Case Reports in Oncology

Case Rep Oncol 2016;9:344–350

DOI: 10.1159/000447352
Published online: June 27, 2016

Case Report

A Case of Malignant Gastrointestinal Stromal Tumor Initially Misdiagnosed as Malignant B-Cell Lymphoma

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Keywords
Stomach · Malignant gastrointestinal stromal tumor · Malignant B-cell lymphoma · Gastric submucosal tumor · Gastrointestinal stromal tumor

Abstract
Errors that occur in anatomic pathology influence the treatment strategy of patients with malignancy. There are four general types of error with three subtypes in the category of defective interpretation. The first subtype is a false-negative diagnosis or undercall of the extent or severity of the lesion, the second is a false-positive diagnosis, and the third is misclassification. We herein report a 65-year-old female patient with malignant gastrointestinal stromal tumor that was diagnosed after reevaluation of the lesion at our hospital – and treated with proximal gastrectomy – after initial diagnosis as malignant B-cell lymphoma on esophagogastroduodenoscopy biopsy of a small gastric fundic mass and subsequent treatment with six cycles of CHOP chemotherapy with aggravation of the mass at another hospital.

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Introduction

Gastric submucosal tumor (SMT) is a mesenchymal neoplasm occurring in 2% of all gastric tumors [1]. The tumors are generally discovered during esophagogastroduodenoscopy (EGD) screening, but preoperative pathologic diagnosis of gastric SMTs is difficult, and the final pathologic diagnosis is often made after surgical resection [2]. Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the stomach with an incidence of 33–63% [3]. The majority of cancer diagnoses are the result of histologic and cytological evaluation. Errors in cancer diagnosis are reportedly 11.8% of all reviewed cytological-histologic specimen pairs [4]. Diagnostic pathology errors may lead to incorrect patient management, including the inappropriate application of treatment regimens. Such errors result in the delay of appropriate treatment and in morbidity and mortality of the patients [4, 5]. In the case of malignant lymphoma, discrepancies in histopathologic diagnosis in surgical pathology have been reported to be from 2.4 to 8.4% [6, 7]. The treatment of malignant lymphoma is mainly chemotherapy with the regimen of cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP). On the other hand, the treatment of GISTs is mainly surgical resection without lymph node dissection. However, in case of unresectable locally advanced GISTs, administration of imatinib mesylate (IM; Gleevec, Novartis Pharma) is the mainstay of treatment [8]. We herein report a case of malignant GIST that was diagnosed after reevaluation of lesion at our hospital – and treated with proximal gastrectomy – after initial diagnosis as malignant B-cell lymphoma on EGD biopsy of a small gastric fundic mass and subsequent treatment with six cycles of CHOP chemotherapy with aggravation of the mass at another hospital.

Case Report

A 65-year-old female patient was admitted due to abdominal pain with a gastric mass. The patient had been admitted to another hospital 14 months before visiting our hospital. The patient's initial chief complaints were night sweat and anemia. At the initially visited hospital, the patient underwent EGD, which found SMT (fig. 1a). They performed endoscopic ultrasonography (EUS)-guided biopsy, and pathologic examination results showed diffuse large B-cell lymphoma with prominent plasma cell differentiation. According to the pathologic diagnosis of diffuse large B-cell lymphoma, they performed staging abdominopelvic CT and diagnosed SMT at the upper body of the stomach with lymphadenopathy at the celiac and paraaortic area. The patient underwent six cycles of chemotherapy with CHOP. At the initially visited hospital, follow-up EGD (fig. 1b) and abdominopelvic CT was done with a more aggravated gastric mass. The patient visited the hemato-oncology department of our hospital after the aggravation of her disease. Another four cycles of chemotherapy with etoposide, methylprednisolone, cisplatin, and sitarabine were administered, according to the initial diagnosis of malignant B-cell lymphoma. After additional chemotherapy, follow-up abdominopelvic CT (fig. 2a–c) and EGD (fig. 3a) revealed an increased gastric mass at the fundus with reactive pleural effusion of the left chest. Consequently, the disease was reevaluated with EGD biopsy at our hospital, and pathological confirmation of GIST was made with positive CD34 and c-kit on immunohistochemical staining. After the diagnosis of malignant GIST, administration of IM (Gleevec, Novartis Pharma) 400 mg p.o. q.d. was started. Five months after the administration of IM, abdominopelvic CT and EGD (fig. 3b) revealed partial response of GIST, and the patient was referred to the general surgical department for sur-

gery. Upon exploration of the abdomen, a huge mass with satellite lesion was noted at the posterior aspect and fundus of the stomach. We performed proximal gastrectomy with esophagogastrostomy without lymph node dissection. The pathologic report was as follows: GIST; size of tumor: 12.0 × 10.5 × 5.5 cm; mitotic count: 78/50 high power fields (HPF) (fig.4a). Immunohistochemical staining showed positivity for CD34 and c-kit on 400 HPF with negative surgical margins from proximal (1.0 cm) and distal (2.0 cm). The TNM stage according to the AJCC 7th edition was T4. After the operation, the patient was discharged without any complications, and administration of IM 400 mg p.o. q.d. continued at the outpatient department. Follow-up abdominopelvic CT (fig. 2d) and EGD (fig. 5), taken 1 year after operation, showed no evidence of recurrence.

Discussion

Gastrointestinal SMT is the general term for an elevated lesion covered by normal-appearing mucosa due to the mass arising in deeper layers of gastrointestinal tract wall. The most common types of gastric SMTs are mesenchymal tumors represented by GIST, myogenic tumors, and neurogenic tumors such as Schwannomas, followed by ectopic pancreas, lipomas, carcinoids, lymphangioma, and hemangioma [9]. Pathologic assessment of tissues and consequent diagnosis is the key process of cancer treatment. Cytology is the most common method for the diagnosis for gastric tumor lesions; nevertheless, cytological diagnosis of gastric SMTs is often difficult before operation. EUS-guided fine needle aspiration (EUS-FNA) is a useful diagnostic tool to obtain tissues for the cytological diagnosis before operation. However, applying EUS-FNA to gastric SMT is often difficult, and the false-positive rate of EUS-FNA biopsy is reportedly 1.6% [10]. In addition, Raab et al. [4] reported that errors in cancer diagnosis occur in up to 11.8% of all reviewed cytological-histologic specimen pairs. Diagnostic pathology error may lead to wrong direction of cancer treatment and result in delays in treatment and, consequently, application of incorrect treatment regimens. False-positive or false-negative cancer diagnosis might affect seriously the correct treatment of cancer patients. According to the categories of error in diagnosing clinical severity given by Raab et al. [4], this case belongs to the 'moderate harm to the patient' category, which refers to major morbidity lasting over 6 months [4] due to unnecessary further diagnostic effort or therapy on the presence of unjustified diagnosis. Error detection in anatomic pathology most often depends on secondary case review. Secondary case review also occurs when the pathology reports do not correlate with clinical findings. The patient in our case was initially diagnosed with malignant B-cell lymphoma at another hospital and underwent chemotherapy according to the pathologic result; however, the lesion was more aggravated despite the chemotherapy. In the literature, there are some reports concerning synchronous occurrence of mucosa-associated lymphoid tissue lymphoma and GIST of the stomach after surgical resection [11]. In our case, there were only components of malignant GIST without any evidence of malignant B-cell lymphoma.

GISTs are the most common mesenchymal tumors of the stomach. Clinically, the most important differential diagnosis of GISTs includes epithelial neoplasms or malignant lymphomas, because the treatment of choice is totally different [12]. The final pathologic diagnosis of SMT is often made after surgical resection. Without sufficient cytological specimens of EUS-FNA, preoperative confirmation of the diagnosis of GIST is difficult. Thus, it is important for the cytologist to be aware of the differential diagnosis of GIST. GISTs can pose significant diagnostic challenge to pathologists because various tumors mimic GISTs. GISTs

with prominent glandular and signet ring cell morphology need to be distinguished from adenocarcinoma [13].

Once the pathologic diagnosis of GIST is made, the treatment modality is surgical resection. For the treatment of GISTs initially considered nonresectable or metastatic GISTs, IM has been demonstrated to be a very effective agent for tumor control [8]. Some reports addressed the role of surgery in IM-pretreated nonresectable or metastatic GISTs. After administration, IM tumor shrinkage resulted in cytoreduction and the mass became less friable from the effect of medication. This enabled surgery of GISTs initially considered nonresectable after IM administration. The median time to best response was 4 months, and it would be reasonable to perform final surgery within 6–12 months [14]. When the patient in our case was admitted to our hospital, abdominopelvic CT showed a huge necrotic mass with increased enhancing solid portion involving the stomach body, fundus, and cardia with left pleural effusion, which suggested progressed disease state of malignant GIST. After 5 months' administration of IM, the operative finding was a huge mass with a hardly nodulated satellite lesion noted at the posterior aspect of the stomach body and fundus, which suggested the effect of IM.

In conclusion, the preoperative pathological diagnosis of gastric SMT is often difficult and the final diagnosis of gastric SMT is often made after surgical resection. The diagnostic accuracy of EUS-guided cytology of gastric SMT has to be improved in the surgeon's view. False-positive results of EUS-guided cytology result in applying a false therapeutic modality to the patient. The cytohistologic discrepancies of malignant tumor affect the outcomes of the patients. The idea of reevaluating the disease and deciding on surgery might be important in case of progression of gastric SMT with nonsurgical treatment.

Statement of Ethics

Written informed consent for the publication of this paper was obtained from the patient.

Disclosure Statement

I wish to confirm that there are no known conflicts of interest associated with this publication and that there has been no significant financial support for this work.

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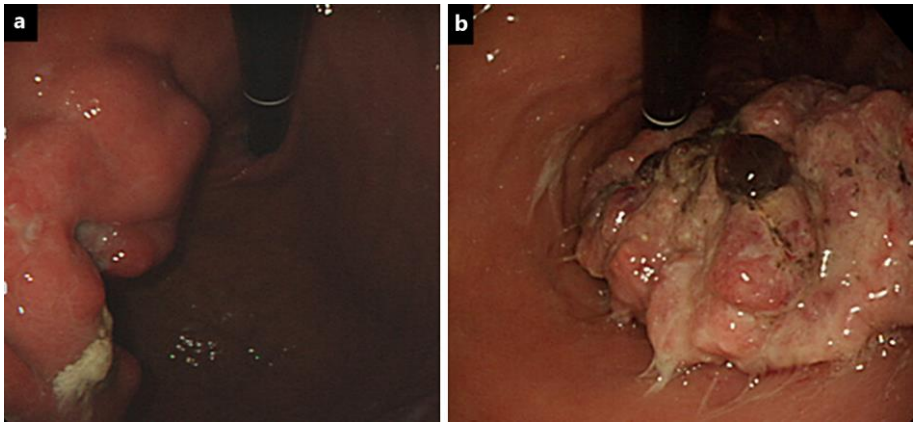

Fig. 1. **a** EGD of the initially visited hospital shows gastric SMT with ulceration at the gastric fundus. **b** EGD finding 4 months after diagnosis and CHOP chemotherapy shows aggravated status of the gastric mass at the gastric fundus at the initially visited hospital.

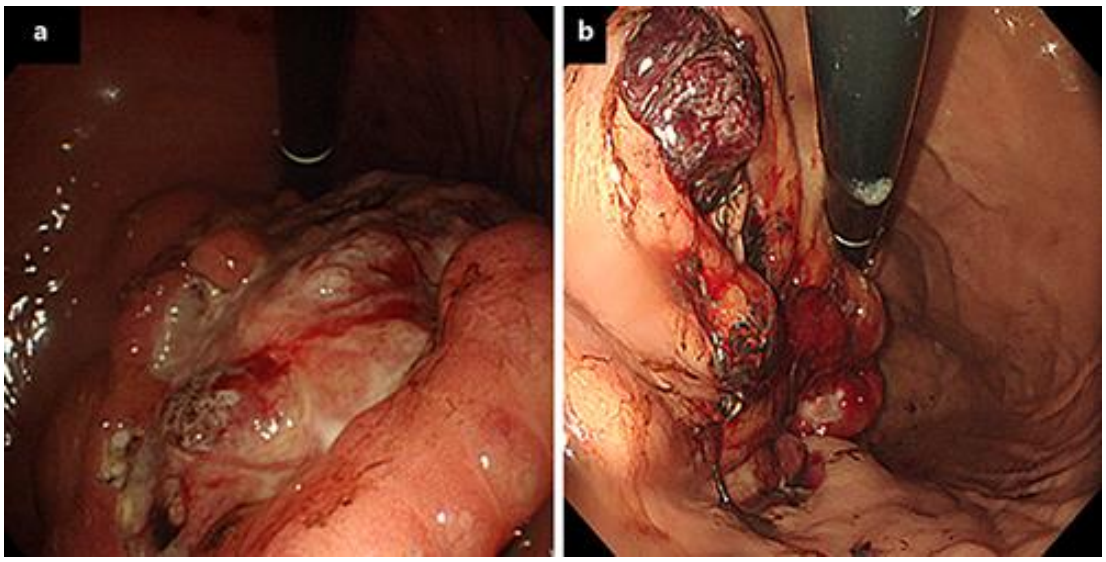

Fig. 2. Abdominopelvic CT findings at 6 (**a**), 12 (**b**), and 18 months (**c**) after initial diagnosis with CHOP chemotherapy shows increased size and cavitation of the mass at the gastric fundus. **d** Abdominopelvic CT findings 1 year after operation shows no evidence of recurrence.

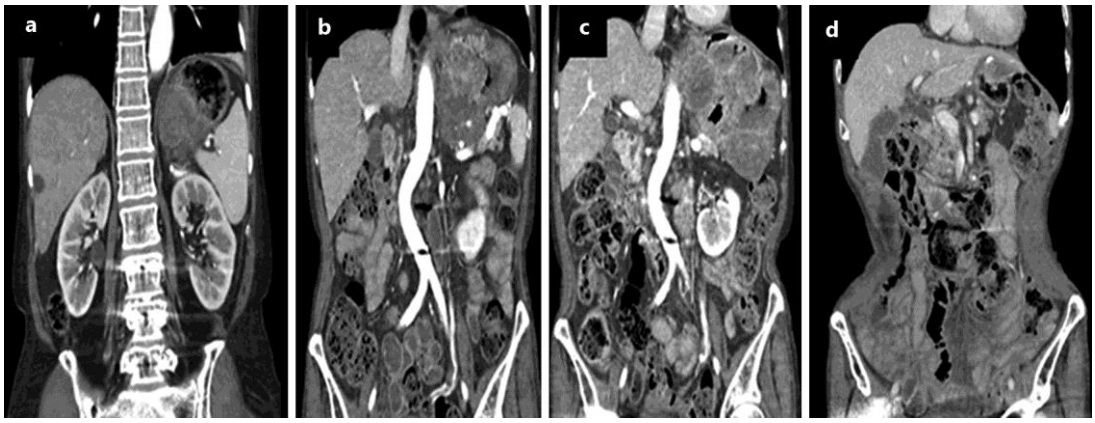

Fig. 3. **a** Fifteen months after initial diagnosis, EGD finding shows increased size of mass at the gastric fundus after CHOP chemotherapy at the initially visited hospital. **b** EGD finding shows a somewhat decreased size of the mass at the gastric fundus 2 years after initial diagnosis and 6 months after administration of Gleevec.

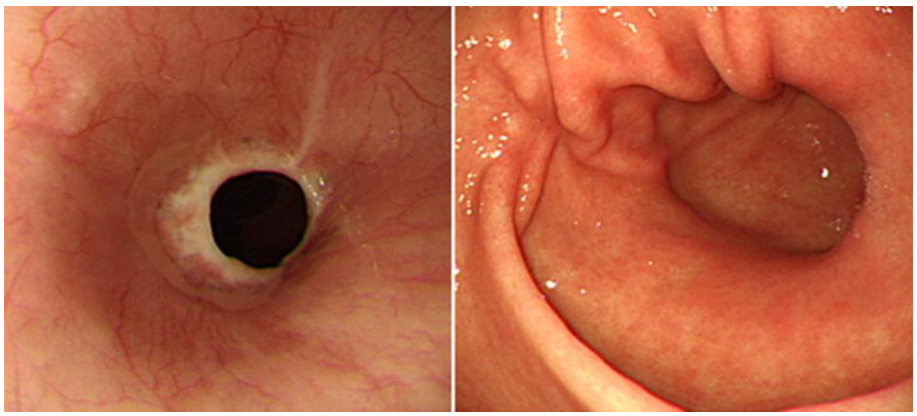

Fig. 4. **a** Pathological reports with malignant GIST with mitosis on ×400 HPF. **b** Immunohistochemical staining shows CD34 on ×400 HPF. **c** Immunohistochemical staining shows c-kit on ×400 HPF.

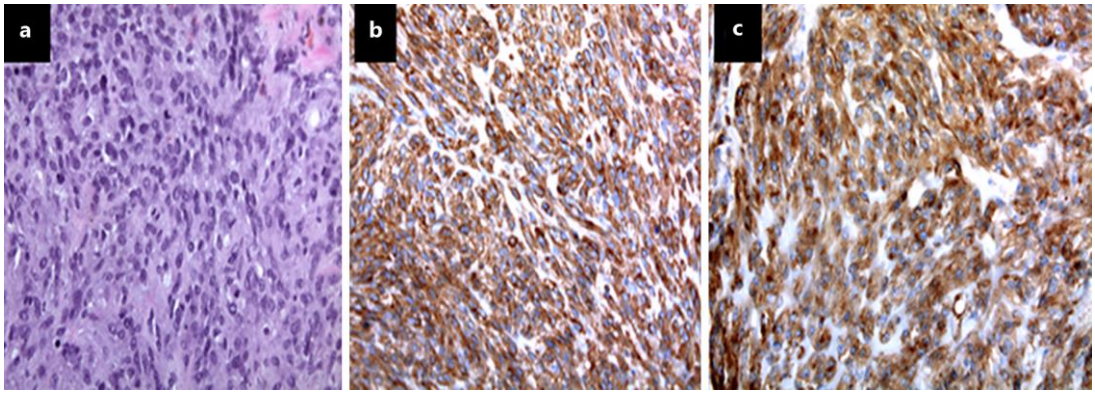

Fig. 5. EGD finding 1 year after proximal subtotal gastrectomy and esophagogastrostomy.