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Kidney Curveball: A Rare Case of a Gastrointestinal Stromal Tumor with Renal Metastasis

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Abstract

Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract, accounting for approximately 1% of primary malignant gastrointestinal tumours. They arise from the interstitial cells of Cajal and are most frequently associated with KIT and PDGFRA mutations. GISTs primarily metastasize to the liver and peritoneum via hematogenous spread. Renal metastasis, however, is exceptionally rare, with only isolated cases reported in the literature. We report the case of a 55-year-old woman with a history of gastric GIST initially diagnosed in 2008, treated with laparoscopic wedge resection. She remained disease-free for 12 years before developing a local recurrence in 2020, for which repeat laparoscopic resection was performed. Histopathology demonstrated spindle and epithelioid tumour cells with a mitotic count of 13 - 15 per 50 high-power fields and positive immunohistochemical staining for CD117 and CD34, consistent with intermediate-risk GIST based on AFIP classification. Adjuvant imatinib was not initiated following either resection. Serial surveillance imaging remained unremarkable until mid-2023, when she presented with a right-sided abdominal mass and constitutional symptoms. Contrast-enhanced computed tomography revealed a large heterogeneously enhancing solid-cystic mass arising from the right kidney with high nephrometry complexity. Percutaneous renal biopsy demonstrated spindle and epithelioid tumour cells positive for CD117, CD34, and DOG1, confirming metastatic renal GIST. The patient was subsequently commenced on systemic tyrosine kinase inhibitor therapy with imatinib and remains under close oncological surveillance. This case highlights an extremely rare site of metastatic spread in GIST, posing

significant diagnostic challenges as it may mimic a primary renal malignancy on imaging. Renal involvement likely reflects aggressive tumour biology and emphasizes the importance of long-term surveillance. In patients with a history of GIST, any new renal mass should prompt consideration of metastatic disease and early histological confirmation to guide appropriate systemic therapy.

Subject Areas

Urology

Keywords

Gastrointestinal Tumour (GIST), Renal Metastasis, Surgical Oncology, Targeted Therapy, Tumour Recurrence

1. Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract, accounting for about 1% of primary malignant GI tumors [1] [2]. The global incidence ranges from 7 to 15 cases per million annually [3] [4], primarily affecting individuals aged 50 - 70, with no gender preference [5]. Studies have shown that GISTs are linked to KIT and PDGFRA mutations in 95% of cases [3] [6]. They arise from interstitial cells of Cajal, which mainly function in regulation of gastrointestinal motility [7]. Based on previous literatures, GISTs most commonly originate in the stomach (60% - 70%), small intestine (20% - 25%), colon/rectum (5%), and esophagus (<5%) [4] [8] [9]. Metastases commonly affect the liver (50% - 60%) and peritoneum (20% - 43%) [8] [10], while renal metastases are extremely rare, with only isolated reports in literature [11] [12].

2. Case Report

This case describes a 55-year-old woman who was diagnosed with recurrent gastrointestinal stromal tumor (GIST) and subsequent renal metastasis. She was initially diagnosed in 2008 with a localized Stomach GIST. She underwent a laparoscopic wedge resection of a gastric GIST. Histology confirmed it as GIST tumor. Subsequently, she remained disease-free for 12 years. However, in 2020, imaging surveillance detected local recurrence of a GIST tumor for which she underwent a second laparoscopic resection. Histopathological examination of the recurrent gastric tumour was composed of spindle and epithelioid cells, with a mitotic count of 13 - 15 per 50 high-power fields. Immunohistochemical staining was positive for CD117 and CD34, consistent with a diagnosis of GIST. As such it was classified under the AFIP classification (Category 5) as intermediate risk. At the time of the initial diagnosis in 2008, adjuvant imatinib was not universally recommended for intermediate-risk gastric GISTs, as clinical guidelines were still evolving and long-term survival benefits had not yet been clearly established. By 2020, although adjuvant imatinib was established, it was mainly recommended primarily for high-

risk GIST, and rarely certain intermediate risk cases. In this patient, therapy was not initiated likely due to perceived complete resection and underestimation of recurrence risk. Following her second resection for the recurrent tumor, subsequent surveillance follow ups with regular computed tomography (CT) scans and oesophagogastroduodenoscopy (OGDS) showed no recurrence until mid-2023.

In June 2023, she presented with a right-sided abdominal mass associated with constitutional symptoms. Contrast-enhanced CT scan revealed a 10.9 × 9.8 × 15.2 cm heterogeneously enhancing solid-cystic mass at the anterior cortex of the right lower pole, crossing the lower pole line with >50% exophytic growth. It showed corticomedullary enhancement with washout on the nephrogenic phase and loss of fat planes with the D2 duodenum, hepatic flexure, and right psoas, but no renal vein or IVC thrombus. The mass was also seen to indent on the liver surface but without hydronephrosis or collecting system obstruction. Based on its size (>7 cm), predominantly exophytic, anterior location, and extension near the renal sinus without invasion, the renal nephrometry score was 9a, denoting high complexity and supporting radical nephrectomy. However, the presence of metastatic disease warranted systemic therapy instead.

A percutaneous renal biopsy was performed which demonstrated spindle and epithelioid cells (as depicted in **Figures 1-5**) consistent with GIST. Furthermore, Immunohistochemical staining was positive for CD117 and DOG1, (as depicted in **Figure 6** and **Figure 7**, respectively) confirming the diagnosis of metastatic renal GIST. The patient was referred to oncology and commenced on imatinib 300 mg once daily from June 2024, which remains ongoing, with serial imaging planned to assess treatment response. KIT and PDGFRA mutational testing was not performed due to unavailability at our center. This represents a limitation, as identifying specific mutations can guide targeted therapy selection and predict treatment response to tyrosine kinase inhibitors such as imatinib and sunitinib.

The patient's demographic details and chronological clinical timeline are summarized in **Table 1**.

Table 1. Patient demographics and clinical timeline.

Parameter	Details
Age/Sex	55-year-old female
Initial Diagnosis	2008 Gastric GIST diagnosed; underwent laparoscopic wedge resection
Disease-Free Interval	2008-2020 (12 years)
Recurrence	2020 Recurrent GIST detected; laparoscopic resection performed
Surveillance Findings	Regular CT and OGDS follow-up until mid-2023, no recurrence
Latest Presentation	June 2023 Right-sided abdominal mass and constitutional symptoms
Imaging Findings	CT: Complex right renal mass suspicious for malignancy
Biopsy Result	Spindle and epithelioid cells consistent with metastatic GIST
Immunohistochemistry	CD34+, CD117+, DOG1+
Current Management	Started on Sunitinib (tyrosine kinase inhibitor) under oncology care

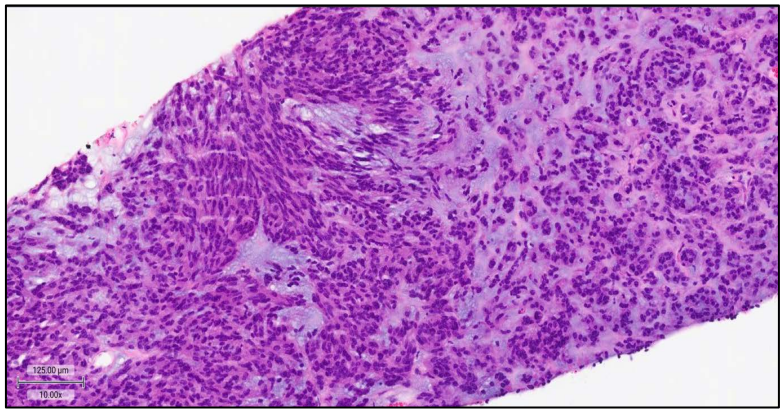

Figure 1. Spindle and epithelioid cells proliferation with myxoid background (×100).

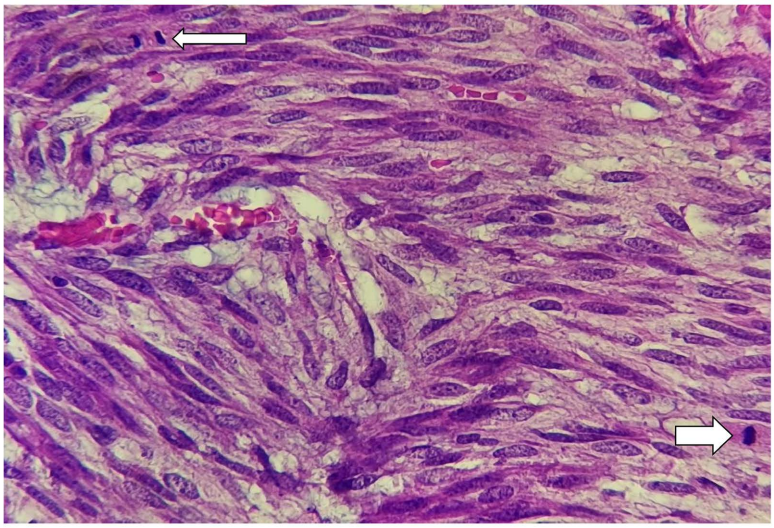

Figure 2. Spindled cells with increased mitotic figures [white arrow] (40× objective/400× magnification).

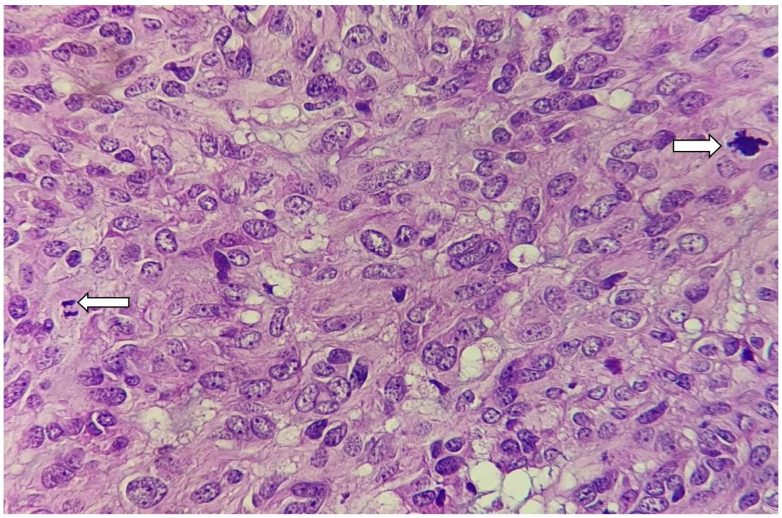

Figure 3. Epithelioid cells with increased mitotic figures [white arrow] (40× objective/400× magnification).

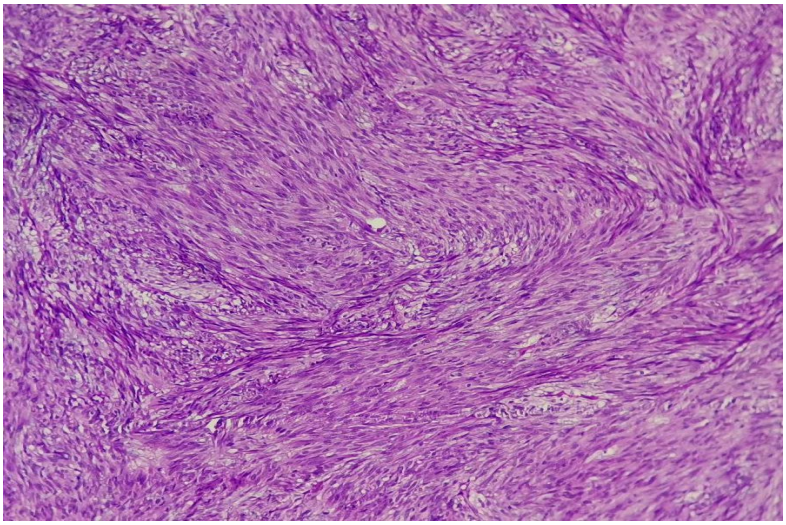

Figure 4. Spindled cells in fascicular pattern (10× objective/100× magnification).

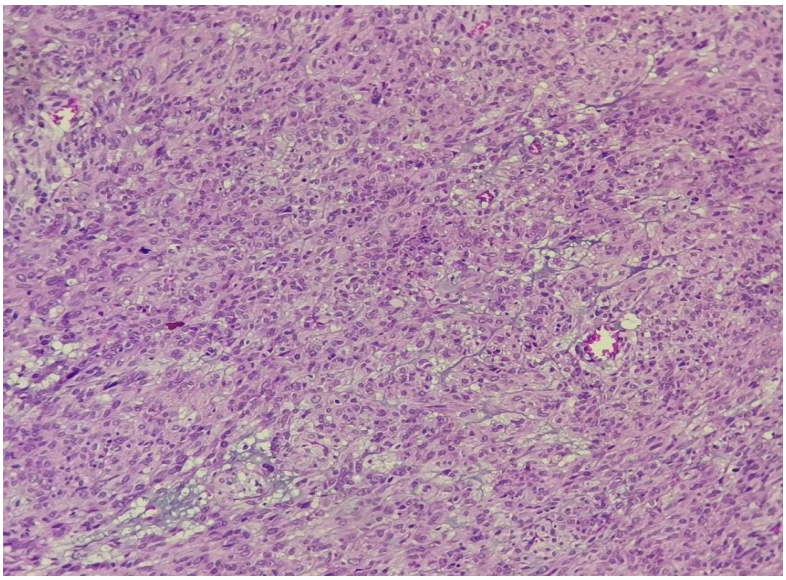

Figure 5. Epithelioid cells in fascicular pattern (10× objective/100× magnification).

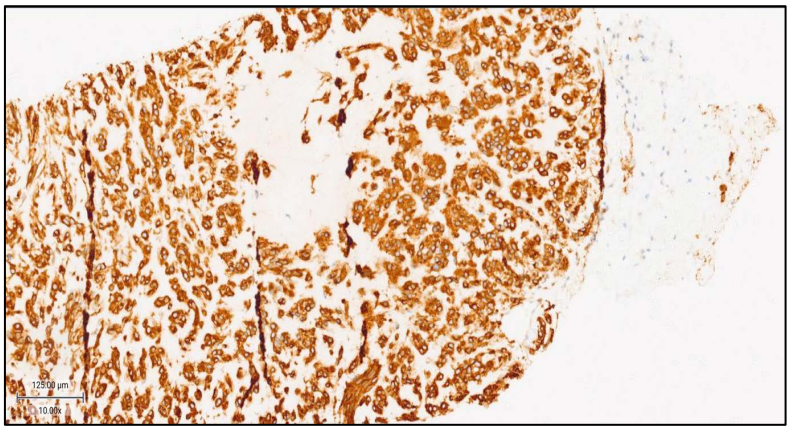

Figure 6. CD117 positive (×100).

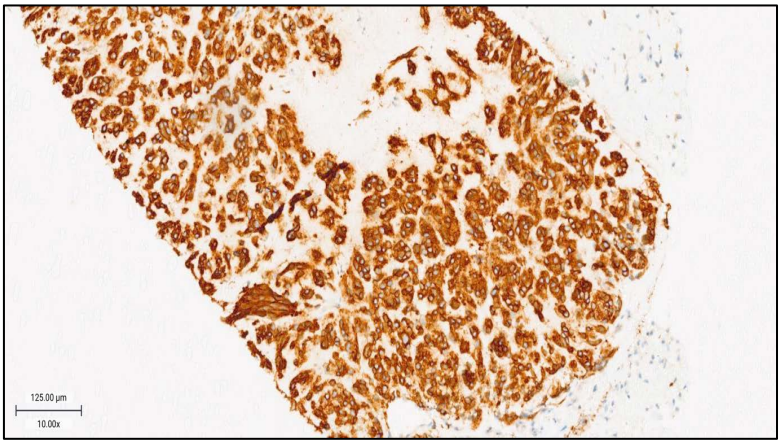

Figure 7. DOG1 positive (×100).

3. Discussion

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract, accounting for ~1% of primary malignant GI tumors [1] [3]. The global incidence is 7 - 15 cases per million annually [4] [5]. GISTs arise anywhere in the GI tract, mostly in the stomach (60% - 70%) or small intestine (20% - 30%), with 5% in the colon and <5% in the esophagus [4] [8]. They originate from interstitial cells of Cajal, which regulate intestinal motility, and are strongly linked to c-KIT (CD117) or PDGFRA mutations (85% - 90%) [2] [6] [10]. Though often benign, up to 30% can be malignant [9] [13]. GISTs rarely spread via lymphatics but metastasize hematogenously, primarily to the liver (50% - 60%) and peritoneum (20% - 43%), with rare lung, bone, or lymph node involvement < 10% [13] [14]. Thus, the most common the sites of metastasis are usually to the liver and peritoneum.

Metastasis to the kidneys from a GIST is an exceptionally rare occurrence, making up <1% metastatic sites of GISTs [11] [14]. Hence, the kidneys are not a common site for secondary involvement, making this case particularly unusual. A recent study by the Departments of Surgery, Biostatistics, and Pathology, Memorial Sloan-Kettering Cancer Centre, New York City reviewed literature from the year 2000 onwards on rare sites of metastasis of GISTs other than the liver and peritoneum. A recent systematic review of unusual metastatic sites identified 98 reported cases that together described 118 non-liver, non-peritoneal metastatic sites (some patients had >1 site). Renal involvement was reported in only one case, underscoring the exceptional rarity of kidney metastasis from GIST [12] [15]. Other recent comprehensive reviews of GIST likewise list renal involvement as an uncommon/isolated occurrence among many rare metastatic sites, supporting the assertion that renal metastasis is exceedingly rare [11] [14] [15].

GIST symptoms vary by location and metastasis site, commonly presenting with GI bleeding, abdominal pain, or a palpable mass [15]. Metastatic symptoms depend on the affected organ, such as respiratory issues in lung metastases or bone pain in bone metastases [11]. In this case, a patient developed an abdominal mass

years after GIST resection. Imaging identified a right kidney mass, initially thought to be a primary renal tumor. However, histological analysis revealed spindle cell morphology consistent with GIST, confirming it as a rare renal metastasis.

Recurrence of disease after resection was predominantly intraabdominal and involved the original tumour site, peritoneum, and liver [13]. The most common anatomic sites of tumour recurrence were the stomach (39%) and the small intestine (32%); colorectal tumours accounted for 15% of the total. A small portion of recurrence of GISTs were from other intraabdominal or retroperitoneal sites where the exact origin is unclear [13] [16].

GIST diagnosis involves imaging, endoscopy, and histopathology. Imaging choice depends on tumor location and clinical presentation, with contrast-enhanced CT as the preferred method. MRI is an alternative if contrast is contraindicated [16]. Endoscopic ultrasound helps differentiate GISTs from other sub-epithelial lesions [8] [15]. However, histopathological examination is vital in establishing the diagnosis of GISTs which can be obtained via endoscopic biopsies, surgical resections, or metastatic site sampling. GISTs are classified into spindle cell, epithelioid, or mixed types. Confirmatory diagnosis is by immunohistochemical staining with CD117 (c-KIT) and CD34, which are specific diagnostic markers for GISTs [7] [8]. In some instances, DOG1 and genetic testing aim in KIT-negative cases [3] [6]. In this case, a renal mass initially suspected as a primary tumor was histologically similar to the patient's previous GIST, confirming it as a rare renal metastasis.

GIST management depends on disease extent, with surgery preferred for localized tumors. Laparoscopic or open surgery is chosen based on tumor size, followed by adjuvant imatinib. ESMO recommends three years of adjuvant imatinib (400 mg daily) for high-risk patients, improving relapse-free and overall survival [17]-[19]. For patients with locally advanced disease, neoadjuvant imatinib can be used to help reduce tumor burden to facilitate better surgical resection. Indications for this use include tumors where negative margins will be difficult to obtain and when reduced tumor burden may allow for function-sparing resection. At this time, there are no clear recommendations guiding the duration of neoadjuvant therapy, but it is recommended that therapy be continued until maximal response has been obtained. While patients are undergoing neoadjuvant therapy, it is recommended to evaluate for the response to therapy [20] [21].

Metastatic GISTs rely on medical therapy, primarily tyrosine kinase inhibitors like imatinib, sunitinib, and regorafenib [16] [22]. The aim of treatment is mainly to slow disease progression. Imatinib is the first-line treatment, as evidence has shown to prolong overall survival from 1.5 to over 5 years [22]. CT scans monitor treatment response, though initial tumor changes may appear misleading. Prognosis depends on tumor site, size, and mitotic count, guiding treatment decisions and long-term outcomes [9] [20] [23].

The mechanism of renal metastasis from GIST remains speculative. A probable theory about renal metastasis of GIST could be linked to arterial dissemination of circulating tumor emboli lodging within the renal cortical microvasculature [11]

[22]. This follows the basis that GISTs predominantly spread hematogenously. Lymphatic spread, however, is improbable due to the absence of direct lymphatic connections between the gastrointestinal tract and kidneys. Another possibility that could favour renal metastasis of GIST is retroperitoneal seeding from peritoneal deposits along the posterior abdominal wall. Despite the kidney's rich blood supply, its vascular structure may be less conducive to tumor cell implantation, which could explain why renal metastases from GIST are exceedingly rare [12] [14].

4. Conclusion

Diagnosing and treating GISTs requires collaboration among specialists, including surgeons, pathologists, radiologists, and oncologists [17] [18]. Renal metastasis of GIST is rare and may indicate aggressive disease with a higher morbidity risk [12] [14]. Limited literature on this further complicates diagnosis. When a renal mass is detected in a GIST patient, metastasis should be considered, prompting early urologist referral and biopsy [7] [15]. Due to its rarity, a proper clinical approach is crucial for GIST patients presenting with a flank mass to prevent misdiagnosis and ensure timely treatment.

Conflicts of Interest

The authors declare no conflicts of interest.

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