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Repeated recurrence of a gastric gastrointestinal stromal tumor on the chest wall after initial curative resection: Report of a case☆

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ABSTRACT

INTRODUCTION: Extra-abdominal recurrence or metastasis of a gastrointestinal stromal tumor (GIST) is very rare. Chest wall recurrence of a resected gastric GIST is extremely rare.
PRESENTATION OF CASE: A 64-year-old Japanese man had undergone proximal gastrectomy for a gastric submucosal tumor 11 years previously. The histopathological diagnosis was GIST (size, 8 cm). He did not receive adjuvant therapy, and underwent imaging evaluations every 6 months for the first 5 years after surgery and then annually. He was admitted to our hospital because of a lump on his right anterior chest wall 7 years after curative resection. We resected the tumor, and histopathologic findings revealed metastatic GIST. Four years after metastasectomy, another lump appeared at a different location on the right anterior chest wall. The patient was diagnosed with a second recurrence of gastric GIST and began adjuvant treatment with imatinib after second resection. He has remained alive without tumor recurrence for 2 years.
DISCUSSION: Most recurrences were predominantly found in the intra-abdominal cavity, either locally or involving the liver or peritoneum. Extra-abdominal recurrence was much less common. Although we assume that the recurrent tumor of our patient was derived from his gastric GIST, based on the histopathological examinations and clinical course, it is possible that the recurrent tumor of our case was an "extragastrointestinal GIST".
CONCLUSION: Because extra-abdominal recurrence can occur many years after curative resection, continued, careful whole-body follow-up is required for patients with high-risk GIST.

1. Introduction

Gastrointestinal stromal tumor (GIST) is a rare mesenchymal tumor originating from the interstitial cells of Cajal in the gastrointestinal tract. GIST, with a yearly incidence of 10–20 cases per 1 million individuals. It is the most common sarcoma of the intestinal tract, accounting for 82% of all gastrointestinal mesenchymal neoplasms.[1,2] The molecular, biological, and clinical characteristics of GIST have recently been elucidated, which has led to improved outcomes. According to the guidelines on GIST, surgical resection is the treatment of choice for resectable primary tumors;[1,3,4] however, nearly half of the patients undergoing curative resection recurred, with a 5-year recurrence-free survival (RFS) rate of 54% and a median RFS time of 66 months.[1] Several clinical trials have indicated that adjuvant therapy after curative resection should be administered to improve outcomes, especially for patients with high-risk GIST.[5–7]

DeMatteo et al. reported that GISTs recur after resection predominantly within the abdominal cavity, either locally or in the liver or peritoneum, and that extra-abdominal recurrence is extremely rare.[1] Furthermore, most GISTs recur during the first 5 years of follow-up and few recur after the first 10 years of follow-up.[7] Therefore, several risk stratification tools have been developed, and mutational analysis has been used to aid assessment of patients for targeted adjuvant treatment.[8] We herein report a patient with a second recurrence of gastric GIST involving his chest wall 11 years after curative resection.

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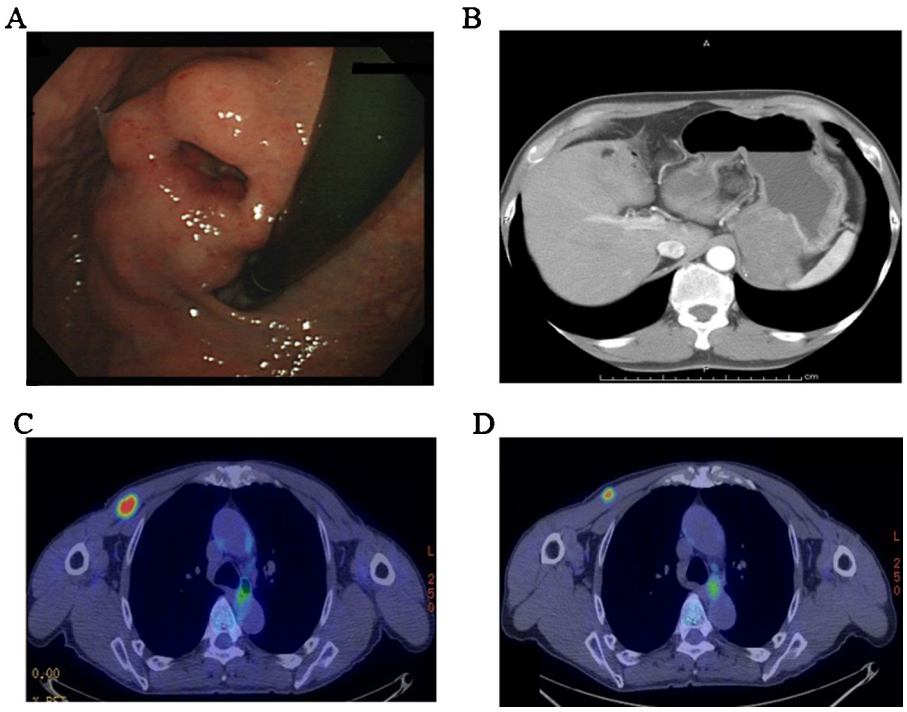

Fig. 1. *Imaging findings.* Upper gastrointestinal endoscopy shows an ulcerated submucosal tumor in the cardiac region of the stomach (A), contrast-enhanced computed tomography (CT) shows a large mass with homogeneous density dorsal to the stomach (B), positron emission tomography/computed tomography (PET/CT) at the time of first recurrence shows a mass with fluorine-18 2-deoxy-2-fluoro-D-glucose (FDG) accumulation in the tumor with an SUV of 7.7 involving his right anterior chest wall (C), PET-CT at the time of second recurrence shows a mass with FDG accumulation in the tumor with an SUV of 7.3 at a distance from the first site of recurrence in his right anterior chest wall (D).

2. Presentation of case

A 64-year-old Japanese man visited our hospital complaining of epigastralgia. An upper gastrointestinal endoscopy revealed an ulcerated submucosal tumor in the cardiac region of the stomach (Fig. 1A). Computed tomography (CT) revealed a large mass with homogeneous density located dorsal to the stomach (Fig. 1B). The patient had undergone a proximal gastrectomy without tumor rupture for gastric GIST via the abdominal approach 11 years prior. Histopathological examination revealed an 8-cm GIST with lymph node metastases (3/9) and a mitotic count of 32/50 high-power field (HPF). The immunohistochemical examination showed *KIT* negative and CD34 positive (Fig. 2A–C). The patient did not receive adjuvant therapy and was followed by imaging every 6 months for the first 5 years after surgery, and then annually.

Seven years after curative resection, he was admitted to our hospital because of a lump on his right anterior chest wall. Positron emission tomography/computed tomography (PET/CT) revealed accumulation of fluorine-18 2-deoxy-2-fluoro-D-glucose (FDG) in the tumor, with a standardized uptake value of 7.7 and no other definitive intra-abdominal lesions (Fig. 1C). We resected the tumor, and histopathologic findings revealed metastatic GIST (size, 3.5 cm; mitotic count, 80/50 HPF). Immunohistochemical examination found spindle-shaped cells positive for *KIT* and CD34 expression (Fig. 2D–F). He did not receive adjuvant therapy and underwent imaging follow-up every 6 months. Four years after his second surgery, he developed a lump at a different location on the right anterior chest wall. Since PET-CT revealed an FDG accumulation in the tumor with an SUV of 7.3 and no other definitive lesions (Fig. 1D), the patient underwent a second resection. The histopathological diagnosis of this tumor was metastatic tumor secondary to gastric GIST. After surgery, the patient began imatinib treatment at a dose of 400 mg/day. He has been alive without recurrence on imaging for 2 years.

3. Discussion

We present a case of repeated recurrence on the chest wall secondary to gastric GIST 11 years after curative resection of the primary tumor. Chest wall recurrence of a resected gastric GIST is extremely rare, although there have been a few case reports on cutaneous and subcutaneous GIST metastases.[9,10] Wang et al. reported that all patients with cutaneous and subcutaneous GIST metastases had multiple concurrent or subsequent abdominal and/or hepatic metastases.[10] We previously reported a patient with pleural dissemination of gastric GIST found 11 years after curative resection.[11] However, to the best of our knowledge, there are no English language reports of repeated recurrence of GIST involving the chest wall.

Most GIST recurrences occur in the abdominal cavity. DeMatteo et al. investigated the recurrence pattern of GIST in patients who had undergone complete resection of their primary tumor. Of the total number of recurrences, most were predominantly found in the intra-abdominal cavity, either locally (52%) or involving the liver (63%) or peritoneum (21%). Extra-abdominal recurrence was much less common, and involved the lung (7%) and bone (7%).[1] There were no cases of chest wall recurrence. However, it is possible that the recurrent tumor of our case was an “extragastrointestinal GIST (EGIST)”. It is reported that EGIST constitutes only 5%-10% of GIST cases.[12] Most EGISTs are derived from the mesentery, omentum, and retroperitoneum. Although our assumption that the recurrent tumor of our patient was derived from his gastric GIST, based on the histopathological examinations and clinical course, gene mutation analysis of the primary and recurrent lesions might provide more information on this case.

Although oral imatinib is the first-line therapy for recurrent or metastatic GIST, surgical treatment can be used to delay or prevent recurrence. However, the benefits of surgical resection for recurrent cases have not been confirmed.[3,4,13] We performed

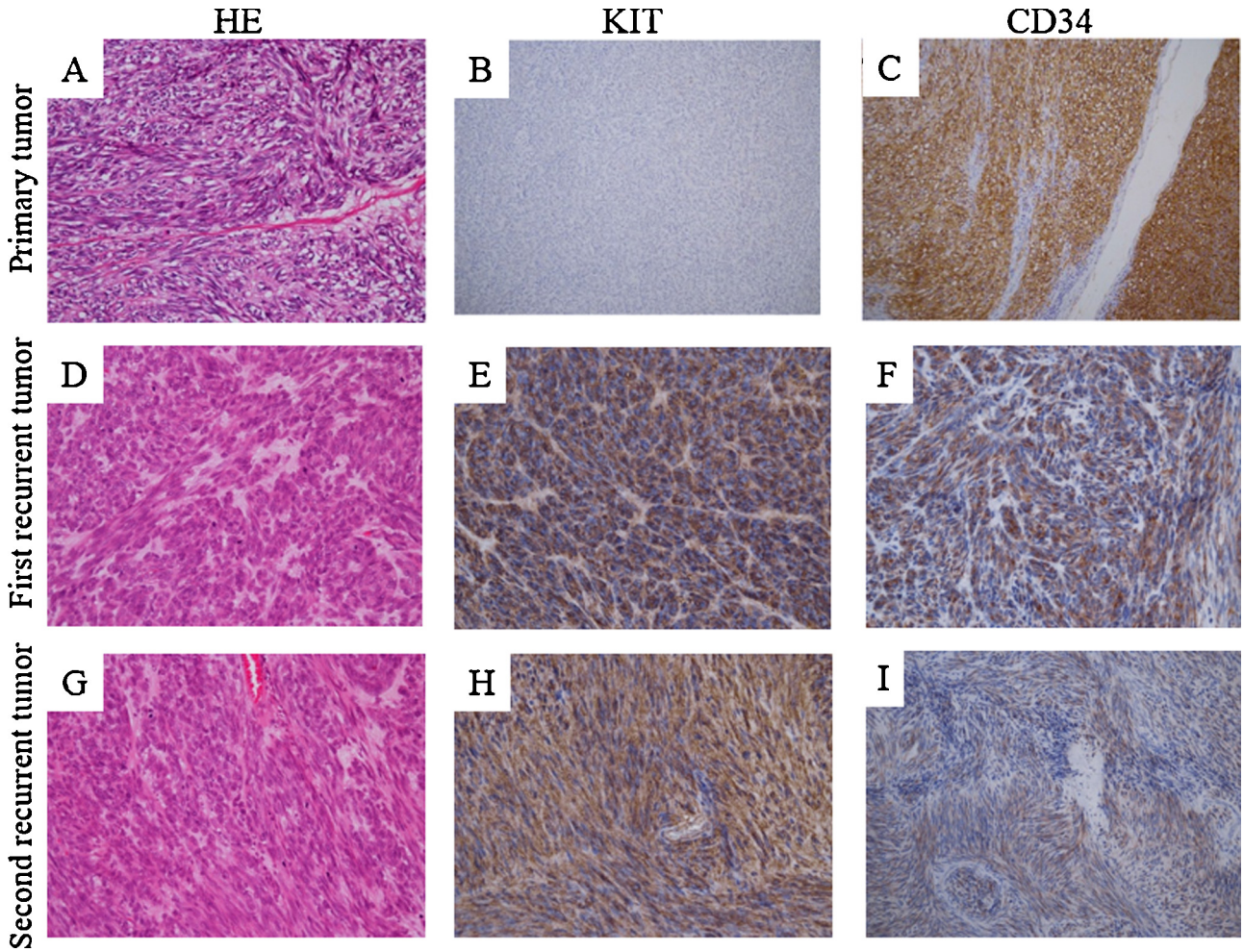

Fig. 2. *Histopathological findings.* Hematoxylin–eosin (HE) staining of primary, first recurrent, and second recurrent tumors shows proliferation of spindle-shaped tumor cells (×20) (A, D, G). Immunohistochemical staining shows *KIT*-negative tumor cells in the primary tumor specimen and *KIT*-positive cells in the first recurrent and second recurrent tumor specimens (×20) (B, E, H). Immunohistochemical staining shows CD34-positive tumor cells in primary, first recurrent, and second recurrent tumors (×20) (C, F, I). The following information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned. If you have nothing to declare in any of these categories then this should be stated.

surgical resections for the 2 recurrences in our patient because the diagnosis of recurrent GIST remained uncertain, and there were no other definitive recurrences except those involving the chest wall. We believe that in our case, the second recurrence after tumorectomy for the first recurrent tumor was not a local recurrence, because a microscopically complete resection had been performed, and the site of the second recurrence was at a distance from the site of the first recurrence. It was intriguing that the histopathological findings of the primary lesion included GIST with osteochrondromatous differentiation. Nada et al. reported that metaplastic changes resembling bone, cartilage, and adipose were only seen in high-risk GISTs.[14] Therefore, a careful long-term follow-up is needed for this patient because it is possible that the primary tumor might have malignant potential.

The SSGXVIII/AIO trial, which was an open-label, multicenter, randomized, phase III study, recently showed that 3 years of adjuvant imatinib improved the recurrence-free and overall survival of GIST patients who were at a high risk of recurrence. Therefore, adjuvant therapy with imatinib for at least 3 years is standard treatment for patients with high-risk GIST.[6] Our patient had not been administered adjuvant therapy after curative resection for his primary gastric GIST, because the efficacy of imatinib as adjuvant therapy was unclear at that time. Currently, a case such as ours would have been treated by primary resection followed by adjuvant imatinib.

4. Conclusion

We report a case of repeated recurrence on the chest wall secondary to gastric GIST 11 years after curative resection of the primary tumor. Because recurrence in unusual sites can occur many years after curative resection, continued careful whole-body follow-up is required for patients with high-risk GIST.

Conflict of interest

We have no conflicts of interest to declare.

Funding

We declare that we have no sources of funding.

Ethical approval

Documented informed consent was obtained from patient.

Author contribution

Masaaki Iwatsuki: writing the paper, study concept or design. Kojiro Eto, Kenji Shimizu, Katsuhiro Ogawa, Kensuke Yamamura,

Nobuyuki Ozaki, Hideyuki Tanaka, Shinichi Sugiyama, Kenichi Ogata and Koichi Doi: data collection, data analysis or interpretation, Takihiro Kamio: pathological diagnosis and interpretation. Hiroshi Takamori and Hideo Baba: reviewed and supervised the report.

Consent

Written informed consent has been already obtained from this patients and we describe about it in our manuscript.

Guarantor

Hiroshi Takamori.

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