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ENDOSCOPIC FULL-THICKNESS RESECTION OF SIGMOID COLON CANCER IN A LIVER RECIPIENT

M.T. Bekov[1], A.R. Monakhov[1, 2], K.S. Smirnov[1], Ya.S. Yakunin[1], R.A. Latypov[1], D.O. Oleshkevich[1], O.M. Tsirulnikova[1, 2], S.V. Gautier[1, 2]

[1] Shumakov National Medical Research Center of Transplantology and Artificial Organs, Moscow, Russian Federation

[2] Sechenov University, Moscow, Russian Federation

Compared with the general population, solid organ transplant recipients have a higher cancer risk. This is mainly due to the use of immunosuppressive therapy. Colorectal cancer is one of the most common cancers in recipients. This paper presents the experience of endoscopic full-thickness resection (EFTR) of a sigmoid colon cancer in a liver recipient.

Keywords: solid organ transplantation, cancer morbidity, colorectal cancer, endoscopic full-thickness resection.

Organ transplantation is the operation of choice for terminal and irreversible organ failure, especially when the limit of conservative therapy has been exhausted [1]. In global practice, there is a persistent trend towards a higher number of vital organ transplants performed from both deceased and living related donors [2]. The number of regional centers in the Russian Federation, where transplantation is performed, is increasing every year. For instance, in 2022, organ transplants performed in Russia increased by 10.0% compared to 2021. In 2022, 2555 solid organ transplants were performed in Russia [3].

Solid organ recipients are at risk of malignant tumors [4]. This is largely due to the use of immunosuppressive drugs at preventing post-transplant immunologic complications [5].

Organ transplant recipients have a higher risk of developing colorectal cancer (CRC) than in the population [6]. In 2016, Safaeian et al. analyzed CRC incidence in solid organ recipients. The authors reviewed 790 CRC cases among 224,098 recipients of various organs. Recipients had elevated proximal CRC risk, while distal colon cancer was not increased, and rectal cancer was reduced compared to the general population.

According to multicenter analyses, CRC risk was significantly higher in lung recipients who were operated upon for cystic fibrosis [6–8].

Park et al. analyzed CRC incidence in kidney recipients [9]. The authors noted an elevated risk of colorectal adenomas and CRC in patients with Epstein–Barr virus and cytomegalovirus.

CRC incidence is significantly higher in liver transplant recipients with primary sclerosing cholangitis and with inflammatory bowel disease [10–11].

The outcome of 6,244 heart transplants was analyzed in a multicenter study by Sagastagoitia-Fornie et al. CRC was diagnosed in 116 recipients. The incidence of CRC increased from 56.6 per 100,000 person-years among under 45-year-olds to 436.4 per 100,000 person-years among over 64-year-olds [12].

Surgery is the main definitive treatment for CRC patients [13]. For early (stage 0–1) CRC, organ-preserving procedures like endoscopic mucosal resection with dissection in the submucosal layer is recommended.

Endoscopic full-thickness resection (EFTR) using a full-thickness resection device (FTRD) can replace surgical resection in some cases. The EFTR procedure is shown schematically in Fig. 1.

Andrisani et al. performed EFTR in 110 patients [14]. Main indications were: recurrent adenoma (39 cases), incomplete resection at endoscopic removal of tumor masses (26), non-lifting lesion (12), adenoma involving the appendix (2), subepithelial lesions (10 cases), suspected T1 carcinoma (16) and others. Mean size of specimens was 20 mm (range 6–42 mm). Residual disease was evident in only seven patients.

P. Aepli et al. reported the use of EFTR in 33 patients with colonic epithelial neoplasms [15]. Main indications were recurrent adenoma and nonlifting colorectal lesions. In 31 cases, complete removal of pathologic tissues was achieved. Three post-procedure bleedings and one perforation were seen.

CASE REPORT

Patient K., 54 years old, in August 2019 complained of general weakness, abdominal enlargement. In September 2019, bloody vomiting episodes and melena were noted. At the same time, toxic liver cirrhosis

Corresponding author: Maksat Bekov. Address: 1, Shchukinskaya str., Moscow, 123182, Russian Federation. Phone: (926) 399-49-75. E-mail: doctorbekov@gmail.com

(regular alcohol consumption every week, abstinence since 2019) with portal hypertension syndrome (ascitic syndrome, grade 3 esophageal varices (EV) according to N. Soehendra, K. Binmoeller) was diagnosed. Several laparocentesis sessions were performed, and a total of up to 30 liters of ascitic fluid were evacuated. Endoscopic variceal ligation (EVL) was performed in October 2019. The postoperative period was uneventful. The patient was diagnosed with extrinsic portal vein thrombosis in November 2019, for which apixaban therapy was administered at a dosage of 2.5 mg twice a day. In 2020, a second endoscopic ligation of grade 3 EV was performed, without complications. One month later, there were signs of progression of portal thrombosis which spread to the superior mesenteric vein. An increase in edematous-ascitic syndrome has been noted since December 2020.

In March 2021, the patient came to Shumakov National Medical Research Center of Transplantology and Artificial Organs. A comprehensive examination was performed, and the diagnosis was: cirrhosis of alimentary toxic genesis, decompensation, Child–Pugh class B, MELD-Na 12, complicated by portal hypertension syndrome (ascites, EV), hepatocellular failure (coagulopathy, hyperbilirubinemia, stage 1 hepatic encephalopathy) was established. The following concomitant diseases were diagnosed: type 2 diabetes mellitus; grade 2 arterial hypertension, risk 3; cholelithiasis with cholecystolithiasis. Due to the severity of the underlying disease and the futility of conservative therapy, liver transplantation (LT) was adopted as the definitive treatment method. The patient was added to the LT waiting list since there were no contraindications.

In April 2021, in preparation for LT, an outpatient colonoscopy was performed, which revealed adenomatous epithelial neoplasms of the colon and rectum. Preparation for the study was carried out with a Macrogol-based drug. The quality of preparation was evaluated as unsatisfactory (4 points on the Boston scale: left side (LS), 1; transverse colon (TS), 1; right side (RS), 2. Scheduled in-hospital endoscopic polypectomy was recommended. However, the patient refused hospitalization.

In July 2021, orthotopic LT from a deceased ABO-compatible donor was performed according to the classical technique. Immunosuppressive therapy was induced with basiliximab 20 mg and methylprednisolone 500 mg, followed by a reduction in methylprednisolone dosage and transition to oral administration with a daily dosage of 6 mg. The postoperative period was uneventful. On day 2, the second drug of the immunosuppressive therapy – Tacrolimus – was initiated, with gradual increase in target drug concentrations. Day 5 saw the start of mycophenolate mofetil at a dose of 1000 mg twice a day. The patient was discharged from the hospital on day 11 following LT under outpatient follow-up due to the situation having stabilized, the graft functioning satisfactorily, and there were no longer any reasons for further inpatient care.

There were regular visits for outpatient follow-up with clinical, laboratory and instrumental monitoring of the graft and general medical status. From August 2021, the patient was converted to prolonged-release tacrolimus with achievement of target drug concentrations in blood.

In December 2021, increased serum alpha-fetoprotein level (17.13 IU/mL) was noted. Diagnostic colonoscopy was performed in January 2022, which revealed: 3 epithelial masses of the ascending colon up to 6 mm in diameter, type 0-Is according to Paris classification, type 2 according to NICE classification; 3 epithelial masses of the transverse colon up to 6 mm in diameter, type 0-IIa

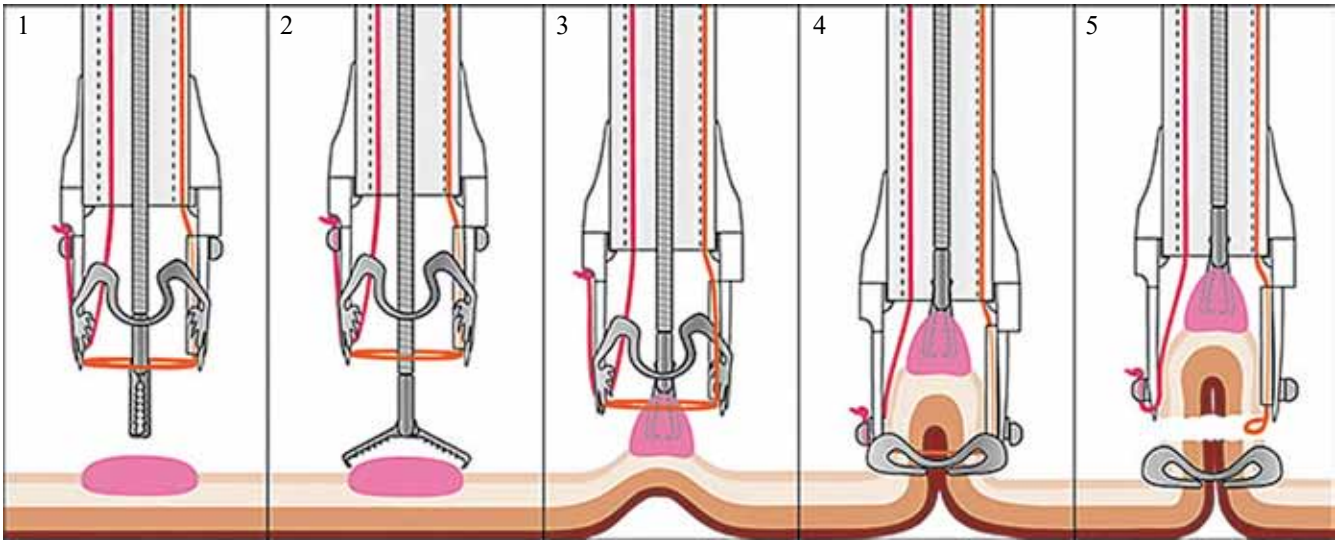

Fig. 1. The EFTR system is presented. 1, marking of the surgical intervention site; 2, grasping of the target tissue with a forceps; 3, retrieval of the target tissue within cap and fixation; 4, release of the clip; 5, closure of the snare and tissue incision using electrosurgery (source: www.ovesco.com)

according to Paris classification, type 2 according to NICE classification; two rectal epithelial masses up to 6 mm in diameter, type 0-Is according to Paris classification, type 2 according to NICE classification. Endoscopic cold snare polypectomy with subsequent histological examination was performed. Also, in the sigmoid colon, at 30–35 cm from the anus, a formation of up to 7–8 mm in diameter, type 0-IIa+IIc according to Paris classification, type 3 according to NICE classification, with central retraction was determined. The epithelial pattern was obliterated in some places; in the narrow band imaging (NBI) mode, curved multilobular vessels were detected (Fig. 2). Instrumental palpation revealed wall infiltration, but slight mobility remained during traction. A biopsy was taken. Also, the tumor was endoscopically marked with a Black Eye marker. Preparation for the study was carried out with a Macrogol-based agent with the addition of ascorbic acid. The quality of preparation was evaluated as satisfactory (6 points on the Boston scale: left side (LS), 2; transverse colon (TS), 2; right side (RS), 2.

Histological examination of the removed epithelial neoplasms revealed colonic tubular adenomas with mild dysplasia. The histologic picture of the epithelial neoplasm in the sigmoid colon was represented by a highly differentiated adenocarcinoma (low-grade).

Oncologic search was performed, including contrast-enhanced computed tomography of the brain, chest and abdominal cavity, esophagogastroduodenoscopy, and positron emission tomography. There were no signs of metastatic lesion. Taking into account the size of the tumor mass, absence of metastases, spread of the process (pT1N0M0, stage I), it was decided to perform EFTR of the sigmoid colon cancer.

In February 2022, in the operating room under intravenous sedation, EFTR of the sigmoid colon cancer was performed using the OTSC clipping system and Ovesco® endoscopic clips (Ovesco AG, Germany) (Olympus Evis Exera III video endoscopy system, CF-190L colonoscope (Olympus Corporation, Japan)). Using alligator biopsy forceps (Endo Stars LLC, Russia), the mass was retrieved within the device for clip application with grasping of the intestinal wall with unchanged mucosa. The next stage was application of Ovesco® clip within the healthy tissues. The epithelial formation was removed in ENDO CUT Q mode (effect 3, cutting width 1, cutting interval 6) (ERBE VIO 300D, Erbe Elektromedizin, Germany). The removed fragment was extracted from the intestinal lumen. No signs of residual tumor tissue were found during revision (Fig. 3).

Histological study revealed numerous colonic mucosa fragments with invasive growth of highly differentiated adenocarcinoma, moderate lymphocytic-leukocytic infiltration in the stroma. The resection margin was intact.

The postoperative period was uneventful. Following surgery, the patient was discharged from the hospital on day 7.

When performing control colonoscopy 6 months and 1 year 6 months after EFTR of a sigmoid colon cancer, no evidence of relapse was found (Fig. 4). At the time of writing, the follow-up period was 2 years.

CONCLUSION

Solid organ recipients have an increased risk of cancer, including CRC, especially with age and time since transplant. This statistical pattern is largely due to the use of immunosuppressive drugs for vital indications.

This patient cohort requires more thorough cancer screening. The gold standard for CRC screening is colonoscopy. The diagnostic value of this technique depends both on quality of preparation (including adherence to a specialized diet with the exclusion of fiber-rich foods),

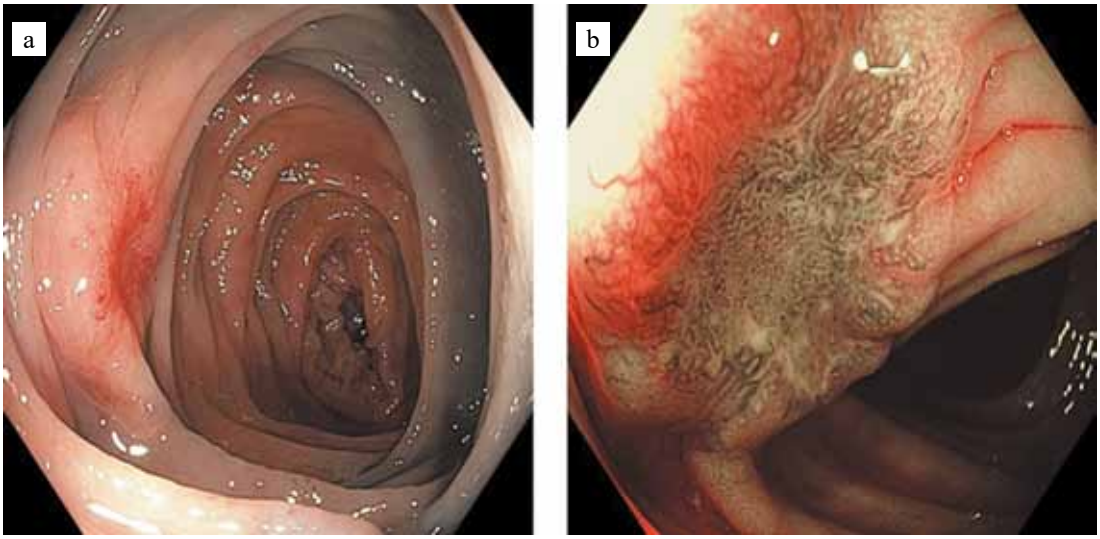

Fig. 2. Epithelial formation of the sigmoid colon: a, in white color; b, in narrow-spectral imaging mode, there is pronounced "neoangiogenesis", a sign of malignant growth

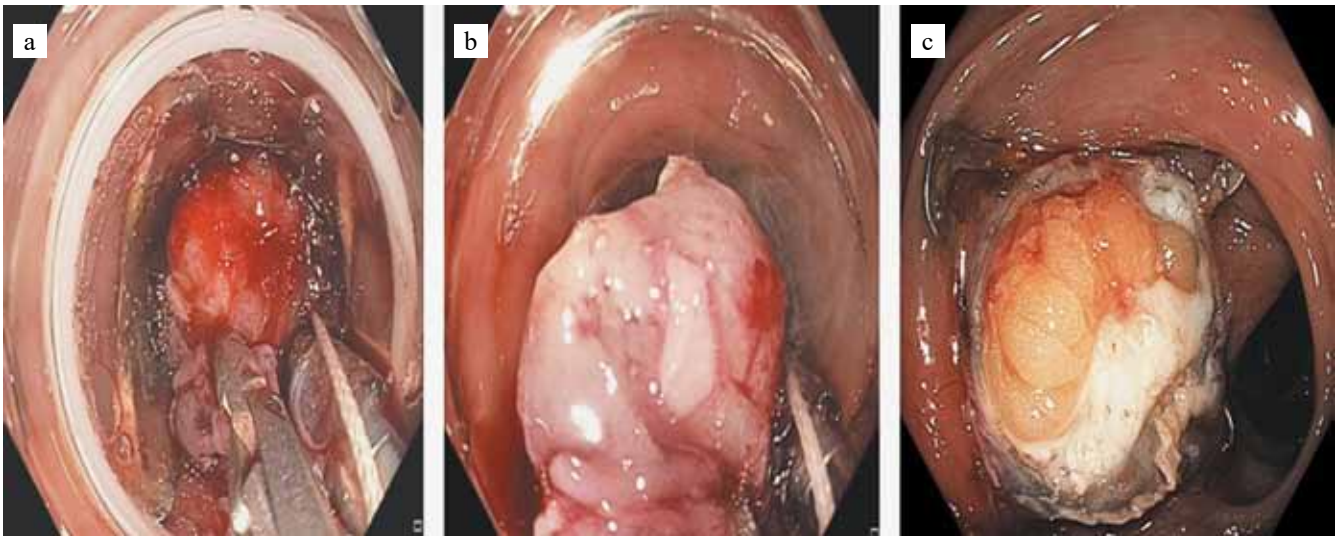

Fig. 3. Surgical intervention stages. a, grasping of the tumor tissue and retrieval within cap; b, fragment of the sigmoid colon wall resected using electrosurgery; c, revision after adenocarcinoma removal

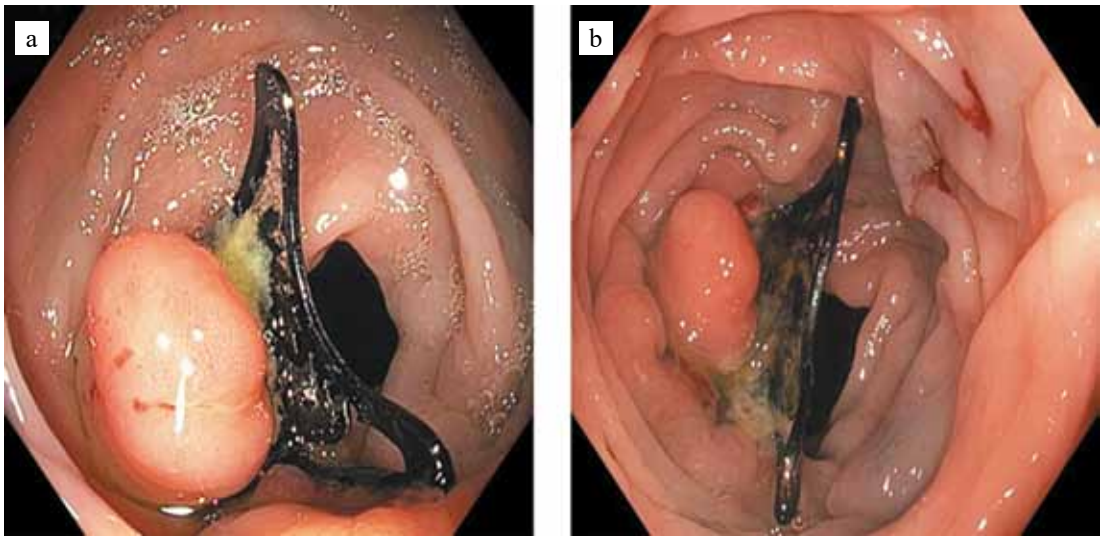

Fig. 4. Control colonoscopy after EFTR of sigmoid colon cancer: a, at 6 months; b, at 1 year 6 months (the clip is still in the intestinal lumen)

on split administration of Macrogol-based drugs, and on conducting an examination using expert-level equipment with a water-jet pump and carbon dioxide insufflator.

The use of EFTR of colonic epithelial neoplasms, if technically feasible and if there are no contraindications, may be an alternative to colon resection. EFTR can reduce the incidence of surgical complications, length of hospitalization, and can be considered in patients for whom abdominal surgery is contraindicated due to high anesthetic risks.

The authors declare no conflict of interest.

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