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Original Article

Management of enormous duodenal gastrointestinal stromal tumor in patients with poor cardiopulmonary function

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Abstract: Duodenal gastrointestinal stromal tumors (GISTs) are uncommon. The duodenal GISTs growing exophytically into enormous mass (the maximum diameter ≥20 cm) is extremely rare and is difficult to deal with clinically. In July, 2013, a 63-year-old Chinese male came to our hospital with a complaint of a mass in the right upper abdomen for almost 4 years, which is growing gradually. The pulmonary function showed severe obstructive ventilatory dysfunction and echocardiography showed left ventricular systolic function. The CT and MRI revealed an exophytic mixed lesion measuring 20×19 cm in the hilar region. The enormous mass raised from the paries lateralis of the second part of duodenum and invaded the V segment of liver close to the hepatic portal. Considering that the patient's poor cardiopulmonary function, and the pancreas and duodenal major papilla were not involved, he received local tumor resection combined with partial hepatectomy and cholecystectomy. The result of histopathology confirmed duodenal malignant GIST. In the second month, the patient received oral imatinib. After a 2-year follow-up, the patient showed no obvious signs of recurrence.

Keywords: Duodenum, GIST, exogenous, poor cardiopulmonary function, local resection

Introduction

Gastrointestinal stromal tumors (GISTs) are defined as mesenchymal solid tumors arising from the gastrointestinal wall, mesentery, omentum or retroperitoneum. Common sites are stomach (40% to 60%), small intestine (30% to 40%). Duodenal GISTs constitute 30% of primary duodenal tumors and only 4.5% of all GISTs [1]. These tumors are mainly located in second part of duodenum followed by third, fourth and the first part. Clinical presentations of duodenal GISTs are nonspecific, varying from gastrointestinal bleeding to different degrees abdominal pain or discomfort [2]. Surgical resection is the first choice for the treatment of duodenal GISTs. The best surgical choice for duodenal GISTs depends not only on the size of the tumor but also on the location in the duodenal wall and the relation to the ampulla of Vater and pancreas [3].

Herein, we report an extremely rare case of duodenum GIST treated by tumor resection combined with peripheral organs resection, which is relatively unusual for two reasons: firstly, the exceptionally huge (the maximum diameter ≥20 cm) duodenum GIST is extremely rare; secondly, limited tumor resection but not PD surgery also made the patient with poor cardiopulmonary function long survival. We suggest that clinicians should pay attention to the presence of enormous duodenal malignant GIST in patients who had poor cardiopulmonary function. Local tumor resection combined with peripheral organs resection and postoperative oral imatinib might also get satisfactory outcome.

Case presentation

A 63-year-old Chinese male was referred to our Hospital with a complaint of a mass in the right upper abdomen for almost 4 years. During this period of time, the mass was gradually growing in size. He denied any history of fever, nausea, gastrointestinal bleeding, jaundice, and weight loss. It was worth noting that he had a more

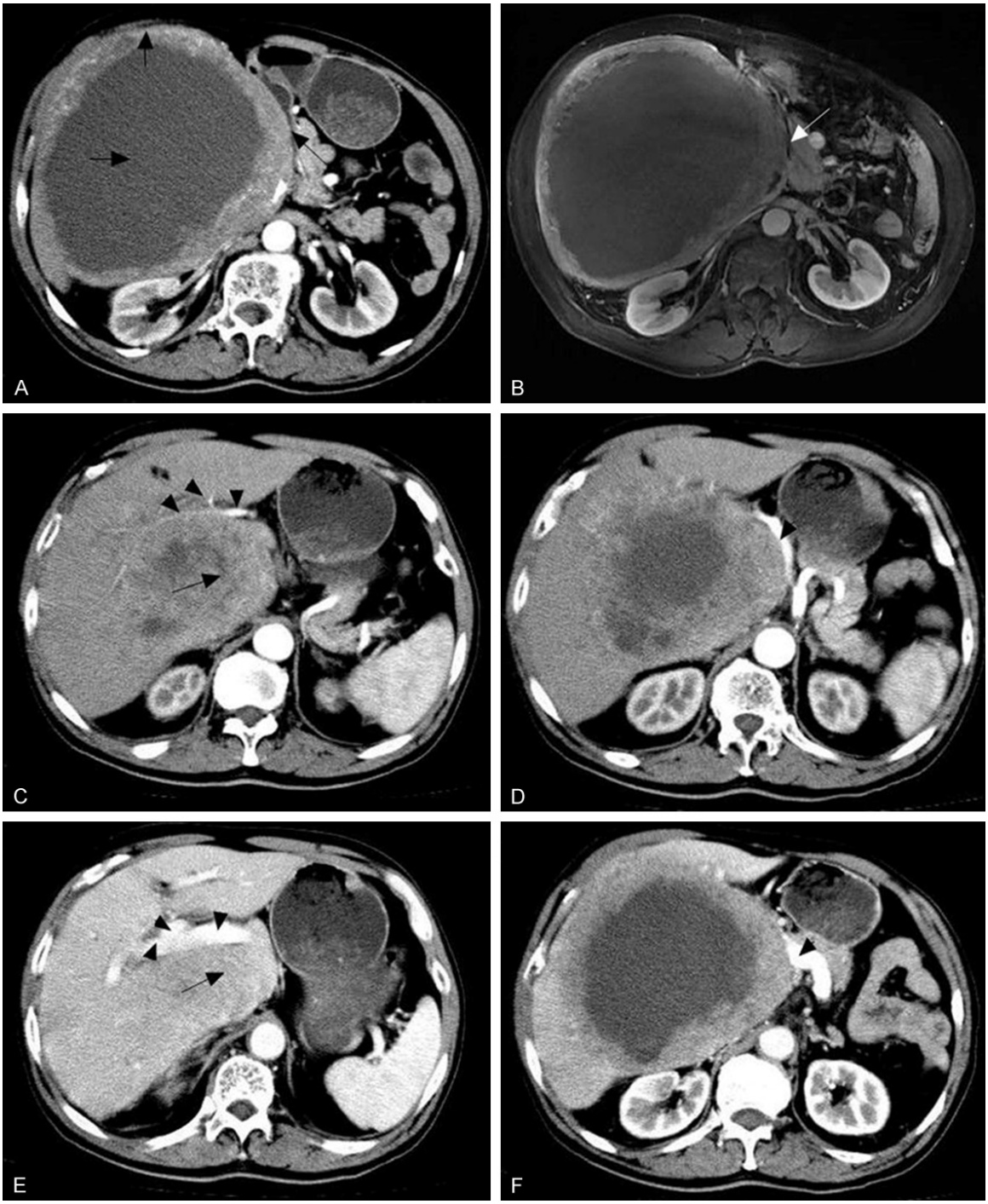

Figure 1. Diagnostic computed tomography (CT) and magnetic resonance imaging (MRI). A. (CT) parieslateralis of duodenum was oppressed by the tumor (slanted arrow), enhancing peripheral component (vertical arrow) and non-enhancing (necrotic) central component (horizontal arrow). B. (MRI) parieslateralis of duodenum was oppressed by the tumor (slanted arrow). C and D. (CT) tumor in the hepatic portal region (arrow), the hepatic artery (main, left and right branch) seemed to be oppressed by the tumor, but not to be invaded (arrowhead). E and F. (CT) portal vein (main, left and right branch) seemed to be oppressed by the tumor, but not to be invaded (arrowhead).

than 40-year history of smoking (average 10-15 cigarettes a day) and 10-year history of hypertension (the highest blood pressure: 190/110 mmHg and taking anti-hypertensive drugs occasionally). On examination, his admission blood pressure was 182/104 mmHg and

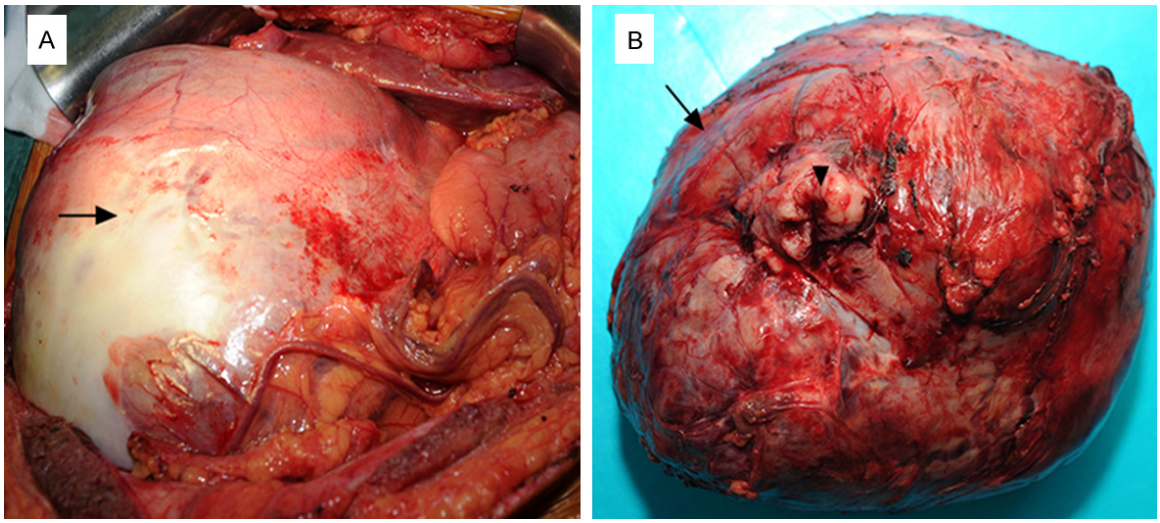

Figure 2. Macroscopic appearance of the tumor. A. Front view of the tumor during operation (arrow). B. Backwall of the resected specimens (arrow), showing tumor grew into the duodenum (arrowhead).

abdominal palpation examination showed: a huge firm mass in the epigastrium, which had round shape, bosselated surface, smooth margins, and was slightly mobile in the transverse direction. The pulmonary function showed severe obstructive ventilatory dysfunction (VCMax 2.07L, FEV 11.2L, FEV1Pred 60.0%, FEV1/FVC 58%, MVV 55L, Tracheal dilation test negative). Left ventricular ejection fraction (LVEF) detected with echocardiography was 59%. Abdominal ultrasound showed a 20×19 cm heterogeneous mass in the hepatic portal region, extending from the right costal margin to right anterior superior spine. The abdominal CT/MRI showed a well-defined mixed solid cystic mass, measuring 20×19 cm in the hepatic portal region had a blurred boundary with the paries lateralis of the second part of duodenum, which had enhancing peripheral component and non-enhancing (necrotic) central component. The hepatic artery and portal vein seemed to be oppressed by the tumor, but not invaded (**Figure 1**). Considering that the patient's poor cardiopulmonary function, and the pancreas and major papilla (4 cm distal from tumor) were not involved, the surgical strategy of local tumor resection combined with peripheral organs resection was made. On laparotomy, there was an enormous mixed solid cystic mass close to the hepatic portal, which appeared to be originated from the right lobe of liver, and the gallbladder was pushed away on the surface of mass. However, in the course of isolating the back wall of mass, it was found growing into the upper end of paries lateralis of the second part of duodenum (**Figure 2**). There was no metastasis in pancreas or peritoneum. Eventually, local tumor resection combined with partial hepatectomy (V segment) and cholecystectomy was performed. Intraoperative frozen section showed spindle cell tumor with palisading pattern and foci of necrosis. Post-operation histopathology showed the mitotic count was more than 10/50 HPF, which revealed malignant duodenal GIST involving muscular is propriety with infiltration in the duodenal epithelial layer and the margin was negative. The tumor was definitely diagnosed as the duodenal GIST with high-grade malignancy, growing exophytically and invading partial liver parenchyma after detailed immunohistochemical study: CD117(+), CD34(+), SMA(+), Nestin(+), Desmin(-), S-100(-), Melan-A(-), CK(-) (**Figure 3**). Post-operatively patient had slight biliary leakage which was managed conservatively and discharged in satisfactory condition. A molecular genetic analysis for KIT protein mutation was not performed because of its unavailability in our hospital. However, the patient was still scheduled for oral imatinib 400 mg/d at the 1 month after surgery. The patient showed no obvious signs of recurrence after a 2-year follow-up and was planned to stop at the end of next year.

Discussion

Gastrointestinal stromal tumors (GISTs) are defined as mesenchymal tumors arising from the gastrointestinal wall, mesentery, omentum

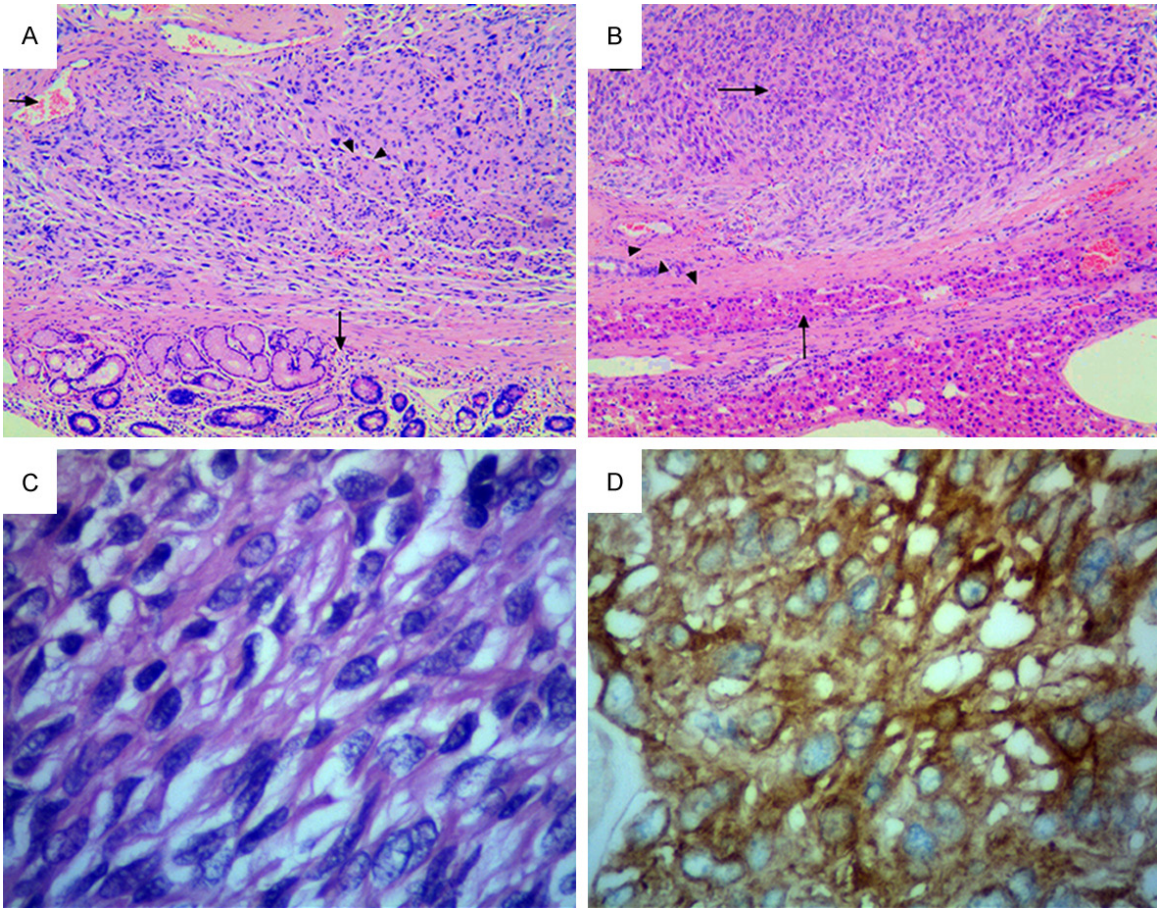

Figure 3. Histopathology and Immunohistochemistry appearance of the tumor. A. Histopathology showed spindle cell tumor with palisading pattern (arrowhead) and foci of necrosis (horizontal arrow) and revealed that tumor was arising from the duodenal wall (vertical arrow) (H&E stain, 50×). B. Histopathology showed tumor (horizontal arrow) invaded partial liver parenchyma (vertical arrow), necrotic and fibrotic hepatocyte (arrowhead) (H&E stain, 50×). C. The mitotic count was more than 10/50 HPF (H&E stain, 400×). D. Immunohistochemistry showing positivity for CD117 (400×).

or retroperitoneum. Common sites are stomach (40% to 60%), small intestine (30% to 40%) [1]. Usually, GISTs are solid tumors. However, as they grow, they can protrude exophytically and undergo cystic changes to present a largely cystic lesion due to liquefaction and hemorrhage. Duodenal GISTs constitute 30% of primary duodenal tumors and only 4.5% of all GISTs. They are mainly located in the second portion of the duodenum and about half of them are malignant. The mean age of patients with GIST is 53 years and only about the 5% of GIST patients are younger than 30 years [4]. Clinical presentations of duodenal GISTs are nonspecific, varying from gastrointestinal bleeding to different degrees abdominal pain or discomfort. Duodenal GISTs always present as smooth submucosal bulge or ulceration at endoscopy, which is often done for nonspecific complaints or gastrointestinal bleeding. Endoscopic ultrasound can help in delineating the sub-mucosal tumor [5]. Alternative diagnostic means include CT, MRI, barium study and ultra-sonography. However, CT and MRI seem to be the best imaging modalities for assessment of the primary lesion and detection of metastases [6]. In the present case, the endoscopy and FNA cytology were not done because of its intense indication for surgery, and the tumor presented as heterogeneous mass with central necrotic at CT/MRI scan [4].

Surgical resection is the first choice for the treatment of duodenal GISTs. Complete resection with an intact pseudocapsule and ensuring negative margins are the most important principles of treatment. The best surgical choice for duodenal GISTs depends not only on the size of

the tumor but also on the location in the duodenal wall and the relation to the ampulla of Vater and pancreas [3]. The surgical management swings between major resections including PD or pancreas-sparing duodenectomy (PSD) and conservative surgery such as partial resection of duodenum with primary closure of duodenum, segmental duodenectomy with duodenal jejunostomy reconstruction or pancreaticoduodenectomy [7]. Due to local and regional lymph node involvement is infrequent in duodenal GISTs, routine lymph node dissection is not advocated [8]. Generally speaking, segmental duodenectomy is indicated for small (<1 cm) tumors of the second part when the distance to the ampulla is enough (>2 cm) or large (>3 cm) located on the third or fourth part of the duodenum. PD is indicated for periampullary GISTs or large tumors on the first or second part of the duodenum, which may be inadequately resected through a PSD. Some authors reported the local resection with tumor free margins including adjacent organs resection, if necessary, is an attractive option in cases without pancreatic/ampullary involvement which can avoid a PD. Therefore, in our case who have poor lungs function, considering that the pancreas and major papilla (4 cm distal from tumor) were not been involved and the tumor is well-encapsulated, tumor resection with primary layered interrupted suture of duodenal crevasse combined with partial hepatectomy (V segment) and cholecystectomy was performed.

Various factors are described to predict the malignant potential of GIST, such as tumor size, mitotic activity, tumor location, non-radical resection, tumor rupture, peritoneal dissemination, metastasis, and invasion into adjacent organs. Fletcher's criteria proposed risk stratification of tumor behavior based upon its size and mitotic activity. Tumors larger than 10 cm in size with any mitotic count or of any size with mitotic count more than 10/50 HPF are at high risk of aggressive behavior [9]. Adjuvant therapy with imatinib has been recommended in patients with substantial risk of recurrence. Risk of recurrence is increased in tumors of large size, increased mitotic activity and resection with positive margins. Adjuvant therapy with imatinib has shown to increase the recurrence-free survival but not overall survival [10]. In our case, adjuvant therapy with imatinib was started in 1 month after surgery considering that the tumor was proved to be high risk grade (size >10 cm and mitotic count more than 10/50 HPF) and have a high recurrence rate. The patient tolerated well to imatinib and showed no obvious evidence of recurrence until now.

In conclusion, the duodenal GISTs grew exophytically into enormous mass (the maximum diameter ≥20 cm) is extremely rare and difficult to deal with clinically, especially in the elderly patients with poor cardiopulmonary function. Herein, we report an extremely rare case of duodenum GIST which is relatively unusual for two reasons: firstly, the exceptionally huge (the maximum diameter ≥20 cm) duodenum GIST is extremely rare; secondly, limited tumor resection but not PD surgery also made the patient long survival. Local tumor resection combined with peripheral organs resection and postoperative oral imatinib may be a useful alternative treatment strategy, when encounted such patients in the future.

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Disclosure of conflict of interest

None.

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References

[1] Marano L, Boccardi V, Marrelli D, Roviello F. Duodenal gastrointestinal stromal tumor: from clinicopathological features to surgical outcomes. Eur J Surg Oncol 2015; 41: 814-22.

[2] Yang F, Jin C, Du Z, Subedi S, Jiang Y, Li J, Di Y, Zhou Z, Tang F, Fu D. Duodenal gastrointestinal stromal tumor: clinicopathological characteristics, surgical outcomes, long term survival and predictors for adverse outcomes. Am J Surg 2013; 206: 360-7.

[3] Everett M, Gutman H. Surgical management of gastrointestinal stromal tumors: analysis of

outcome with respect to surgical margins and technique. J Surg Oncol 2008; 98: 588-93.
[4] Al-Thani H, El-Menyar A, Rasul KI, Al-Sulaiti, M, El-Mabrok J, Hajaji K, Elgohary H, Tabeb A. Clinical presentation, management and outcomes of gastrointestinal stromal tumors. Int J Surg 2014; 12: 1127-33.
[5] Poves I, Burdio F, Alonso S, Seoane A, Grande L. Laparoscopic pancreas-sparing subtotal duodenectomy. JOP 2011; 12: 62-5.
[6] Mennigen R, Wolters HH, Schulte B, Pelster FW. Segmental resection of the duodenum for gastrointestinal stromal tumor (GIST). World J Surg Oncol 2008; 6: 105.
[7] Tien YW, Lee CY, Huang CC, Hu RH, Lee PH. Surgery for gastrointestinal stromal tumors of the duodenum. Ann Surg Oncol 2010; 17: 109-14.
[8] Buchs NC, Bucher P, Gervaz P, Ostermann S, Pugin F, Morel P. Segmental duodenectomy for gastrointestinal stromal tumor of the duodenum. World J Gastroenterol 2010; 16: 2788-92.
[9] Miki Y, Kurokawa Y, Hirao M, Fujitani K, Iwasa Y, Mano M, Nakamori S, Tsujinaka T. Survival analysis of patients with duodenal gastrointestinal stromal tumors. J Clin Gastroenterol 2010; 44: 97-101.
[10] Eisenberg BL, Trent JC. Adjuvant and neoadjuvant imatinib therapy: current role in the management of gastrointestinal stromal tumors. Int J Cancer 2011; 129: 2533-42.