Multiple Sarcomatoid Carcinomas of the Jejunum with Postoperative Lung and Brain Metastases: A Case Report and Literature Review (Postprint)

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Abstract

Objective: To investigate the clinical manifestations, treatment, and prognosis of sarcomatoid carcinoma of the jejunum, and to provide references for clinical diagnosis and treatment. Methods: This article reports a case of a patient with postoperative lung and brain metastases from multiple sarcomatoid carcinomas of the jejunum admitted to our hospital, and analyzes 14 case reports comprising a total of 18 cases. Results: The patient underwent partial jejunectomy due to intussusception with gastrointestinal bleeding, developed multiple metastases to the brain and lungs at 4 months postoperatively, and died of multiple organ failure at 8 months postoperatively. Sarcomatoid carcinoma of the jejunum has no unified nomenclature domestically or internationally, and its diagnosis is difficult, particularly early definitive diagnosis, with pathological examination and immunohistochemistry constituting the main diagnostic basis. Currently, there are no clear treatment guidelines; extensive surgical resection including the tumor is the main effective treatment modality, but the prognosis is extremely poor, with a median survival of only 5.5 months (0.36–36 months), and most patients die from recurrence and metastasis. Conclusion: Sarcomatoid carcinoma of the jejunum is relatively rare; multiple lesions in the jejunum with metastases to the brain and other sites as in this case is even rarer. Standardized nomenclature, early diagnosis, identification of additional cancer lesions through whole-body multi-site imaging, comprehensive assessment of disease course, and prompt initiation of treatment are all crucial. Surgery forms the cornerstone of treatment, and various locoregional therapeutic modalities may be considered. The potential value of Ki-67 for prognostic assessment and PD-L1-targeted immunotherapy requires further investigation.

Full Text

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Abstract

Objective: We report a rare case of multiple sarcomatoid carcinoma of the jejunum with postoperative lung and brain metastases. The patient underwent segmental jejunectomy for intussusception and gastrointestinal bleeding. Multiple metastases to the brain and lung occurred 4 months after surgery, and the patient died of multiple organ failure 8 months postoperatively. Primary sarcomatoid carcinoma is difficult to diagnose at an early stage, and diagnosis relies on microscopic and immunohistochemical examination. Currently, no treatment guidelines are established for sarcomatoid carcinoma of the jejunum, and surgical resection remains the optimal therapeutic approach. Previous reports documented poor prognosis with a median survival time of 5.5 months (range 0.36–36 months), with tumor recurrence and metastasis being the primary causes of death. Ki-67 as a potential prognostic marker and the value of PD-L1-targeted immunotherapy warrant further investigation.

Keywords: primary sarcomatoid carcinoma; jejunum; lung and brain metastases; literature review

Introduction

Sarcomatoid carcinoma is a very rare malignant tumor composed of malignant epithelioid cells and numerous spindle cells [1-3]. Various terms, including sarcomatoid carcinoma, undifferentiated carcinoma, pleomorphic carcinoma, metaplastic carcinoma, and anaplastic carcinoma, have been used to describe such tumors. The latest WHO classification of digestive system tumors categorizes these lesions as undifferentiated carcinoma and has not recognized sarcomatoid carcinoma as an independent type or subtype [4]. However, based on its pathological structure and immunohistochemical characteristics, sarcomatoid carcinoma is currently the most widely accepted term and is recommended for diagnostic surgical pathology reports [2-3]. Sarcomatoid carcinoma most commonly occurs in the respiratory tract, breast, thyroid, pancreas, kidney, bladder, and esophagus, with rare reports involving the small intestine and even rarer involvement of the jejunum. Upon reviewing the literature, only 18 cases have been reported to date, with just 3 cases of multiple lesions; this article reports the 4th case of multiple tumors. Notably, compared with other jejunal tumors, sarcomatoid carcinoma demonstrates greater metastatic potential and invasiveness [5], resulting in extremely poor patient prognosis. This study reports a case of multiple sarcomatoid carcinoma of the jejunum with postoperative lung and brain metastases and includes a relevant literature review.

Case Report

A 72-year-old male was admitted to our gastroenterology department on June 17, 2016, with a 4-month history of recurrent upper abdominal pain, melena, and dizziness. The upper abdominal pain was intermittent and distending, mostly self-resolving, occasionally accompanied by vomiting without coffee-ground material or hematemesis. He experienced intermittent melena in small amounts and recurrent dizziness without syncope, blurred vision, profuse sweating, or palpitations. Three days prior, a stool occult blood test was positive at another hospital. He had a history of hypertension for over 2 years, controlled with regular antihypertensive medication.

Physical examination revealed moderate anemia, normal cardiopulmonary findings, mild upper abdominal distension, upper abdominal tenderness without rebound tenderness, no palpable abdominal mass, active bowel sounds at 6 times per minute, and no succussion splash. Laboratory tests showed white blood cells 10.86×10 /L, hemoglobin 76 g/L, hematocrit 0.25, platelets 577×10 /L, carcinoembryonic antigen 21.78 ng/mL, and positive stool occult blood. Gastroscopy and colonoscopy revealed no significant lesions. Chest radiography suggested mild inflammation in both lower lungs. After admission, the patient received fasting, proton pump inhibitor (PPI) therapy for acid suppression, hemostatic agents, somatostatin, fluid replacement, and other supportive measures, but upper abdominal pain persisted with intermittent melena.

On June 24, 2016, abdominal CT revealed [Figure 1: see original paper][Figure 2: see original paper]: thickened jejunal wall with a soft tissue density mass in the right upper abdomen, suspicious for tumor; additionally, local small bowel wall thickening with intussusception changes in the left middle abdomen, possibly complicated by tumor, with mild obstructive dilation of proximal jejunum. Considering small bowel tumor with intussusception, obstruction, and bleeding, exploratory laparotomy was performed on June 25, 2016. Intraoperatively, a firm mass approximately 5 cm in size was palpable in the jejunum about 50 cm from the Treitz ligament, mostly intraluminal with serosal layer invasion. Intussusception of about 5 cm was observed approximately 60 cm from the Treitz ligament, which could not be reduced, containing a firm tumor approximately 3 cm in size, considered tumor-related. Multiple enlarged lymph nodes were visible in the associated mesentery, with the largest measuring about 1.5 cm. Partial jejunectomy was performed: approximately 40 cm of jejunum was resected, with the proximal margin about 10 cm from the tumor and the distal margin about 10 cm from the intussusception lesion, including fan-shaped resection of the corresponding jejunal mesentery.

Postoperative pathology showed [Figure 3: see original paper]: a 35 cm segment of small intestine with intussusception measuring 6 cm long, internal diameter 2 cm, external diameter 3 cm, and intestinal diameter 3–4.5 cm. An ulcerative mass measuring 5 cm×3 cm×0.7 cm was located about 10 cm from one resection margin, and a polypoid mass approximately 3.5 cm×3 cm×3 cm was seen

deep in the intussuscepted bowel. Microscopy [Figure 4: see original paper] revealed diffuse sheet-like proliferation of atypical cells, locally forming nest-like structures, with abundant eosinophilic cytoplasm, large round or irregular nuclei, visible nucleoli, numerous tumor giant cells, and frequent mitotic figures. Pathological diagnosis: sarcomatoid carcinoma of the jejunum, 2 tumors measuring 5 cm×3 cm×0.7 cm and 3.5 cm×3 cm×3 cm; invasion of the entire bowel wall; vascular tumor emboli present, no neural invasion, both intestinal resection margins negative for cancer; no mesenteric lymph node metastasis (0/29). Immunohistochemistry: CK, CK19, Vimentin (+), CEA, CK20, Villin, CDX2, AFP, Hepatocyte (-), Ki-67 approximately 75% (+).

The patient recovered smoothly and was discharged but refused adjuvant chemotherapy. Four months postoperatively, he returned due to mental abnormalities. Brain MRI [Figure 5: see original paper] showed multiple abnormal enhanced nodules in bilateral cerebral hemispheres and right cerebellar hemisphere, considered metastases, with brain atrophy. Chest CT [Figure 6: see original paper] showed a mass in the apical posterior segment of left upper lobe with cavity formation; a mass in the posterior segment of right upper lobe bronchus-right hilum with obstructive pneumonia in right upper lobe; multiple scattered nodules and masses in both lungs; bilateral emphysema with multiple bullae; and multiple enlarged lymph nodes in mediastinum and bilateral hilar regions, some with necrosis. Enhanced abdominal and pelvic CT showed no obvious masses or enlarged lymph nodes. Considering postoperative lung and brain metastases of jejunal sarcomatoid carcinoma, the patient died of respiratory failure 8 months postoperatively.

Literature Review and Discussion

We searched PubMed for all reports on sarcomatoid carcinoma of the jejunum published up to May 2017 using the terms: "sarcomatoid carcinoma," "undifferentiated cancer," "pleomorphic cancer," "metaplastic carcinoma," "anaplastic carcinoma," "jejunum," and "small intestine." After excluding reports involving sarcomatoid carcinoma at small intestinal sites other than the jejunum, we identified 14 case reports comprising 18 cases. There were 9 males and 9 females with a mean age of 59.2 years (range 35–85 years). Detailed clinical data and treatment information are summarized in Table 1 .

Sarcomatoid carcinoma of the small intestine is rare, occurring primarily in the ileum, followed by the jejunum and duodenum [2]. To date, only 18 cases of jejunal sarcomatoid carcinoma have been reported. The disease predominantly affects middle-aged and elderly individuals. One study reported male predominance with a male-to-female ratio of 1.5:1.0 [2]; however, our data showed no significant gender difference (1.0:0.9). Jejunal sarcomatoid carcinoma typically presents as a single lesion, with only 4 reported cases (including this case) showing multifocal tumors [6].

Among 15 patients with relatively complete clinical records (including this case),

the most common presenting symptom was anemia (60.0%), followed by abdominal pain (46.7%), gastrointestinal bleeding (33.3%), fatigue (33.3%), abdominal mass (26.7%), and weight loss (26.7%). Additional common symptoms included small bowel obstruction (20.0%), shortness of breath (13.3%), palpitations (13.3%), vomiting (20.0%), fever (13.3%), nausea (6.7%), diarrhea (6.7%), dyspepsia (13.3%), and anorexia (6.7%). Two patients required emergency laparotomy due to carcinomatous intra-abdominal hemorrhage [9], and another 2 required emergency laparotomy due to gastrointestinal perforation with acute peritonitis [11,13]. Our case also required emergency laparotomy due to gastrointestinal bleeding and obstruction. Because clinical manifestations are nonspecific and the small intestine is anatomically concealed, most patients are diagnosed at middle-to-advanced stages.

Jejunal sarcomatoid carcinoma typically appears as an endophytic or polypoid protruding mass, often with central ulcerative necrosis and hemorrhage, averaging 7.75 cm (range 3–16 cm); 76.4% measured 5–10 cm. Tumors can occur anywhere in the jejunum and frequently exhibit local lymph node metastasis (81.8%) and direct invasion of adjacent tissues including small intestine (42.9%), colon (28.6%), mesentery (28.6%), omentum (28.6%), and ovary (14.3%). Additionally, 58.3% showed invasion of surrounding lymphatic vessels, blood vessels, or nerves. Despite surgical resection in all patients, tumor progression and metastasis were rapid. The most common metastatic site was lung (53.8%), followed by distant lymph nodes (para-aortic, supraclavicular, axillary, parametrial) and liver; brain and pelvic metastases also occurred. Among 19 reported patients (including this case), 17 with complete follow-up died from the disease, essentially all due to tumor metastasis or recurrence, demonstrating the highly aggressive and metastatic nature of this tumor. Overall prognosis is extremely poor, with a median survival of only 5.5 months (range 0.36–36 months) after diagnosis. Our case had 2 tumors in the jejunum—the larger endophytic lesion with ulcerative necrosis and hemorrhage and the smaller polypoid lesion—representing the first reported case with two simultaneous growth patterns and the second reported case with brain metastasis, with death occurring 8 months after diagnosis.

Histologically, jejunal sarcomatoid carcinoma may exhibit monophasic or biphasic patterns [5]. The monophasic pattern consists primarily of mesenchymal cells with minimal or absent epithelioid cells, while the biphasic pattern contains both epithelioid and mesenchymal components. Diagnosis cannot be established by HE staining alone and requires immunohistochemical examination of multiple biomarkers [1-3]. All reported cases were positive for cytokeratin (CK), and all cases with complete data were positive for vimentin, indicating that these tumors almost exclusively represent the biphasic pattern with both epithelial and mesenchymal components. Our case showed positive CK and vimentin expression, confirming the diagnosis. Individual case reports have suggested relatively better prognosis associated with lower Ki-67 expression [13]. In our case, Ki-67 was approximately 75% positive, correlating with poor prognosis and consistent with other reports of poor outcomes in patients with higher Ki-67 positivity [16].

High Ki-67 positivity may correlate with the clinical characteristics of high invasiveness and metastatic potential. Therefore, Ki-67 may serve as a prognostic marker for patients with jejunal sarcomatoid carcinoma.

Currently, no treatment guidelines exist for this disease, and wide resection including the tumor remains the main effective treatment. Some reports have described postoperative adjuvant chemotherapy with 5-fluorouracil and/or cisplatin and radiotherapy, but none have effectively improved prognosis. Clinical trials targeting the programmed death receptor-1 (PD-1) and its ligand PD-L1 immune checkpoint pathways have reported benefits in several malignant tumors. Upregulated PD-L1 expression in tumor cells mediates immune escape by activating the PD-1/PD-L1 pathway and inhibiting effective immune responses, ultimately leading to tumor cell proliferation [17]. Previous literature has demonstrated upregulated PD-L1 expression in sarcomatoid lung carcinoma [18], and studies have also found abnormal PD-L1 protein expression in jejunal sarcomatoid carcinoma [16]. Therefore, PD-L1-targeted immunotherapy may be effective for this cancer type. PD-L1 testing should be routinely performed in patients with jejunal sarcomatoid carcinoma to provide potential effective treatment options.

Whether jejunal sarcomatoid carcinoma represents multiple primary origins or a single primary lesion prone to multiple metastases remains unclear [19]. In our case, multiple metastatic lesions in the brain and lung were discovered 4 months postoperatively, which cannot exclude the possibility that this patient had multiple primary tumors or that small metastatic lesions already existed in the brain and/or lung at the time of surgery but were not detected due to lack of comprehensive whole-body multi-site scanning. Abdominal and pelvic CT at 4 months postoperatively showed no tumor recurrence, suggesting that thorough local tumor clearance may effectively delay local recurrence. If these metastatic lesions could be detected early and treated with R0 resection or various effective local treatment modalities (such as radiofrequency ablation, gamma knife, radioactive seeds, etc.), patient prognosis might be improved.

As shown in Table 1, case reports of jejunal sarcomatoid carcinoma have increased significantly since 2009, with new cases reported almost every year, indicating a certain incidence rate. The previously low number of reported cases may be due to backward diagnostic techniques or failure to establish definitive diagnoses in patients who died from this disease. With improvements in diagnostic technologies such as imaging and immunohistochemistry, reported cases may increase substantially. Since jejunal sarcomatoid carcinoma is a highly metastatic and aggressive tumor with extremely poor prognosis, its diagnosis and treatment warrant attention. Utilizing current advanced examination methods for early detection and comprehensive multi-site scanning after definitive diagnosis to identify multiple or metastatic lesions, along with thorough disease assessment and radical surgical resection, may effectively improve patient prognosis. For multiple or metastatic lesions, R0 resection or application of various local treatment modalities is worth attempting. Furthermore, the tu-

mor pathogenesis, Ki-67 as a prognostic biomarker, and the potential value of PD-L1-targeted immunotherapy require further investigation.

References

[1] Fukuda T, Kamishima T, Ohnishi Y, et al. Sarcomatoid carcinoma of small intestine: histologic, immunohistochemical ultrastructural features of three cases and its differential diagnosis [J]. Pathol Int, 1996, 46(9): 682-8.
[2] Reid M, Idrees M, Perino G, et al. Sarcomatoid carcinoma of the small intestine - A case report and review of the literature [J]. Arch Pathol Lab Med, 2004, 128(8): 918-21.
[3] Lee HM, Cho MS, Kim YI. A surgically resected large sarcomatoid carcinoma of the jejunum: a case report and literature review [J]. J Gastric Cancer, 2015, 15(2): 143-6.
[4] Bosman FT, Carneiro F, Hruban RH, et al. WHO classification of tumours of the digestive system [M]. Lyon: IARC Press, 2010: 125-31.
[5] Robey SS, Silva EG, Cleary KR. Anaplastic and sarcomatoid carcinoma of the small intestine: a clinicopathologic study [J]. Hum Pathol, 1989, 20(9): 858-63.
[6] Kwok CM. Sarcomatoid carcinoma of the jejunum with gastric metastases: a case report and review of the literature [J]. Int J Surg Case Rep, 2016, 28(11): 161-4.
[7] Bak M, Teglbjaerg PS. Pleomorphic (giant cell) carcinoma of the intestine: an immunohistochemical and electron microscopic study [J]. Cancer, 1989, 64(12): 2557-64.
[8] Lam KY, Leung CY, Ho JW. Sarcomatoid carcinoma of the small intestine [J]. Aust J Surg, 1996, 66(9): 636-9.
[9] Tsukadaira A, Koizumi T, Okubo Y, et al. Small-intestinal sarcomatoid carcinoma with superior vena cava syndrome [J]. J Gastroenterol, 2002, 37(6): 471-5.
[10] Moriwaki Y, Sugiyama M. Severe anemia inducing preshock caused by sarcomatoid carcinoma of the small intestine [J]. Int Surg, 2009, 94(2): 164-70.
[11] Yucel AF, Kocakusak A, Arikan SA, et al. A rare cause of acute abdomen: Perforated primary sarcomatoid carcinoma of the small intestine - Report of a case, with a brief review of the literature [J]. J Cancer Res Ther, 2011, 7(3): 348-50.
[12] Pata F, Sengodan M, Tang CB, et al. Concomitant jejunal sarcomatoid carcinoma and gastric GIST in patient with polymyalgia rheumatica: A case report [J]. Int J Surg Case Rep, 2013, 4(5): 449-52.
[13] Han N, Han QH, Liu YZ, et al. Perforated sarcomatoid carcinoma of the jejunum: case report [J]. Oncol Lett, 2013, 6(2): 562-4.
[14] Kang K, Yoon JH, Kang G. Sarcomatoid carcinoma of the small intestine: a case report and review of the literature [J]. J Korean Soc Radiol, 2013, 69(4): 295-9.
[15] Alfonso PN, Jimenez C, Higuera MI. Sarcomatoid carcinoma of the jejunum presenting as obscure gastrointestinal bleeding in a patient with a history of gliosarcoma [J]. Gastroenterol Rep (Oxf), 2014, 2(2): 150-3.

[16] Zhang B, Cheng BO, Wang L, et al. Primary sarcomatoid carcinoma of the jejunum with massive intra-abdominal hemorrhage: a case report and review of the literature [J]. Molec Clin Oncol, 2016, 4(5): 703-6.
[17] Brahmer JR, Tykodi SS, Chow LQ, et al. Safety and activity of anti-PD-L1 antibody in patients with advanced cancer [J]. N Engl J Med, 2012, 366(26): 2455-65.
[18] Velcheti V, Rimm DL, Schalper KA. Sarcomatoid lung carcinomas show high levels of programmed death ligand-1 (PD-L1) [J]. J Thorac Oncol, 2013, 8(6): 803-5.
[19] Han XY, Liu J, Pan Q, et al. Multiple sarcomatoid carcinoma of the small intestine: a case report [J]. Chinese Journal of Pathology, 2017, 46(2): 118-9.

Note: Figure translations are in progress. See original paper for figures.