



Colonic Medullary Carcinoma: A Rare Case

Kolonun Meduller Karsinomu; Nadir Bir Olgu

Halis Bağ¹, Haldun Kar¹, Necat Cin¹, Arzu Avcı², Yasin Peker¹, Evren Durak¹

Medullary carcinoma is a rare subtype of colorectal cancer making up less than 0.1% of all colorectal malignancies. This subtype can be confused with poorly differentiated colorectal carcinoma due to undifferentiated complex morphology and high mitotic activity. Medullary carcinoma is a subtype of colonic adenocarcinoma with a better prognosis than other subtypes. This subtype is important because of the expansive growth pattern and high microsatellite instability. Medullary carcinoma is often right sided and is more frequent in older females and has lower incidence of lymph node metastases. In our case, the patient presented with complaints of abdominal pain and rectal bleeding due to a 5 cm wide colonic mass located at the transverse colon. Resection of the specimen revealed medullary colonic carcinoma.

Keywords: Medullary, colon, carcinoma

Medüller karsinomlar tüm kolorektal kanserlerin % 0.1'inden azını oluşturan ve nadir saptanan tümörlerdir. Bu tümörlerin andiferansiyasyon görünümü ve yüksek mitotik aktivitesi nedeni ile özellikle kötü diferansiyasyonlu kolorektal karsinomlar ile tanı karışıklıklarına yol açabilmektedir. Andiferansiyasyon görünümüne karşın prognozu iyi olan kolonik adenokarsinomların bir alt tipidir. Solid büyüme paterni göstermesi ve yüksek mikrosatellit instabiliteye sahip olması medüller karsinomları diğer kolorektal karsinomlardan ayıran önemli özelliklerdir. Sıklıkla sağ kolonda yerleşir, ileri yaş bayan hastalarda görülür ve lenf nodu metastaz insidansı düşük olan tümörlerdir. Bu olguda, karın ağrısı ve rektal kanama şikayeti ile başvuran, transvers kolon lokalizasyonunda 5 cm çaplı kitle lezyonu saptanan, rezeksiyon sonrası patoloji sonucu kolonun medüller karsini olarak gelen hastayı sunmayı amaçladık.

Anahtar Kelimeler: Medüller, kolon, kanser

Introduction

Medullary carcinoma (MC) is a rare subtype of colorectal cancer making up less than 0.1% of all colorectal malignancies (1). MC presents like conventional colonic carcinoma and can be confused with poorly differentiated colorectal carcinoma (PDC) due to undifferentiated complex morphology and high mitotic activity (2, 3). MC of the colon is accepted as a subtype of colonic adenocarcinoma with a better clinical course and prognosis than other subtypes (1, 4). There are few reports in the literature, but it has been shown that MC is frequently located at the proximal parts of the colon with low incidence of lymph node metastases. It also has a female tendency according to the literature (2, 4, 5). It has also been reported that it might have an expansive growth pattern and an association with Lynch syndrome and high microsatellite instability (MSI) (3, 6). In recent years, the incidence of MC has increased due to increased incidence of colon cancer and improved histopathological investigation methods. In this report, we present an MC of the colon in a 72-year-old male patient along with a literature review.

Case Report

A 72-year-old male patient was admitted to our unit with a one-month history of abdominal pain and rectal bleeding. The patient had no family history of colon cancer. The colonoscopy revealed a huge lobulated polypoid tumor protruding into the lumen located in the middle part of the transverse colon. The pathological diagnosis obtained by colonoscopic biopsy was fibrinopurulent exudate. Blood carcinoembryonic antigen (CEA) level was measured as 1.9 ng/mL. Computed tomography showed that there was a well-defined 5 cm round lesion compressing the periintestinal fat tissue homogeneously, and there was no invasion into the surrounding tissues (figure 1). The patient was scheduled for elective laparotomy after the diagnosis of the colonic mass.

Midline laparotomy was performed, and a mobile polypoid tumor 5.5 cm in diameter with no serosal invasion in the middle part of the transverse colon was detected (Figure 2). The lesion was totally intraluminal and felt like a lipoma during the palpation. Multiple reactive lymphadenopathies were also observed within the transverse mesocolon. There was no additional pathological finding during the exploration. The patient underwent segmental colon resection with proper mesocolon excision consisting of palpable lymph nodes. The frozen section revealed that lymph

¹Department of General Surgery, Katip Çelebi University Atatürk Training and Research Hospital, İzmir, Turkey
²Department of Pathology, Katip Çelebi University Atatürk Training and Research Hospital, İzmir, Turkey

Address for Correspondence

Yazışma Adresi:

Haldun Kar

E-mail: haldunkar@hotmail.com

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Figure 1. Large luminal mass lesion located in the transverse colon (arrowhead)



Figure 2. During the laparotomy, a mobile polypoid tumoral mass was observed in the transverse colon



Figure 3. Pedunculated polypoid mass originating from the transverse colon

nodes were not metastatic. Thus, the operation was ended as a segmental colon resection with end-to-end anastomosis (Figure 3). The postoperative period was uneventful, and the patient was discharged on postoperative day 8.

The pathological diagnosis was reported as MC of the colon. The tumor had invasion into the superficial muscularis propria (pT2), all of the lymphnodes (18/18) were reactive (N0), the proximal and distal surgical margins were negative, and there was no invasion into the lymphatics or vascular tissue. The tumor had no necrosis, and it was moderately differentiated (G2). Immunohistochemical evaluation showed the following profile: cytokeratin 20 negative, synaptophysin negative, chromogranin negative, CDX2 negative, CD56 negative, CEAmmono negative, p53 (20% positive +), e-cadherin (diffuse positive +), Cyclin D1 (5% nuclearexpression), CD44 (80% positive +), KI-67 (80% cytoplasmic and membranous expression positive +), Calretinin negative, and p16 positive (Figure 4).

Positron emission tomography was performed at 1 month after the index operation and showed no recurrence, residual tumor, or lymph node involvement. The patient was referred to the oncology department, and it was decided to follow him without chemotherapy. At 2 years after the operation, the patient was engaged normally in daily activities.

Informed consent was obtained from the patient who participated in this case.

Discussion

MC has been categorized as a rare variant of colorectal adenocarcinoma composed of sheets of malignant cells with vesicular nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm with prominent infiltration by intraepithelial lymphocytes (Crohn's like lymphoid reaction). In recent years, many investigators have focused on the differentiation of MC retrospectively. Thrinavukarasu et al. (6) reported that MC is seen in only 5–8/10,000 patients with colon cancer in their database between 1973-2006 in The surveillance, Epidemiology and End Results (SEER) study, while Knox et al. (1) have reported a higher incidence of this entity compared with previous reports.

MC mostly locate in the cecum (38% of cases), the ascending colon (36%), the transverse colon (12%), and the sigmoid colon (6%) (6). In the literature, the median diameter of the tumor is reported to be 7 cm. In our case, the tumor was 5.5 cm in diameter, and it originated from the transverse colon. According to the literature, MC of the colon is usually diagnosed at stage 2 with less than 10% distant metastasis. The relative survival rates in the first and second years are reported to be 92.7% and 73.8%, respectively (6).

In previous decades, MCs have been misdiagnosed as neuroendocrine carcinomas or poorly differentiated adenocarcinomas due to the lack of immune histochemical parameters that are crucial for its diagnosis. Interestingly, some of the MCs might have abortive foci of adenocarcinoma. It is also a controversial issue as to whether MCs have endocrine differentiation (3, 7). CDX2 is a spe-

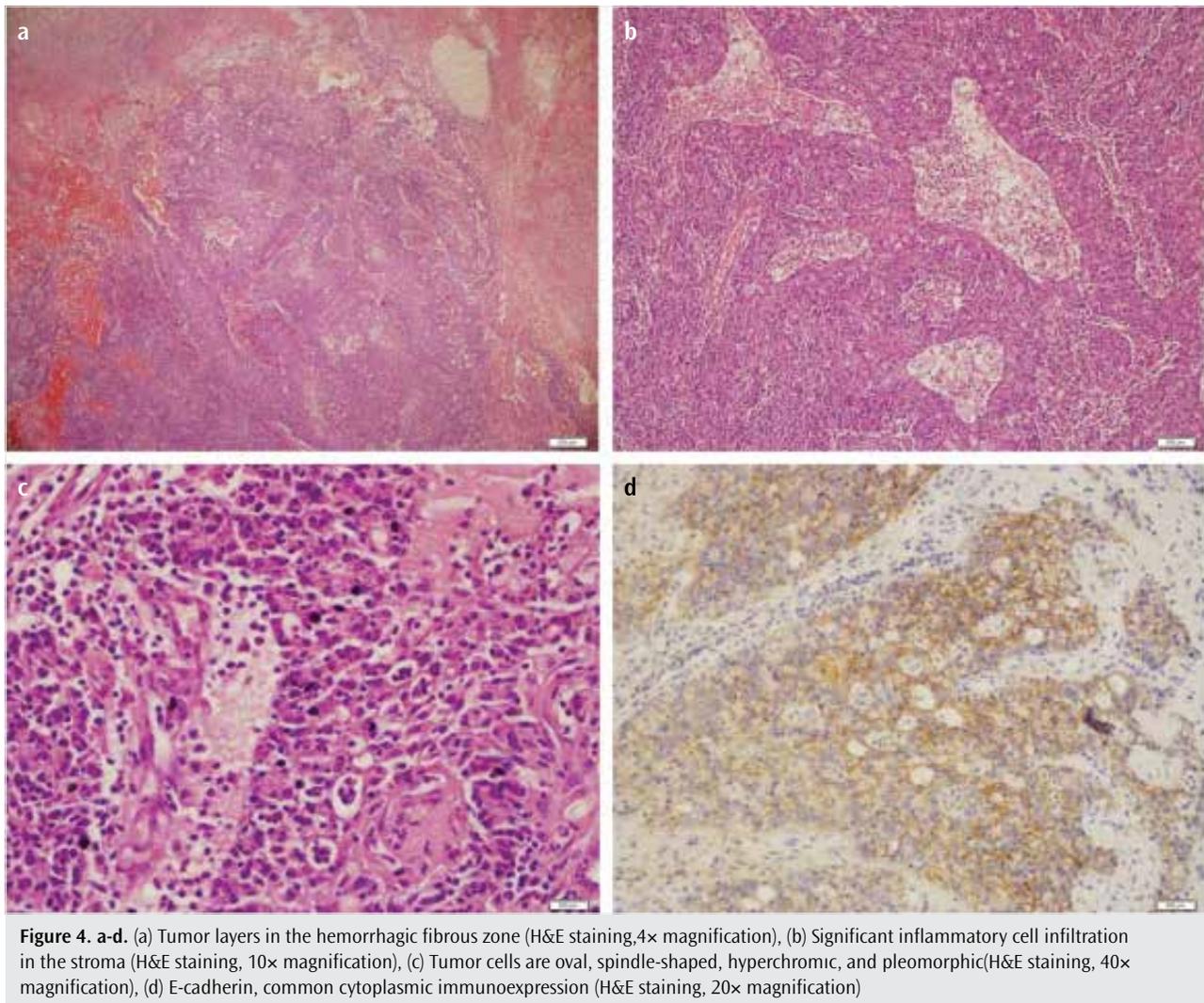


Figure 4. a-d. (a) Tumor layers in the hemorrhagic fibrous zone (H&E staining, 4× magnification), (b) Significant inflammatory cell infiltration in the stroma (H&E staining, 10× magnification), (c) Tumor cells are oval, spindle-shaped, hyperchromatic, and pleomorphic (H&E staining, 40× magnification), (d) E-cadherin, common cytoplasmic immunorexpression (H&E staining, 20× magnification)

cific marker related to intestinal differentiation. Win et al. (5) have reported that the CDX2 negative, MLH1 negative, Calretinin positive phenotype has an 82% predictive value in MC diagnosis. Our case was CDX2 negative and Calretinin negative.

MCs are tumors that have MSI (8). Micro satellites are repeating sequences in the human genome, and they appear because of a disorder in the mismatch repair system (MMR) that corrects replication mistakes in the DNA (3). MSI is reported to be seen in 10–15% of sporadic colorectal carcinomas, while it is seen in 100% of Lynch syndrome-associated tumors (2, 3). The tumors with mutations in MMR genes are proposed to be categorized as low grade without considering histological differentiation (1). The tumors with high MSI are less aggressive, have lower recurrence ratios, and have reduced response to 5-fluorouracyl compared with tumors with lower MSI rates. Furthermore, a high B-RAF mutation rate and low K-ras mutation rate are associated more with MC than PDC and conventional adenocarcinoma (4).

Conclusion

Our case is in concordance with the literature that the tumor is localized at the proximal colon, has a polypoid structure, and has an expansive growth pattern without necrosis or lymphovascular invasion. Because of having good prognosis and specific clinico-

pathologic features, clinicians must be aware that MC, although rare, is one of the possibilities in patients diagnosed with a large colonic mass located in the proximal colon. colonoscopic biopsy is usually nondiagnostic in these patients, and colon resection is required for definitive histopathological diagnosis.

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