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WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

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CASE REPORT

Metachronous multifocal carcinoma: A case report

Dan-Dan Wan, Xiao-Ju Li, Xing-Ru Wang, Tian-Xi Liu

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Abstract

BACKGROUND

The incidence of multiple primary carcinomas (MPC) varies greatly, ranging from 0.73% to 11.70% in foreign countries, with duo-duplex carcinoma being the most common, trio-duplex carcinoma and above being rare, and simultaneous multigenic carcinoma being even rarer, accounting for 18.4% to 25.3% of the incidence of MPC. However, there is no report regarding patients presenting with simultaneous dual-origin carcinoma of the liver and colon and heterochronous pancreatic cancer.

CASE SUMMARY

We report a special case of multifocal carcinoma, in which one patient had a medical condition of primary liver and colon cancer and pancreatic cystadenocarcinoma 2 years after surgery. Through aggressive advanced fluorescent laparoscopic techniques, standardized immunotherapy, targeting, and chemotherapy, a better prognosis and a desirable survival period were achieved for the patient.

CONCLUSION

There is a need to clarify the nature of MPC through advanced surgical means to ensure better diagnosis and treatment.

Key Words: Multiple primary carcinomas; Metachronous multifocal carcinoma; Heterochronous pancreatic cancer; Comprehensive diagnosis and treatment; Case report

Core Tip: This study describes an uncommon case of simultaneous dual-origin carcinoma of the liver and colon and heterochronous pancreatic cancer, which was verified through histopathological and immunohistochemical analyses. Our findings suggest that patients can benefit from comprehensive diagnosis and treatment.

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INTRODUCTION

Multiple primary carcinomas (MPC) were refer to the occurrence of two or more primary malignant tumors in the same patient. Currently, the diagnostic criteria proposed by Warren and Gates[1] are primarily used. The incidence of MPC varies greatly, ranging from 0.73% to 11.70% in foreign countries[2], with duo-duplex carcinoma being the most common, trio-duplex carcinoma and above being rare[3-5], and simultaneous multigenic carcinoma being even rarer, accounting for 18.4% to 25.3% of the incidence of MPC[6,7]. Accurate diagnosis prior to surgery poses challenges, necessitating postoperative immunohistochemistry of the specimen for a definitive diagnosis. As of reporting this case, there is no report regarding patients presenting with simultaneous dual-origin carcinoma of the liver and colon and heterochronous pancreatic cancer. Herein, we report the clinical case of a 60-year-old male patient who was diagnosed with metachronous multifocal carcinoma and subsequently underwent comprehensive treatment.

CASE PRESENTATION

Chief complaints

The patient was a 60-year-old male. He was admitted to the hospital due to right-sided abdominal pain that had lasted for a week.

History of present illness

The patient report abdominal pain, and there were changes in bowel habits. But, there were no signs of hematemesis or melena.

History of past illness

He had a history of hepatitis B, hypertension, diabetes, and sequelae of cerebral infarction.

Personal and family history

He also had a family history of colon cancer.

Physical examination

The physical examination of the patient showed some abnormality that right abdominal tenderness, no rebound pain and muscle tension, not touched the mass.

Laboratory examinations

The post-hospitalization laboratory results were summarized as follows: The count of white blood cell, red blood cell and platelet are all normal, alpha-fetoprotein level of 530 ng/mL, cancer antigen 199 level of 100 U/mL, and carcinoembryonic antigen level of 3.5 ng/mL. Abnormal prothrombin level of 54.46 μg/L.

Imaging examinations

He was admitted to the hospital for a complete examination, including abdominal-enhanced magnetic resonance imaging, abdominal-enhanced computed tomography (CT), and gastrointestinal scintigraphy (Figure 1). Postoperative examination and immunohistochemical results confirmed that the colon lesion was a low-to-moderately differentiated adenocarcinoma, and the liver lesion was a moderately differentiated hepatocellular carcinoma (Figure 2). Two years post-surgery, the patient was re-admitted to the hospital due to recurrent abdominal pain and diarrhea that had lasted for 1 wk. After abdominal CT and colonoscopy (Figure 3A-E), intestinal obstruction and pancreatic cystadenoma were considered.

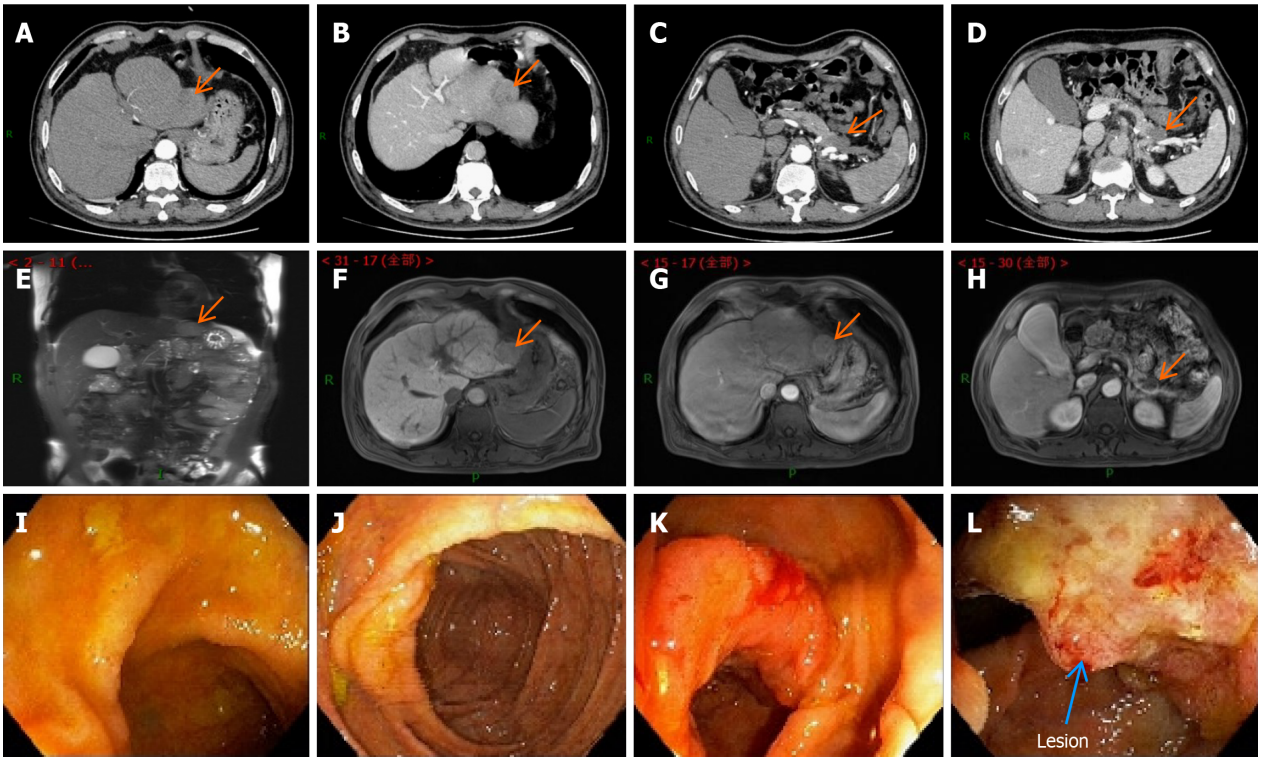


Figure 1 Schematic diagram of the enhanced computed tomography, magnetic resonance imaging, and colonoscopy results before the first surgery. A: Contrast-enhanced abdominal computed tomography (CT) image of the liver during the arterial phase; B: Contrast-enhanced abdominal CT image of the liver during the portal phase; C: Contrast-enhanced abdominal CT image of the arterial pancreatic lesion; D: Contrast-enhanced abdominal CT image of the arterial pancreatic lesion; E-H: Contrast-enhanced magnetic resonance imaging (MRI) images of the liver and pancreatic foci at different levels. They suggest that the hepatic fissure was widened, and the edge of the liver was not smooth. The left lobe could be seen as a nodular abnormal signal shadow of about 35 mm × 31 mm in size. There was a low signal in T1-weighted image (T1WI) and a high signal in T2WI. There was mild enhancement in the arterial phase after enhancement, which receded in the delayed phase and was considered to be hepatocellular carcinoma. Pancreatic atrophy and the caudal part of the pancreas could be seen as cystic foci of about 25 mm × 28 mm in size. There was a low signal in T1WI and a high signal in T2WI. There was no enhancement in the arterial phase after enhancement, which was considered a cystic adenoma; I: Electron enteroscopic image of the end of the ileum; J: Electron enteroscopic image of the cecum; K: Electron enteroscopic image of the liver region; L: Electron enteroscopic image of the liver region, suggesting neoplasm in the liver region of the colon, a longitudinal change of 3 cm, and narrowing of the intestinal lumen by half. The results of the sampling pathology suggested moderately differentiated adenocarcinoma of the colon.

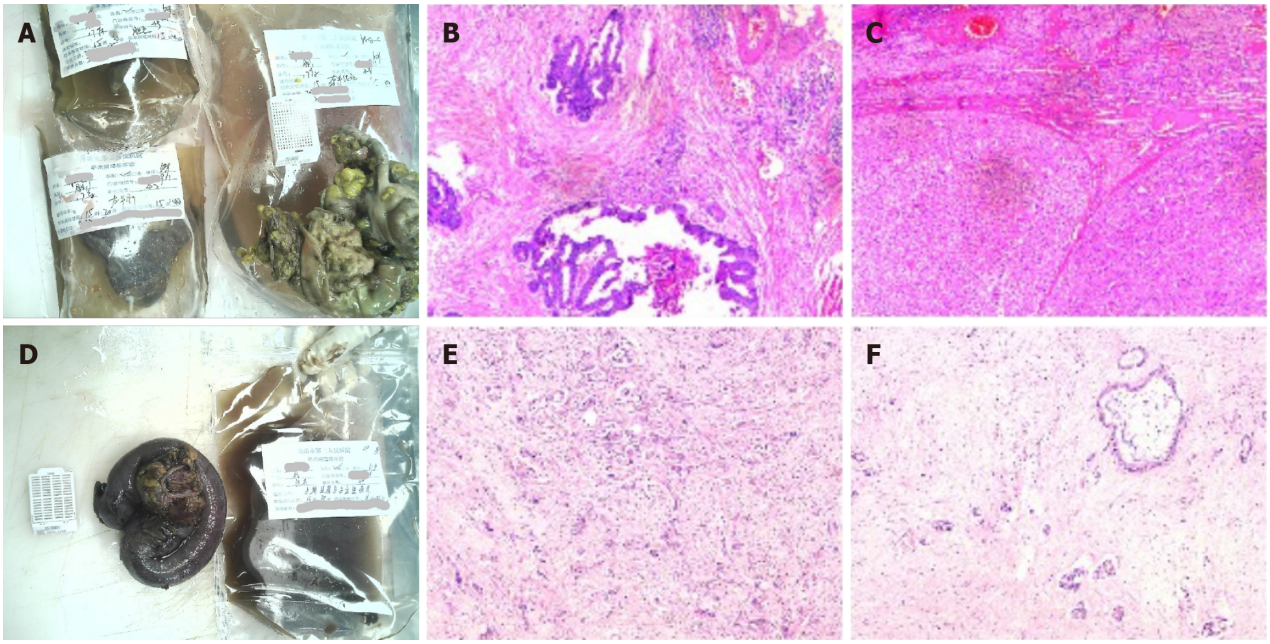


Figure 2 Schematic diagram of the pathological results of the lesions after the first and second operations. A: Gross images of the first surgery

specimen; B and C: Light microscopic images of the first surgery specimen with the following immunohistochemical results: CD34+, D2-40+, CK7-, CK19-, hepatocyte+, CD34+, endothelial vascularization of hepatic sinusoids, carcinoembryonic antigen-. Pathological diagnosis: (Right hemicolon) low-moderately differentiated adenocarcinoma infiltrating the plasma membrane layer in the fibro-fatty tissues (there was choroidal carcinoma embolus and there were no nerve invasion, negative margins, or metastasis in the lymph nodes); (left liver) moderately differentiated hepatocellular carcinoma (there was no choroidal carcinoma embolus or nerve invasion, negative margins, or cirrhotic changes); D: Gross images of the second surgical specimen; E and F: Light microscopic images of the second surgical procedure. The immunohistochemical results were as follows: Tumor cells CK7+, CK20-, villin+, hepatocyte few cells+, glypican-3-, CK8/18+, CDX2 few+, D2-40 lymphatic vessels+, CD34 vascular+, Ki67 hotspot area+ in about 50%-60%. Pathological diagnosis: (Terminal ileum and occupying lesion) moderately-lowly differentiated adenocarcinoma (the tumor invaded the intestinal wall tissue from the plasma membrane upward and focally invaded the mucosal musculature. Combined with the history and immunohistochemistry results, the colonic origin and hepatocellular carcinoma origin were not supported at this time, and pancreatic origin was considered. Moreover, vascular cancer embolism and nerve invasion could be observed in the interior).

FINAL DIAGNOSIS

He was diagnosed with cystadenoma of the pancreas and double-origin cancer of the liver and colon.

TREATMENT

He underwent total fluorescence laparoscopic hepatic segmental 2 resection and radical surgery for right hemicolonic cancer. His operation proceeded smoothly and lasted for 4 h. The volume of blood lost due to bleeding was approximately 100 mL, and he was discharged 12 d after the surgery. The intra-operative images and operation schematic diagrams are presented in Figures 4 and 5. The patient underwent regular postoperative follow-ups, regular oral lenvatinib therapy, and 12 cycles of single oral gemcitabine chemotherapy. Two years post-surgery, the patient was re-admitted to the hospital due to recurrent abdominal pain and diarrhea that had lasted for 1 wk. The patient was not suitable for conservative treatment because of his poor condition; therefore, intestinal resection was performed. The site of the obstruction was observed during surgery (Figure 3F).

OUTCOME AND FOLLOW-UP

The patient recovered well after the operation and underwent the FOLFIRINOX chemotherapy program 1 month after the surgery. Currently, his condition is stable, and he is being followed up further. Furthermore, we provided the key indicators during follow-up and the timeline of the disease progression in Figures 6 and 7.

DISCUSSION

Owing to its dual blood supply, the liver is a common metastatic organ for malignant tumors, accounting for approximately 40% of all malignant tumors, with colorectal cancer being the most common source. Although the vast majority of colon and liver tumors reported simultaneously in clinical settings are liver metastases from intestinal cancer sources, the incidence of multi-origin cancers has increased in recent years, and dual primary malignant tumors of the liver and colon also exist simultaneously[8]. The postoperative pathology and immunohistochemistry of our patient confirmed that the two tumors were primary tumors without a clear basis for metastasis. Moreover, the canceration of the patient's original cystadenoma in the tail of the pancreas involved the original intestinal-intestinal anastomosis and led to intestinal obstruction after 2 years of follow-up. This has not been reported in the domestic and international literature. Data have shown that the prognosis of concurrent MPC is worse than that of heterochronous MPC and solitary carcinoma. Moreover, tumor treatment is an important independent prognostic factor.

First, in the face of multi-site tumor lesions, doctors should break through the inertia of diagnosis and treatment thinking, and target screening for multi-source cancer should be considered. They should also avoid thinking subjectively regarding metastatic cancer and conducting non-surgical interventions. Even when it is uncertain whether the patient's systemic condition can tolerate simultaneous surgeries, active surgical interventions can be considered, and adjuvant treatments can be performed after the surgery. In our case, further exclusion of microscopic metastases and anatomical resection of the liver by fluorescent laparoscopy and three-dimensional reconstruction, intra-operative ultrasound, and fluorescent staining techniques were performed to achieve surgical refinement. Doctors should prioritize malignant lesions. Furthermore, the patient's condition and malignant foci of the liver and colon can be assessed simultaneously. Pancreatic foci were considered to be benign and asymptomatic, which, on balance, could be temporarily left untreated.

Second, the standardization of multi-source cancer surgery is a key factor in determining patient prognosis. For each part of the tumor, with the help of advanced equipment and under the guarantee of patient safety, doctors can achieve refined R0 resection and carry out standardized lymph node dissection. In the presence of stenosis of the original anastomosis, it is important not to blindly assume that it is caused by the recurrence of the original lesion, which, in this case, was ultimately confirmed to be caused by pancreatic cancer invading the original anastomosis.

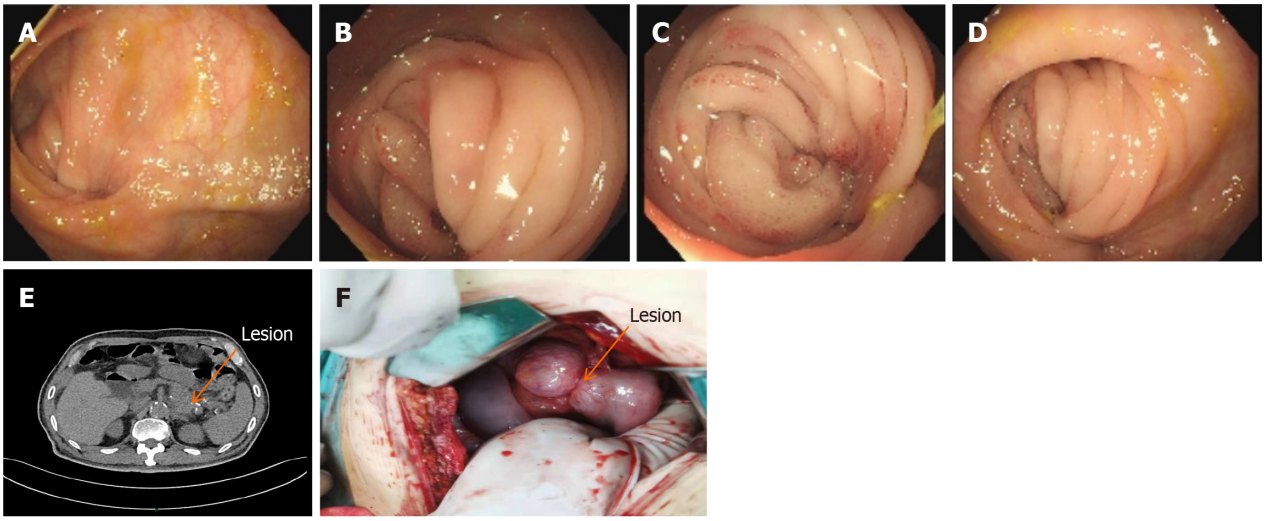


Figure 3 Schematic diagram of the colonoscopic and abdominal computed tomography results before the second operation and the lesion during the operation. A-D: Entering the scope 70 cm from the anus. Anastomotic changes were visible. There was mucosal congestion and entanglement, and it was difficult to enter the scope; E: Dilatation and pneumatization of the bowel in the upper abdomen. When wide and large air-fluid planes could be seen, intestinal obstruction was considered. When the original lesion in the tail of the pancreas was enlarged compared with the previous one with unclear borders, cystadenoma was considered; F: Intra-operatively, the original anastomosis was found to be entangled and narrowed, and the posterior pancreatic lesion invaded the original anastomosis, which was confirmed by pathological examination.

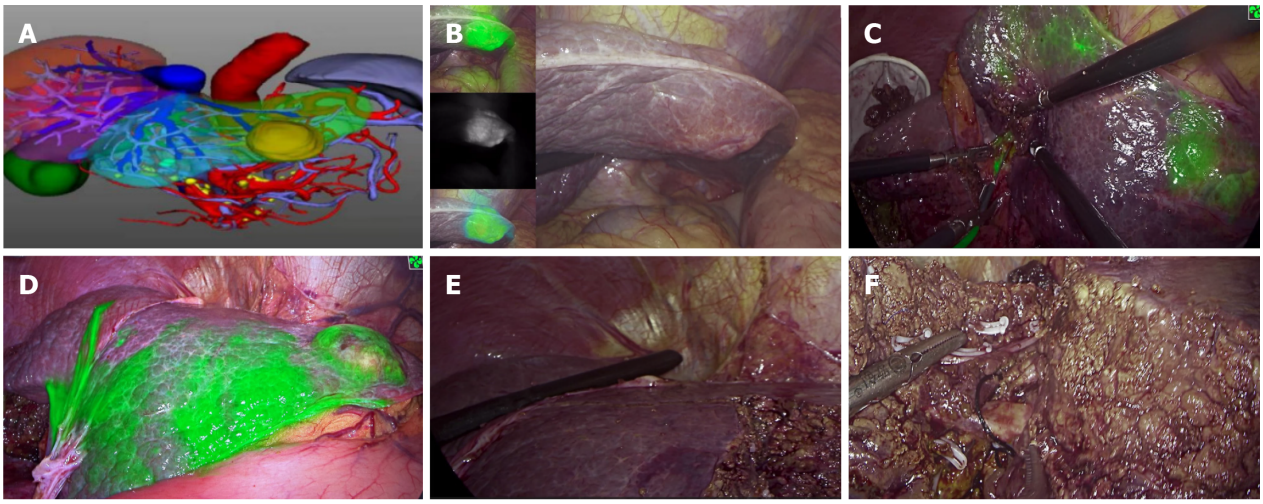


Figure 4 Intraoperative images during the first operation. A: Preoperative three-dimensional reconstruction for the watershed analysis; B: Different fluorescence modes of liver lesions were visualized, and micrometastases in the liver could be screened simultaneously; C: Indocyanine green was injected into the portal watershed of the S3 segment, and the S3 segment was stained; D: The tumor boundary and boundaries of the S3 and S2 segments were clearly visible; E: Intra-operative ultrasonography was used to investigate the remaining part of the liver. Simultaneously, the location and course of the left hepatic vein were investigated with the aid of ultrasonography, which ensured that the left hepatic vein was intact and exposed; F: Cross-section of the liver after resection of segment S2. The morphology and course of the left hepatic vein could be clearly seen.

In addition, multigenic cancers require strict follow-up and subsequent postoperative treatment. This typical case suggests that after surgery for simultaneous dual-origin cancer, there is still the possibility of heterochronic multiple-origin cancer, which requires clinical attention. Moreover, individualized regimens of immunotherapy, targeting, and chemotherapy can be formulated based on the results of genetic testing. This case suggests that irregular postoperative follow-up and missed visits may prevent physicians from noting the optimal treatment time for heterochronic multigenic cancers.

CONCLUSION

There is an urgent need to learn more about MPC and clarify the nature of the tumor through advanced surgical means. This can help ensure better diagnosis and treatment, which will benefit patients with MPC by allowing them to receive a

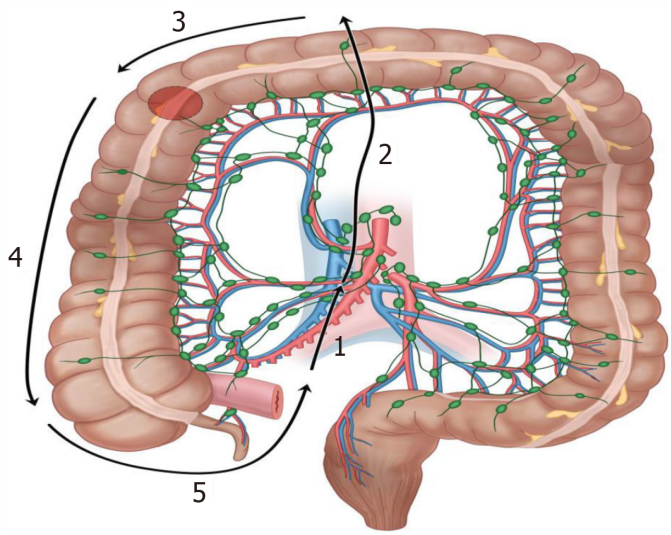
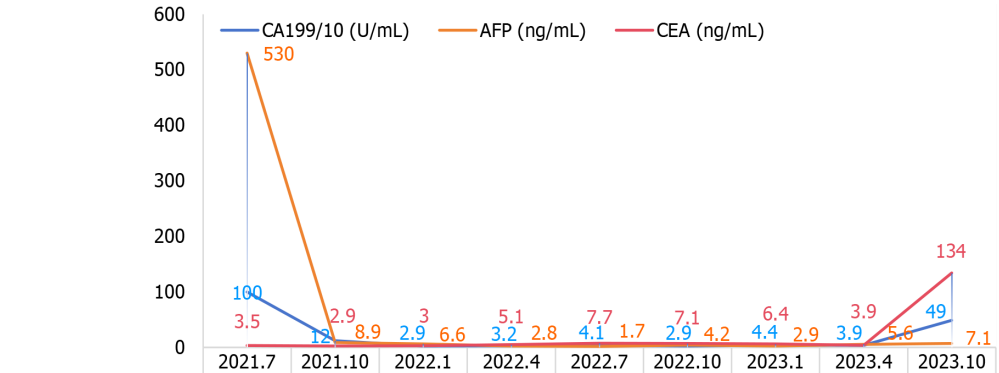


Figure 5 Schematic diagram of the unidirectional loop laparoscopic radical right hemicolectomy pathway for right hemicolectomy using the caudal medial approach during the first operation. 1: Dissect the terminal ileocecal mesentery; 2: Sweep the surgical trunk; 3: Dissect the gastrocolic ligament; 4: Spare the right lateral peritoneum; 5: Free the ileocecal region.



	2021.7	2021.10	2022.1	2022.4	2022.7	2022.10	2023.1	2023.4	2023.10
CA199/10 (U/mL)	100	12	2.9	3.2	4.1	2.9	4.4	3.9	49
AFP (ng/mL)	530	8.9	6.6	2.8	1.7	4.2	2.9	5.6	7.1
CEA (ng/mL)	3.5	2.9	3	5.1	7.7	7.1	6.4	3.9	134

Figure 6 Schematic diagram of the trends of carbohydrate antigen 199, alpha fetoprotein, and carcinoembryonic antigen indices in the follow-up of the disease course. CA199: Carbohydrate antigen 199; AFP: Alpha fetoprotein; CEA: Carcinoembryonic antigen.

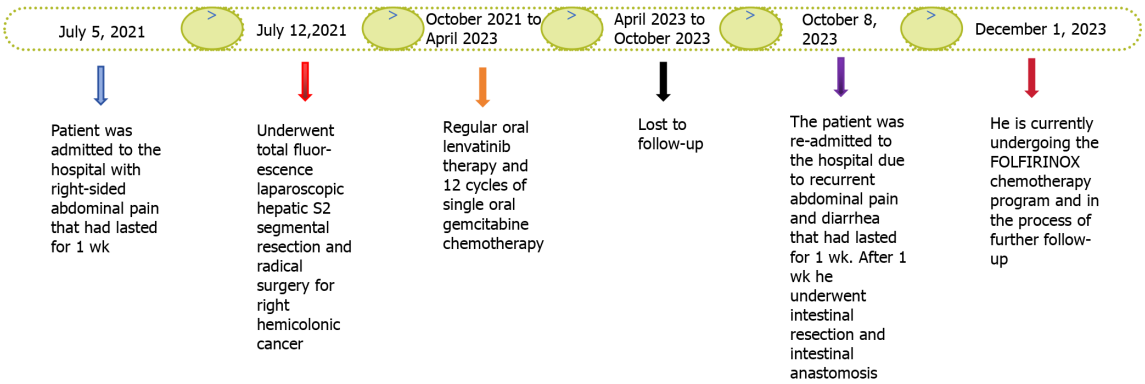


Figure 7 Timeline of the disease progression.

more rigorous diagnostic and treatment plan, improving the probability of survival. However, data on the influence of comprehensive treatment after simultaneous multiple primary carcinoma surgeries on the occurrence of metachronous multifocal carcinoma are still lacking.

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