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Case Report / Приказ болесника

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Signet-ring colorectal carcinoma

Карцином колона типа печатног прстена

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Signet-ring colorectal carcinoma

Карцином колона типа печатног прстена

SUMMARY

Introduction Colorectal cancer is the third most common cancer worldwide. Signet ring carcinoma is an extremely rare subtype of colorectal cancer, with frequency ranges 0.3–4.6%. The diagnosis of this type of cancer is based on pathohistological analysis.

Case outline A 58-year-old patient was admitted due to abdominal pain and abdominal swelling. The physical findings indicated abdomen above the level of the chest, soft, painfully sensitive in the left hemiabdomen, with positive clinical signs of ascites. Laboratory analyzes indicated: positive inflammatory syndrome, elevation of D-dimer and CA-19.9. Ascites analysis showed the presence of malignant cells. Computed tomography revealed: hepatomegaly, liver steatosis, as well as multiple secondary deposits in the liver, ascites and peritoneal implants. Colonoscopy showed ulceration of the right colon, which was covered with fibrin. The pathohistological findings indicated poorly differentiated, invasive adenocarcinoma of the signet ring carcinoma type. The patient was treated with analgesics, diuretics, proton pump inhibitors, beta 2 blockers, angiotensin converting enzyme inhibitors, low molecular weight heparin, antibiotics and supportive therapy. The patient was discharged after 10 days of hospitalization. He was presented to the multidisciplinary team, which decided on further symptomatic therapy.

Conclusion Signet ring colon cancer is a rare, aggressive tumor with a poor prognosis. Although it is most often localized in the stomach, it is necessary to think about the colorectal localization of this tumor in the differential diagnosis of patients with colonic complaints, especially if they have "alarm symptoms" and if they are younger.

Keywords: colorectal cancer; signet-ring carcinoma; peritoneal carcinomatosis; ascites; colonoscopy

САЖЕТАК

Увод Карцином дебелог црева је трећи најчешћи карцином у свету. Карцином печатног прстена је изузетно редак подтип колоректалногкарцинома, чија учесталост износи 0.3–4.6%. Дијагноза ове врсте карцинома је базирана на патохистолошкој анализи.

Приказ болесника Болесник стар 58 година је примљен због болова и отока трбуха. Физикални налаз је указао на абдомен изнад нивоа грудног коша, мек, палпаторно болно осетљив у левом хемиабдомену, са позитивним клиничким знацима асцитеса. Лабораторијски је установљен: позитиван запаљенски синдром, повишење Д-димера и карбохидратног антигена-19.9 (*CA*-19-9). Анализа асцитеса је указала на присуство малигних ћелија. Компјутеризованом томографијом су откривени: хепатомегалија, стеатоза јетре, као и мултипли секундарни депозити у јетри, асцитес и перитонеални имплантати. Колоноскопијом је детектована улцерација десног колона која је прекривена фибрином. Патохистолошки налаз је указао на слабо диферентован, инвазивни аденокарцином типа карцинома печатног прстена. Пацијент је лечен аналгетицима, диуретицима, инхибиторима протонске пумпе, бета-2 блокаторима, инхибиторима ангиотензин конвертујућегензима, хепарином ниске молекулске масе, антибиотицима и супортивном терапијом. Болесник је отпуштен након 10 дана хоспитализације. Представљен је онколошком конзилијуму који је донео одлуку за даљу симптоматску терапију.

Закључак: Карцином колона типа печатног прстена је редак, агресиван тумор са лошом прогнозом. Иако је најчешће локализован у желуцу, о колоректалној локализацији овог тумора је потребно размишљати у диференцијалној дијагнози код болесника са колопатским тегобама, нарочито уколико су удружене са „алармним симптомима" и ако се јављају у млађој популацији.

Кључне речи: колоректални карцином; карцином печатног прстена; карциноматоза перитонеума; асцитес; колоноскопија

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer worldwide [1]. In terms of mortality, it ranks third, in both genders [1]. Mortality from colorectal cancer is declining, except in Japan where it is stable [2].

The most common colorectal cancer is adenocarcinoma. There are three main types of colorectal adenocarcinoma: conventional adenocarcinoma (AC), mucinous adenocarcinoma, and signet ring adenocarcinoma (SRAC) [3, 4].

Signet ring carcinoma is an extremely rare subtype of colorectal cancer [3, 5, 6]. Its frequency ranges from 0.3-4.6% [3, 7, 8]. Five-year survival ranges from 11-46% [9]. This subtype of colon cancer was first described by Laufman and Saphir in 1951 [10].

CASE REPORT

A 58-year-old patient was admitted to the Department for Gastroenterology due to abdominal pain and abdominal swelling. The complaints started a month before admission. The pains are localized in the entire abdomen, occasionally occur in the left lumbosacral region and spread to the left leg. The pain occurs in bursts, of the "tearing and pulling" type, with an intensity of 8/10. It gets worse when lying down. Stools are for 2-3 days, normally formed, without blood and mucus. Due to the aforementioned complaints, the patient was initially examined by a general practitioner, ultrasound and abdominal and pelvic CT were performed, and the patient was referred to our Clinic for further diagnosis and therapy.

In history, the patient had a cerebrovascular insult two months ago. He has dilated cardiomyopathy, extrasystolic arrhythmia and hyperlipoproteinemia. He does not take regular therapy. He had no surgeries and no allergies. There are no hereditary diseases. Former smoker, does not consume alcohol.

On admission, the patient is conscious, oriented, afebrile, eupneic, acyanotic, anicteric, hemodynamically stable (TA 120/80 mmHg, HR 90/min), with normal nutrition. The head and neck are normal. Auscultatory findings on the heart and lungs are normal. Abdomen above the level of the chest, soft, painfully sensitive in the left hemiabdomen. Liver and spleen are not palpable. Positive clinical signs of ascites. Rectal examination was normal. The findings on the extremities are normal.

Laboratory analyzes on admission are shown in Table 1. Malignant cells were detected by cytological analysis of ascites. ECG showed sinus rhythm, right bundle branch block and q in D2, D3 and aVF. A chest X-ray showed a banded, oblique shadow between the middle and lower left lung fields.

Abdominal ultrasonography showed an enlarged, inhomogeneous liver with multiple heteroechoic lesions with a hypoechoic halo. Ascites is present in the abdomen, as well as

diffuse edema of the mesentery. Along the anterior abdominal wall, hypoechoic oval changes with a diameter of 11 mm were visualized.

Computed tomography (CT) of the abdomen and pelvis was performed before admission to our Clinic. The findings indicated hepatomegaly, liver steatosis, as well as multiple secondary deposits in the liver. Ascites and numerous cystic necrotic peritoneal implants are present, predominantly along the anterior and lateral abdominal wall. The colon and rectum were without signs of infiltration, with transverse colon diverticulum and bilateral iliac lymphadenopathy. In addition to the above, an infrarenal aortic aneurysm was detected.

Esophagogastroduodenoscopy showed hyperemia of the antral mucosa with suspicious areas of focal atrophy, hiatus hernia and angiodysplasia of the D2 part of the duodenum, 5 mm in diameter. Pathohistological findings of gastric biopsies indicated reactive gastropathy of the antral mucosa. H. pylori status is negative.

A colonoscopy was performed. At 90 cm from the anocutaneous line, an ulceration was detected,covered with fibrin (Figure 1). Biopsies were taken, the pathohistological findings indicated poorly differentiated, invasive adenocarcinoma of the signet ring carcinoma type. At 45 cm from the anocutaneous line, a hyperemic induration of the mucosa was detected, which is harder during biopsies (Figure 2). Pathohistological findings indicated interstitial chronic colitis (grade I). In addition to the above, diverticula of the transverse colon were detected.

The patient was treated with analgesics, diuretics, proton pump inhibitors, beta 2 blockers, angiotensin converting enzyme inhibitors, low molecular weight heparin, antibiotics and supportive therapy. The initial analgesics were: tramadol, fentanyl and metamizole, and then tapentadol (50 mg, q6h.), paracetamol iv. (1000 mg, q8h) and morphine iv. (5 mg, as needed).

The patient was discharged after 10 days of hospitalization, in a stable general condition. He was presented to the multidisciplinary team, which decided on further symptomatic therapy.

We confirm that we have read the journal's position on issues involving ethical publication and affirm that this work is consistent with those guidelines. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written consent to publish all shown material was obtained from the patient.

DISCUSSION

We present the case of a 58-year-old patient with colonic SRAC. By the way, SRAC occurs more often in the younger population [5, 7, 8, 11, 12, 13]. Cases have also been described in the pediatric population, where CRC is uncommon [14, 15, 16].

In addition to the difference in frequency and time of presentation, there are differences in clinicopathological characteristics between colonic AC and SRAC. Namely, SRAC is more often localized in the right colon [4, 8, 17]. It occurs in the rectum in 20% of patients [7]. In some earlier manuscripts, it was described that the most common localization of this type of cancer is the rectum [18]. In our patient, the cancer was localized in the right colon. Compared to conventional adenocarcinoma, SRAC colon is a more aggressive tumor, usually of larger dimensions, of higher histopathological grade with frequent neurovascular infiltration and involvement of lymph nodes, and greater metastatic potential [8, 11, 19]. In general, the prognosis of this type of tumor is worse than that of colon adenocarcinoma [4, 7, 8, 11, 19]. In addition to being a primary colon cancer, SARC can also be a metastasis of this cancer from other organs (e.g., stomach) [20].

The clinical presentation of SRAC is similar to conventional colon adenocarcinoma. Very often, patients are asymptomatic. If they are symptomatic, the dominant symptoms are: changes in bowel habits (constipation, diarrhea), blood in stool, symptoms/signs of anemia, etc. [7]. Symptomatology is primarily determined by tumor localization. If the tumor is localized in the right colon, it can be asymptomatic until obstruction or perforation occurs. This localization of the tumor can be manifested only by symptoms/signs of anemia [21]. If there is a distal location of the tumor, the dominant symptoms are changes in bowel emptying and blood in stool. Given that the tumor primarily involves the wall of the large intestine, the mucosa may be intact, and the fecal occult blood test may be negative [9]. SRAC colon metastasizes more often in the peritoneum than in the liver [8, 11]. Peritoneal dissemination occurs in half of patients [7]. After the lymph nodes, the peritoneum is the most common site of SRAC metastasis [18, 22]. Our patient did not have symptoms typical of colon cancer, which is most likely due to the proximal localization of the tumor. The dominant symptoms were severe abdominal pain and abdominal swelling. The aforementioned complaints are the result of peritoneal dissemination of the disease. Due to the lack of any other complaints, the disease was diagnosed at an advanced stage.

The diagnosis of colonic localization of SRAC is established on the basis of colonoscopy. This type of cancer causes ulcerative lesions in 41.2% of cases [19], which was also the case

with our patient. In addition to ulcerative forms, SRAC can also have infiltrative and exophytic forms [19, 23]. Endoscopically, this cancer can look like a depressed, polypoid or, rarely a flat lesion [17]. Also, the early stage of SRAC can be in the form of a discolored flat-elevated lesion with a central depression [17]. In our patient, another lesion was detected colonoscopically, more distal than the previous one, which macroscopically could correspond to SRAC, however, this was not confirmed by histopathology. The histopathological characteristic of SRAC is the presence of >50% of tumor cells containing intracytoplasmic mucin [7, 19]. Mucin causes peripheral displacement of the nucleus [8, 19]. This configuration of cells is called a signet ring. The molecular features of SRAC differ from conventional colon adenocarcinoma. Namely, in SRAC there is a higher frequency of microsatellite instability, loss of heterozygosity (e.g., 18q, 3p14.2, etc.), K-ras codon 61 and b-Raf V600E mutations [7, 23, 24].

Most SRAC is diagnosed on CT as a thickening of the longer segment of the colon, while an intraluminal mass is rarely present [19]. This is due to the infiltrative nature of this tumor. Namely, the tumor infiltrates the entire thickness of the wall of the affected segment of the colon, leading to a thickening of the wall. As a result, a rigid and contracted wall occurs, which is a feature of "linitis plastica" [25]. In our patients, CT indicated the presence of peritoneal dissemination of the disease and ascites, while thickening of the colon wall was not detected.

The only curative treatment modality for SRAC is surgery. Surgery can be curative only if it is applied in the early stages of the disease, which is quite rare because this type of cancer is most often diagnosed in advanced stages [6, 22]. An initial treatment with endoscopic mucosal resection was described, however, due to the risk of disease dissemination, the patients subsequently underwent laparoscopic resection [17]. In advanced stages, chemotherapy (5-fluorouracil, capecitabine, oxaliplatin, irinotecan, bevacizumab) can be used with varying success [7, 26, 27, 28]. In the case of peritoneal dissemination, the use of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy has been described [28, 29]. However, there are no clear recommendations.

Signet ring colon cancer is a rare, aggressive tumor with a poor prognosis. Although it is most often localized in the stomach, it is necessary to think about the colorectal localization of this tumor in the differential diagnosis of patients with colonic complaints, especially if they have “alarm symptoms” and if they are younger.

Conflict of interest: None declared.

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Table 1. Laboratory analyses at admission

Variable	SI unit	Value	Reference range
Leukocytes	10^9/L	22.7	4–10
Erythrocytes	10^{12}/L	5.24	3.8–6
Hemoglobin	g/L	148	115–165
Mean Corpuscular Volume	fL	83	80–98
Platelets	10^9/L	440	150–400
Blood glucose	mmol/L	6.2	4.1–5.6
Urea	mmol/L	7.4	3–9.2
Creatinine	μmol/L	61	53–115
Sodium	mmol/L	133	136–146
Potassium	mmol/L	5.3	3.5–5.1
Chlorides	mmol/L	90	98–107
Total bilirubin	μmol/L	14.8	3.4–20.5
Aspartate-transaminase	IJ/L	60	11–34
Alanine-transaminase	IJ/L	65	< 45
Gamma-glutamyltransferase	IJ/L	220	< 55
Alkaline phosphatase	U/L	155	40–150
Lactate-dehydrogenase	IJ/L	823	125–220
Total proteins	g/L	73	64–83
Albumins	g/L	47	35–50
Amylase	IJ/L	25	28–100
Lipase	IJ/L	11.0	< 60
C-reactive protein	mg/L	97.5	< 5.0
Alpha-fetoprotein	IU/ml	1.6	< 7.0
Carcinoembryonic antigen	ng/mL	< 0.5	< 10
Carbohydrate antigen 19-9	U/ml	48.87	< 37.00
Free prostate-specific antigen / total prostate-specific antigen		0.3	>0.20
B-type natriuretic peptide	pg/ml	1475.0	< 125
Prothrombin time	s	1.15	11.7–15.5
Activated partial thromboplastin time	s	29.5	24.8–34.4
D-dimer	mg/L	9.88	< 0.7

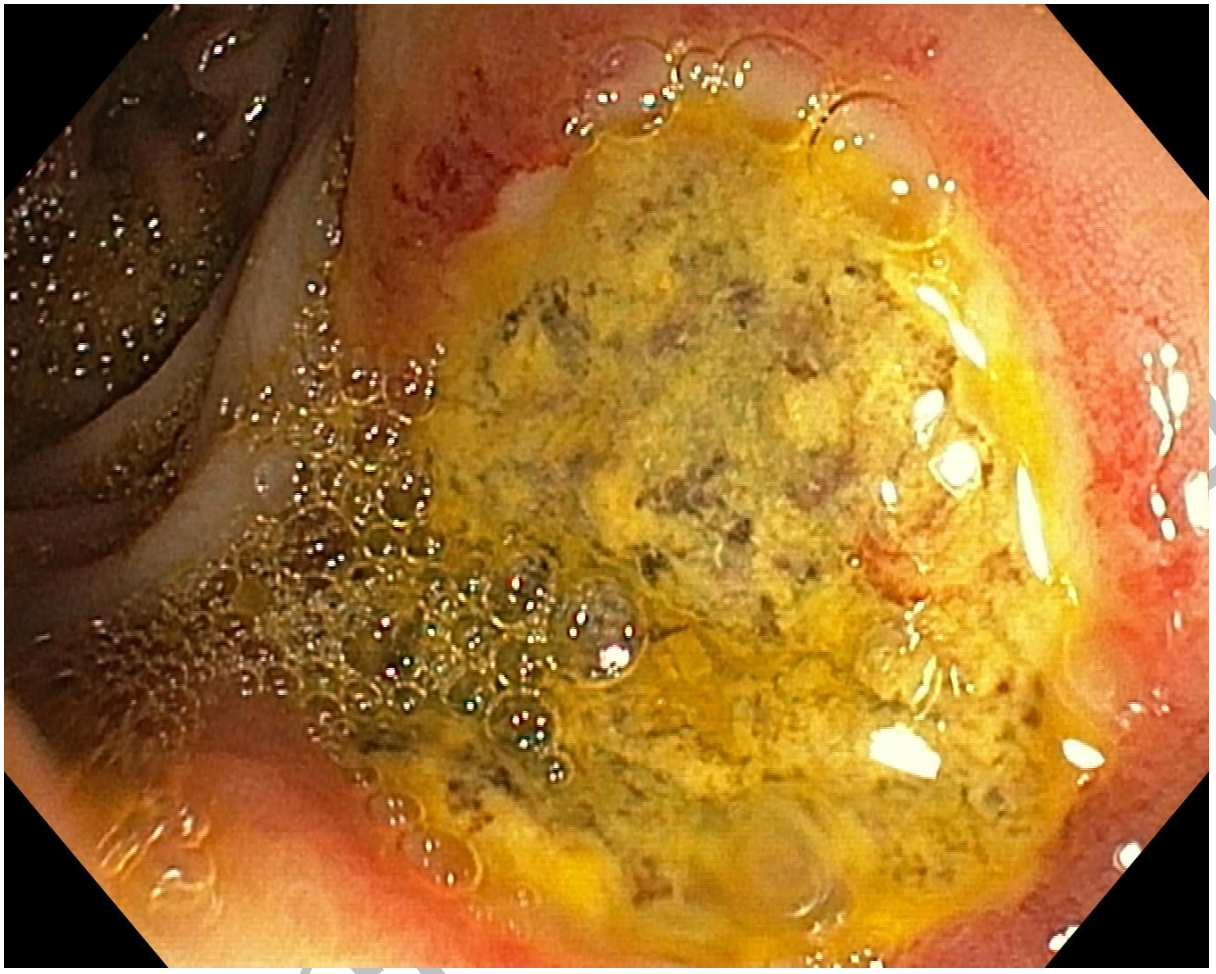

Figure 1. Ulceration of the right colon, covered with fibrin (histopathology: poorly differentiated, invasive adenocarcinoma of the signet-ring carcinoma type)

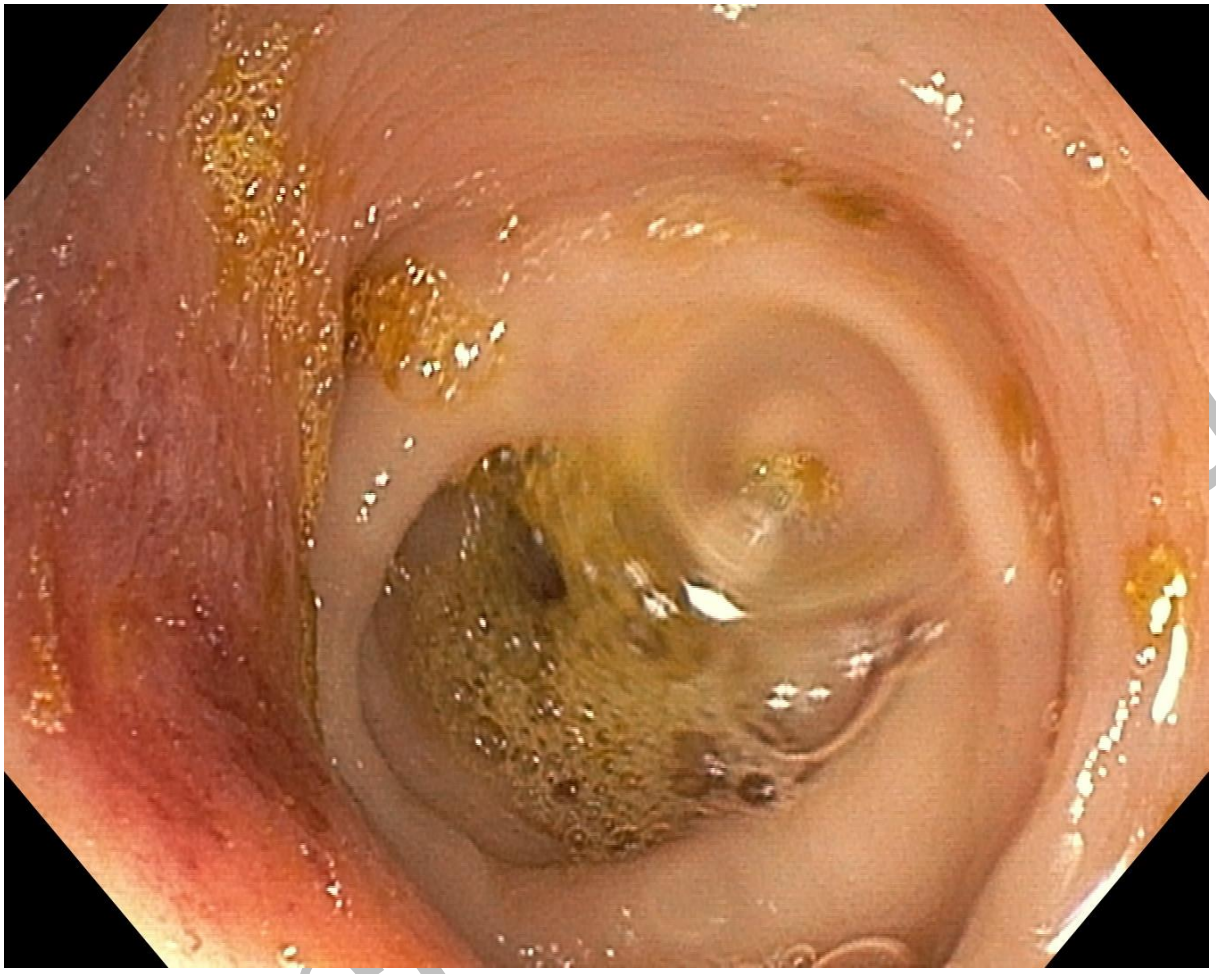

Figure 2. Hyperemic induration of the colonic mucosa (histopathology: interstitial chronic colitis grade I)

