Then, a double barrel ostomy was performed on the two ends of the remaining colon, and a drain was placed in Douglas pouch. The layers of the abdomen were closed and a sterile dressing was applied. The section of the colon that had been removed was examined at the pathology department. It showed 30 cm long left colon with a maximum diameter of 6 cm. Two tumor masses that had penetrated the serous layer were visible in the middle.

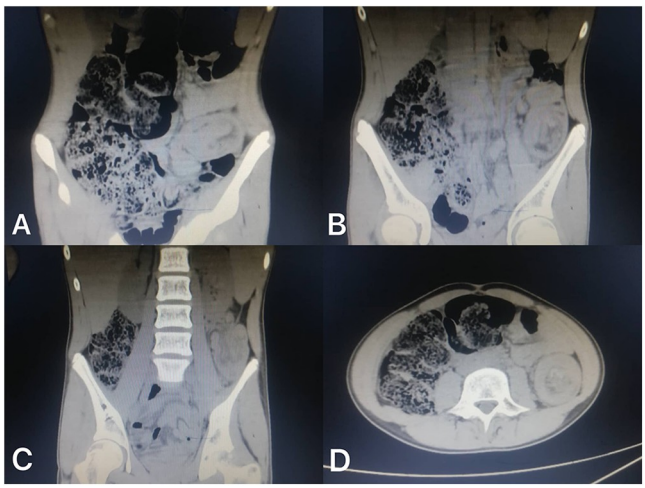

Figure 1. (A–D) Computed tomography scan: Performed preoperatively upon admission of the patient. (B) Showing a mass at the level of the descending colon with severe dilation that appeared on the level of the ascending and transverse colons. (C) Computed tomography scan in the longitudinal section showing the Pseudokidney sign which indicates colon intussusception as an initial diagnosis. (D) Computed tomography scan in the transverse section showing the Target sign which indicates colon intussusception as an initial diagnosis.

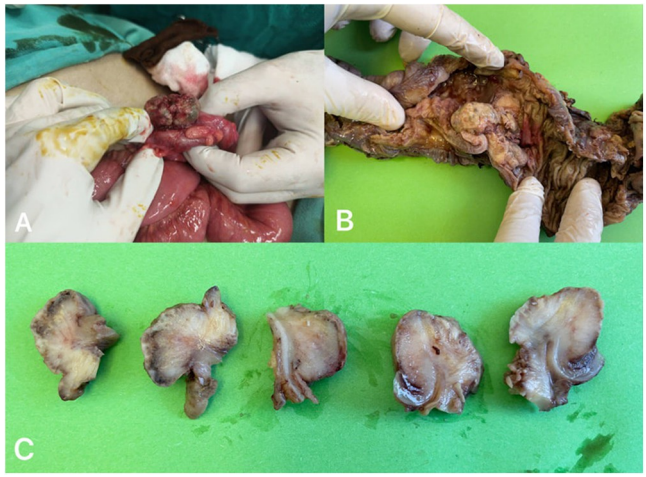

Figure 2. (A) Upon opening the colon wall and examining the mass, a tumor was found. Because initially, it was suspected that there was an intussusception, not a tumor. (B) Shown in the middle, are two tumor masses that had penetrated the serous layer. The diameter of the first was 3 cm, while the second was 4 cm. (C) Thirteen specimens were taken: two from the upper and lower borders, five from the tumor, and six from the lymph nodes.

The diameter of the first was 3 cm, while the second was 4 cm measuring 4 cm in maximum dimension (Fig. 2B). Thirteen specimens were taken: two from the upper and lower borders, five from the tumor, and six from the regional lymph nodes (Fig. 2-C).

Microscopic description revealed malignant, well circumscribed neoplasm with solid growth pattern and pushing border with neuroendocrine features Fig. 3 (A + B + C), suggestive of neuroendocrine carcinoma (NEC). The neoplastic cells invaded muscularis and subserosa (pT3). The pericolic lymph nodes showed two positive metastatic nodes (2/12) – pN1. All margins of surgical resection were free from tumor cells.

Immune stains showed positivity for cytokeratin (Fig. 3D) and calretinin (Fig. 3E), whereas chromogranin A (Fig. 3F), and melan A (Fig. 3G) were negative, high rate Ki67 ~70% (Fig. 3H). Histologically, the tumor is very similar to NEC, but the positivity of calretinin and cytokeratin in the immune stains, and the negativity of the neuroendocrine marker (chromogranin A) supported the diagnosis of MC of the colon. In addition, the solid growth pattern of the neoplasm, and either absence or very focal mucin production, along with the positivity of Calretinin, helped differentiate MC from other AC.

Post-operative follow-up: The patient's overall health is good, with stable vital signs. A CT scan of the abdomen, pelvis, chest, and brain with contrast was carried out and showed that there were no metastases. Laboratory tests conducted before the first surgery are listed in (Table 1). While being prepared for colostomy closure surgery, the patient started chemotherapy, consisting of oxaliplatin (50 mg) and 5-fluorouracil (50 mg) administered intravenously once every 13 days. No treatment adjustments were made for the patient's age and rare diagnosis. After 3 months from the first surgery, colostomy closure procedure was performed successfully. The results were normal with no complications. The patient was followed up for 1 month after colostomy closure procedure. The patient remains in good health, experiencing only a well-managed wound infection after the surgery.

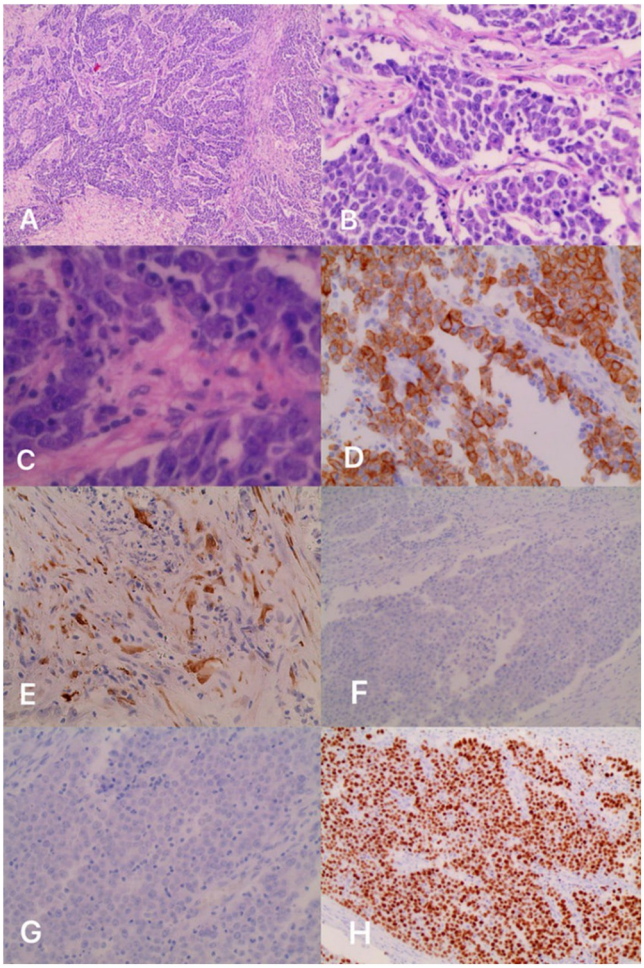

Figure 3. (A) H&Ex40. (B) H&Ex200. (C) H&Ex400. (D) IHC-CK+. (E) IHC-Calretinin+. (F) IHC-Chromogranin A-. (G) IHC-Melan A-. (H) IHC-Ki67 ~70%.

Table 1

Laboratory tests analysis showing normal results

Parameter	Results
White blood cells	4.5×10^9/L
Lymphocytes%	39.8%
Mid-range cells%	8.7%
Granulocytes%	51.5%
Lymphocytes	1.8×10^9/L
Mid-range cells	0.4×10^9/L
Granulocytes	2.3×10^9/L
Red blood cells	4.94×10^{12}/L
Hemoglobin	13.1 g/dL
Hematocrit	41.1 %
MCV	83.3 fL
MCH	26.5 pg
MCHC	31.8 g/dL
RDW-CV	15.4 %
RDW-SD	40.7 fL
Platelet count	17.4×10^9/L
MPV	12.1 fL
PDW	17.9 fL
Procalcitonin	0.21%
P-LCR	44.6%
PLCC	77×10^9/L
Creatinine	0.73 mg/dL
Urea	19.5 mg/dL
CRP-M	1.7 mg/L

Discussion

Medullary carcinoma of the colorectal tract is a rare subtype of colorectal cancer (CRC), accounting for approximately 0.29% of all CRC cases[1,5]. First described by Jessurun *et al* in 1999[6], MC is a type of AC characterized by a solid structure and minimal glandular differentiation[3]. Thirunavukarasu *et al* in 2010 reported that MC can present as minimally differentiated AC (0.03%), poorly differentiated (72%), and undifferentiated (22%), complicating histological differentiation[6]. Despite its rarity, MC presents unique challenges in diagnosis and management[5]. The clinical presentation of MC can vary widely, often resembling symptoms commonly associated with CRC, including abdominal pain, changes in bowel habits, rectal bleeding, and signs of bowel obstruction[1].

The incidence of CRC in the pediatric population is extremely low. According to data from the Surveillance, Epidemiology and End Results (SEER) Program, the yearly incidence rate is 1.78/1 000 000 for patients aged 15–19 and 0.12/1 000 000 for the group aged 0–14[7]. In our case, we are dealing with a 16-year-old male patient whose primary tumor mass is situated in the left colon. This rarity is further accentuated by the fact that MC typically manifests in elderly Caucasian women, with a median age of 69 years, and is more commonly observed in the right colon[5,8]. According to Thirunavukarasu *et al*, the average age of diagnosis of MC of the colon was 69.3 ± 12.5. Males were diagnosed at an average age of 64.3 ± 13.3, much younger than the average age of females, 72.1 ± 11.2 years (*t*-test, two tailed p = 0.009)[9]. MC of the colon (MCC) is predominantly located in the cecum (36%) and the ascending colon (38%), and is less frequently found in the transverse colon (12%) and the sigmoid colon (6%). Compared to MCs in the rest of the colon, sigmoid colon MCs tended to appear earlier (mean age of 59.7 ± 7.2 years) (two-tailed P = 0.05). Locations such as the hepatic flexure, splenic flexure, descending colon, and rectum are uncommon for MCC[9].

In our case, the tumor was localized in the descending colon, which is an unusual site for this type of tumor. MCC unfolds a diagnostic conundrum owing to its histological resemblance to NEC[10] or poorly differentiated AC[5]. The distinct histological features of MCC include intratumoral lymphocyte infiltration and infrequent lymph node and perineural invasion. Genetic factors such as MSI-high (MSI-H), mismatch repair deficiency, and specific molecular alterations like MLH1 promoter hypermethylation and BRAF V600E mutations are common. MCC often does not exhibit markers linked to colonic differentiation such as CDX2 and CK20, but can display positive staining for calretinin and CK7, as well as the absence of ARID1A expression, in addition to a higher frequency of BRAF (V600E) mutation[1,2]. Essential to its differential diagnosis is the absence of neuroendocrine marker expression, a critical distinction from NEC[5]. In our case, the pathological examination following surgical resection revealed a poorly differentiated carcinoma, demonstrating invasive tumor growth involving the mucosal and submucosal layers. These histological findings are consistent with the characteristic

features of MCC, including solid growth patterns, poorly differentiated neoplastic cells, and prominent lymphocytic infiltration[11]. Additionally, the detection of MSI further supports the diagnosis of MCC and underscores the significance of molecular profiling in refining diagnostic accuracy and guiding therapeutic strategies[12]. To further confirm the diagnosis of MCC, immunological tests were conducted, testing negative for Melan-A, and indicating a non-melanocytic origin of the tumor. Additionally, it was negative for Chromogranin A, which ruled out NEC, but positive for CK and calretinin with high rate of Ki67 which confirm the diagnosis of MCC. Despite typically presenting at an early stage (stage II), MCC can metastasize to uncommon sites like the abdominal wall and scapula. In a population-based analysis study, it was found that this tumor had metastasized in 10% of the patients[9]. In our case, there was no evidence of metastasis, with only two lymph nodes showing metaplastic changes. A well-planned surgical approach combined with chemotherapy is typically regarded as the optimal treatment option for these rare tumors to prevent metastasis[3]. In our case, a colostomy was carried out, and a double barrel ostomy was performed on the two ends of the remaining colon. Then a drain was placed in Douglas pouch. Along with early treatment with chemotherapy consisting of oxaliplatin (50 mg) and 5-fluorouracil (50 mg) administered intravenously once every 13 days, the patient remains in good health, experiencing only a well-managed wound infection after the surgery.

Conclusion

The peculiarity of this case of MC is by its occurrence in a 16-year-old male patient, defying the typical demographic and anatomical expectations associated with this neoplasm. Therefore, recognition of medullary colonic carcinoma in children and adolescents as a separate clinical entity should be considered. MC in children has a different clinical presentation and maybe prognosis & outcome.

The pivotal role of immunohistochemistry (IHC) in diagnosis was demonstrated, with the expression profile supporting the medullary phenotype. Notably, this cancer subtype typically manifests with less lymphatic dissemination, therefore finding two positive regional lymph nodes represents a deviation from the norm. Raising awareness among pathologists and clinicians for this rare type of colonic carcinoma.

This unprecedented case report not only enriches the understanding of MC of colon, but also emphasizes the critical importance of considering this rare diagnosis in atypical presentations, thereby influence the early diagnosis and a multidisciplinary approach in rare cases like this. The need to consider MC in atypical presentations and the role of IHC, would be helpful for clinicians.

Ethical approval

Ethical approval was not required, because it is a case report without intervention; however, a written informed consent was obtained from the patient's parents for publishing this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Consent

Written informed consent was obtained from the patient's parents/legal guardian for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author's contributions

L.R.: design of the study, data interpretation and analysis, drafting of the article. M.M.: data interpretation and analysis. G.M.H.: data interpretation and analysis, drafting of the article. A.N.M.: data collection. S.M.: data collection, drafting of the article. A.M.: patient care, critical revision. Z.A.: supervisor and the approval of the final revision.

Conflicts of interest disclosure

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Zuheir Alshehabi is the guarantor of this work.

Provenance and peer review

The paper was not invited to publish in other journals.

Data availability and materials

All data (of the patient) generated during this study are included in this published article and its supplementary information files.

References

[1] Al-Ishaq F, Al-Dhaheri M, Toffaha A, *et al*. Colonic medullary carcinoma: an exceedingly rare type of colorectal malignancy: a case report and review of the literature. J Med Case Rep 2023;17:434.
[2] Fatima Z, Sharma P, Youssef B, *et al*. Medullary carcinoma of the colon: a histopathologic challenge. Cureus 2021;13:e15831.
[3] Martinotti M, Cirillo F, Ungari M, *et al*. Microsatellite instability in medullary carcinoma of the colon. Rare Tumors 2017;9:6541.
[4] Agha RA, Franchi T, Sohrabi C, *et al*. SCARE Group. The SCARE 2020 Guideline: updating Consensus Surgical CAse REport (SCARE) Guidelines. Int J Surg 2020;84:226–30.
[5] Abada E, Jang H, Kim S, *et al*. Medullary colonic carcinomas present with early-stage disease and do not express neuroendocrine markers by immunohistochemistry. Ann Gastroenterol 2023;36:321–26.
[6] Jessurun J, Romero-Guadarrama M, Manivel JC. Medullary adenocarcinoma of the colon: clinicopathologic study of 11 cases. Hum Pathol 1999;30:843–48.
[7] Matheya M, Pennella C, Zubizarreta P. Colorectal carcinoma in children and adolescents. Arch Argent Pediatr 2021;119:e487–98.

[8] Knox RD, Luey N, Sioson L, *et al*. Medullary colorectal carcinoma revisited: a clinical and pathological study of 102 cases. Ann Surg Oncol 2015;22:2988–96.
[9] Thirunavukarasu P, Sathaiah M, Singla S, *et al*. Medullary carcinoma of the large intestine: a population based analysis. Int J Oncol 2010;37: 901–07.
[10] Wick MR, Vitsky JL, Ritter JH, *et al*. Sporadic medullary carcinoma of the colon: a clinicopathologic comparison with nonhereditary poorly differentiated enteric-type adenocarcinoma and neuroendocrine colorectal carcinoma. Am J Clin Pathol 2005;123:56–65.
[11] Colarossi C, Mare M, La Greca G, *et al*. Medullary carcinoma of the gastrointestinal tract: report on two cases with immunohistochemical and molecular features. Diagnostics 2021;11:1775.
[12] Blakely AM, Nelson RA, Hamilton SA, *et al*. Sidedness determines clinical characteristics and survival outcomes in medullary adenocarcinoma of the colon. Sci Rep 2021;11:20481.