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A Rare Case Report of Primary Gastric Synovial Sarcoma

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Background	Synovial sarcoma (SS) is a rare type of soft-tissue tumor that typically occurs in the extremities and joints. However, it can also manifest in the gastrointestinal tract, where it often mimics other mesenchymal, fibrous, and spindle cell neoplasms. Accurate diagnosis is crucial and requires a combination of morphological assessment, molecular testing (specifically for the SYT-SSX fusion transcript), and immunohistochemical confirmation. Due to the tumor's aggressive nature and the need for complete excision, a partial or total gastrectomy is often the recommended treatment for primary gastric synovial sarcoma.
Summary	This case report presents a 42-year-old female with primary gastric synovial sarcoma discovered incidentally during an esophagogastroduodenoscopy. The diagnosis was confirmed through molecular identification of the characteristic t(X:18) translocation and supported by immunohistochemical findings. To better understand this rare presentation, a comprehensive literature review was conducted, analyzing the clinical characteristics of all 47 reported cases of primary gastric synovial sarcoma.
Conclusion	This case highlights the importance of considering synovial sarcoma in the differential diagnosis of spindle cell neoplasms within the GI tract. By utilizing a combination of morphological, molecular, and immunohistochemical techniques, clinicians can ensure accurate diagnosis and guide appropriate surgical management (often gastrectomy) to minimize the risk of recurrence. Further investigation into this rare entity is warranted.
Key Words	surgical oncology; sarcoma; robotic surgery

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Case Description

Synovial sarcoma (SS) is a rare mesenchymal malignancy, comprising 5-10% of all soft tissue sarcomas. Typically manifesting in the second and third decades of life,[1] SS is most often associated with extremity joints, with an annual diagnosis rate of just 0.81 per million children and 1.42 per million adults.[2] While rare, extra-articular manifestations can occur in the heart, fallopian tubes, kidneys, lungs, and mediastinum. SS has also been reported in the gastrointestinal tract, primarily affecting the stomach, with the first primary gastric SS case documented in 2000.[3]

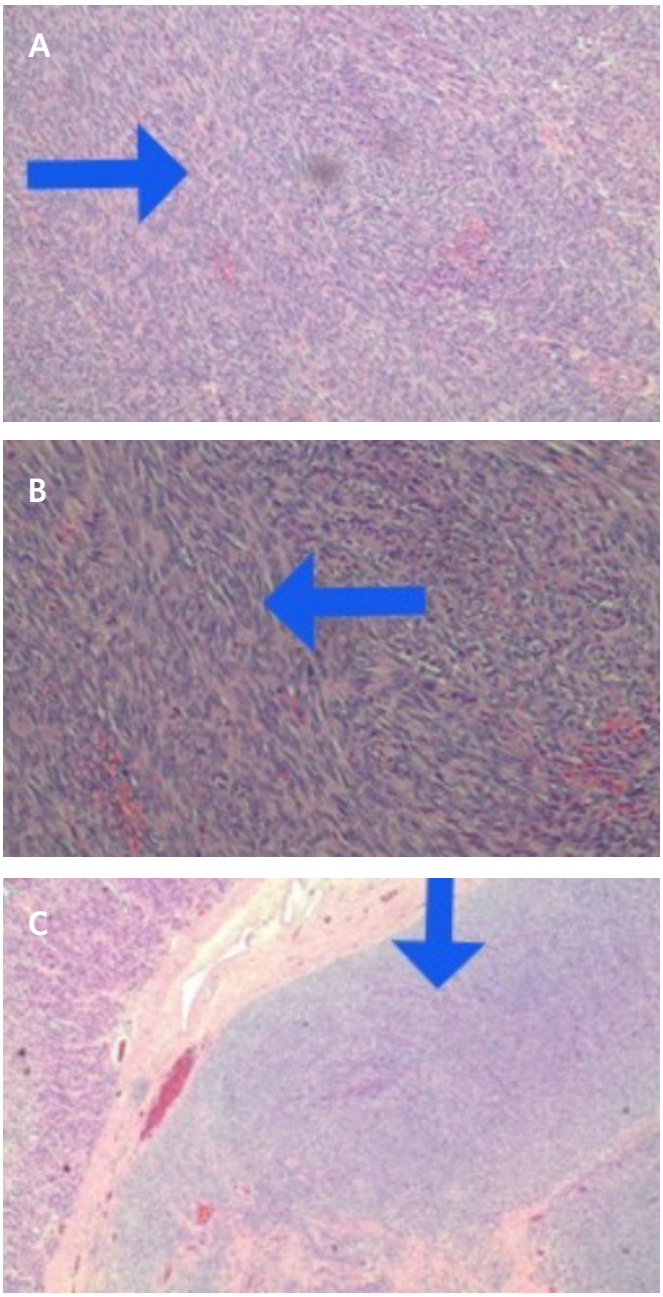
Due to the similar histological presentation of fascicles and sheets of spindle cells,[4] gastric SS can be mistaken for gastrointestinal stromal tumors (GIST). Definitive diagnosis relies on immunohistochemical confirmation of the characteristic t(X;18)(p22;q11) translocation, resulting in the SYT-SSX fusion transcript. While SYT expression is ubiquitous, SSX genes are typically found in the testis and thyroid. SSX1 and SSX2 variants account for over 90% of SS cases. Antibodies targeting these fusion genes offer high sensitivity (95%) and specificity (100%) for SS diagnosis.

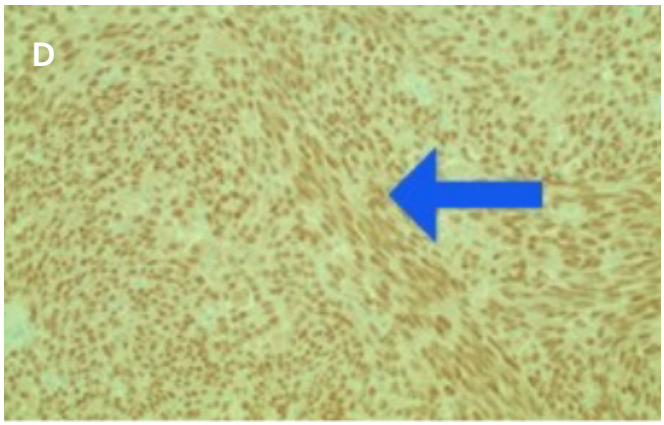
Currently, no specific guidelines exist for gastric SS. However, NCCN guidelines for sarcomas in the limbs, outer torso, head, and neck recommend R0 surgical resection with or without radiation. Reported gastric SS cases have been managed with various procedures, including partial, wedge, or total gastrectomy, via open or laparoscopic approaches.[1,2,5]

A 42-year-old woman with no significant medical history presented to her primary care physician after a tick bite suffered on a hike. She was prescribed prophylactic doxycycline for Lyme disease. Subsequently, she developed abdominal pain and melena, prompting a gastroenterology consultation. Esophagogastroduodenoscopy (EGD) revealed a medium-sized, submucosal, non-circumferential mass on the lesser curvature of the stomach, with no evidence of bleeding. Endoscopic ultrasound (EUS) further characterized the lesion as an intramural, subepithelial mass located 5 cm distal to the gastroesophageal junction. Biopsy results were negative for C-KIT but positive for CD34, suggesting a spindle cell neoplasm, most likely a leiomyoma. After further imaging to guide surgical planning, the patient underwent a robotic-assisted partial gastrectomy with intraoperative EGD for precise lesion localization. The patient recovered as expected and was discharged in stable condition.

Pathology of the mass, however, revealed a surprise. The mass demonstrated uniform cells with oval, vesicular nuclei and eosinophilic inclusions. Immunohistochemistry was negative for CD117, DOG1, S100, desmin, and ERG. Critically, PCR identified diffuse positivity for SS18-SRX, confirming the diagnosis of synovial sarcoma (Figure 1). Worryingly, the tumor focally extended to the inked margin, indicating potential incomplete resection.

Figure 1. Histological Appearance of SS with Characteristic Spindle Cell Morphology and Diffuse Positivity for SS18-SSX Translocation (D). Published with Permission





Following a negative biopsy for malignancy proximal to the staple line from a repeat gastrectomy, the patient underwent a second robotic-assisted gastrectomy. EGD and direct visualization were used to identify the target lesion. The stomach was then resected both proximally and distally to the lesion with a 60mm blue cartridge stapler, ensuring a margin negative for disease as confirmed by frozen section analysis. Although reconstruction was initially considered, the surgical plan was revised intraoperatively to a gastro-gastro anastomosis at the patient's request. Two gastrotomies were created with electrocautery on either side of the staple line, and indocyanine green (ICG) angiography was used to assess anastomotic perfusion. The anastomosis was then created with a 60mm blue cartridge stapler, forming a common channel. This common channel was closed in two layers using 2-0 absorbable Stratifix suture. Finally, a leak test was performed by submerging the anastomosis in saline and insufflating air via an orogastric tube.

The patient's postoperative course was uncomplicated, with minimal nausea and incisional pain. Discharged on postoperative day two on a clear liquid diet, she progressed to a regular diet by her six-week follow-up, at which time she reported no issues with eating or drinking and had returned to normal activity levels. Pathology from the second surgery confirmed clear margins with no residual malignancy. Although the patient missed her six-month follow-up, she remains scheduled for her one-year follow-up.

Discussion

Synovial sarcoma (SS) of the gastrointestinal tract is a rare entity, infrequently documented in the medical literature. While most SS cases arise in large joints, this tumor type can occur in the gastrointestinal tract, named for its histological resemblance to developing synovium. Although the precise tissue origin remains uncertain, current hypotheses, supported by transgenic mouse studies, suggest that SS may be derived from immature myoblasts.[6]

Diagnosis of SS can be challenging based solely on histopathological examination, as it can be easily mistaken for gastrointestinal stromal tumors (GIST). However, unlike GIST, which typically stains positive for C-kit and lacks a chromosomal translocation, SS is usually C-kit negative and characterized by a specific reciprocal translocation t(X;18) or the presence of the SYT-SSX fusion gene. These molecular markers offer high specificity and sensitivity, making them crucial for definitive diagnosis.[7]

In addition to molecular testing, immunohistochemical analysis can further aid in differentiating SS from other spindle cell tumors. While less specific than the genetic markers, diffuse expression of bcl-2, positive staining for CD99, expression of NY-ESO-1, and diffuse nuclear staining for the transcriptional corepressor TLE1 can be helpful in this distinction.[8]

Once diagnosed, SS can be categorized into three subtypes: monophasic, biphasic, and poorly differentiated.[2] Monophasic SS, composed entirely of spindle cells, presents the greatest diagnostic challenge due to its resemblance to other mesenchymal tumors, such as leiomyoma, leiomyosarcoma, schwannoma, solitary fibrous tumors, and gastroblastomas. It can also mimic cytokeratin-positive tumors like sarcomatoids and poorly differentiated carcinomas.[9] Biphasic SS, in contrast, is distinguished by the presence of both spindle cells and an epithelial component. Poorly differentiated SS exhibits increased nuclear atypia and high mitotic activity, exceeding 6 mitoses/mm^2 or 10 mitoses per 1.7 mm^2.[8,10]

A comprehensive review of the literature identified 46 documented cases of primary gastric SS. A comparative analysis of these cases, including the one presented in this study, is essential for refining diagnostic approaches and establishing effective treatment protocols for primary gastric SS. It is important to note that one previously reported case of metastatic gastric involvement secondary to SS was excluded from this analysis to maintain a focus on primary gastric SS.

Analysis of 46 cases[1,3-5,7,9,11-16,17-30] reveals an average patient age of 45 years (range 13-72) with a nearly equal male-to-female ratio (23:24), confirming the lack of sex predilection for SS. Primary gastric SS tumors averaged 52 mm in size (range 6-160 mm). Consistent with the presented case, the most common clinical presentations were epigastric pain and anemia.

Among the cases with reported subtypes (n=42), the majority (86%) were monophasic, followed by biphasic (12%) and a single poorly differentiated case (2.4%). Resection with adjuvant chemotherapy was performed in 8 cases (20.5%), primarily for larger tumors with transmural or perivisceral involvement.

Minimally invasive approaches are becoming increasingly common. Laparoscopic resection was utilized in 18% of cases, while robotic-assisted laparoscopy, including the presented case, was employed in 5.1%. The remaining cases (77%) presumably underwent open procedures.

Reported surgical procedures included total gastrectomy (7.7%), partial gastrectomy (46%), wedge resection (28%), and simple resection without further specification (18%).

Outcome data was available for 37 cases, with a disease-specific mortality rate of 16% (6 deaths). The majority of patients (84%) were alive at the time of publication, with one death attributed to an unrelated cause. The increasing adoption of laparoscopic and robotic-assisted techniques suggests a trend towards improved prognosis, likely due to enhanced visualization and precision, facilitating complete resection and reducing recurrence and mortality.

Based on these findings, the optimal management of primary gastric SS involves surgical resection with wide margins, prioritizing the preservation of normal gastric anatomy through meticulous surgical planning and advanced techniques. Historically, SS has demonstrated a high degree of localization and a low propensity for metastasis. Consequently, there are no specific recommendations regarding the use or efficacy of adjuvant chemotherapy, and routine investigation of regional lymph node involvement is not considered necessary.[41] However, complete tumor removal remains the overarching goal. The specific surgical approach may vary depending on the tumor's location, depth of invasion, and the ability to achieve clear margins.[2]

Table 1. Summary of Reported Cases and Management Strategies for Primary Gastric SSs.

Case No.	Year, Author	Sex	Age	Tumor Size (mm)	Subtype	Treatment	Outcome
1	2000, Billings	M	47	52	Biphasic	Gastrectomy with partial esophagectomy	AWD
2	2000, Billings	F	55	160	Monophasic	Hemigastrectomy	DD
3	2007, Akhunji	M	42	115	Biphasic	Resection, adjuvant chemotherapy	DD
4	2008, Makhlouf	F	67	8	Monophasic	Partial gastrectomy	AWD
5	2008, Makhlouf	M	49	20	Monophasic	Wedge resection	DD
6	2008, Makhlouf	F	68	20	Monophasic	Wedge resection	AWD
7	2008, Makhlouf	M	29	28	Monophasic	Partial gastrectomy	AWD
8	2008, Makhlouf	F	54	30	Monophasic	Antrectomy with gastroduodenal resection	NR
9	2008, Makhlouf	F	58	30	Monophasic	Wedge resection	AWD
10	2008, Makhlouf	F	37	40	Monophasic	Partial gastrectomy	DFOC
11	2008, Makhlouf	M	50	60	Monophasic	Resection, adjuvant chemotherapy	AD
12	2008, Makhlouf	M	42	80	Biphasic	Partial gastrectomy, adjuvant chemotherapy	DD
13	2008, Makhlouf	F	66	150	Monophasic	Gastrectomy with partial esophagectomy	LTF
14	2012, Sinniah	F	44	47	Monophasic	Laparoscopic wedge resection	AWD

15	2012, Wang	F	38	72	Monophasic	Wedge resection, adjuvant chemotherapy	AD
16	2013, Kamata	F	42	35	Monophasic	Partial gastrectomy	AWD
17	2013, Sahara	M	22	25	Monophasic	Wedge resection	NR
18	2014, Torres	M	44	150	Monophasic	Total gastrectomy	AWD
19	2014, Michot	M	62	38	Monophasic	Total gastrectomy, adjuvant chemotherapy	AWD
20	2015, Romeo	F	50	80	Monophasic	NR	LTF
21	2015, Romeo	M	36	60	Poorly Differentiated	NR	AD
22	2015, Romeo	M	37	20	Monophasic	NR	NR
23	2015, Romeo	M	26	NR	Monophasic	NR	AD
24	2015, Romeo	M	58	100	Monophasic	NR	DD
25	2015, Romeo	M	21	100	Monophasic	NR	DD
26	2015, Romeo	M	36	60	Biphasic	NR	LTF
27	2015, Romeo	F	54	38	Monophasic	NR	NR
28	2015, Wong, N	F	49	35	Monophasic	Resection	AWD
29	2015, Wong, N	F	35	120	Monophasic	Resection, adjuvant chemotherapy	AD
30	2017, So	F	51	17	Monophasic	Laparoscopic distal gastrectomy	AWD
31	2018, Ogino	F	27	20	NR	Laparoscopic gastrectomy	AWD
32	2018, Olsen	F	57	18	Monophasic	Wedge resection	NR
33	2017, Hu	M	58	63	Monophasic	Robotic-assisted, wedge resection	AD
34	2018, Fuente	M	42	30	Monophasic	Resection	AWD
35	2019, Bialik	M	26	80	Monophasic	Partial gastrectomy, adjuvant chemotherapy	AWD
36	2020, Wong, H	M	54	16	Monophasic	Laparoscopic wedge resection	AWD
37	2020, Krupinska	F	48	90	Monophasic	Distal gastrectomy, adjuvant chemotherapy	NR
38	2020, Manohar	M	13	110	Monophasic	Total gastrectomy	AWD
39	2021, Kuboyama	M	22	10	NR	Laparoscopic partial gastrectomy	AWD
40	2021, Kuboyama	F	38	10	NR	Resected	NR
41	2021, Kuboyama	M	72	13	NR	Resected	NR
42	2021, Marchand Crety	F	32	35	Biphasic	Wedge resection	AWD
43	2021, Rivelli 2021,	F	43	10	Monophasic	Laparoscopic intragastric resection	AWD
44	Kinowaki	F	59	26	Monophasic	Resection	NR
45	2021, Shibata	M	59	8	NR	Laparoscopic endoscopic cooperative surgery	AWD
46	2021, Yoshiyasu	F	61	6	Monophasic	Laparoscopic wedge resection	NR
47	**Present Case**	**F**	**42**	**40**	**Monophasic**	**Robotic-assisted resection with gastro-gastric anastomosis**	**AWD**

AWD, alive without disease; AD, alive with disease; DD, died of disease; NR, not reported; LTF, loss to follow-up; DFOC, died from other cause.

Conclusion

Synovial sarcoma of the stomach is a rare and likely underdiagnosed malignancy due to its histologic similarities to other tumor types. Increased awareness of SS in the gastrointestinal tract is crucial for accurate diagnosis and differentiation from other spindle cell and mesenchymal neoplasms, particularly C-kit-negative GISTs. Confirmation relies on immunohistochemical identification of the characteristic t(X;18) translocation or SYT-SSX fusion gene transcript. While surgical excision remains the primary treatment, the literature lacks specific surgical guidelines. However, there is a trend toward utilizing advanced minimally invasive techniques, including laparoscopic and robotic-assisted approaches. Due to the limited number of reported cases, predicting the prognosis of gastrointestinal SS remains difficult. Continued documentation and analysis of cases are needed to establish optimal management protocols and prognostic indicators.

Lessons Learned

This case highlights the challenges in diagnosing and managing gastric SS. A gastric mass on the lesser curvature of the stomach, initially presumed to be a GIST based on endoscopic and endoscopic ultrasound findings, was resected via robotic-assisted partial gastrectomy. However, final pathology revealed SS with positive margins, necessitating a second surgical intervention. To avoid a complex gastric bypass reconstruction, a gastro-gastro anastomosis was performed, deviating from the standard techniques reported in other cases. While successful in this instance, this approach may not be suitable for all patients, particularly those with comorbidities, due to the risk of severe complications.

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