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#### **ABOUT COVER**

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#### **AIMS AND SCOPE**

The primary aim of World Journal of Gastrointestinal Oncology (WJGO, World J Gastrointest Oncol) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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.

#### **INDEXING/ABSTRACTING**

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CASE REPORT

### Jejunal sarcomatoid carcinoma: A case report and review of literature

Qian Feng, Wei Yu, Jing-Hui Feng, Qiao Huang, Gui-Xiang Xiao

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#### Abstract

#### BACKGROUND

Sarcomatoid carcinoma (SCA) of the jejunum is a rare and aggressive neoplasm affecting the smooth muscle cells of the jejunum. This study presents a recent case of jejunal SCA, detailing its diagnosis and treatment, thereby providing a reference for clinical practice.

#### CASE SUMMARY

A 65-year-old male presented to Yichang Central People's Hospital with a chief complaint of hemorrhoids. A computed tomography (CT) scan incidentally revealed multiple abnormal signals in the liver. Subsequent positron emission tomography/CT at Wuhan Union Hospital indicated malignant tumor progression, with a primary duodenal tumor and multiple metastases in the upper left abdomen. Intraoperatively, a large tumor was identified on the omentum. Histopathological and immunohistochemical analyses of the resected specimen confirmed the diagnosis of jejunal SCA. The patient received a combination therapy of sintilimab, nanoparticle albumin-bound paclitaxel, and anlotinib. Follow-up imaging demonstrated significant reduction of hepatic and peritoneal lesions. The patient has remained stable for over one year postoperatively.

#### **CONCLUSION**

This case suggests that chemotherapy, immunotherapy, plus targeted therapy may represent an optimal treatment for intestinal SCA, meriting further investigation.



Key Words: Jejunal sarcomatoid carcinoma; Targeted therapy; Immunotherapy; Chemotherapy; Case report

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Core Tip: Sarcomatoid carcinoma (SCA) of the jejunum is a rare and aggressive malignancy. Currently, there are no established treatment guidelines for SCA. This study reports a patient who achieved favorable outcomes with a combination of immunotherapy, targeted therapy, and chemotherapy. A review of the literature was also conducted. We propose that this therapeutic approach may represent a novel treatment option for jejunal SCA.

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#### INTRODUCTION

Sarcomatoid carcinoma (SCA) is a rare neoplasm characterized by both malignant epithelial and mesenchymal components<sup>[1]</sup>. First described by Virchow in 1864<sup>[2]</sup>, the majority of malignant tumors in the small intestine are either adenocarcinomas or neuroendocrine tumors. Primary SCA of the small intestine is particularly uncommon, typically manifesting in the ileum, jejunum, and duodenum. The incidence is approximately 0.5-0.8 cases per 100000 individuals annually[3], with a median age of onset at 57 years, predominantly affecting middle-aged and elderly men[4,5]. Clinical presentation of small intestine SCA is often nonspecific, with common symptoms including abdominal pain, anemia, and bowel obstruction. The tumor usually presents with a polypoid or fungating appearance, occasionally exhibiting ulceration, but frequently accompanied by necrosis and hemorrhage. Computed tomography (CT) scans generally reveal circumferential thickening of the bowel wall or intraluminal rounded soft tissue masses, which may extend to adjacent mesenteric lymph nodes and surrounding tissue. Enhanced CT scans typically show moderate and heterogeneous enhancement. Secondary complications such as bowel obstruction, intussusception, small bowel dilation, and intestinal fistula can also occur. Pathomorphological analysis and immunohistochemical staining remain the gold standards for diagnosing small intestine SCA. Radical surgery is the preferred treatment modality for early-stage disease. Previous studies have indicated that small intestine SCA is largely unresponsive to chemotherapy and radiotherapy, which are reserved for palliative care. Recent research has demonstrated high expression of programmed death-ligand 1 (PD-L1) in small intestine SCA cells[4,5]. Consequently, immunotherapy targeting the PD-L1 pathway may offer potential therapeutic benefits. This article reports on a recent case of small intestine SCA admitted to our hospital. Clinical data are collected and reviewed alongside the relevant literature to enhance clinicians' understanding of this rare disease.

#### **CASE PRESENTATION**

#### Chief complaints

A 65-year-old Chinese man was admitted to our hospital for a hemorrhoidectomy. During a preoperative CT scan, multiple abnormal signals were detected in his liver.

#### History of present illness

The patient, with no prior medical history, was scheduled for a hemorrhoidectomy at our hospital. A preoperative CT scan revealed multiple abnormal signals in his liver. Subsequent magnetic resonance imaging (MRI) at our hospital demonstrated numerous low-density circular lesions of varying sizes and heterogeneous signals within the liver (Figure 1). The largest lesion, measuring 2.1 cm × 2.0 cm, was located in the right posterior lobe. A positron emission tomography (PET)/CT scan conducted at Wuhan Union Hospital in March 2022 indicated increased metabolic activity in various regions of the intestinal wall, mesentery, omentum, and peritoneum, suggestive of a malignant tumor [maximum standardized uptake value (SUVmax): 16.3] (Figure 2). Exploratory surgery and biopsy revealed a large polypoid tumor in the omentum, measuring 5 cm × 4 cm. This tumor exhibited invasive growth through the muscularis propria into the subserosal soft tissue. Lymphovascular invasion was also observed. Pathological analysis suggested the diagnosis of SCA.

#### History of past illness

The patient has a documented history of hepatitis B, for which he is currently receiving entecavir therapy. Additionally, he has had hypertension for over a decade and is being treated with metoprolol; however, his blood pressure remains suboptimally controlled.

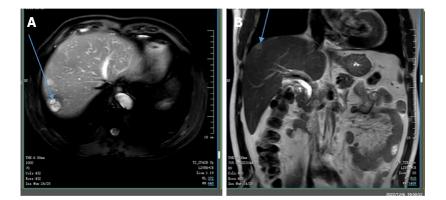


Figure 1 Liver magnetic resonance images. Magnetic resonance images performed at Yichang Central People's Hospital on February 9, 2022. Wellcircumscribed, heterogeneous, and hypodense masses are located in the right posterior lobe of the liver, measuring 2.1 cm × 2.0 cm (indicated by the arrow). A: Transverse view; B: Coronal view.

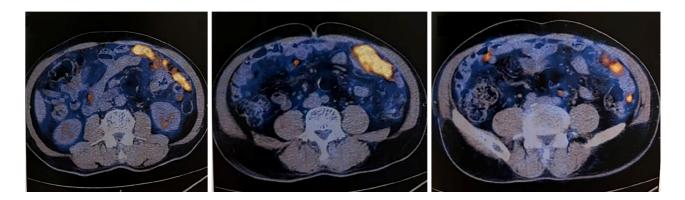


Figure 2 Positron emission tomography-computed tomography images from March 2022 showing multiple masses in the mesentery, omentum, and peritoneum with increased abnormal tracer metabolism.

#### Personal and family history

The patient denied any family history of malignant tumors.

#### Physical examination

On physical examination, the vital signs were as follows: Body temperature, 36.4 °C; blood pressure, 138/105 mmHg; heart rate, 84 beats per minute; and respiratory rate, 18 breaths per minute.

#### Laboratory examinations

Serum tumor markers were within normal limits (carcinoembryonic antigen, 1.6 ng/mL; carbohydrate antigen 19-9, 4.7 U/mL; alpha-fetoprotein, 4.5 ng/mL). Routine blood and urine analyses revealed no abnormalities.

#### Imaging examinations

A preoperative CT scan revealed multiple abnormal signals in the liver. MRI of the liver performed at our hospital identified numerous low-density circular lesions of varying sizes and heterogeneous signals within the liver parenchyma (Figure 1); the largest lesion, located in the right posterior lobe, measured 2.1 cm × 2.0 cm. A PET/CT scan conducted at Wuhan Union Hospital in March 2022 demonstrated increased metabolic activity in various regions of the intestinal wall, mesentery, omentum, and peritoneum, suggesting a potential malignant tumor (SUV max: 16.3) (Figure 2).

#### MULTIDISCIPLINARY EXPERT CONSULTATION

Exploratory surgery and biopsy revealed a large polypoid tumor in the omentum, measuring 5 cm × 4 cm, which had invaded through the muscularis propria into the subserosal soft tissue. Lymphovascular invasion was also observed. Pathological analysis suggested a diagnosis of SCA.

Immunohistochemical staining confirmed the presence of tumor cells in the surgical specimen. The postoperative pathology analysis results consistent with SCA were as follows: PCK (+), CK8/18 (+), CK7 (+), GATA-3 (+), EMA (-), caveolin-1 (weakly positive), calretinin (-), WT1 (-), D2-40 (-), CK5/6 (-), HMHE-1 (-), BAP1 (±), P16 (-), P40 (-), CD34 (-),



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CD117 (-), DDG-1 (-), SDHB (+), SMA (-), desmin (-), S100 (-), SOX10 (-), HMB45 (-), CD31 (-), ERG (-), E-cadherin (-), ALK (-), CK19 (-), villin (-), CDX2 (-), CEA (-), β-catenin (partially positive), INI-1 (no expression deficiencies detected), and Ki67 (LI > 70%) (Figure 3). Fluorescence in situ hybridization testing indicated a deletion at the cyclin-dependent kinase inhibitor 2A locus on chromosome 9; however, malignant mesothelioma was excluded. The p16 gene deletion test was negative.

#### FINAL DIAGNOSIS

Based on the patient's medical history and the diagnostic findings, a diagnosis of jejunal SCA was confirmed.

#### TREATMENT

The patient accepted the treatment regimen at our hospital. However, he was unable to complete PD-L1 gene testing due to financial constraints. With informed consent from the patient and his family, he commenced treatment with a combination of albumin-bound paclitaxel [200 mg (125 mg/m<sup>2</sup>) on day 1] and sintilimab (200 mg on day 1), administered in 21-day cycles. He completed four cycles in total. During treatment, the patient developed significant abdominal ascites, requiring daily drainage of 1000-1500 mL for one week. Cytological analysis of the ascitic fluid showed no malignant cells. The ascites was attributed to abdominal metastases and hypoalbuminemia (serum albumin: 25 g/L). After the first cycle, a CT scan showed no abdominal fluid and a slight enlargement of liver lesions, indicating stable disease. Following the third cycle, CT imaging revealed a reduction in liver nodules and abdominal lesions compared to previous scans. The patient's abdominal fluid and tumor burden was well-controlled, although a complete response was not achieved. Subsequently, the patient underwent three additional cycles of the same treatment regimen, combined with targeted therapy using anlotinib [12 mg orally once daily (days 1-14, 21 days per cycle)]. A CT scan following this treatment indicated a significant reduction in the size of the liver nodule compared to prior imaging (Figure 4), demonstrating a partial response. The patient continued maintenance therapy with anlotinib and sintilimab for an extended period. Unfortunately, due to financial difficulties, the patient discontinued treatment but remained stable for over one-year postsurgery.

#### OUTCOME AND FOLLOW-UP

The patient remained stable for over one year following surgery.

#### DISCUSSION

Primary small intestinal epithelial tumors constitute a mere 2% of all gastrointestinal malignancies, making clinical cases of small intestinal epithelial neoplasms rare<sup>[3]</sup>. SCA predominantly affects middle-aged and elderly men. Clinical symptoms are often nonspecific and may include abdominal pain, anemia, bowel obstruction, vomiting, and weight loss. The diagnosis of small intestinal SCA cannot rely solely on hematoxylin and eosin staining; a comprehensive assessment incorporating immunohistochemical examination of multiple biomarkers is essential. Due to its nonspecific clinical presentation, small intestinal SCA is frequently misdiagnosed. Differential diagnosis should consider epithelioid angiosarcoma, smooth muscle sarcoma, gastrointestinal stromal tumor, lymphoma, and melanoma. The risk factors for small intestinal SCA remain unclear, though previous studies suggest a potential association with long-term regional intestinal inflammation[6]. The prognosis for this disease is extremely poor, with most patients succumbing to metastasis and recurrence. The 5-year survival rate is essentially 0%, and the median survival time following diagnosis is only 8.25 months[7]. Therefore, small intestinal SCA represents a rare, easily misdiagnosed, and challenging-to-treat malignant tumor.

Currently, no standard treatment guidelines exist for SCA. Surgery is generally recognized as the preferred treatment for early-stage patients. Chemotherapy is utilized for recurrent and metastatic cases, although outcomes are often suboptimal[8]. Earlier studies[8] demonstrated no significant difference in survival rates between patients treated with chemotherapy and those who did not receive it. Radiation therapy is primarily limited to palliative care (Table 1). In 2015, the Marshall University School of Medicine reported a case involving a patient with small bowel SCA and lung metastases who declined surgery. The patient initially received oxaliplatin plus capecitabine for four months, but the disease progressed. Subsequently, the treatment regimen was switched to irinotecan plus capecitabine for four cycles, yet the lung and mediastinal lesions continued to advance[9]. In 2017, the Hofstra School of Medicine reported a case of a 58year-old woman with a sarcomatoid tumor of the terminal ileum causing small bowel obstruction. A CT scan of the abdomen and pelvis upon admission showed no evidence of metastatic disease. The patient underwent a robotic-assisted right hemicolectomy with resection of the terminal ileum and ileocolic anastomosis. She was followed up for six months and recovered well[10]. The MD Anderson Cancer Center reported a case involving a patient with small bowel SCA who underwent distal pancreatectomy, splenectomy, right hepatectomy, subtotal gastrectomy, and cholecystectomy.

Table 1 Summary of diagnostic information for all sarcomatoid carcinoma cases reviewed in this study										
Age/sex	Diagnosis	Tumor Site	No. of lesion (s)	Maximal diameter (cm)	Morphology	Metastasis	Treatment method	OS (months)	Ref.	
56/F	SCA	Jejunum	1	6.7	Ulcerating	Yes	Operation	6	[41]	
62/M	SCA	Lleum	1	15	Ulcerating	No	Operation + chemotherapy	3	[ <mark>42</mark> ]	
54/M	SCA	Jejunum	NA	2.6	Polypoid	No	Operation	3	[ <mark>18</mark> ]	
56/M	SCA	Jejunum	NA	14	Polypoid	Yes	Chemotherapy	4 <sup>1</sup>	[ <mark>9</mark> ]	
58/F	SCA	Lleum	1	3	Polypoid	No	Operation + chemotherapy	6 <sup>1</sup>	[10]	
NA	SCA	NA	1	15	Polypoid	Yes	Operation + chemotherapy	12	[ <mark>11</mark> ]	
68/M	SCA	Lleum	1	9.4	Polypoid	No	Operation	0.43	[3]	
60/M	SCA	Jejunum	NA	5	Polypoid	Yes	Operation	0.36	[ <b>7</b> ]	
67/M	SCA	Jejunum	2	6.5	Ulcerating	Yes	Operation	24	[4]	
90/F	SCA	Small intestine	1	4	Polypoid	Yes	Operation	15	[ <mark>12</mark> ]	

#### <sup>1</sup>Alive when presented.

OS: Overall survival; NA: Not available; F: Female; M: Male; SCA: Sarcomatoid carcinoma.

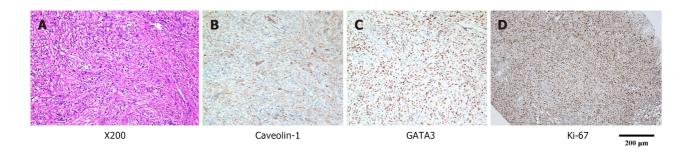


Figure 3 Pathology after laparoscopic exploration of the greater omentum. The tumor cells are spindle-shaped or cluster-shaped, with oval and deeply stained nuclei. A: Shows hematoxylin and eosin staining under a × 200 microscope; B-D: Show immunohistochemical staining: Cytoplasmic vacuoles are observed in some cells. Tumor cell membranes are positive for Caveolin-1, and the nuclei are positive for GATA3 and Ki-67 (Li > 70%).

Pathological examination revealed a high-grade sarcomatoid malignancy involving the pancreas, liver, adrenal gland, and gastric wall. One month later, a PET-CT scan detected abdominal retroperitoneal nodules, indicating disease progression. The patient was treated with four cycles of a gemcitabine plus docetaxel regimen, achieving stable disease. Subsequently, the patient received the FOLFIRINOX regimen (oxaliplatin 85 mg/m<sup>2</sup>, irinotecan 180 mg/m<sup>2</sup>, leucovorin 400 mg/m<sup>2</sup>, and fluorouracil 2400 mg/m<sup>2</sup> intravenously every 14 days for six cycles), which resulted in progressive disease. Following this, the patient was treated with a combination of docetaxel, cyclophosphamide, and bevacizumab, but the disease continued to worsen, with new liver metastases developing. The patient succumbed to the disease 12 months after the initial diagnosis[11]. In 2021, Hiroshima University in Japan reported a case of small intestinal SCA with mesenteric lymph node metastasis, abdominal metastasis, and retroperitoneal lymph node metastasis. The patient did not receive additional adjuvant therapy post-surgery and died 15 months after the operation[12]. Previous case reports have indicated that treatments involving moxifloxacin, dacarbazine, cyclophosphamide, gemcitabine, docetaxel, paclitaxel, and platinum compounds did not yield satisfactory outcomes[11,13,14]. In conclusion, the data suggest that surgery is optimal for early-stage SCA patients. However, due to the occult nature of the disease, most patients are diagnosed with lymph node or distant metastases, rendering chemotherapy insufficient. Thus, current chemotherapeutic drugs demonstrate low efficacy for SCA, highlighting the need for exploring alternative treatment options.

In recent years, targeted therapies and immunotherapy have been increasingly applied to various solid tumors, yielding sustained survival benefits for patients. In 2019, the MD Anderson Cancer Center reported a case involving a patient who presented with painless lumps in the left axilla. The patient underwent surgical excision of two lymph nodes and was diagnosed with SCA based on biopsy analysis. Following axillary disease progression, the patient received four cycles of gencitabine plus albumin-bound paclitaxel chemotherapy (administered in a 2-week regimen). Next-generation sequencing identified *BRAF V600E* and *TP53* mutations in the patient. Consequently, the patient was treated with dabrafenib plus trametinib for three months and underwent post-treatment efficacy evaluation. Subsequent axillary

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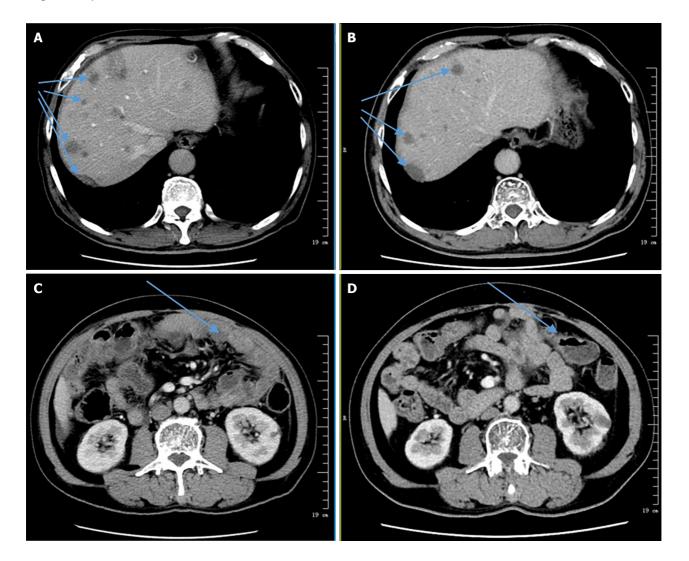


Figure 4 Comparison of Computed tomography. A: Computed tomography (CT) images from May 18, 2022; B: CT images from September 14, 2022; A and B: The total number of liver lesions has decreased, and some lesions have reduced in enhancement compared to the previous images (indicated by the arrow); C: CT images from May 18, 2022; D: CT images from September 14, 2022; C and D: Showing decreased peritoneal thickening, reduced omentum opacity, and decreased size of some nodules in the abdominal cavity. There is also a reduction in abdominal and pelvic fluid accumulation (indicated by the arrow).

clearance was performed, followed by 12 months of adjuvant dabrafenib therapy. At the latest follow-up visit, 45 months post-surgery, the patient's disease remained stable[11]. Additionally, a systematic review and meta-analysis[15] indicated that uterine leiomyosarcoma is almost exclusively driven by the inactivation of tumor suppressor genes, highlighting the necessity of genetic testing. These findings suggest that conventional chemotherapy is less effective for intestinal SCA and may even lead to drug resistance. Therefore, it is recommended to conduct genetic mutation detection and administer appropriate targeted therapies for pathogenic genes, potentially resulting in improved therapeutic outcomes.

Upregulated PD-L1 expression on tumor cells can facilitate immune escape by activating the programmed cell death protein 1 (PD-1)/PD-L1 pathway and inhibiting immune responses[16]. Patients with high levels of PD-1 expression are often treated with PD-L1 inhibitors, which block the interaction between PD-1 and PD-L1, enabling immune cells to maintain their activity and restore their ability to recognize and destroy tumor cells. Consequently, PD-1 inhibitors have demonstrated optimal efficacy in various solid tumors, including lung, cervical, esophageal, and colorectal cancers. Velcheti et al[16] reported that 9 out of 13 (69.2%) patients with lung SCA were PD-L1 positive, with levels higher than those in conventional non-small cell lung cancer (NSCLC)[16]. A case of jejunal SCA with significantly increased PD-L1 protein expression was also reported by Tachibana *et al*[4]. Although there are currently no published reports on the application of immunotherapy in small intestine SCA, this therapeutic approach has shown excellent anti-tumor efficacy in other cancers, sarcomas, and hematological malignancies. For example, in a study evaluating pembrolizumab for advanced soft tissue sarcoma, 9 out of 40 patients achieved objective remissions, yielding an objective response rate of 23%[17]. Given the overall poor effectiveness of chemotherapy, PD-L1 and driver gene mutation testing, along with immunotherapy and targeted therapy, may be preferred options for patients with SCA.

In 2020, the Department of Oncology at The First Affiliated Hospital of Kunming Medical University identified several key driver gene mutations in small intestinal SCA, including KRAS, TP53, and EGFR[18]. Anlotinib, a novel smallmolecule multi-target tyrosine kinase inhibitor, targets vascular endothelial growth factor receptor and platelet-derived growth factor receptor. AnIotinib received its first approval in China on May 10, 2018, as a monotherapy for patients with locally advanced or metastatic NSCLC who have experienced progression or recurrence after at least two lines of

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systemic chemotherapy. Anlotinib has demonstrated significant antitumor effects in lung cancer and soft tissue sarcoma [19]. Sintilimab, a humanized monoclonal antibody developed in China, binds to PD-L1 expressed on T cells and competes effectively and specifically with PD-1/PD-L1/L2 binding, thereby blocking the immunosuppressive response mediated by the PD-1 pathway. Preclinical data suggest that sintilimab has a potentially greater affinity for PD-1 compared to pembrolizumab or nivolumab due to its distinct structural binding mode to PD-1[20]. By 2020, sintilimab had been approved by the National Medical Products Administration of China to treat relapsed or refractory classical Hodgkin lymphoma<sup>[21]</sup>. Sintilimab has also shown favorable antitumor effects in lymphoma<sup>[22]</sup>, NSCLC<sup>[23]</sup>, and digestive system cancers<sup>[24]</sup>. Anti-angiogenesis combined with immunotherapy has a synergistic effect. Mechanistically, anti-angiogenesis can promote antigen presentation and T cell immune responses to tumor antigens by inhibiting dendritic cell maturation disorder[25]. Additionally, anti-angiogenesis can normalize tumor vasculature, enhancing T cell infiltration into the tumor and reducing the number and activity of immunosuppressive cells such as myeloid-derived suppressor cells, tumor-associated macrophages, and regulatory T cells. This combination therapy can transform the tumor microenvironment from immunosuppressive to immunopermissive states [26]. Immunotherapy has demonstrated promising results in the treatment of SCA[17,27,28]. The synergistic effect of combining targeted therapy with immunotherapy in SCA has garnered significant attention [29-31]. Dai et al [32] reported a case where a patient with advanced pulmonary SCA was successfully treated with a combination of sintilimab and anlotinib[32]. Similarly, Piao et al[31] described an advanced pulmonary SCA patient who responded optimally to a regimen of anlotinib, sintilimab, and platinum doublet chemotherapy[31]. Chemotherapy agents such as paclitaxel and docetaxel remain crucial in the treatment of advanced sarcomas[33-38]. Recent clinical trials have demonstrated the promising efficacy of albumin-bound paclitaxel in treating various malignancies, including gastric cancer, melanoma, gynecological malignancies, urothelial carcinoma, head and neck squamous cell carcinoma, biliary carcinoma, and nasopharyngeal carcinoma[38-40]. In the case under discussion, the patient's condition stabilized following treatment with anlotinib, sintilimab, and albumin-bound paclitaxel. The liver and multiple abdominal nodules showed a significant decrease in size compared to their initial presentation, and the patient experienced no disease progression for over a year post-surgery, indicating substantial therapeutic benefits. The patient reported only mild side effects, such as fatigue and peeling of the hands and feet. However, the patient did not complete genetic testing due to financial constraints and subsequently discontinued treatment. It is crucial to encourage patients who cannot undergo surgery or tolerate chemotherapy to complete genetic testing, as it can significantly inform their treatment responses. Targeted therapy and immunotherapy represent promising treatment options, but further clinical trials are necessary to fully assess their side effects and clinical efficacy.

#### CONCLUSION

In conclusion, jejunal SCA is an extremely rare, highly metastatic, and invasive tumor with a very poor prognosis. Surgery is effective for early-stage patients, but for those with late-stage or recurrent disease, chemotherapy remains the mainstay of treatment, often following protocols used for sarcoma and colon cancer. However, the overall efficacy of chemotherapy is limited, and the duration of response is typically short. In the present case report, the patient achieved long-term stability, optimal tolerance, and minimal side effects through a combination of immunotherapy and targeted therapy. This suggests that anti-angiogenic-targeted drugs combined with immunotherapy may offer a novel treatment option for small intestinal SCA. Nevertheless, further clinical research is needed to validate these findings.

#### FOOTNOTES

Author contributions: Feng Q drafted the manuscript; Feng Q and Yu W revised the manuscript; Huang Q critically revised the article and ensured that questions related to the integrity of any part of the work were appropriately investigated and resolved; Feng JH and Xiao GX provided guidance on professional knowledge; Feng Q, Yu W, Feng JH, Xiao GX confirm the authenticity of all the raw data; All authors read and approved the final version of the manuscript.

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