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Case Report

Sigmoid Colon Perforation during Colonoscopy in a Case of Carcinoid Tumor

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ABSTRACT

Background: Carcinoids tumors are slow-growing tumors which originate mainly from the small intestine and can produce biogenic peptides and amines. These products could cause carcinoid syndrome, and also, fibrosis in the peritoneum and mesentery.

Case report: A 50-year-old man complaining of lower limb edema, ascites, and weight loss presented for evaluation. CT scan of the abdomen and pelvis revealed liver enlargement and the increased thickness of cecum and terminal ileum. The patient consented to an exploratory colonoscopy, which led to laparotomy resulting from sigmoid colon perforation. Large retroperitoneal fibrosis developing with colon and mesentery of sigmoid was found during surgery. Hepatomegaly with microscopic tumoral infiltration of the liver was observed and diagnosis of metastatic carcinoma in the liver was confirmed by pathological examination.

Conclusion: The most common sites of primary carcinoid tumors are appendix, ileum, and cecum. One of the less common manifestations of carcinoid tumors is fibrotic reactions around or beyond the tumor that in the reported patient, there was a very extensive fibrosis in the mesentery and peritoneum and serosa covering the colon and intestines, which presented with edema of the lower extremities because of the pressure on the IVC and with perforation of the colon during colonoscopy.

Keywords: Carcinoid, Colon perforation, Neuroendocrine

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Introduction

Carcinoid tumors are rare and have an incidence rate of 2.47 to 2.58 per 100,000 in men, which are more prevalent in women and blacks. Many of these tumors are asymptomatic. Anatomical studies have reported an incidence rate of 8.4 per 100,000 (1). These tumors are seen in various organs of the body such as the gastrointestinal tract (70%) and the respiratory system (25%), and rarely seen in the gonads, gallbladder, biliary tract, thymus, spleen, breast, and kidneys (2). Neuroendocrine tumors (NETs) are a heterogeneous group of neoplasms that probably consist of neuroendocrine cells and their precursors throughout the body. These tumors are characterized by variable biological behaviors. They are also classically differentiated by their ability to secrete peptides and amines, leading to hormonal syndromes. The World Health Organization (WHO) categorized neuroendocrine tumors as G1, G2, and G3, according to Ki-67 proliferation index and mitotic count (MC).

Type G1 has a benign nature and mitotic count less than 2 and Ki-67 less than 3%. Type G2 has a benign nature and mitotic count between 2 to 20 and Ki-67 between 3 to 20%. And type G3 has a malignant nature and mitotic count above 20 and Ki-67 is above 20% (3).

Carcinoid tumors may be characterized based on the anatomical site or their endocrine cell type. There is a significant association between age, metastatic pattern, and survival with tumor location. Carcinoid tumors are divided into three categories on the basis of their embryologic origin: Foregut carcinoids (esophagus, stomach, pancreas, duodenum), mid gut carcinoids (jejunum, ileum, appendix, cecum, ascending colon, 2/3 of right-sided transverse colon), and hindgut carcinoids (1/3 of horizontal colon, descending colon, Sigmoid colon, rectum). The small intestine is the most common site of carcinoids (ileum 30% followed by the appendix 20%) (4).

Carcinoid tumors can synthesize and secrete a large amounts of biological amines, which in the case of midgut, if carcinoid is accompanied by liver metastasis, can cause carcinoid syndrome in the form of flushing attacks, bronchospasm, diarrhea, and fibrotic heart problems. On the other side, other properties of these biological amines (especially serotonin) is stimulation of fibrosis around and beyond the tumor, such as endocardial fibrosis in the right cavities of the heart and peritoneal fibrosis in midgut tumors (5).

Case report

The patient was a 50-year-old man who referred to Department of Gastroenterology, Afzalipour Hospital of Kerman, with lower limb edema from 10 days before admission. His legs were already swelling up and gradually progressed. He suffered from shortness of breath with the onset of edema and severe weakness in the past 10 days. He did not complain of chest pain, coughing, urinary problems, night sweats, and appetite loss. Over the past few months, he had a significant weight loss. In blood tests, all factors except the high alkaline phosphatase (ALP) were normal. Physical examinations did not reveal any other positive side effects, except pitting edema of the lower limb up to the knee. Vital signs were blood pressure (BP: 130/80), PR: 80, RR: 20, and T: 37.5. Table 1 shows laboratory findings in patients at admission.

Table 1. Laboratory testing on the patient reported

Test	Test	Test	Test	Test
HBC-Ab: 1.53	PH: 7.33	K: 3.9	Bs: 98	WBC: 6.5
AFP: 1.85	PCO2: 33.9	Urea: 17	AST: 47	HB: 12.3
PSA: 0.46	HCO3: 17.6	Cr: 1.1	ALT: 40	MCV: 83.7
CA 125: 243	T3: 127	Alb: 3.4	ALK.P: 1837	MCH: 26.7
CEA: 3.31	T4: 10.4	Prt: 8	Bili total: 1	PLT: 317
CA 19/9: 204	TSH: 6.06	LDH: 438	Bili Direct: 0.6	PT: 13
	Retic: 1.6	Lipase: 36	Ca: 4.4	PTT: 35
	Iron: 46	GGT: 215	CRP: 7	INR: 1
	TIBC: 280	Ferritin: 242	Amylase: 281	Na: 140

The EKG tracing showed a regular rhythm and echo report was EF: 50 and PAP:NL, and Mild AI/Mild TR/No PE/No cloth/Mild RV. Doppler ultrasonography of the lower limb showed no DVT. Abdominal sonography revealed mild pelvic ascites as well as hepatomegaly with an echogenic focus in the right lobe of the liver. The CT scan revealed a 6-mm lesion in the eighth section of the liver, which was in favor of hepatic hemangioma. A

slight increase was observed in the thickness of the gallbladder wall. Also, an increase in the thickness of the ileum and cecum, accompanied by an increase in the posterior peritoneal thickness in the sacrum region without lymphadenopathy was observed. A mild ascites and bilateral pleural effusion were reported (Figure 1).

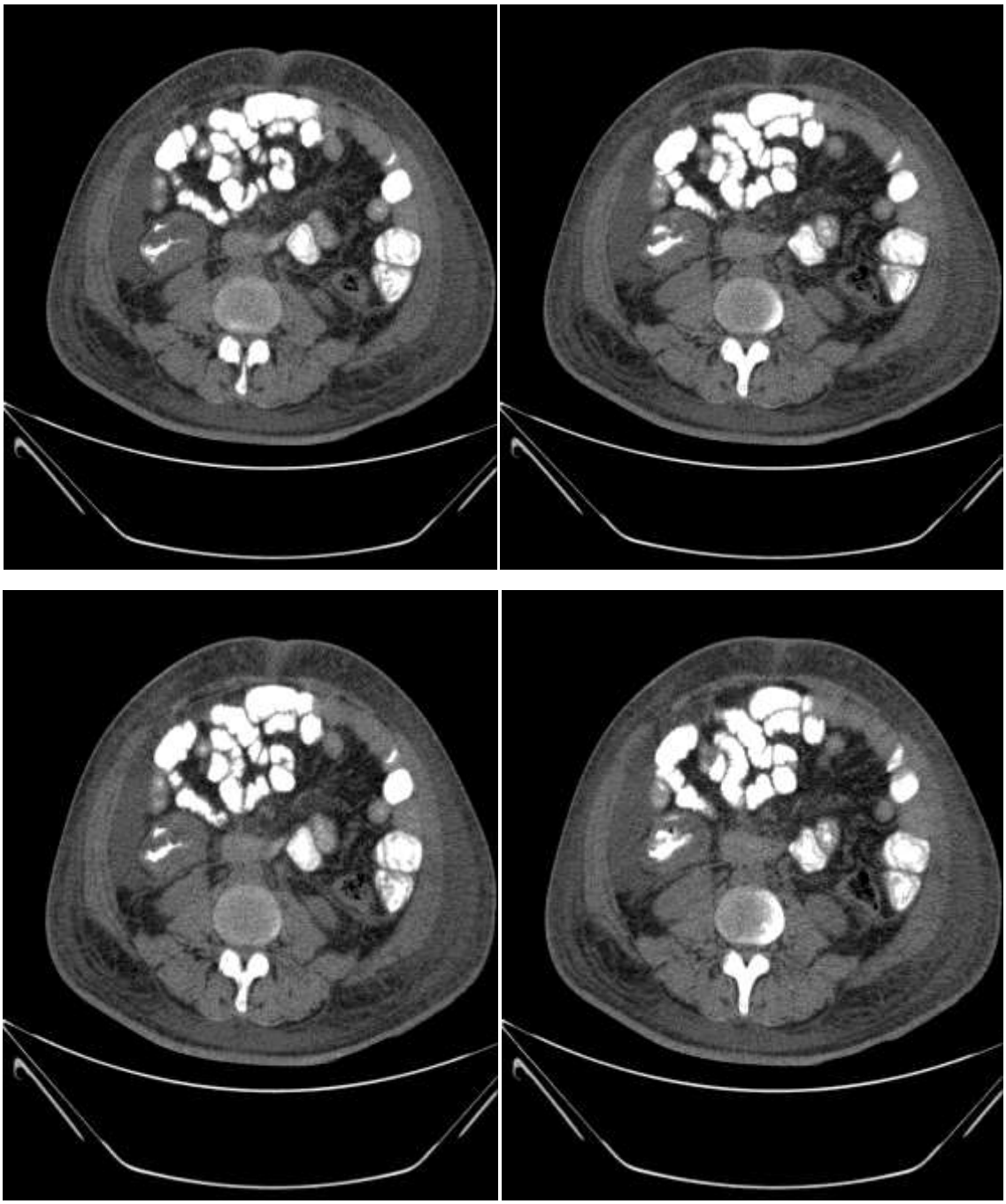

Figure 1. Abdomen and pelvic CT scan (transverse section).

Due to the increase in alkaline phosphatase level, the papillary region was detected by ERCP that revealed normal results. No significant pathology was observed in the biliary tree in MRCP. Only hepatomegaly and elevation of the diameter of the caudate lobe of the liver were seen (Figure 2).

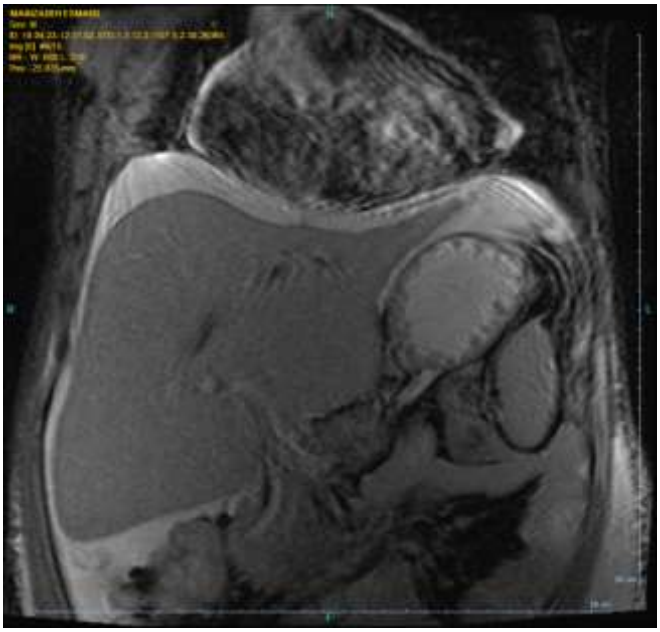

Figure 2. Enlarged liver and caudate lobe: coronal image.

Colonoscopy of the colon was performed in order to examine the cecum or terminal ileum and to take the biopsy samples, but during the colonoscopy, while the control head was in the transverse colon, with a forward pressure to the scope, sudden perforation of colon occurred and the patient underwent emergency laparotomy as the urgent surgical treatment. Laparotomy revealed a 3-cm perforation at the rectosigmoid junction. 1500 cc of peritoneal fluid was removed from the abdomen. There was also a large retroperitoneal fibrosis that involved the inferior vena cava, ureters, intestines and mesentery associated with marked adhesion. Because of intestinal fibrosis, stiffness, and adhesion, there was no possibility of colostomy and only the perforation was sutured and ileostomy was established. During laparotomy, it was observed that the liver was large and infiltrative. Consequently, the liver sample was taken and sent to the frozen section, the results showed a metastatic neuroendocrine tumor. In fact, fibrosis and severe stiffness in the sigmoid colon and its mesenteric region led to an unexpected perforation in the intestine. After surgery, the patient was transferred to the ICU, and the next day, he was suddenly suffering from respiratory distress and tachycardia, and after a few hours, despite all the restoration measures, he unfortunately died. Immunohistochemical stain obtained from liver biopsies showed a low-grade neuroendocrine tumor (Figure 3).

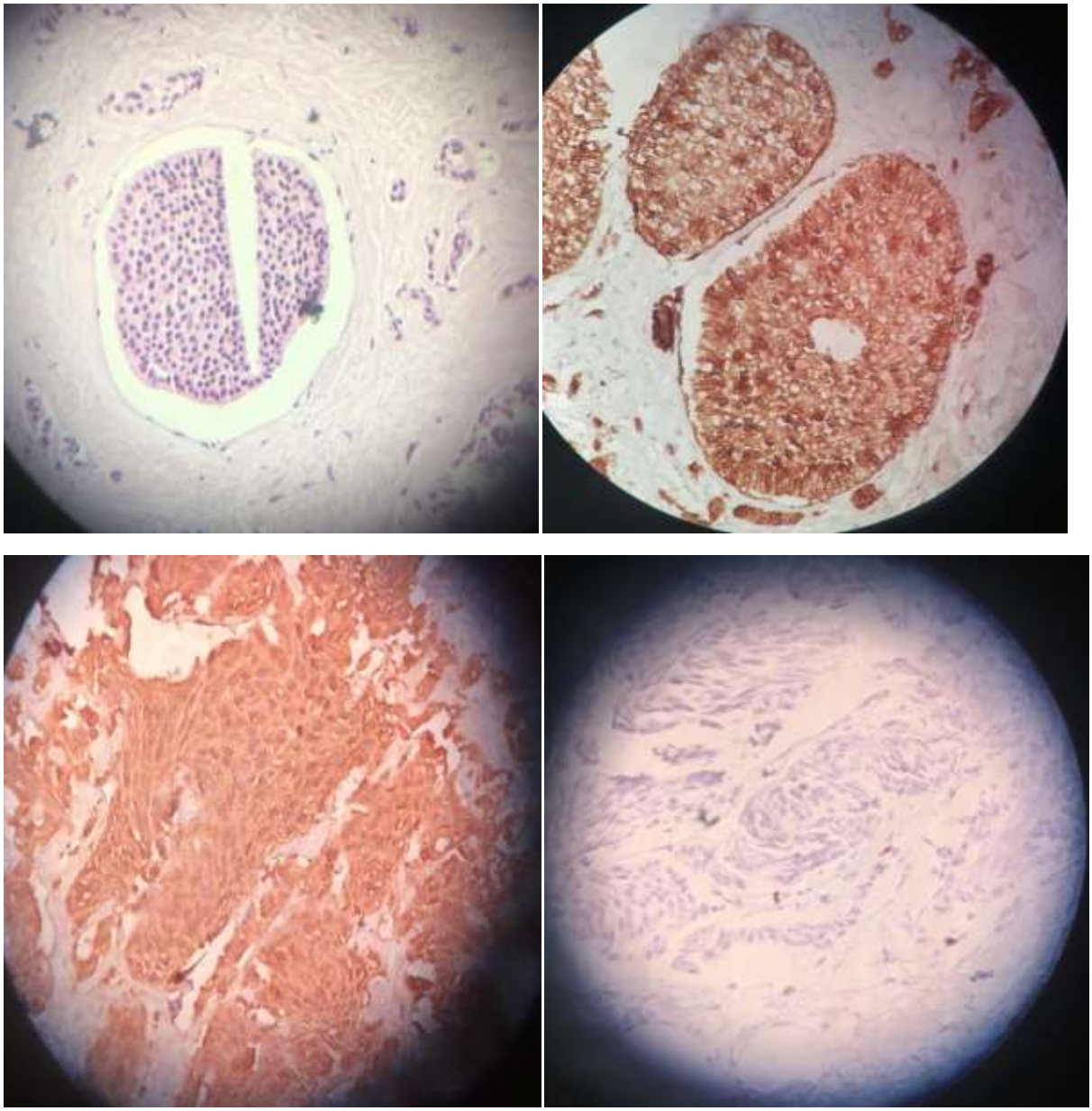

Figure 3. The liver biopsy specimen.

Discussion

According to the CT scan findings, the patient was probably suffering from a low-grade carcinoid tumor in the cecum and terminal ileum with bulky and extensive micro metastases in the liver. Despite the pathological evidence of liver metastasis, metastatic masses were not seen on imaging with ultrasound, CT, and MRI. Enlarged liver and particularly of the caudate lobe was the only finding seen in MRI. High level of alkaline phosphatase was also detected in liver tests, demonstrating infiltrative liver disease. While normal biliary ducts were reported in visual modalities. Interestingly, despite extensive carcinoid metastases to the liver, no signs of carcinoid syndrome (such as diarrhea, asthma, and flushing) were observed. Also, the patient had no fibrosis and stenosis in the right ventricle of the heart in echocardiographic evaluation. The profile of some carcinoid tumors in the intestine is localized fibrosis around the tumor that is due to the local secretion of serotonin. In this case, the fibrosis was very extensive and included all of the intestinal mesentery, and retro peritoneum and colon walls, causing symptoms such as lower extremity edema, due to the effect of compression on the inferior vena cava.

Neuroendocrine cells are spread widely all over the body. Well-differentiated GEP-NETs

have very variable clinical behavior. While some patients have clinically evident symptoms either from tumor bulk or peptide hormone hypersecretion, indolent tumors in some untreated patients remain asymptomatic for years. The secretion of serotonin and other vasoactive substances causes carcinoid syndrome in patients with metastatic gastrointestinal NETs, with presentations as wheezing, episodic flushing, diarrhea, and probable right-sided valvular heart disease (6). The histological grade is another excellent prognostic factor, based on the mitotic rate or Ki-67 labeling index (7, 8). The major site of metastasis is the liver. Liver function tests indicate uncertainty in the involvement of the tumor. Serum alkaline phosphatase, despite extensive liver involvement, is often normal. Contrast-enhanced CT (CECT) images or an MRI scan should be considered in suspected cases to rule out liver metastases.

While in metastatic carcinoid tumors to the liver, in most cases, clear multiple hyper vascular masses were observed on CT scan or liver MRI, but in this patient, despite performing a three-phase hepatic CT scan and MRI, it was not observed a clear mass in favor of the liver metastasis. But during surgery, infiltrative liver with tumor cells was observed, which it is an unusual manifestation of metastatic carcinoid to the liver. Another interesting point is that the patient did not show any signs of carcinoid syndrome despite extensive liver metastasis.

In a study conducted by Druce et al. (2010) on 31 patients with carcinoid tumors and peritoneal fibrosis, it was found that in 55% of cases of peritoneal fibrosis on abdominal CT scan, there was a mesenteric mass with soft tissue opacities that exit from it and create a solar shape, causing incomplete or complete obstruction of the intestine. In 35% of cases, fibrosis occurs only as an increase in the thickness of the small intestinal wall on CT scan of the abdomen, and in 6% of cases, it produce as a misty mesenteryand a decrease in the attenucity of mesenteric fat on CT scan (9).

Whereas in abdominal CT scan of the reported patient, the only obvious finding in favor of peritoneal fibrosis was a slightly increase in the thickness of the peritoneum in the sacral promontory. And only in laparotomy, it was observed an extensive fibrosis, which had spread to the entire abdominal cavity.

Colon perforation during diagnostic colonoscopy has a prevalence of about 0.3 to 0.8% and although it is rare, it is a major complication with major morbidity and mortality (10).

Risk factors of colon perforation during diagnostic colonoscopy include age (above 75 years), female gender, history of abdominal surgery, history of diverticular disease in the colon, patients with multiple comorbidities, and total colonoscopy compared to sigmoidoscopy (11-13).

In the reported case, the most important cause of iatrogenic perforation of the colon during colonoscopy was a decrease in the elastic capacity of the sigmoid mesentery and the colon wall due to peritoneal fibrosis. Because the colon wall in this patient could not withstand the usual pressures of the colonoscope scope during the procedure and a rupture of the colon occurred with a little pressure.

In examination of laparotomy after perforation, extensive fibrosis was present in the mesentery and intestinal wall and omentum, and no evidence of tumoral seeding was found in the peritoneal areas.

In this patient, all laboratory and imaging examinations and clinical findings before surgery did not confirm the definitive diagnosis. Only high ALKP and high tumor markers and a mass in the ileosecal showed indistinct evidence of a tumor disease, but colon perforation during colonoscopy and after laparotomy confirmed the certain diagnosis. It was revealed that ileosecal carcinoid tumor and massive microscopic metastasis to the liver, as well as extensive peritoneal fibrosis and pressure to the IVC, are the causes of all the unusual manifestations of the patient.

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