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Neuroendocrine neoplasm of the colon in a patient with a severe relapse of ulcerative colitis. A case report

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ABSTRACT
This article describes a patient with a severe relapse of newly diagnosed ulcerative colitis, with toxic megacolon, sclerosing cholangitis, and a Bauhin valve neuroendocrine neoplasm. The relationship between inflammatory diseases of the colon, cancer risk including neuroendocrine tumors, the potential impact of these tumors on the course of the underlying disease, and clinical differences between ulcerative colitis with and without coexisting sclerosing cholangitis are discussed based on the latest literature.
Keywords: ulcerative colitis; primary sclerosing cholangitis; neuroendocrine neoplasms; megacolon; inflammatory bowel disease; large intestine.

INTRODUCTION

Ulcerative colitis (UC) is a nonspecific inflammatory bowel disease (IBD). The inflammatory process affects the rectal and colonic mucosae. The disease is present all over the world; its incidence ranges between 1.2–20.3 cases per 100,000 people per year and is constantly increasing [1]. Ulcerative colitis most often affects people between the ages of 20–30, but it can also occur between the ages of 50–80. The etiology of the disease remains unknown, and it is assumed that genetic, environmental, and immunological factors all contribute to the development of the lesions. Ulcerative colitis patients have an increased risk of developing colorectal neoplasms, most commonly cancer including neuroendocrine tumors – 21.5% of which appear in the large intestine and rectum [2, 3]. Colorectal cancer risk factors in UC patients include an early age of onset and the extent and duration of the UC. Inflammatory lesions of the entire colon (pancolitis) and/or coexistence of primary sclerosing cholangitis (PSC) are strongly associated with increased risk [4, 5].

About 3–8% of UC patients may have PSC, while 70–80% of PSC patients have UC [6]. Primary sclerosing cholangitis is hypothesized to result from a disturbance of the intestinal microflora in which microbial particles are transferred from the inflamed intestine to the liver and portal vein system. An inflammatory reaction then develops. The accumulation of T lymphocytes along with more toxic bile causes damage to the biliary epithelium [6, 7]. Most patients have no clinical symptoms at the onset of the disease, which may be suspected on the basis of elevated markers of cholestasis. Laboratory criteria for the diagnosis of PSC include elevated levels of alkaline phosphatase for more than 6 months. The characteristic picture of strictures with subsequent dilatation of the bile ducts found in the magnetic resonance cholangiopancreatography examination is decisive in the diagnosis of PSC. The diagnosis of PSC may precede the diagnosis of IBD. Sometimes PSC can even be diagnosed in a patient after colectomy due to IBD [8]. Patients with PSC and IBD have a 4-times higher risk of colorectal cancer compared with patients with only IBD, and a 10-times higher risk of colorectal cancer than healthy people [9, 10].

Here we describe a 53-year-old patient with a severe relapse of newly diagnosed UC, with toxic distension of the colon, sclerosing cholangitis, and a neuroendocrine neoplasm of the Bauhin valve. The relationship between inflammatory diseases of the colon, the risk of neoplasms including neuroendocrine tumors, their potential impact on the course of the underlying disease, and clinical differences between UC with or without coexisting sclerosing cholangitis are discussed based on the latest literature.

A CASE REPORT

A 53-year-old patient with moderate arterial hypertension was admitted to the Gastroenterology Department of the Pomeranian Medical University in Szczecin, Poland, with suspected UC. On admission, the patient complained of pain in the left iliac region, flatulence, loose stools with blood (6 times a day) and weight loss (about 10 kg) that had been present for 3 weeks. Additionally, he complained of periodic, very severe, paroxysmal abdominal pain corresponding to permeable mechanical obstruction. When asked, he reported that for about 3 years he had periodically loose stools, 2–3 times

a day, without pathological admixtures. These symptoms were so mild that he did not go to the doctor. On admission, the patient's general condition was good. Physical examination revealed pain in the middle epigastric region and in the left iliac fossa. Laboratory tests revealed mild normocytic anemia, thrombocythemia, elevated D-dimers and inflammatory markers, cholestasis, elevated transaminase activity, and hypoalbuminemia. Bacteriological tests and examination of feces for parasites were negative. The ultrasound examination revealed inflammatory lesions covering the entire colon (pancolitis) and single focal lesions in the liver corresponding to most hemangiomas. Rectosigmoidoscopy revealed severe inflammatory changes of Mayo grade 3. Magnetic resonance cholangiography (MRI) revealed sclerosing cholangitis and single focal lesions. The patient received the usual treatment for a severe relapse of UC (aminosalicylates, intravenous steroid therapy, an antibiotic, anticoagulant therapy). After a temporary improvement, there was a sudden deterioration in the patient's condition, with symptoms of toxic megacolon, and the patient was operated on urgently. He had a colectomy with an end ileostomy. The postoperative material revealed a mucosa with a purulent inflammatory infiltrate and numerous ulcerations. The entire thickness of the wall and the entire colon were inflamed. In the ileocecal valve, a 12 mm neuroendocrine tumor was diagnosed (G1, infiltration of nerve trunks and vessels, metastases to the surrounding lymph nodes). After discharge from the hospital, the patient remained under the care of our Gastroenterology Clinic and Endocrinology Clinic. Liver metastases were confirmed in PET/CT 68Ga-DOTA-TATE. He was treated with a long-acting somatostatin analogue and a beta-emitter-conjugated somatostatin analogue (PRRT-177Lu-DOTA-TATE). Five years have now passed since hospitalization. Imaging tests (MRI of the abdominal cavity, PET/CT 68Ga-DOTA-TATE), demonstrate that the changes in the liver remain stable. The patient feels well. The medical team considered liver transplantation, to which the patient did not consent.

DISCUSSION

Our patient sought medical attention for bowel movements with blood and abdominal pain. He was newly diagnosed with severe UC, which did not respond to conservative treatment. Due to toxic megacolon, the patient had to undergo urgent surgery. Considering that the bowel disease coexisted with sclerosing cholangitis and the patient reported a tendency to diarrhea for several years, there is a high probability that the IBD occurred much earlier. In patients with UC and PSC, the clinical picture of IBD may be atypical. In these patients, a milder, sometimes subclinical and even asymptomatic course of UC is observed. A characteristic feature is that inflammatory changes usually affect the right half of the large intestine and can also occur in the ileum (so-called "backwash ileitis"), sparing the rectum. Blood in bowel movements, a symptom that usually signals patients to seek medical attention, does not occur. There is a significantly increased risk of gastrointestinal malignancies, including colorectal cancer, especially on the right side of the intestine. Cordes et al. hypothesized that UC–PSC is a unique subgroup of IBD. Their hypothesis is supported by the fact that pre-existing colitis worsens in UC–PSC patients after orthotopic liver transplantation, and conversely, the risk of PSC recurrence is lower in colectomy patients after such transplantation [4]. Numerous studies have shown an increased incidence of colorectal cancer in patients with IBD–PSC. There are hypotheses as to why patients with PSC and UC have a significantly increased risk of developing neoplastic changes, mainly in the proximal part of the colon. One of them concerns bile acids. Patients with PSC develop cholestasis and the accumulation of secondary bile acids, which may be carcinogenic. However, the risk of colon cancer does not decrease after liver transplantation. Another hypothesis proposes that the development of colorectal cancer in this group of patients is associated with a prolonged course of subclinical activity of the inflammatory disease [11]. There is also hypothesis that the intestinal microflora are different in patients with PSC and UC [12]. The current treatment strategy for UC aims to heal the intestinal mucosa, which reduces the risk of further complications and the need for colectomy [13]. Interesting data have been provided by de Chambrun et al. on the use of oral vancomycin. This antibiotic has been observed to cause a sustained and profound remission in patients with UC and PSC, who achieved clinical remission and healing of the intestinal mucosa [14].

In the course of UC, neoplastic lesions including neuroendocrine tumors may form and develop [15, 16, 17]. The persistence of long-term, chronic inflammation of the colonic mucosa and a lack of adequate control and treatment are of great importance in the development of cancer. The coexistence of a neuroendocrine neoplasm with UC may be influenced by altered intestinal microflora and pro-inflammatory cytokines such as tumor necrosis factor, interferon gamma, and interleukin 2, which stimulate the proliferation of enteroendocrine cells [18]. Some authors have expressed doubts about the higher incidence of neuroendocrine neoplasms in UC [19].

The development of a neuroendocrine neoplasm exacerbates UC. Toxic intestinal dilatation may be caused by the impact of a neuroendocrine tumor on the body and locally in the form of intestinal infiltration, exacerbation of inflammation, metastasis to mesenteric lymph nodes of the intestine, and disruption of the intestinal blood supply [20]. Some of the symptoms reported by the patient resulted from the presence of a neuroendocrine tumor. The 2 diseases had probably been developing in the patient for many years. The patient's tendency to loose stools could have been a symptom of both. Had he consulted a doctor earlier, a correct diagnosis would probably have allowed the implementation of optimal therapy and hence a good prognosis.

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