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Pelvis metastasis with rectal infiltration in hepatocellular carcinoma - a rare case report

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ABSTRACT

Background: Hepatocellular carcinoma (HCC) is the most prevalent primary hepatic neoplasm, with approximately 50% of cases eventually developing metastasis. HCC metastasis to the pelvis is exceedingly rare due to the significant anatomical distance and intricate metastatic pathways involved.

Case Presentation: In this case report, we present a 60-year-old male with HCC metastasis to the pelvis that had infiltrated the rectum. Initially, we suspected the pelvic mass to be a gastrointestinal stromal tumor, but histopathological and immunohistochemical examinations revealed it to be HCC metastasis. The dissemination of the tumor was suspected to have occurred through peritoneal implantation following a radiofrequency ablation (RFA) procedure that the patient had undergone 10 months prior. A resection surgery of the sigmoid colon up to the tumor-free mid-rectum was performed. The patient is currently stable and undergoing routine outpatient care, now in the third-month post-surgery.

Conclusion: This case report unveils a rare HCC metastasis to the pelvis with rectal infiltration. We conclude that in HCC patients presenting with obstructive symptoms, suspicion of metastasis to the pelvis should be considered, especially in patients who have undergone an RFA procedure. Limited diagnostic support from computed tomography scans and colonoscopies made establishing a definitive diagnosis before surgery challenging. However, patients can attain a favorable prognosis with effective surgical intervention, underscoring the importance of prompt and effective treatment in such cases.

Keyword: Carcinoma, hepatocellular, neoplasm metastasis, pelvis, rectum, case reports.

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Background

Hepatocellular carcinoma (HCC) constitutes the preeminent primary malignancy of the liver and represents the most pervasive subtype of primary hepatic neoplasms, accounting for an overwhelming 90% of all primary hepatic tumors. Globally, HCC ranks fifth among the most prevalent cancers, with an unfortunate distinction as the second leading cause of cancer-related mortality in males, trailing only lung carcinoma [1]. Asia and Africa bear the heaviest burden of HCC incidence, with male populations exhibiting an incidence rate 2-4 times higher than their female counterparts. Notably, infection with hepatitis B virus and hepatitis C virus (HCV) emerges as a prominent etiological factor, conferring a considerable 10%-20% risk of HCC development in afflicted individuals [2].

Extrahepatic metastasis afflicts a substantial proportion, roughly 30%-50%, of patients diagnosed with HCC. This spread occurs via hematogenous or lymphatic routes, often manifesting in the lungs, intra-abdominal lymph nodes, skeletal structures, spleen, adrenal glands, central nervous system, pleural space, and kidneys [3,4]. However, in recent years, rare metastatic locations of HCC have been reported, including the auricle, musculature, bone marrow, gingiva, nasal cavity, integumentary tissue, parotid gland, seminal vesicle, pharynx, and nail bed [4].

Metastasis in the pelvis alone is an exceptionally rare event. This rarity is primarily attributed to the considerable anatomical distance from the liver and the complex nature of its metastatic dissemination pathway. The subsequent case report presents a unique case of HCC metastasis to the pelvis, complicated by its infiltration into the rectum, which prompted a provisional diagnosis of a primary gastrointestinal stromal tumor (GIST). To the best of our knowledge, such an occurrence has not previously been reported.

Case Presentation

A 60-year-old male was diagnosed with hepatitis B 20 years ago and has received regular Tenofovir treatment. Three years ago, the patient was diagnosed with HCC in

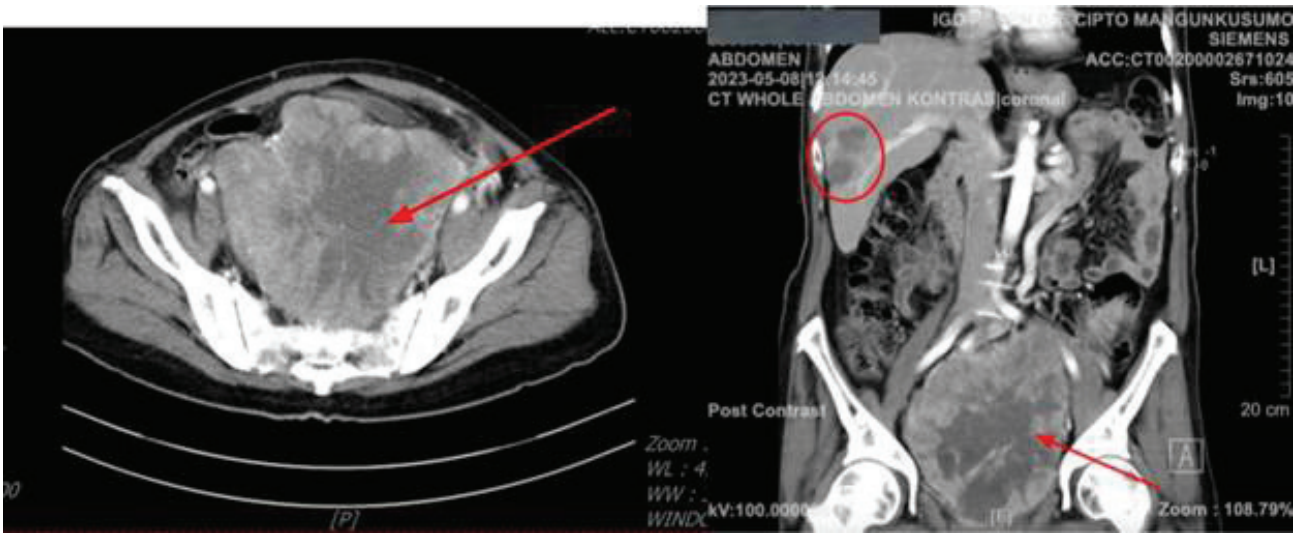

Figure 1. *Abdominal CT scans showed liver nodule (red circle) and pelvic mass (red arrow).*

segment 5 of the liver, measuring 3 × 4 × 5 cm. The patient underwent radiofrequency ablation (RFA) four times, resulting in no viable components remaining.

Ten months after finishing RFA regiments, the patient presented to the hospital complaining of a lower left abdomen mass, pain, weight loss, and obstructive symptoms during urination and bowel movements. There was no history of melena, hematochezia, or vomiting. Physical examination revealed a palpable mass in the left hemiabdomen and suprapubic region. Laboratory results showed PSA 0.39, CEA 1.8, and AFP 1.73, with reactive HBsAg and non-reactive in HCV panels. There was a slight elevation in SGOT (71) and normal SGPT (18) with a PT/APTT ratio of 1.15×. A fibroscan examination showed a value of 5.9 kPa.

An abdominal computed tomography (CT) scan revealed a viable nodule in liver segment 5 measuring 2.8 cm and a solid necrotic mass with characteristic hypervascular features in the pelvis (Figure 1). There were no signs of tumor thrombus in the portal vein or new pathological lesions in other liver segments. Based on these findings, we suspected the pelvic mass to be a rectal GIST. A colonoscopy was performed with no significant findings, except for varices in the rectosigmoid segment and no abnormalities in the colon or cecum mucosa. Three months later, a repeat CT scan showed an enlargement of the solid hypervascular necrotic mass in the pelvis by 60%-87%, with adhesions to the rectosigmoid wall (Figure 1). We performed a repeat RFA for the segment 5 HCC and pelvic mass resection.

During surgery, a solitary pelvic mass that had infiltrated the rectosigmoid segment was found (Figure 2). Therefore, a resection of the sigmoid and rectum to the level of mid-rectum was performed (Figure 3), creating an end stoma of the descending colon (Figure 4). The surgery went well, with intraoperative bleeding of 2,600 ml and an

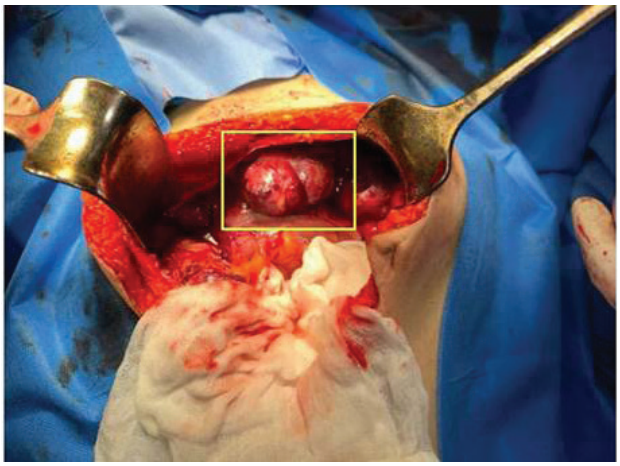

Figure 2. *Tumor located in the pelvis before (yellow square).*

intraoperative complication of a bladder injury that was repaired during the surgery. The bladder injury occurred iatrogenically when attempting to separate the posterior part of the bladder from the anterior part of the tumor. No infiltration was identified in the bladder, both on the CT scan and intraoperatively.

The histopathological examination of the pelvic mass revealed a poorly differentiated carcinoma suspicious for HCC with vascular invasion. In addition, there was infiltration into the muscular layer of the large intestine without involving the mucosal layer. No tumor infiltration was found in the lymph nodes. The immunohistochemical examination indicated positivity for CAM5.2 and glypican 3, partial positivity for HepPar-1 in some cells (Figure 5), local positivity for CK20 and CD56, and limited positivity for AFP, A1/3, and CK19. It showed negativity for the markers CEA, arginase-1, CK7, synaptophysin, chromogranin, CD34, melan A, DOG1, SMA, Desmin, SALL4, Inhibin, and Vimentin. This immunohistochemical profile supported a diagnosis of poorly differentiated HCC.

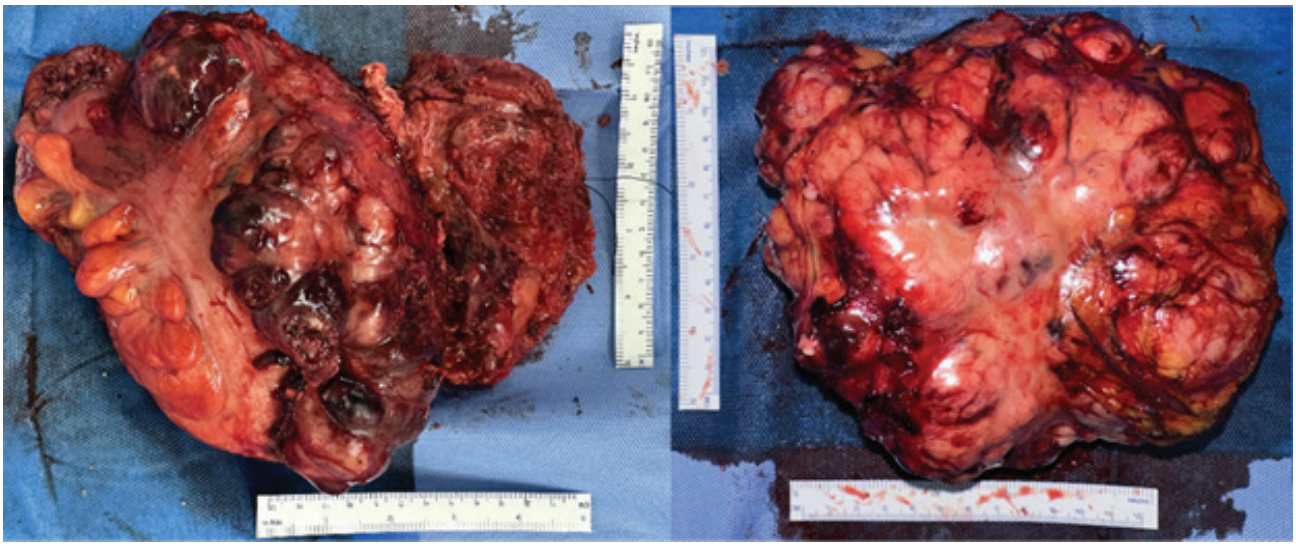

Figure 3. *Tumor excised from the pelvis. The tumor could not be resected in its entirety due to its significant size; hence, we had to divide it into two parts.*

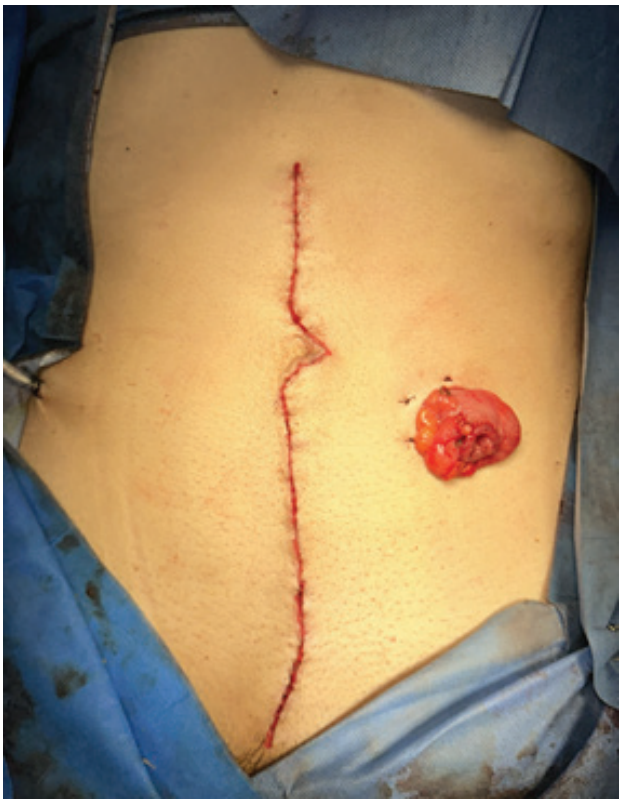

Figure 4. *End colostomy was made after the resection.*

The patient was discharged on the sixth-day post-surgery in stable condition and is presently receiving routine outpatient care.

Discussion

Extrahepatic metastasis in HCC is not uncommon. According to a study by Targe et al. [5] common sites of metastasis in HCC include the lung (39.5%), lymph nodes (34.2%), bone (25.4%), adrenal glands (8.8%), and less frequently, the spleen (0.6%) and breast (0.3%). However, in recent years, numerous reports of HCC metastasizing to uncommon sites have been reported. Boldo et al. [4] documented 15 cases of uncommon HCC metastasis reported over the past decade. Of these 15 cases, only 1 reported HCC metastasis to the uterus that is located in the pelvis. However, in that case report, metastasis to the pelvis was accompanied by metastasis elsewhere, namely the lungs, in contrast to this case report, which indicated the presence of metastasis to the pelvis without any other metastases [4,6]. Moreover, infiltration to the rectosigmoid is even rarer. Previous literature that reported metastasis to the rectal region showed metastasis to the mucosa layer of the rectum, which was also initially diagnosed as primary rectal carcinoma [7]. In this case, however, the tumor infiltrates the serosa layer of the rectum.

In this case report, the patient presented with the primary complaint of a mass in the lower left abdomen, accompanied by pain and obstructive symptoms like constipation and difficulty urinating. These symptoms were clearly attributed to the mass developed in the pelvis and were exacerbated by its infiltration into the rectum. However, it is important to note that the infiltration of the tumor into the gastrointestinal (GI) tract, especially the colorectal region, typically causes symptoms such as bloody stool, as reported in previous literature, rather than the presence of an abdominal mass or obstructive symptoms [7,8]. This difference is due to the location of the tumor's infiltration in the pelvis, which involves the muscular layer of the rectum, as opposed to the mucosal layer as commonly reported in HCC metastasis to the colorectal region.

Extrahepatic metastasis in HCC manifests through various routes, notably hematogenous spread or lymphogenous spread and direct invasion. The majority of distant extrahepatic metastases of HCC (approximately 56%) occur hematogenously or lymphogenously,

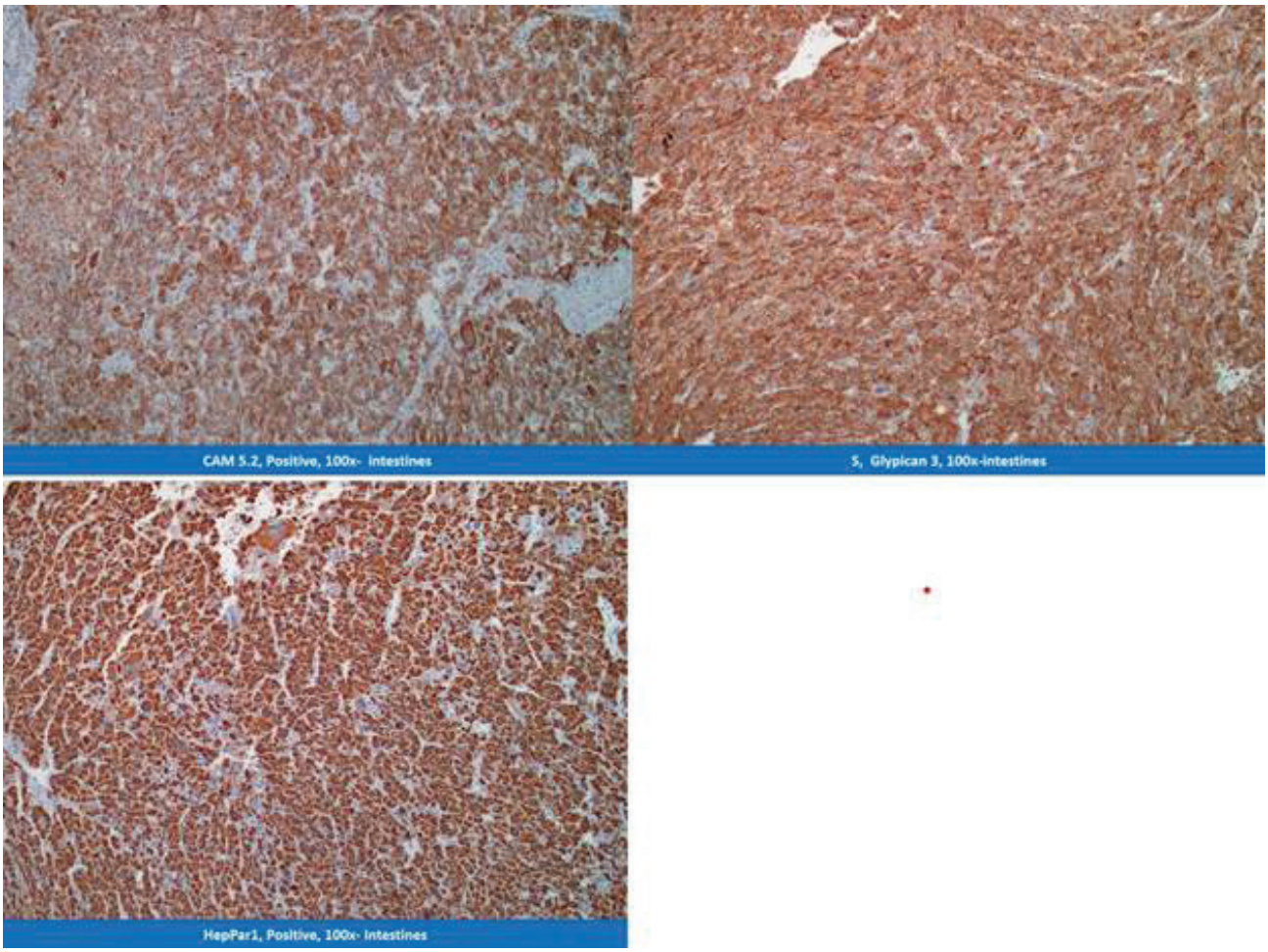

Figure 5. *Immunohistochemistry examination for CAM5.2, Glypican 3, and HepPar1 indicates positivity.*

including metastasis to the pelvis [7-9]. The previous case report indicated metastasis to the uterus via the hematogenous route due to its involvement with pulmonary metastasis [6]. In addition, other case reports that documented colorectal metastasis of HCC also indicated a hematogenous route of metastasis. The hematogenous spread of HCC primarily involves vascular invasion. Tumor thrombosis in the portal vein is a key factor that can lead to alteration in blood flow dynamics, reduced portal blood flow, and reversed retrograde blood flow, allowing HCC to metastasize hematogenously to the GI tract [7-9]. However, the occurrence of retrograde portal flow is not solely linked to the presence of liver cirrhosis [7].

Metastasis through direct invasion is often observed in patients previously undergoing trans-arterial embolization (TAE) or trans-arterial chemoembolization (TACE). These interventional procedures have the potential to incite exophytic growth of HCC, primarily as a result of inflammatory responses and alterations in the tumor's blood supply dynamics [9,10]. Consequently, such exophytic growth may facilitate the direct extension of tumor cells into adjacent anatomical structures. Metastasis via direct invasion is often encountered in cases of metastasis to adjacent structures of the liver, such as the stomach, duodenum, ascending, or transverse colon [8,10].

It is also worth noting that metastasis through peritoneal implantation can manifest, particularly in scenarios involving the rupture of exophytic HCC into the peritoneal cavity. In such instances, the tumor cells may disseminate within the peritoneal space, giving rise to seeding metastasis. This phenomenon is more commonly observed in patients presenting with massive ascites [9].

In this case, the hematogenous spread of the metastatic tumor is less likely, considering the absence of tumor thrombosis in the portal vein as well as signs of portal hypertension. Moreover, the tumor's localization in the serosa layer, rather than the more typical mucosal involvement seen in hematogenous spread to the colon region, further mitigates the plausibility of this mechanism. Direct invasion is also less likely due to the distant location of the metastasis from the primary HCC site.

The possibility of peritoneal implantation becomes more likely, even in the absence of any signs of HCC rupture. A previous study by Liu et al. [11] mentioned the potential for tumor seeding after an RFA procedure, with an interval diagnosis time ranging from 4.8 to 63.8 months following the procedure. In this case, the patient

had undergone RFA 10 months before the diagnosis of tumor seeding, which falls within the previously mentioned range. The possible mechanism behind this phenomenon may involve viable cancer cells being extruded into the pelvis during the RFA procedure or cancer cells being shed during needle withdrawal [11]. It is noteworthy that the CT scan results for the pelvic mass revealed hypervascular and necrotic characteristics, which further support the diagnosis of peritoneal implantation, as previously described in the literature [9].

Several risk factors contribute to neoplastic seeding after the RFA procedure, including subcapsular location, poor tumor differentiation grade, multiple RFA sessions, multiple electrode placements, and needle size. A meticulous approach to RFA should be employed, especially for individuals with these identified risk factors, to minimize the occurrence of this event. Minimizing needle probe repositioning and performing tract ablation during needle withdrawal are also crucial measures. The latter can effectively obliterate any detected tumor cells [11-13].

In this patient, the initial suspicion was that the metastatic tumor resembled a GIST, as seen on the CT scan. GISTs typically exhibit central necrosis, heterogeneous enhancement, cavitation that gives the appearance of gas-like features within the tumor, and an absence of enlarged lymph nodes, as described in previous literature [14]. In the presented case, there was evidence of necrosis without enlarged lymph nodes. The infiltration into the rectum led us to consider the possibility that this tumor originated primarily from the rectum, further strengthening our suspicion of a GIST diagnosis. Furthermore, the exceedingly rare incidence of HCC metastasis to the pelvis led us to conclude that this diagnosis was less likely. However, post-surgery pathology examination as well as immunohistochemistry examination revealed that the tumor in the pelvis was a metastasis from the HCC.

Surgery remains the primary treatment option for HCC metastasis to the pelvis, especially that infiltrates the GI tract, as noted in previous case reports [7,8,10]. TAE or TACE is deemed less effective, while RFA carries a high risk of GI tract perforation. Moreover, the median survival time for patients undergoing surgery for HCC metastasis to the GI tract is higher than other management approaches [10]. In addition, RFA is used only for small tumors, less than 3-5 cm. Therefore, despite the risk of GI tract perforation that may occur, this pelvic mass is too large for RFA, hence RFA was not indicated [15]. Furthermore, we initially suspected this mass to be a GIST, which was also not an indication of RFA.

In this patient, the surgery involved the resection of the sigmoid colon up to the tumor-free mid-rectum, creating a descending colon end stoma. We opted for an end colostomy to anticipate potential tumor seeding in the distal part of the resected colon. In addition, there was significant bleeding amounting to 2,600 cc, as the extensive size of the tumor excised which required more than 10 hours for this surgery. This resulted in intraoperative hemodynamic instability, making it impractical to perform an anastomosis, which would have required a longer duration.

Meanwhile, for the liver mass, we initially planned to resect it simultaneously with the pelvic mass. However, considering the size and the complexity of the pelvic mass resection, we determined that simultaneous resection would cause more harm than benefit to the patient. Therefore, we decided against liver mass resection and instead proceeded with RFA. Subsequent pathology examination revealed that the pelvic mass was a metastasis from the liver, making liver mass resection unnecessary due to systemic metastasis.

Survival times for patients with HCC metastasis to the colorectal region who undergo surgery vary based on previous case reports, ranging from 1 month to over 60 months [7,8,10]. The patient in our case was discharged in stable condition sixth day post-surgery and is presently receiving routine outpatient care, now in the third month.

Conclusion

This case report unveils a rare HCC metastasis to the pelvis with rectal infiltration. We conclude that in HCC patients presenting with obstructive symptoms, suspicion of metastasis to the pelvis should be considered, especially in patients who have undergone an RFA procedure. Limited diagnostic support from CT scans and colonoscopies made establishing a definitive diagnosis before surgery challenging. However, patients can attain a favorable prognosis with effective surgical intervention, underscoring the importance of prompt and effective treatment in such cases.

What is new?

HCC metastasizing to extrahepatic organs is common. However, metastasis to the pelvis is extremely rare. Moreover, pelvic metastases infiltrating the rectosigmoid are even rarer.

List of Abbreviations

AFP	Alpha-fetoprotein
APTT	Activated partial thromboplastin time
CEA	Carcinoembryonic antigen
CT	Computed tomography
GI	Gastrointestinal
GIST	Gastrointestinal stromal tumor
HBsAg	Hepatitis B surface antigen
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
PSA	Prostate-specific antigen
PT	Prothrombin time
RFA	Radiofrequency ablation
SGOT	Serum glutamic oxaloacetic transaminase
SGPT	Serum glutamate pyruvate transaminase
TACE	Transarterial chemoembolization
TAE	Transarterial embolization

Conflicts of interest
The authors declare that they have no conflict of interest regarding the publication of this case report.

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Consent for publication
Written consent was obtained from the parents of the patient.

Ethical approval
Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	Male, 60 years old
2	**Final Diagnosis**	Pelvis metastasis with rectal infiltration in HCC
3	**Symptoms**	Lower left abdominal mass, pain, weight loss, obstructive symptoms during urination and bowel movements
4	**Medications**	-
5	**Clinical procedure**	Resection of the sigmoid colon up to the tumor-free mid-rectum as well as creating a descending colon end stoma
6	**Specialty**	Digestive surgery