**Multifocal colorectal cancer in ulcerative colitis patient with sclerosing cholangitis – case report**

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**ABSTRACT:**

**Introduction:** Ulcerative colitis (CU) is an inflammatory disease predisposing to colorectal cancer. Colorectal cancer in ulcerative colitis is more often metachronous or synchronous.

**Case report:** In this case report we present a patient with multifocal colorectal cancer in the course of CU and operative treatment that was implemented. Additionally, primary sclerosing cholangitis was diagnosed in this patient post-operatively.

**KEYWORDS:**

adenocarcinoma, multifocal colorectal cancer, primary sclerosing cholangitis, ulcerative colitis

**ABBREVIATIONS**

CCA – cholangiocarcinoma
CU – ulcerative colitis
IBD – Inflammatory Bowel Diseases
MRCP – magnetic resonance imaging cholangiography
PSC – primary sclerosing cholangitis

**CASE REPORT**

A forty-year-old female patient with many years of ulcerative colitis (CU) was admitted in February of 2015 with a diagnosis of cecal cancer for surgical treatment. Colonoscopy performed prior to hospitalization showed a change in the caecum. The remaining sections of the large intestine showed fragile, contact bleeding mucosa devoid of vascular pattern, and furthermore anal stenosis. Beside typical CU symptoms, the patient complained of rectal bleeding persisting for one year with a bowel movement, and reported sporadic abdominal pain in the left iliac region.

The woman was treated with sulfasalazine, azathioprine and folic acid. In addition, her clinical history included: iron-deficiency anemia treated with iron intramuscularly for a year, status post appendectomy due to acute appendicitis 10 years ago, status post hysterectomy with removal of the right appendix due to fibrosis 3 years ago. Negative family history.

On the basis of interview and physical examination as well as additional tests, the patient was qualified for surgery. After presenting all aspects of the disease and discussing them with the patient, it was proposed to perform restorative proctocolectomy. Due to the advanced pathological process and a suspicion of multifocal cancer, the surgery was divided into stages. On February 27, 2015, a colectomy was done with preservation of the rectum and construction of an end ileostomy. Cecal cancer was confirmed, but a second, hard lesion could be felt in the mid-way along the length of the transverse colon. There was a noticeable narrowing in the rectum. The large bowel was removed by Hartmann’s procedure, leaving a 12 cm rectum. An end ileostomy was exteriorized. No metastatic lesions were found in the liver or in the small intestine.

Histopathological examination of resected intestinal fragments showed as many as four adenocarcinoma lesions. Two were palpable and macroscopically visible during surgery for changes in the cecum and transverse colon. However, the other two were not visible during the procedure: 1 cm lesion-, the nearest 2 cm from the incision line. Joint histopathological diagnosis: adenocarcinoma multifocale invasivum coli G2, pT4a, pN2a, Dukes C, Astler-Coller C2.

This was followed by qualification of the patient for chemotherapy according to the FOLFOX 4 regimen. However, she only underwent 9 out of 12 treatment cycles. Subsequent cycles were abandoned due to agranulocytosis.

Over a year of colectomy, the patient was hospitalized for jaundice with signs of cholangitis. Laboratory tests showed bilirubin 7.6 mg/dl, CRP 198.5 mg/l, ALT 268 U/l, AST 172 U/l. Abdominal ultrasonography revealed slightly expanded intrahepatic bile ducts peripherally up to 3 mm, with a predominance of the left lobe. ERCP showed critical narrowing with complete separation from the lobar ducts, expanded lobar ducts with a jagged image of the ducts of right lobe at the height of the division of the common hepatic duct. Papillotomy and bile duct dilatation were performed and discharge of purulent biliary content was obtained. A bile duct prosthesis was inserted. The status of the patient improved.

MR examination of the liver performed for the purpose of further diagnosis revealed an abnormal picture of extrahepatic and intrahepatic bile ducts with numerous multilevel stenoses. This aroused the suspicion of primary sclerosing cholangitis (PSC). Since then, the patient was hospitalized three times for cholangitis with replacement of prostheses. Imaging examinations reveal progressive narrowing of intrahepatic bile ducts. The patient remains under the care of a transplant clinic and liver transplantation is under consideration.

**DISCUSSION**

Ulcercative colitis (CU) is an inflammatory disease predisposing for colorectal cancer [1]. Research shows that the risk of its occurrence
The treatment of CU-related colorectal cancer is in most cases the same – it involves proctocolectomy with the formation of an intestinal reservoir with ileoanal anastomosis [6]. Such radical management results from the increased risk of synchronous and metachronous cancers in patients with CU [7]. This treatment can consist in one stage or be divided into two or three stages [8]. The described patient underwent a complete resection of the large intestine using Hartmann’s procedure with the exteriorization of an end ileostomy and the use of adjuvant chemotherapy. Due to the multifocality of colorectal cancer, a severe postoperative course and the need for further oncological treatment, with the patient’s approval, it was decided to abandon further stages of surgical treatment. The woman lives to this day with an exteriorized ileostomy.

Just under a year after surgery, the woman was diagnosed with primary sclerosing cholangitis (PSC). PSC is an autoimmune disease that accompanies IBD in 2/3 patients in Northern Europe and the United States. However, only 5% of IBD patients will develop PSC [9]. Diagnosis of PSC may precede the diagnosis of IBD, but we could also encounter a reverse situation in which PSC is diagnosed after colectomy due to CU – just like in the described patient. There is an increased risk of colorectal cancer and bile duct cancer—cholangiocarcinoma (CCA) in people with PSC. PSC is diagnosed by excluding other diseases that could cause sclerosing cholangitis, such as: CCA, Vater’s papillary stenosis, carcinoma of the papilla of Vater, chronic pancreatitis, pancreatic cancer, hilar lymphadenopathy, recurrent purulent cholangitis, congenital biliary atresia, parasitic diseases and others. The diagnosis is made on the basis of a radiological image – the most effective according to modern research is magnetic resonance cholangiography [10], which shows characteristic stenoses with subsequent expansion of bile ducts – both in the intra- and extrahepatic segments [11]. This is usually accompanied by biochemical exponents of cholestasis. PSC is a degenerative disease; over the years, bile duct fibrosis increases leading to cirrhosis, and eventually most patients develop extreme liver failure or CCA. The most common symptoms of PSC include: weakness, fatigue, itching, abdominal pain, and recurrent cholangitis. The latter, if it occurs often and reduces the patient’s quality of life, can be an indication for liver transplantation. After diagnosing PSC, the patient requires constant supervision in the form of: clinical examination, measurement of liver enzymes and cholestasis markers, AFP level, CA19.9 marker measurement, abdominal ultrasound, possibly magnetic resonance cholangiography (MRCP) every 6–12 months. Furthermore, due to the heightened risk of colorectal cancer, it is recommended to perform colonoscopy once a year in IBD-related PSC; chromoendoscopy is also advised [10].

In patients with IBD, cholangitis may be initially asymptomatic, therefore it is recommended to perform annual PSC screening in the form of liver enzymes and serum cholestasis markers. In patients after colectomy due to IBD, it is also recommended to perform the abovementioned tests at the same time intervals due to the still heightened risk of PSC compared to the general population. Cholangiography is performed with elevated liver markers – the abovementioned MRCP is the gold standard. Regarding the
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that the network of adhesive molecules and chemokine receptors normally found in the gut is also expressed in the liver. Hence the possibility of treatment with vedolizumab antibodies (an antibody directed against the alpha4beta7 adhesive molecule) that could have anti-inflammatory effects in the liver [9].

The patient has been in a good general condition since the surgery in 2015, and she has remained under the control of a transplant clinic. Due to frequent episodes of cholangitis, she could be qualified for liver transplantation. Other indications for liver transplantation in patients with PSC include: end-stage liver disease, cirrhosis and biliary tract cancer. Due to the degenerative course of the illness, approximately 40% of patients will receive a transplant. Unfortunately, on average a quarter of patients after liver transplantation will experience recurrence of PSC within 10 years of surgery [12].

REFERENCES
