Isolated Synchronous Multiple Splenic Metastases From Rectal Cancer: a Case Report and Review of the Literature

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Case report

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Abstract

Background: Isolated splenic metastasis emanating from colorectal cancer is an extremely rare finding, which usually indicates widely disseminated and multiple metastatic cancer. There have only been 39 cases of isolated splenic metastasis reported in the English literature to date.

Case presentation: We report a case of synchronous and isolated multiple splenic metastases derived from rectal cancer. An 84-year-old woman, who presented with and an increased serum carcinoembryonic antigen (CEA) level, was diagnosed with rectal cancer with splenic metastases by abdomen computed tomography (CT). The patient underwent a radical resection of rectal cancer and splenectomy, and the postoperative histopathology confirmed that the splenic lesions were derived from the adenocarcinoma of the rectum. After surgery, the patient recovered well and was recommended for further chemotherapy.

Conclusion: Our findings enrich the database of this rare clinical entity and provide experience in the management of splenic metastasis. In addition to revealing a rare case, we also performed a literature review, including a brief discussion about the atypical isolated splenic metastasis from colorectal cancer (CRC).

Background

Colorectal cancer (CRC) is the third most common cancer worldwide and the fourth leading cause of death(1, 2). In particular, CRC-related mortality in elderly patients is very high, even after radical surgical resection and new chemotherapy treatments(2). During clinical examination and diagnosis, most patients with CRC present tumor metastasis to regional lymph nodes, liver, lung, bone, and brain(2, 3). However, unlike the above sites, the spleen consists of a mass of lymphoid tissue, thus both the primary and metastatic tumors of the spleen are considered to be exceptions(4). More specifically, the rarity of splenic metastasis can be explained by the special anatomical structure and immunological features of the spleen(5). Splenic metastasis has been discovered from primary tumors of liver, breast, colorectum, lung, and ovarian cancer; however, the most common is from melanoma(6, 7). In this context, isolated splenic metastasis derived from colorectal carcinoma is even rarer, and is usually reckoned as part of disseminated metastatic disease(8). Based on the formation time of metastasis, splenic metastasis can be divided into synchronous and metachronous metastasis. Synchronous metastasis means that the splenic lesion is discovered by imaging studies together with the primary tumor; however, the diagnosis of metachronous metastasis is usually made during the follow-up of patients in the post-surgical period. Most patients with splenic metastasis are asymptomatic. To date, only a few cases have presented with spontaneous rupture of the spleen and splenic abscess(9). For example, one patient presented with abdominal pain, hyperpyrexia (40 °C), shaking and chills. Further clinical examination discovered synchronous isolated splenic metastasis and a concomitant splenic abscess(10). In the present study, we report a case of synchronous splenic metastasis in an 84-year-old woman, which was derived from a moderately differentiated adenocarcinoma of the rectum.

Case Presentation

An 84-year-old female patient came to our department with dark-red bloody stool that has persisted for one month. The patient also complained of abdominal pain and abdominal distension. She had no symptoms of vomiting, diarrhea, fever, or weight loss, and there was no splenomegaly and hypersplenism. Her blood pressure was 125/60 mmHg and the pulse rate was 56/min. Other physical examinations were normal. She denied any history of cancer, hypertension, and diabetes. She had a surgery history of cholecystectomy two years previously in our hospital.

The preoperative laboratory examinations demonstrated total white blood cells(WBC)of 2.7×10^9/L (normal: $(3.5–9.5) \times 10^9$/L) and total protein (TP) of 58.1 g/L (normal: 65–85 g/L). The serum levels of alpha-fetoprotein and carbohydrate antigen 19 – 9 (CA19-9) were within normal limits, except for carcinoembryonic antigen (CEA), which was 57.57 ng/mL (normal 0–3 ng/mL). A colonoscopy showed a rectal mass located 3 cm from the anal margin, which was 45 mm in diameter, with surface depression, erosion, and a propensity for bleeding. The tumor prevented endoscope insertion for further examination of the intestines. The histopathological results revealed that the tumor was a moderately differentiated adenocarcinoma. The abdomen enhanced computed tomography (CT) revealed wall thickening of the upper rectum (Fig. 1C) and multiple low-density shadows in the spleen (Fig. 1B), among which the largest diameter was 39.2 mm (Fig. 1A). The radiologist suspected a rectal tumor with splenic metastasis. Magnetic resonance imaging (MRI) showed irregular wall thickening of the middle and upper rectum, and the rectal lesion was about 59 mm from the anal margin. The clinical-stage assessed by MRI before surgery was cT3N1 (Fig. 1D, E and F).

Subsequently, the patient underwent a radical resection for rectal cancer and splenectomy after a series of preoperative tests. Intraoperatively, we did not find any metastasis and dissemination to other organs. Therefore, a subtotal proctectomy with side-to-side sigmoid colon-rectum anastomosis was performed. The postoperative histopathological results confirmed that the splenic lesions were consistent with adenocarcinoma of the rectum (Fig. 2), which supports the diagnosis of isolated splenic metastasis.

Intraoperatively, seventeen lymph nodes were removed; however, there was no metastasis and the postoperative pathological stage was pT3N0M1 (stage IV). On postoperative day 15, the CEA level dropped to 10.13 μg/L, and the patient was finally discharged. The patient was recommended for further chemotherapy; however, the postoperative course was uneventful.

Discussion

Tumor metastasis is a complex process, which is influenced by anatomical structures, mechanical factors, the immunological tissue microenvironment, and the intrinsic characteristics of tumor cells(11). Compared with the liver, lung, and kidney, metastatic tumors of the spleen are difficult to implant, which might be caused by its specific anatomical factors and immune surveillance functions. Especially for rectal cancer, it is difficult to form a splenic metastasis by blood vessel invasion. On the one hand, the venous blood flow above the dentate line can directly flow into the splenic vein through the inferior mesenteric

artery, and then enter into the portal vein system. Thus, the blood flow is from the spleen to the liver, and the retrograde venous blood from the portal vein system to the spleen is very rare, making it difficult for tumor cells to reach the spleen. On the other hand, the venous blood flow below the dentate line is capable of flowing into the inferior vena cava through the internal iliac vein and internal pudendal vein, making it is almost impossible to directly enter the vasculature of the spleen. In addition, the acute angulations of the spleen artery and the rhythmic contraction of the splenic capsule significantly limit the ability of the tumor embolus to implant in the spleen(12). Besides, the reticuloendothelial system of the spleen is capable of inhibiting tumor cell proliferation. Furthermore, the lack of afferent lymphatics also limits lymphogenic metastases. More interestingly, some researchers proposed that splenic cells possess a phagocytic capability and are capable of producing anti-tumor substances, which can effectively inhibit the progression of tumors(13). Significantly, one study also proposed that although disseminated cancer cells can easily reside in splenic parenchyma, the special microenvironment of the spleen may suppress the growth and progression of these cells(4). Consequently, the splenic micrometastatic foci cannot be detected through traditional clinical methods, resulting in the clinically detectable isolated metastases of the spleen being reported as 4.4% for colon cancer and 1.6% for rectum cancer(14). In comparison, the incidence of splenic micrometastases at autopsy is approximately 7.1%(15).

Splenic metastasis has to be distinguished from the primary splenic lesion, such as malignant lymphoma, vascular tumors, infections disease, septic emboli, and granulomatous diseases(4). Recently, with the development of medical imaging techniques, such as positron emission tomography (PET)-CT and PET-magnetic resonance imaging (MRI), it has become easier to detect splenic metastases, thereby increasing their apparent incidence. Consequently, it is important to trace the patient's disease history, in which a history of malignancy increases the possibility of splenic metastasis(16). Interestingly, one study reported a patient with rectosigmoid adenocarcinoma with splenic lesions; however, the postoperative pathological diagnosis revealed a primary splenic malignant lymphoma(17). Therefore, histopathology remains the gold standard for diagnosis.

In this study, we analyzed 39 previously published cases (22 male, 17 female; age range, 33 to 84 years; mean, 64 years) of isolated splenic metastasis derived from CRC (Table 1(2)[,(7),(5, 8, 10, 14, 18–47)]). Among them, 35 cases were metachronous metastasis and only 4 cases were synchronous metastasis. Interestingly, in terms of splenic lesions, there were only 4 cases of multiple metachronous splenic metastases, and most cases (35) were solitary. In this study, we described the first case of a synchronic splenic metastasis from a malignant tumor of the rectum. Our case was also (47)previous reports.

Table 1
Isolate splenic tumor metastasis derived from CRC.

No	Ag/Gender	Primary tumor site	Stage	Size (cm)	Synchronous/Metachronous	DFI	Solitary/ Multiple	CEA ng/mL	Imaging	Treatment	The prognosis
1	48/F	sigmoid	III	0.4-3	Metachronous	21 month	Multiple	206.8	PET and MRI	S, Cmt, TT	7 month alive
2	73/M	hepatic flexure	IV	5.7	Synchronous	NA month	Solitary	6.9	CT	S, Cmt	6 month alive
3	76/F	descending	III	1.6	Metachronous	28 month	Solitary	NA	PET	S, Cmt	21 month alive
4	84/F	cecum	III	8	Metachronous	5 month	Solitary	205	CT and MRI	S	NA
5	53/M	sigmoid	NA	NA	Metachronous	12 month	Solitary	NA	PET	S, Cmt	36 month died
6	59/M	descending, sigmoid	NA	NA	Metachronous	3 month	Solitary	NA	PET	S, Cmt	12 month alive
7	64/F	cecum	I	4.9	Metachronous	6 month	Solitary	38	CT	S, Cmt	10 month alive
8	62/F	sigmoid	III	3–6	Metachronous	36 month	Multiple	NA	CT	S. Cmt	10 month alive
9	74/M	descending	IV	7.5–8.5	Synchronous	NA	Multiple	242	CT	S, Cmt	NA
10	74/M	cecum	III	7	Metachronous	36 month	Solitary	38.6	PET	S, Cmt	12 month alive
11	58/M	cecum	III	3.5–5.5	Metachronous	20 month	Solitary	4.62	PET	Cmt	7 month alive
12	70/M	splenic flexure	III	10	Metachronous	24 month	Solitary	NA	CT	S, Cmt	12 month alive
13	73/M	hepatic flexure	III	1,5	Metachronous	62 month	Solitary	132	CT-PET	S, Cmt	36 month alive
14	52/F	sigmoid	III	4.5	Metachronous	37 month	Solitary	16	PET	S, Cmt	NA
15	69/F	sigmoid	II	4	Metachronous	24 month	Solitary	20	CT	S, Cmt	60 month alive
16	80/F	transverse	III	8	Metachronous	9 month	Solitary	52.3	NA	S	NA
17	54/F	splenic flexure	III	4,5	Synchronous	NA	Multiple	31.1	CT	S, Cmt	NA
18	52/M	sigmoid, rectum	II	13	Metachronous	72 month	Solitary	7.2	CT	S, Cmt	22 month alive
19	76/M	splenic flexure	III	6.5	Metachronous	14 month	Solitary	95	CT and PET	S	12 month alive
20	52/F	sigmoid	NA	NA	Metachronous	24 month	Solitary	rise	CT	S	22 month died
21	62/M	sigmoid	II	3	Metachronous	25 month	Solitary	NA	CT	S	21 month alive
22	65/M	ascending	II	5	Metachronous	36 month	Solitary	10.9	CT	S	18 month alive
23	78,F	rectum	III	18	Metachronous	48 month	Solitary	64	CT	S	84 month alive

F: female; M: male

DFI: disease-free interval between treatment of primary tumor and diagnosis of the spleen metastasis

US: Ultrasonography; LSS: Liver splenic scintigraphy; CT: Computed tomography; PET: Positron emission tomography; MRI: Magnetic resonance imaging

S: Surgery; Cmt: Chemotherapy; TT: Target therapy

NA: not available.

No	Ag/Gender	Primary tumor site	Stage	Size (cm)	Synchronous/Metachronous	DFI	Solitary/ Multiple	CEA ng/mL	Imaging	Treatment	The prognosis
24	72,M	sigmoid	III	9	Metachronous	48 month	Solitary	106	LSS	S	6 month alive
25	81,M	cecum	III	NA	Metachronous	30 month	Solitary	7.5	LSS	S	12 month alive
26	51,F	rectum	II	2.8	Metachronous	51 month	Solitary	13.5	CT	S	14 month alive
27	72,F	descending	II	3	Metachronous	144 month	Solitary	223	CT	S	12 month alive
28	62,F	descending	III	4	Metachronous	42 month	Solitary	rise	CT	S	12 month alive
29	74,M	sigmoid	II	9.5	Metachronous	24 month	Solitary	23.4	CT	S	24 month alive
30	52,M	ascending	NA	NA	Metachronous	12 month	Solitary	NA	US and CT	S	6 month alive
31	48,M	ascending	NA	NA	Metachronous	24 month	Solitary	NA	US and CT	S	3 month alive
32	33,F	sigmoid	III	3.5	Metachronous	3 month	Solitary	9	CT and MRI	S	12 month alive
33	51,M	sigmoid	III	13	Metachronous	72 month	Solitary	NA	CT	S	6 month alive
34	72,M	rectum	III	NA	Metachronous	18 month	Solitary	rise	CT	S	NA
35	59,M	ascending	III	4	Metachronous	15 month	Solitary	37	CT	S	24 month alive
36	78,M	cecum	III	7	Metachronous	37 month	Solitary	38.6	CT and PET	S, Cmt	9 month alive
37	76,F	descending	III	1.6	Metachronous	24 month	Solitary	NA	PET	S, Cmt	21 month alive
38	62,M	sigmoid	III	3.5	Metachronous	23 month	Solitary	2.5	US and CT	S	19 month alive
39	52,F	descending		5	Synchronous	NA	Solitary	rise	CT	S	12 month died

F: female; M: male

DFI: disease-free interval between treatment of primary tumor and diagnosis of the spleen metastasis

US: Ultrasonography; LSS: Liver splenic scintigraphy; CT: Computed tomography; PET: Positron emission tomography; MRI: Magnetic resonance imaging

S: Surgery; Cmt: Chemotherapy; TT: Target therapy

NA: not available.

Among these cases, based on their primary tumor sites, we observed that the most common lesion was in the sigmoid colon (12 cases), accounting for 30.8%. In comparison, the two most uncommon sites were the transverse colon in one case and the hepatic flexure in two cases. Others included six cases in the cecum, four cases in the ascending colon, three cases in the splenic curvature, six cases in the descending colon, and three cases in the rectum. In particular, two patients presented with multiple primary cancers. For the one patient, the primary tumors were found in the descending colon and sigmoid colon together, and the tumors of the other patient were located in the sigmoid colon and rectum. Based on these findings, we deduced that the primary tumors of splenic metastasis are most commonly found in the left hemi-colon in 24 cases, accounting for 61.5%, which might reflect the fact that these tumor cells can enter counter-currently into the splenic vein via the inferior mesenteric vein. In terms of primary tumor stage (1 case with stage I, 7 cases with stage II, 23 cases with stage III, 3 cases with stage IV, and 5 cases in which the stage was not mentioned), indicating that most isolated splenic metastasis is derived from the median or advanced colorectal cancer.

Among reported cases, 29 of the 39 patients presented with an elevated CEA level. In accordance with the above results, the CEA level reached a maximum of 57.57 ng/mL in our case. In terms of cases of metachronous splenic metastasis cases, the disease-free interval ranged from 3 to 144 months (average, 31.7 months). In addition, for most of the patients, the isolated splenic metastases were found during postoperative follow-up by radiological examinations, such as abdomen computed tomography (CT), magnetic resonance imaging (MRI), ultrasound (US), fine-needle aspiration, and even fluorodeoxyglucose-positron emission tomography (FDG-PET). According to the literature, only one patient did not undergo curative splenectomy. For most patients, splenectomy and chemotherapy were the two main optimal treatment strategies.

In our case, both the primary rectal cancer and metastasis splenic lesions showed caudal type homeobox 2 (CDX2) expression (Fig. 2). CDX2, a homeobox protein, is believed to be an important factor in maintaining the intestinal phenotype and regulating colorectal tumor metastasis(48). Importantly, we observed that splenic lesions express special AT-rich sequence-binding protein 2 (SATB2) (Fig. 2), which is used as a diagnostic marker of colorectal origin cancer(49). One study found that more than 93% of colorectal origin tumors showed SATB2 positive staining, which was consistent with our results(50).

Conclusion

We reported a case of the rare occurrence of isolated synchronous multiple splenic metastases from rectal cancer. Our findings enrich the database of this rare clinical entity and provide experience in the management of splenic metastasis. To the best of our knowledge, splenic metastasis of colorectal carcinoma is very uncommon. With improvements in examining techniques, increased numbers of patients with isolated splenic metastasis might be found. Over the long term, it is essential to follow up patients with colorectal cancer postoperatively, which could effectively improve the management and prolong the survival of these patients with isolated splenic metastases. The common therapeutics options include splenectomy, chemotherapy, targeted therapy, and radiotherapy. However, to date, only a small number of cases have been reported and long-term follow-up is absent; therefore, standardized clinical treatment strategies for splenic metastasis have not been established. In future studies, more attention should be paid to this rare entity.

Abbreviations

CEA: carcinoembryonic antigen; CT: computed tomography; CRC: colorectal cancer; WBC: white blood cells; TP: total protein; CA19-9: carbohydrate antigen 19-9; MRI: Magnetic resonance imaging; US: ultrasound; FDG-PET: fluorodeoxyglucose-positron emission tomography; CDX2: caudal type homeobox 2; SATB2: special AT-rich sequence-binding protein 2

Declarations

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Not applicable

Authors' contributions

Linxian Zhao: project development, data analysis, and writing the manuscript. Lanqing Cao: pathological diagnosis. Fengwen Cui: project development and data analysis. Wei Li: writing and editing the manuscript. Tongjun Liu and Kai Zhang: editing the manuscript. Jiannan Li: project development, surgical procedures and editing the manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Competing interests

The authors declare that they have no competing interests

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Figures

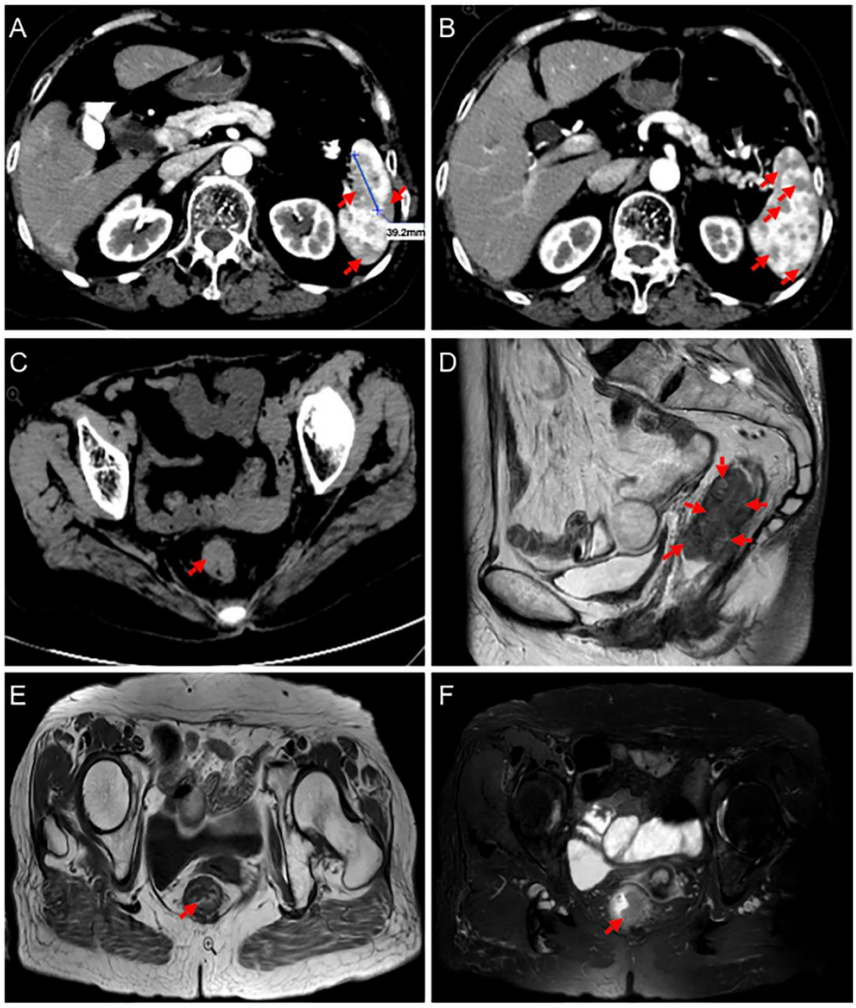

Figure 1

Imaging examinations of the spleen and the rectum. A and B: Abdomen enhanced computed tomography (CT) showing multiple low density shadows in the spleen (red arrow) , the largest diameter of which is 39.2 mm (blue lines). C: Abdomen CT showing wall thickening of the upper rectum (red arrow). D: Magnetic resonance imaging (MRI; T2W-TSE-HR) showing that the cumulative length of the tumor was about 57 mm, the lower margin of the tumor was higher than the rectal ring, and the distance from the anorectal ring was about 20 mm (red arrow). E: MRI (TSE-Axial) showing irregular wall thickening of the middle and upper rectum, and the rectal lesion is about 59 mm from the anal margin (red arrow). F: MRI (T2W-SPAIR-tra) showing a slightly high signal of the rectal lesion (red arrow).

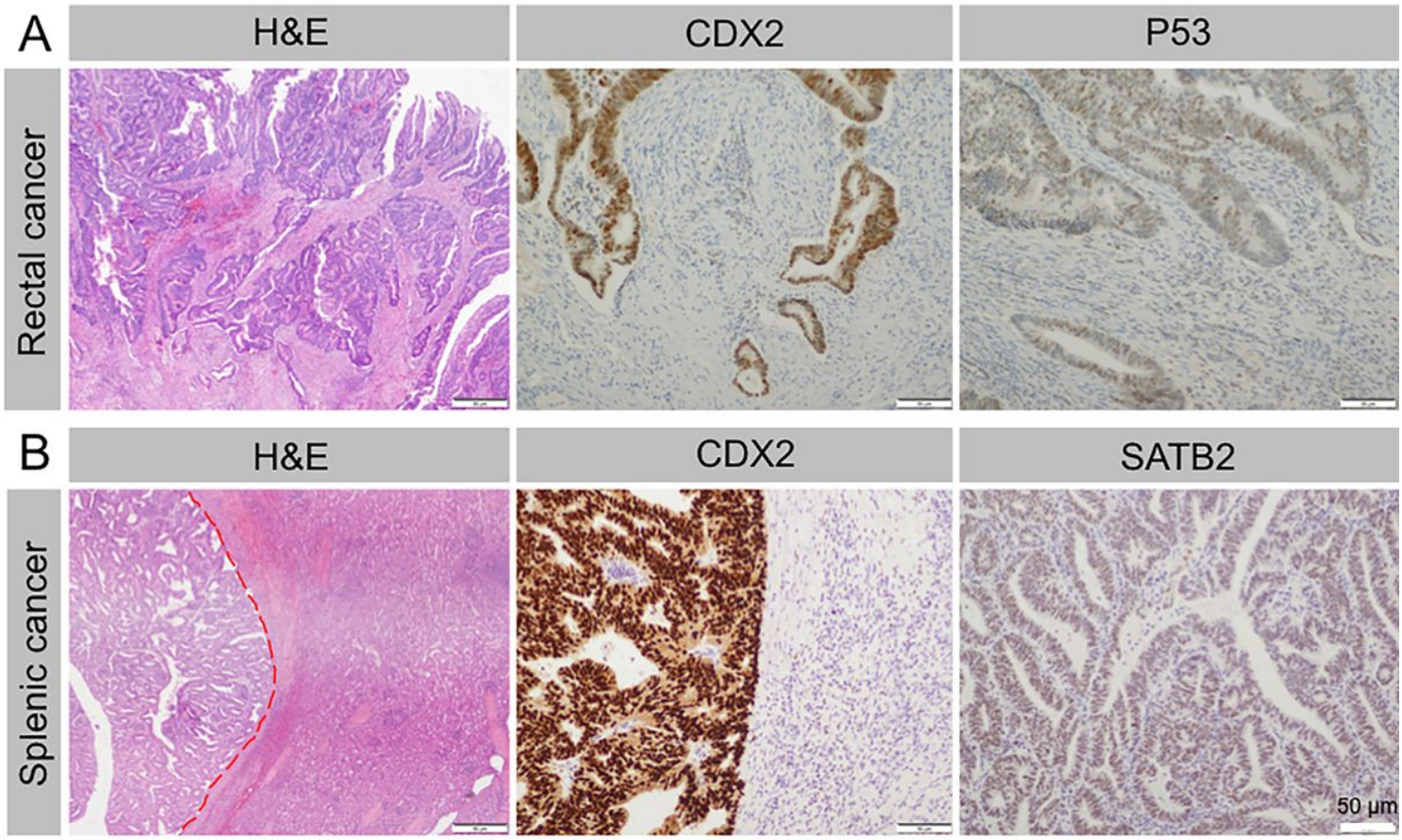

Figure 2

Histological findings of the primary rectal cancer (A) and splenic metastasis (B). A: Moderately differentiated adenocarcinoma (HE, ×50); CDX2 positively expressed (CDX2, ×50); P53 gene mutation positive (P53, ×50) B: Splenic tumor showing glandular pattern consistent with metastasis from rectal cancer (HE, ×50); CDX2 positively expressed (CDX2, ×50); SATB2 positively stained (SATB2, ×50)