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CASE REPORT

New Abdominal Mass After Surgery for Gastrointestinal Stromal Tumor: Desmoid-Type Fibromatosis Difficult to Distinguish from Mesenchymal Tumor – A Case Report

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Abstract: A new lump in patients with a history of gastrointestinal stromal tumor (GIST) may indicate resistance to medication and recurrence. It is important to monitor for recurrence or metastasis after surgery for GIST, especially in cases of high-risk GIST, as it determines the subsequent treatment. However, it is difficult to differentiate between GIST and DF by imaging. Tissue biopsy and final diagnosis through pathological analysis are usually required. Here, we report 2 cases of primary diagnosis with high-risk GIST and suspected tumor recurrence during Imatinib treatment. The mass was not located where the previous GIST lesion had been. After the complete excision of the mass through laparoscopic surgery, the pathological findings revealed that it was not a recurrence of GIST, but a desmoid-type fibromatosis.

Keywords: lumpectomy, pathological diagnosis, GIST, imatinib

Introduction

Gastrointestinal stromal tumors (GIST) are the most prevalent type of sarcoma. The incidence rate of GIST is approximately 10–15 per million.[1,2] Approximately 70% to 80% of GIST has mutations in the KIT receptor tyrosine kinase gene. About 5–10% of GISTs have mutations in the platelet-derived growth factor receptor-α (PDGFRA), while 10–15% of GIST are referred to as wild-type GIST, which do not have detectable mutations in either KIT or PDGFRA.[3–5] The majority of GISTs are positive for KIT (CD117) and DOG-1. Other markers include CD34 antigen (70%), smooth muscle actin (SMA, 30–40%), S100 protein (10%), and desmin (< 5%).[5,6] The treatment of GIST was revolutionized by the introduction of KIT inhibitors, with imatinib being the most representative drug due to the prevalence of exon 11 mutations in KIT mutations (80%).[7] However, most patients sensitive to imatinib develop resistance after 2–3 years of treatment. Although the second-line drug sunitinib and the third-line drug regorafenib have been utilized, the response rates and patient benefits have been limited. In recent years, two fourth-line drugs, ripretinib and avapritinib, have been approved for marketing. These drugs specifically target PDGFRA exon 18 mutations.[3]

Desmoid-type fibromatosis (DF) is a rare neoplasm that arises from deep tissues. The prevalence rate of fibromatosis is low, with an estimated occurrence of 2–5 cases per 1,000,000.[8] DF may be associated with familial adenomatous polyposis, a history of abdominal surgery, or abdominal trauma.[9] It mainly consists of fibroblastic and myofibroblastic cells and has the potential to invade nearby organs.[10] Some articles have shown that GIST and intra-abdominal DF are frequently misdiagnosed.[11–14] In patients with a history of GIST, the presence of DF may give the impression of recurrence and interfere with subsequent treatment. The endoscopic findings, such as the expression of CD117, CD34, DOG-1, or β-Catenin, may provide the most accurate means of distinguishing between DF and GIST.[14] In our present study, we present findings on two patients with a history of GIST who developed abdominal masses after surgery. The

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mass was not located in the same place as the previous GIST lesion. After the complete excision of the mass through laparoscopic surgery, the pathological findings revealed that it was not a recurrence of GIST, but rather a DF.

Case Presentation

A 45-year-old man was first diagnosis with GIST in September 2020. Bleeding, tumor rupture, and gastric perforation occurred during gastroscopy, leading to subsequent complete removal of the lesion by emergency surgery. Genetic testing indicated exon 11 mutations in the KIT gene, with no other mutations identified. Due to rupture and gastric perforation during the endoscopic resection, the patient received postoperative treatment with Glivec (Imatinib). The patient was regularly monitored after the operation. In October 2022, a whole abdomen enhanced CT scan indicated a small mesenteric mass in the small intestine with a maximum diameter of approximately 3.6 cm and mild enhancement (Figure 1A). The PET-CT also indicated a soft tissue density mass in the lower abdominal mesentery with increased FDG metabolism. Considering the medical history, this finding initially raised the possibility of GIST metastasis and suggested a biopsy to clarify the pathology. The imaging indicated that the patient had only one isolated lesion, and the possibility of GIST recurrence was being considered. Consequently, in October 2022, the patient underwent a lumpectomy to completely remove the lesion. Postoperative pathological findings indicated the following: CD117 (-), DOG-1 (-), CD34 (-), Ki-67 (+, 5%), SDHB (+), CK (pan) (-), S-100 (+), Desmin (partially +), SMA (+), β-Catenin (nuclear/plasma +). The final pathological findings indicated diffuse fibrosis (Figure 1B). The second patient, a 57-year-old man, was initially diagnosed with a duodenal mesenchymal tumor with liver metastases. The duodenal mesenchymal tumor and liver metastases were surgically removed. Postoperative pathology revealed a duodenal tumor measuring 5×3 cm, with a mitotic index of 6/50 high-power fields (HPFs). The tumor tested positive for SDHB, CD117, DOG-1, and Ki-67 (44%). Genetic test results suggest a mutation in exon 11 of the KIT gene. The patient received oral Imatinib at a dosage of 400 mg/day, and our hospital conducted regular post-operative follow-ups after the surgery. The patient's condition was well controlled during treatment with Imatinib. In August 2022, the patient underwent a re-examination, which revealed the presence of a mesenteric mass in the small bowel. Considering the patient's medical history, a mesenchymal tumor was considered as a potential diagnosis (Figure 2A). Due to the tumor's location in a difficult-to-access area, the patient underwent a lumpectomy to remove the mass. Intraoperative cryosection indicated the presence of a spindle cell soft tissue tumor. The final pathology, in combination with immunohistochemistry, suggested that the Ki-67 was positive (5%), CD117 was negative, S-100 showed scattered positivity, Desmin showed less positivity, CD34 was negative, SMA

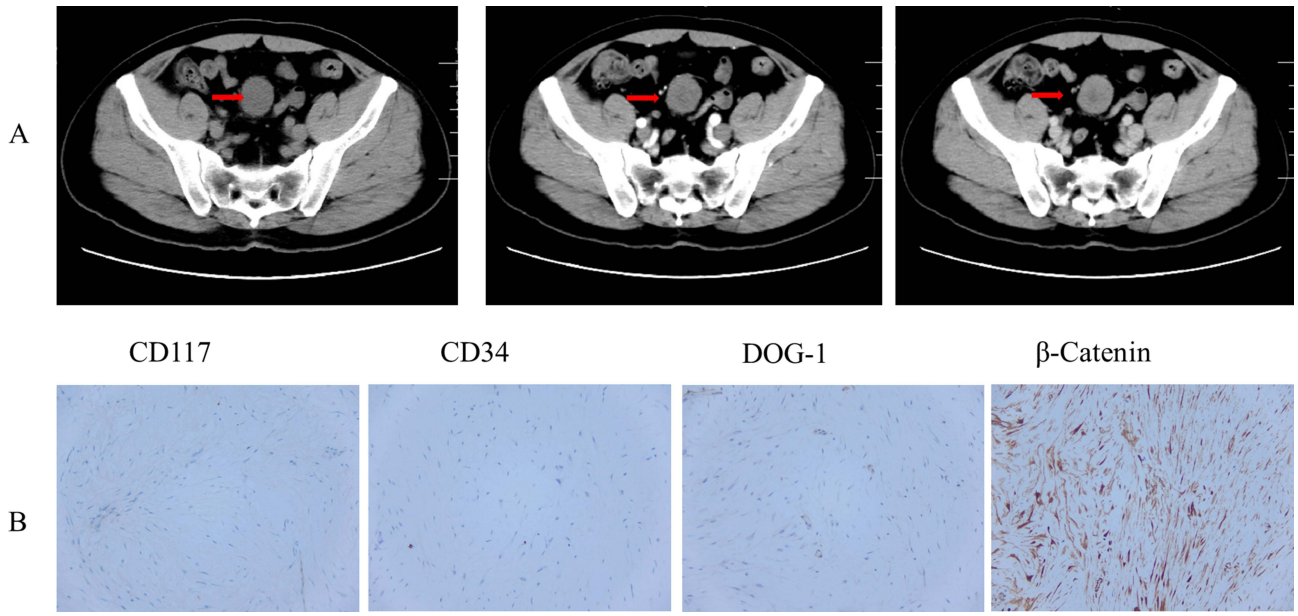

Figure 1 (A) Enhanced CT scan of the patient indicates the presence of a new mass outside the primary tumor. A soft tissue mass in the mesentery of the small intestine with enhancement suggests a possible recurrence of a GIST. (**B**) Pathological results showed negativity for CD117, CD34, DOG-1, and positivity for β-catenin.

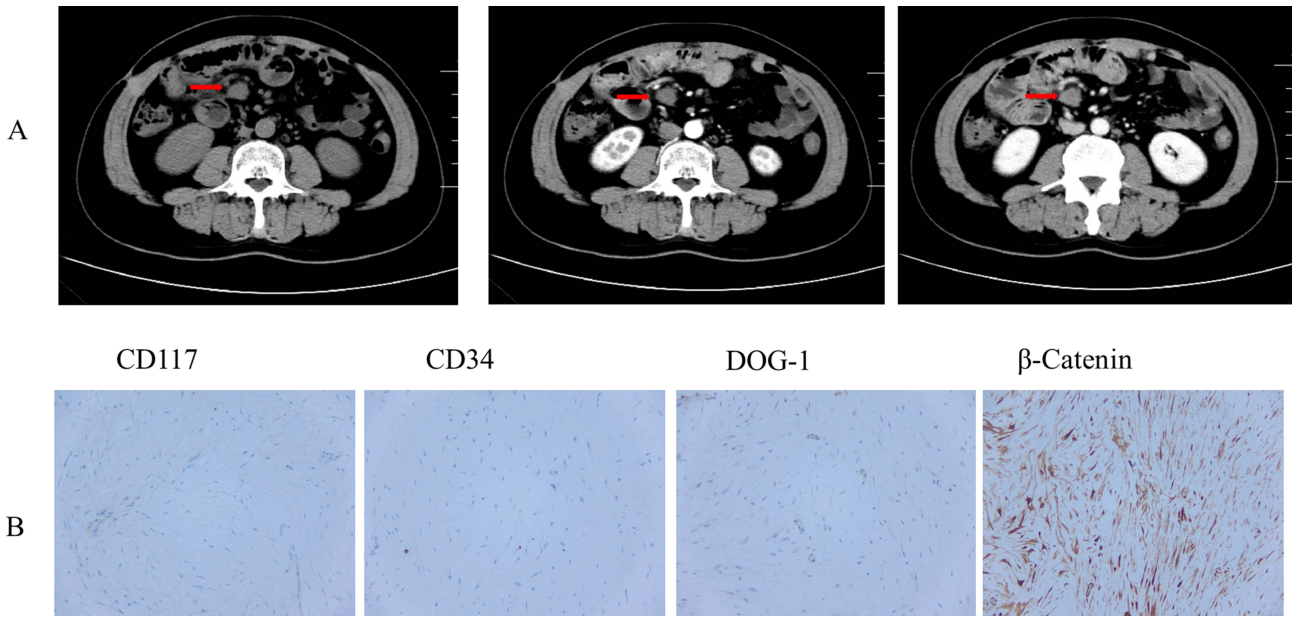

Figure 2 (**A**) Enhanced CT scans of the patient indicates the presence of a new mass outside the primary tumor. A soft tissue mass is present in the root of the mesentery of the small intestine with increased enhancement, indicating a potential recurrence of a GIST. (**B**) Pathological results showed negativity for CD117, CD34, DOG-1, and positivity for β-catenin.

showed partial positivity, DOG-1 was negative, and β-Catenin showed nuclear positivity. These findings are consistent with DF (Figure 2B).

Discussion

The introduction of tyrosine kinase inhibitors (TKIs) has revolutionized the treatment of GIST. Imatinib, one of the most widely used TKIs, revolutionized the treatment of unresectable, metastatic, and/or recurrent GIST. While imatinib improves the prognosis of patients with advanced GIST, increasing the median progression-free survival to 2 years and overall survival to 5 years, most patients eventually develop drug resistance. Several mechanisms of acquired resistance to imatinib have been proposed, including the development of secondary mutations and the potential activation of other metabolic pathways.[15–17] Patients with imatinib-resistant GIST should consider changing treatment regimens. Second- and third-line treatment options include sunitinib and regorafenib, respectively. However, response rates are low, and the clinical benefit is limited. Recently, the FDA has approved several drugs for treating GIST, such as rilpretinib for fourth-line treatment and avapritinib for PDGFRA exon 18 mutant GIST. Therefore, it is crucial to clarify whether the tumor is experiencing recurrence, metastasis, etc. during GIST treatment.

GIST and DF are different types of abdominal masses. DF may exhibit local aggressiveness but generally lacks the ability to metastasize and is considered non-malignant.[18] In the past, DF was primarily treated through surgical resection and radiotherapy.[19] Both tumors may present as a mass in the abdomen. The presence of DF in the abdomen post-operatively in patients with GIST is a rare phenomenon. Thway, K. et al reported a case of DF in anastomosis after the resection of sigmoid GIST in 2016.[20] A definitive diagnosis is crucial because detecting metastatic GIST is essential for determining subsequent treatment. However, some reports have shown that it is difficult to differentiate between GIST and DF using imaging.[21] Diagnosis based on molecular markers may be the most reliable method for diagnosis. In our study, obtaining tissue through puncture was challenging due to the location being obscured by the small intestine. Based on the clinical features, the surgeon decided to perform an exploratory open laparotomy to remove the tumor. Further pathological analysis suggested that the patient did not have a recurrence of GIST. Therefore, we concluded that the patients did not develop resistance to Imatinib. During the next follow-up, neither patient experienced a recurrence of GIST metastasis. In patients with high-risk GIST, obtaining an accurate pathological diagnosis is crucial for selecting appropriate therapeutic agents.

Pathology reports and immunohistochemistry analyses play a crucial role in differentiating between DF and GIST. On CT scan results, DF and GIST exhibit similar characteristics, making them challenging to distinguish. Given the medical history of GIST in both patients, diagnosing GIST was straightforward. The negativity for CD117, CD34, and DOG-1 effectively ruled out GIST, while the presence of β-catenin indicated a diagnosis of DF. Currently, there are limited reports of independent recurrences in patients with a history of GIST that have pathological findings consistent with DF. Furthermore, there is a scarcity of studies addressing the differentiation between GIST and DF, and the etiology of DF remains unclear. The emergence of DF may suggest the onset of progressive resistance to Imatinib. Alternatively, the presence of DF could indicate that Imatinib remains effective. In future studies, we will continue to monitor these two patients to assess their GIST treatment outcomes.

Conclusion

Pathology reports and immunohistochemistry analysis play a vital role in distinguishing between DF and GIST. On CT, DF and GIST behave similarly and are difficult to distinguish. Combined with the medical history of GIST in both patients, it was easy to diagnose GIST directly. CD117, CD34, and DOG-1 negativity ruled out GIST, and β-catenin indicated a diagnosis of DF. Currently, there are few reports of independent recurrences in patients with a history of GIST with pathological findings considered to be DF. Moreover, there are few studies addressing the distinction between GIST and DF, and the formation of DF is unknown. Perhaps the emergence of DF may suggest the beginning of progressive resistance to Imatinib. Or, the presence of DF may be a sign that Imatinib is still effective. In subsequent studies, we will continue to follow these two patients to observe the GIST treatment.

Abbreviations

GIST, Gastrointestinal stromal tumors; DF, Desmoid-type fibromatosis; PDGFRA, platelet-derived growth factor receptor-α; TKI, tyrosine kinase inhibitors.

Ethical Approval

A report of 2 cases is described in the article. Consequently, no further approval from our Ethics Committee was necessary (First Affiliated Hospital School of Medicine, Zhejiang University).

Consent

The patient has approved and written informed consent for the publication of this case report including the images.

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Disclosure

The author(s) report no conflicts of interest in this work.

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