Hyperthermic intraperitoneal chemotherapy and ileal pouch-anal anastomosis: A case report

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Case report

Keywords: Familial adenomatous polyposis, peritoneal carcinomatosis, metastatic cancer, cyto-reductive surgery, Hyperthermic intraperitoneal chemotherapy, J-Pouch, colorectal cancer

Posted Date: February 7th, 2020

DOI: https://doi.org/10.21203/rs.2.22880/v1

Abstract

Background: CRS and HIPEC are established treatments for peritoneal carcinomatosis that prolong survival in carefully selected patients, considered to be a loco-regional disease. At the time of diagnosis 4-7% of patients have metastasis to the peritoneum. There is a lack of evidence in the literature if J-pouch can be applied simultaneously with HIPEC in order to improve quality of life of this patient group.

Case presentation: We describe a rare case of a 41 year-old Caucasian male with Familial Adenomatous Polyposis which was diagnosed as metastatic colorectal cancer in the liver and peritoneum. He was treated with systemic chemotherapy followed by total proctocolectomy with a J-shaped IPAA, liver metastasectomy, right hemidiaphragm resection, CRS and HIPEC. This is the first reported case of J-Pouch formation along with HIPEC

Conclusions: J-Pouch after CRS and HIPEC can be offered as a treatment as long as the patient is carefully being selected, in high experienced centers and the perioperative findings allow it.

Background

Familial adenomatous polyposis (FAP) is an autosomal dominant syndrome with an incidence of 1:10000, however approximately 20% of cases appear as de novo mutations. The driving mutation is in the APC gene. Hereditary polyposis syndromes represent 5–10% of all colorectal cancers (CRC). FAP usually progresses to CRC by the 4th decade of life unless prophylactic colectomy or proctocolectomy is performed (1). Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) is considered to be the ‘gold standard’ in the management of FAP in order to prevent cancer development and preserve fecal continence, improving quality of life.

FAP may present as metastatic CRC with liver and peritoneum as the most common sites of metastasis. Liver metastases occur in 25–30% of patients with CRC (2). Peritoneum is the second most common site of CRC metastasis (4–13%), found in 4–7% of patients at the time of diagnosis (3,4). Treatment of peritoneal carcinomatosis is multimodal; the standard of care in carefully selected patients is cytoreductive surgery (CRS) with hyperthermal intraperitoneal chemotherapy (HIPEC) and systemic chemotherapy, the combination of which has been shown to expand the overall survival from 6 months if left untreated to 20–63 months (5). On the other hand, CRS with HIPEC has been criticized as a surgical procedure with high morbidity and mortality, correlated with increased rates of anastomotic leak (6).

We present the case of an adult man with FAP which was diagnosed as metastatic CRC in the liver and peritoneum. that was treated with systemic chemotherapy followed by total proctocolectomy with a J-shaped IPAA, liver metastasectomy, right hemidiaphragm resection, CRS and HIPEC. This is the first reported case of IPAA surgery in combination with HIPEC.

Case Presentation

We report the case of a 41 year-old Caucasian male with FAP and metastatic colonic cancer who was referred to our institution. The patient was not under screening although he had a family history of FAP. He presented 2 years ago with epigastric pain and symptoms of obstructive ileus. Abdominal Computerized Tomography (CT) revealed stenosis at the transition of the descending to sigmoid colon, multifocal metastatic disease of the liver and a mesenteric nodal mass (1.9 cm). (Fig. 1) An exploratory laparotomy was performed, in which diffuse peritoneal carcinomatosis was revealed in combination with an obstructing neoplastic mass in the aforementioned by the CT segment of descending colon. A diverting loop ileostomy was created and biopsies were obtained from the liver and the greater omentum.

Colonoscopy after surgery revealed multiple polyps of the rectum, sigmoid and distal descending colon; a total colonoscopy was not achieved due to the neoplastic stenosis of the descending colon. Upper gastrointestinal tract endoscopy showed multiple cystic polyps at the gastric fundus and body and multiple duodenal adenomas at the ampulla of Vater (Fig. 2). Histopathological examination of the surgical specimens revealed moderately differentiated adenocarcinoma. Immunohistochemistry tests were positive for the markers CDX2 and CK20, whereas the CK7 marker was negative. KRAS/BRAF screening of pathological specimens found wild-type KRAS, wild-type NRAS,was negative for BRAF mutations and the tumour was microsatellite stable (MSS).

Chemotherapy (ChT) was given for a period of 15 months, consisting of Oxaliplatin and Bevacizumab regimens. Subsequent CT and Magnetic Resonance Imaging (MRI) revealed an impressive response of metastatic liver disease; only a single metastatic lesion in liver segment VI had remained, which had been downsized from 3.5 cm before ChT to 1.8 cm after ChT. Moreover, multiple small focal lesions were shown in liver segments III and VI, possibly corresponding to “cured” metastases. (Fig. 3). Positron emission tomography–computed tomography (PET- CT) revealed only one hypermetabolic area (SUVmax = 4.2) in liver segment VI. Interestingly, PET-CT showed absence of hypermetabolic neoplastic activity elsewhere in the abdominal cavity, including the already known site of the primary tumor in the descending colon. (Fig. 3).

The hospital’s multidisciplinary tumor board concluded that a second exploratory laparotomy in combination with possible restorative proctocolectomy, liver metastasectomy, peritonectomy and HIPEC was decided as the best option for the patient.

Abdominal cavity exploration revealed seven liver metastases(segment II and right lobe), metastatic lesions to the right hemidiaphragm and three suspicious lesions in the mesentery. Peritoneal carcinomatosis Index (PCI) was 7.

He then underwent total proctocolectomy with J-Pouch formation with diverting ileostomy, liver metastasectomy, part of right hemidiaphragm resection and HIPEC.

The small bowel mesentery was mobilized adequately and J-Pouch was constructed from the terminal 40 cm of small intestine. A side to side anastomosis was performed with multiple firings of a GIA 75 linear stapler via enterotomy at the pouch apex.

The blind loop of the J-pouch was closed with a linear stapler and a second reinforcing overstich line. Insufflation with normal saline confirmed the integrity of the pouch. The IPAA anastomosis was performed with a circular stapler. Care was taken for prevention of twisting of small bowel mesentery. The doughnuts were checked and the air-leak test was negative for leak of the anastomosis. Moreover, a diverting ileostomy was performed.

Completeness of cytoreduction (CCR) score was 0. Open coliseum technique was utilized for HIPEC, suspending the edges of the abdominal wall with a running suture over a self-retaining retractor. HIPEC with mitomycin C was administered for 90 min, at a temperature of 42 °C simultaneously with intravenous administration of 5-Fluoruracil and leucovorin. After HIPEC, washout of the abdomen was performed.

The postoperative course was complicated with persistent fever and resolved after intra-port removal. This prolonged his hospital stay to 15 days.

He then underwent ChT for six months with bevacizumab and capecitabine regimens. Six months after surgery and before closure of the diverting ileostomy, the pouchogram was performed and it was normal (Fig. 4). The patient is free of metastasis (CT, MRI), his pouch is uncomplicated as seen by colonoscopy and is going to reverse his ileostomy.

Discussion And Conclusions

FAP is an autosomal dominant inherited syndrome characterized by multiple large bowel adenomas being formed in the early childhood, progressing to adenocarcinoma usually by the 4th decade of life if not treated. According to the number of colorectal polyps, FAP is categorized as classical (> 100 polyps) or attenuated (10–100 polyps) (7). Approximately 20% of patients have de novo mutations; due to the lack of family history these patients seek for medical consultation only when the disease becomes symptomatic (polyps, CRC) (8) .

Our patient had shown poor compliance in medical consultation and was not under screening, although he had a family history of FAP. As a result, he presented with CRC that caused bowel obstruction with concomitant liver and peritoneal metastases.

Peritoneal carcinomatosis standard therapy for certain types of cancer (e.g CRC)has been established as complete CRS with HIPEC.(4) There are theories that have been proposed regarding the possible negative effect of CRS and HIPEC in the process of anastomotic healing; intestinal edema caused by this longstanding surgical procedure, the need for excessive fluid resuscitation, as long as the thermal pressure and the cytotoxicity of the regimens used during HIPEC have been considered as aggravating factors in the process of anastomotic healing.(9, 10)

CRS and HIPEC has been implicated with high morbidity and mortality rates. A major independent risk factor correlated with high morbidity is anastomotic failure. Anastomotic leakage rates range from 0

to9% in experienced centers (6). The German DGAV StuDoQ Registry(Studien-, Dokumentations- und Qualitätszentrum der Deutschen Gesellschaft für Allgemein- und Viszeralchirurgie), the largest published national registry on CRS and HIPEC with 2149 patients, reports anastomotic leakage rates of 6% with rectal anastomosis being an independent prognostic factor (11). Anastomotic failure seems to be dependent on patient's gender or tumour histology but not on anastomotic technique (12). However, Paul Sugarbaker, who first developed CRS and HIPEC (Sugarbaker procedure) published a series of 29 patients without anastomotic leak .This was attributed to a second, reinforcing overstitch line in the stapled colorectal anastomosis. (13)

Ileal pouch–anal anastomosis (IPAA) is well-established after total proctocolectomy as it improves quality of life of patients and is related to high patient satisfaction and good or excellent functional outcomes for up to 95% of patients who have it (14). Nevertheless, its complications-acute postoperative or late- range from 30–60% in series of studies. They include septic such as anastomotic leak, fistula or pouchitis and non-septic such as small bowel obstruction, stricture, pouchitis, cuffitis. They can lead to pouch failure and excision or death.(15) Mortality rates when complications happen range from 3.5 to 17%. Anastomotic leak occurs in 9% of patients with FAP and J-Pouch. (16)

Inflammatory bowel disease, body mass index greater than 30, patient older than 50 years and surgeon inexperience have all been demonstrated as risk factors (17)

Our patient was treated with CRS, restorative proctocolectomy- J pouch and HIPEC. This is the first reported case of J- Pouch formation along with HIPEC. The patient is free of metastasis 10 months later (CT, MRI), his pouch is uncomplicated as seen by colonoscopy and is going to reverse his ileostomy.

It seems that J-Pouch after CRS and HIPEC can be offered as a treatment as long as the patient is carefully being selected, in high experienced centers and the perioperative findings allow it. However, this is a single case report and this kind of treatment should be under research, so patients with peritoneal malignancies have not only a prolonged overall survival but also a more qualitative one.

List Of Abbreviations

CT
Computerized tomography
MRI
Magnetic Resonance Imaging
PET CT
Positron emission tomography–computed tomography
HIPEC
Intraperitoneal hyperthermic chemotherapy
IPAA
Ileal pouch–anal anastomosis
StuDoQ Registry

Studien-, Dokumentations- und Qualitätszentrum der Deutschen Gesellschaft für Allgemein- und Viszeralchirurgie

Declarations

Ethics approval and consent to participate

Not applicable

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no competing interests

Funding

None

Authors' contributions

LC designed the structure of the article and wrote the paper. AG revised the article.IS provided imaging findings as figures for the manuscript. EV carried out gastroscopy and colonoscopy. JK carried out the surgical procedure IP carried out the surgical procedure and gave the final approval of the version to be published. All authors read and approved the final manuscript.

Acknowledgements

Not applicable

References

1. Patel R, Hyer W. Practical management of polyposis syndromes. Frontline Gastroenterol. 2019;10(4):379-87.
2. Engstrand J, Nilsson H, Stromberg C, Jonas E, Freedman J. Colorectal cancer liver metastases - a population-based study on incidence, management and survival. BMC Cancer. 2018;18(1):78.

3. Vatandoust S, Price TJ, Karapetis CS. Colorectal cancer: Metastases to a single organ. World J Gastroenterol. 2015;21(41):11767-76.
4. Aoyagi T, Terracina KP, Raza A, Takabe K. Current treatment options for colon cancer peritoneal carcinomatosis. World J Gastroenterol. 2014;20(35):12493-500.
5. Hallam S, Tyler R, Price M, Beggs A, Youssef H. Meta-analysis of prognostic factors for patients with colorectal peritoneal metastasis undergoing cytoreductive surgery and heated intraperitoneal chemotherapy. BJS Open. 2019;3(5):585-94.
6. Chua TC, Yan TD, Saxena A, Morris DL. Should the treatment of peritoneal carcinomatosis by cytoreductive surgery and hyperthermic intraperitoneal chemotherapy still be regarded as a highly morbid procedure?: a systematic review of morbidity and mortality. Ann Surg. 2009;249(6):900-7.
7. Mitchem JB, Hall JF. Adenomatous Polyposis Syndromes: Diagnosis and Management. Clin Colon Rectal Surg. 2016;29(4):321-9.
8. Tudyka VN, Clark SK. Surgical treatment in familial adenomatous polyposis. Ann Gastroenterol. 2012;25(3):201-6.
9. Whealon MD, Gahagan JV, Sujatha-Bhaskar S, O'Leary MP, Selleck M, Dumitra S, et al. Is Fecal Diversion Needed in Pelvic Anastomoses During Hyperthermic Intraperitoneal Chemotherapy (HIPEC)? Ann Surg Oncol. 2017;24(8):2122-8.
10. Lopez-Lopez V, Lynn PB, Gil J, Garcia-Salom M, Gil E, Gonzalez A, et al. Effect of Paclitaxel-based Hyperthermic Intraperitoneal Chemotherapy (HIPEC) on colonic anastomosis in a rat model. Clin Transl Oncol. 2019;21(4):505-11.
11. Piso P, Nedelcut SD, Rau B, Konigsrainer A, Glockzin G, Strohlein MA, et al. Morbidity and Mortality Following Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: Data from the DGAV StuDoQ Registry with 2149 Consecutive Patients. Ann Surg Oncol. 2019;26(1):148-54.
12. Wiseman JT, Kimbrough C, Beal EW, Zaidi MY, Staley CA, Grotz T, et al. Predictors of Anastomotic Failure After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: Does Technique Matter? Ann Surg Oncol. 2019.
13. Sugarbaker PH. Avoiding Diverting Ileostomy in Patients Requiring Complete Pelvic Peritonectomy. Ann Surg Oncol. 2016;23(5):1481-5.
14. Fazio VW, Kiran RP, Remzi FH, Coffey JC, Heneghan HM, Kirat HT, et al. Ileal pouch anal anastomosis: analysis of outcome and quality of life in 3707 patients. Ann Surg. 2013;257(4):679-85.
15. Sherman J, Greenstein AJ, Greenstein AJ. Ileal j pouch complications and surgical solutions: a review. Inflamm Bowel Dis. 2014;20(9):1678-85.
16. Fazio VW, Ziv Y, Church JM, Oakley JR, Lavery IC, Milsom JW, et al. Ileal pouch-anal anastomoses complications and function in 1005 patients. Ann Surg. 1995;222(2):120-7.
17. Kiran RP, da Luz Moreira A, Remzi FH, Church JM, Lavery I, Hammel J, et al. Factors associated with septic complications after restorative proctocolectomy. Ann Surg. 2010;251(3):436-40.

Figures

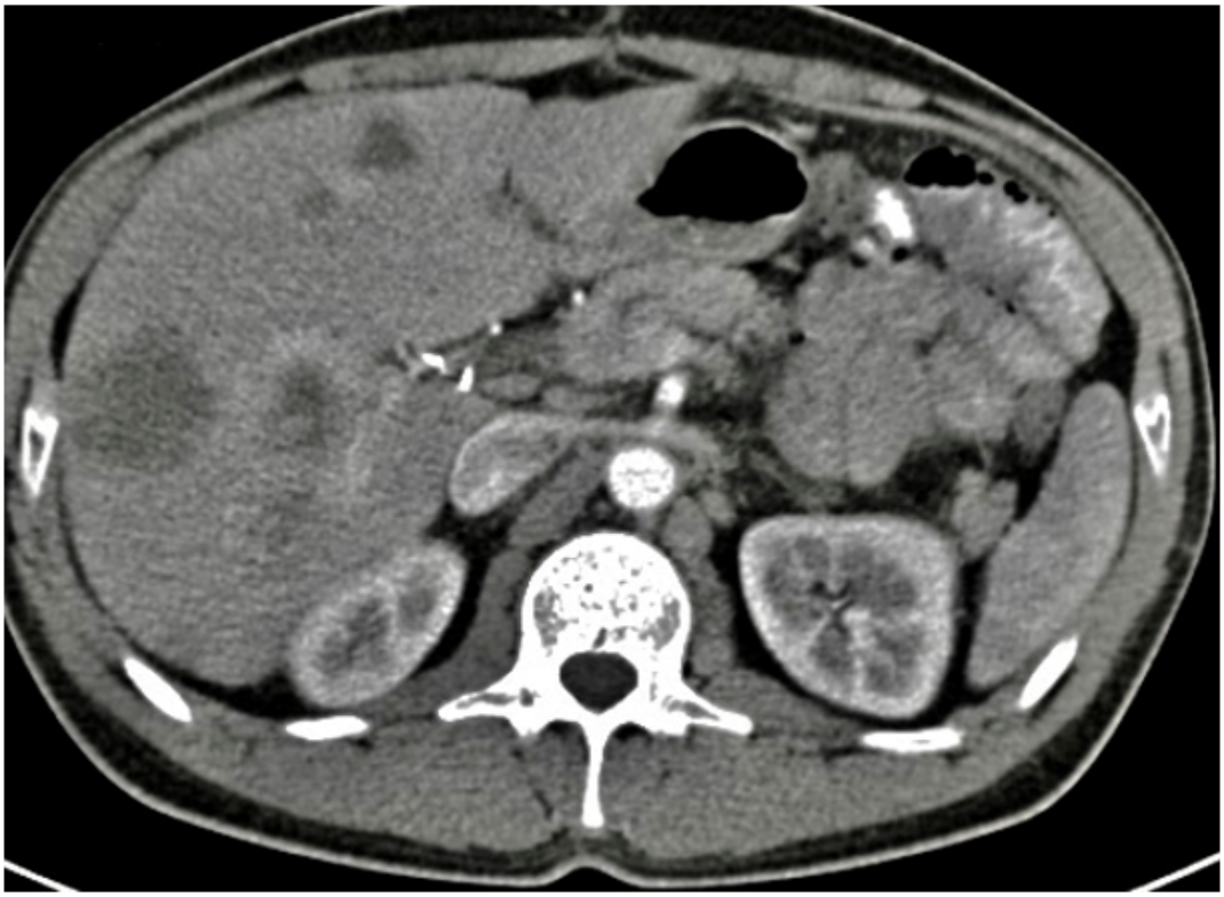

Figure 1

Abdominal computed tomography image demonstrating liver metastasis at the time of the diagnosis

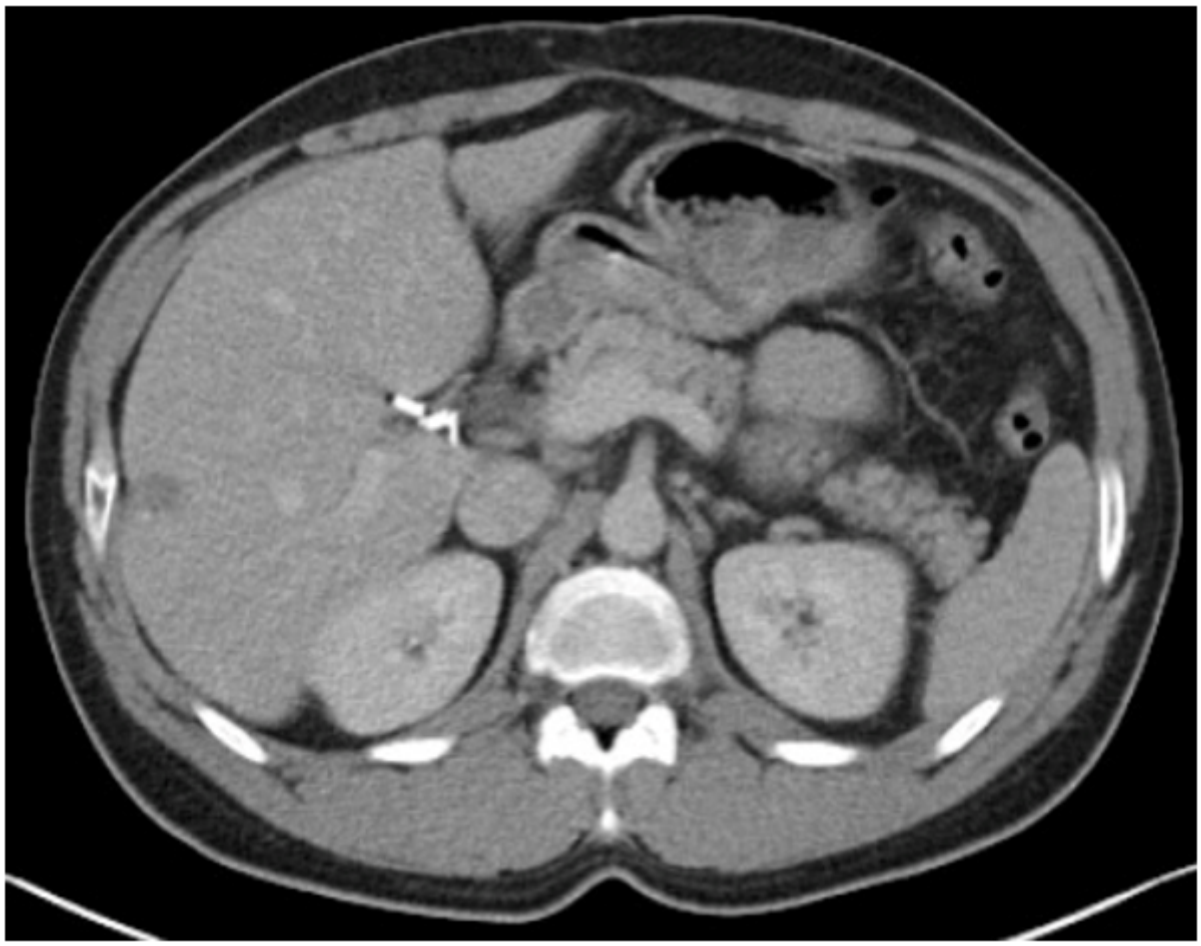

Figure 2

Abdominal computed tomography image demonstrating liver metastasis after chemotherapy

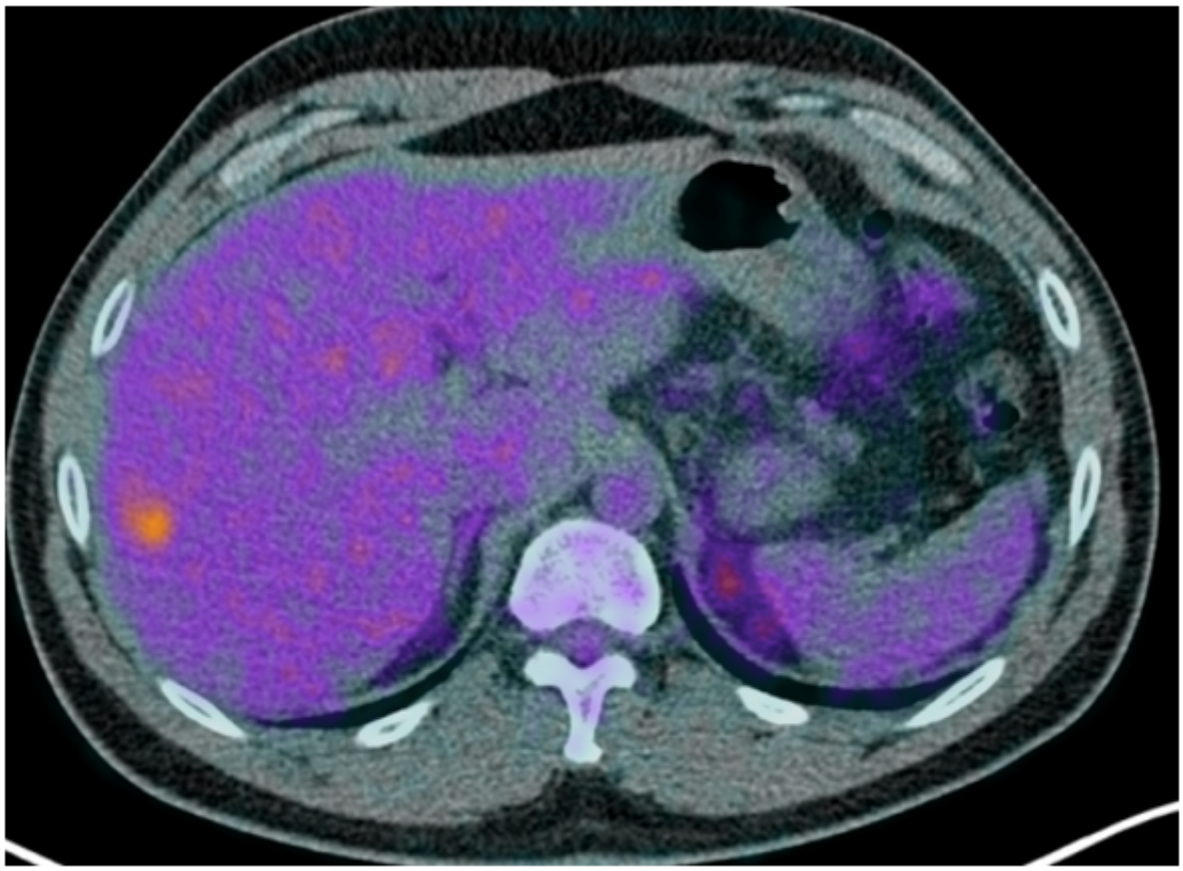

Figure 3

Positron emission tomography–computed tomography after chemotherapy revealed only one hypermetabolic area (SUVmax=4.2) in liver segment VI

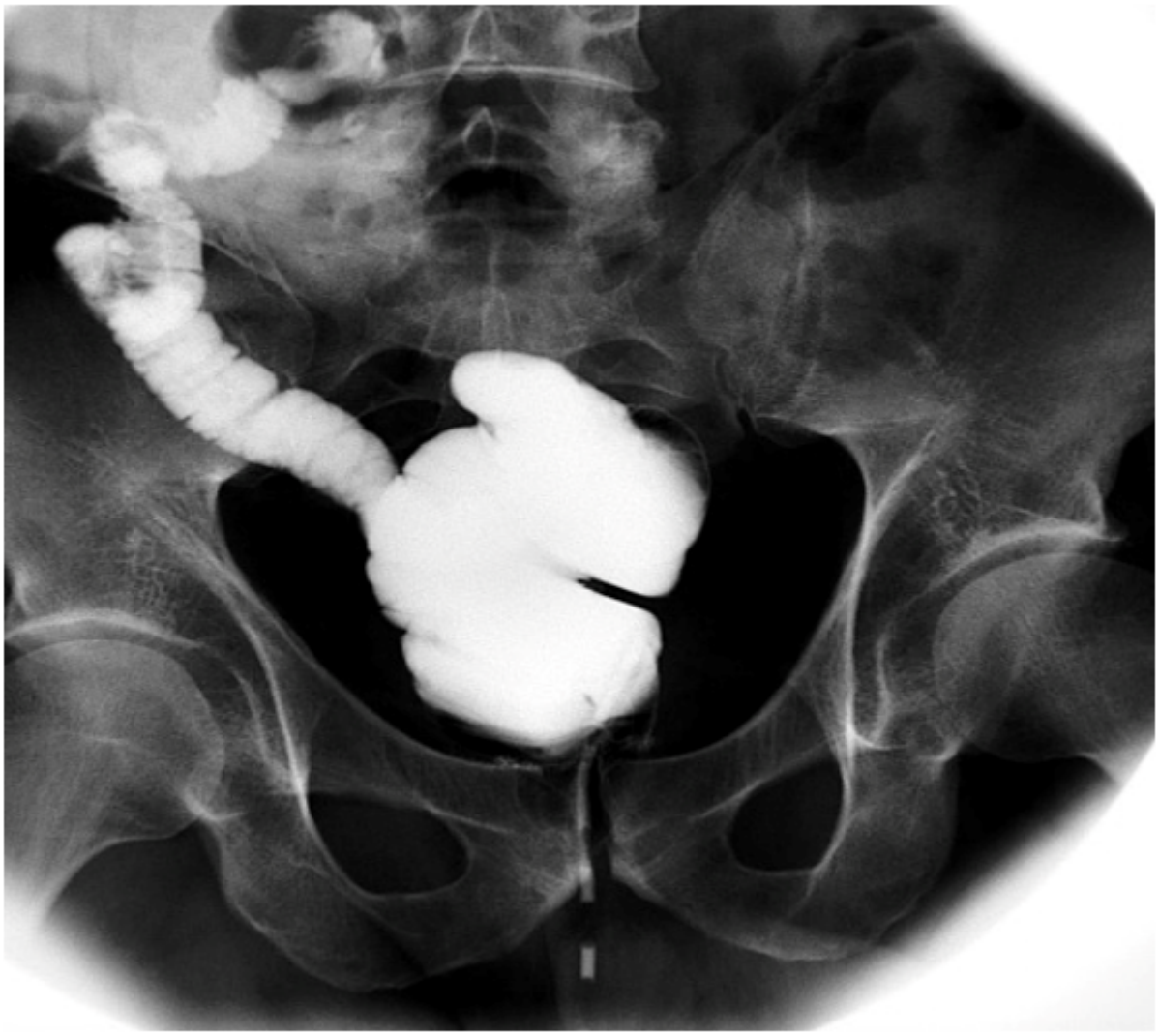

Figure 4

A pouchogram of the patient 6 months after ileal pouch-anal anastomosis performed before diverting stoma closure