

Case Report of Duodenal Gastrointestinal Stromal Tumor Masquerading a Pancreatic Head Tumor

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Abstract

Gastrointestinal stromal tumor (GIST) represents the most common kind of mesenchymal tumor that arises from the alimentary tract. Tumors arising from the first and the second part of the duodenum (DI and DII, respectively) can be wrongly diagnosed as pancreatic mass. We report a case of a 58-year-old male patient with the history of vomiting just after eating, loss of appetite, lethargic and weight loss for 25 days. CT scan of abdomen and pelvis showed a soft tissue mass with slight heterogeneous enhancement at the region of the uncinate process of the head of pancreas and (MPR) on CT enhanced showed the closely attached mass to the head of the pancreas. On operative exploration, the mass was found to be originated from duodenum. Then, surgical resection of the duodenal tumor was performed by wedge resection successfully. Postoperative laboratory diagnosis was "low risk" duodenal gastrointestinal stromal tumor.

Keywords

Gastrointestinal Stromal Tumor, Mesenchymal Tumor, Imatinib, Pancreatoduodenectomy

1. Introduction

Gastrointestinal stromal tumor (GIST) is currently defined as a gastrointestinal tract mesenchymal tumor containing spindle cells (or less commonly epithelioid cells or rarely both) and showing CD117 (c-kit protein) positivity [1] [2] [3]. GISTs may occur in the entire gastrointestinal tract. The stomach is the most

common location of GIST (60% - 70%), followed by other uncommon sites like small bowel (25%), rectum (2%), and the esophagus (2%), with other various locations accounting for the rest of the presentations. Small intestinal GIST can occur anywhere along the length of the bowel and can be multiple. The duodenum is involved in about 10% to 20% of small intestinal GIST. Some GISTs are primary in the omentum, mesentery or retroperitoneum, but most GISTs in these sites are the results of metastases from gastric or intestinal sites [4] [5] [6]. Duodenal GISTs comprise less than 5% of all cases and it can be diagnosed under upper gastrointestinal endoscope due to formation of a gross ulceration in the mucosa or an intramural mass with a centrally ulcerated umblication [7]. The diagnosis of duodenal GISTs is based on: histological features (tumor arising from duodenal wall), immunohistochemical staining (positive for CD117, CD34 and alpha-smooth muscle actin) and molecular features (oncogenic c-kit mutation) [8]. Although duodenal GIST is pathologically similar to that involving other organs, they do have some peculiar features. GISTs in the duodenum pose particular challenges for diagnosis and management. Pinpoint analysis is of great concern in imaging diagnosis of duodenal GIST.

We present a case that we encountered at our hospital of duodenal GIST mimicking pancreatic head tumor in a 58-year-old male patient who was confirmed following surgical exploration. The imaging findings, clinical course and treatment options are reviewed.

2. Case Report

A 58-year-old male patient presented in our hospital with the chief complaint of vomiting just after eating, lethargy and loss of appetite since 25 days. There was history of gradual loss of weight for past few months. There was no any history of abdominal pain, gastrointestinal bleed, diarrhea or constipation. Contents of vomit was nongreasy with undigested food particles. There was no any history of infectious disease such as hepatitis, tuberculosis etc. There was no any significant past medical history of diabetes mellitus, hypertension, drugs or food allergy. There was no any history of surgical intervention and the history of blood transfusion.

On physical examination, there was no pallor, no jaundice, no lymphadenopathy and bilateral thyroid gland were intact. His temperature was recorded to be 37°C, pulse-78b/m, respiratory rate-22 br/m and BP-150/90 mm of Hg. The bilateral breathe sound was clear and heart rate, rhythm was regular with no any pathological murmur. The abdominal wall was soft, non-tender, no rebound tenderness and abdominal mass were not palpable. Bilateral upper and lower limb movement was intact and there was no any swelling present.

CT scan of the abdomen and pelvis showed homogeneous, eqidensity, soft tissue tumor mass at the uncinate process of the head of pancreas (Figure 1). Enhanced CT revealed slightly heterogeneous enhancement of the tumor mass (Figure 2). The Coronal CT enhanced MPR demonstrated exophytic growth of the tumor mass at the uncinate process of the head of the pancreas showing



Figure 1. Axial plain CT showing homogeneous, eqidensity, soft tissue tumor mass in the uncinate process of the head of pancreas.



Figure 2. Axial enhanced CT exhibits soft tissue tumor mass showing slight heterogeneous enhancement. (1-pancreatic head. 2-tumor mass. 3-duodenum).

slightly heterogenous enhancement but couldn't clearify the exact location (**Figure 3**). But, the site of the origin of the tumor mass was not clear. On MR studies, the tumor mass showed low signal intensity in T1 weighted image (**Figure 4**) and high signal intensity in T2 weighted image (**Figure 5**) at the head of pancreas.

According to these findings, the head of pancreas was strongly suspected for the tumor and surgical management was planned. Then the patient underwent surgery in our hospital during which the tumor was found to be located in the lower part of duodenum. The size of the tumor was about 3.7 cm * 4 cm, soft, lobulated and rich in superficial blood vessels. There was no obvious invasion of the surrounding structures seen. There was a clear separation between the tumor and the pancreas but a white bulge like lesion was seen on the wall of gallbladder. So, the successfully wedge resection with cholecystectomy was performed. In further staging examinations, there was no pathological finding for the tumor markers CEA, Ca-19.9, gastrin and chromogranin.

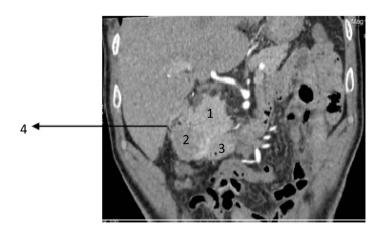


Figure 3. Coronal CT enhanced MPR exhibits soft tissue tumor mass showing slightly. heterogeneous enhancement at the uncinate process of head of pancreas. (1-Head of pancreas, 2-tumor mass, 3-2nd part of duodenum, 4-colon.)

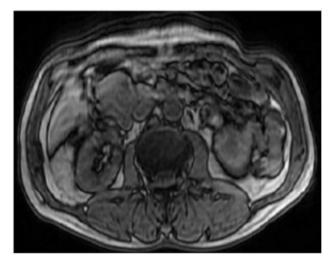


Figure 4. Axial T1-weighted image demonstrating soft tissue mass of slightly low signal intensity at the head of pancreas.

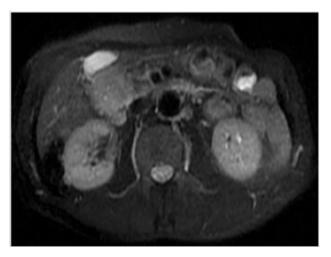


Figure 5. Axial T2-weighted image demonstrating soft tissue mass of slightly high signal intensity at the head of pancreas.

Immunohistochemistry showed CD34 (+), CD117 (+), Dog-1 (+), S-100 (-) Ki67Li about 3% (Figure 6 and Figure 7). Expression of CD117 and DOG-1 was determined using a semiquantitative method and assessed as positive (reaction visible in >20% of tumour cells) or negative (lack of reaction, or reaction present in <20% of cells). MIB-1amarkerforproliferationshoweda rate of 1%. Further examinations showed an exon11 mutation in the c-KIT gene. Histologically it was a mesenchymal, sharply margined tumor consisting of spindle cells and isolated apoptosis but without necrosis, size of tumor was 4.2 cm * 4.1 cm * 3 cm, and mitotic activity was <5/50 HPF suggestive of "Low risk" duodenal gastrointestinal tumor according to risk classification of duodenal GISTs modified after Miettinen and Lasota (Table 1). The patient is under regular follow up and has shown no sign of disease.

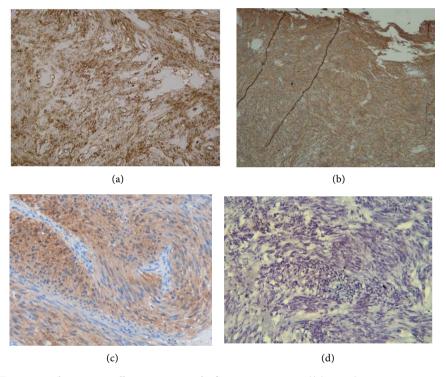


Figure 6. The tumor cells react positively for CD34 positive ((a) $\times 200$), CD117 positive ((b) $\times 200$), DOG-1 positive ((c) $\times 20$) and S100 negative ((d) $\times 40$) on immunohistochemistry.

Table 1. Risk classification of duodenal	GISTs modified after Miettinen and Lasota [23]	
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Amount of mitosis Size (cm)		Size (cm)	Risk
≤2	No risk		
≤5 per 50 HPF		2 - 5	Low
5 - 10			High
≤2	No data		
>5 per 50 HPF		2 - 5	High
5 - 10			High

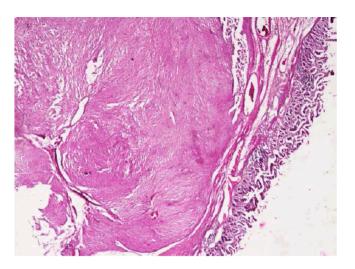


Figure 7. Histopathology showing tumor involving duodenal Wall (H & E stain, 40×).

3. Discussion

GISTs are quite rare tumors with an incidence of annually only 10 - 15 per million [2]. Gastrointestinal stromal tumor (GIST) arises from the interstitial cells of Cajal which are located in the submucosal and myentric plexus of gastrointestinal tract and are the most common form of tumors of the gastrointestinal tract. The main pathogenesis of most GISTs is the mutation of one of the two tyrosine kinase receptor genes (KIT and PDGFRA). Among all GISTs, only 4.5% - 5% arises in the duodenum and are frequently located into the DII [7]. GISTs can occur anywhere in the GI but mostly affect the stomach (60%), jejunum and ileum (30%) only 45% arise in den duodenum. Depending on the size and location of the tumor, they often present with abdominal discomfort, full feeling and gastrointestinal bleeding, if the tumor grows invasively into the epithelial layer. The diagnosis of GIST is done by immunohistochemistry and electron microscopy where the presence of staining for tyrosine kinase receptor KIT (CD 117) is confirmatory for the presence of the interstitial cells of Cajal. On estimation of over 95% of GISTs shows positive staining results for CD 117 in the diagnosis of GIST [9]. It also shows positive results for nestin (90% - 100%) and CD34 (70%) but they are less specific in comparison to CD 117. Smooth muscle actins (SMA) (20% - 30%) and heavy caldesmon (80%) are often expressed, whereas desmin is usually absent. Histologically, the structures of GISTs vary from cellular spindle cell tumors to epithelioid and pleomorphic ones, and morphology varies depending on the lesion sites. The expression of CD34 and SMA is often reciprocal.

GISTs can occur throughout the gastrointestinal tract, but may also occur in the peritoneum and extragastrointestinal sites. Duodenal GISTs most frequently involve the second portion of the duodenum, followed by the third portion, fourth portion, and first portion [7]. GISTs express an uncertain clinical behavior that ranges from benign to malignant, and there is no any rule of staging system developed yet. The various features of the tumor like initial size, anatomical location, mitotic activity, histologic subtype, presence/absence of intra-tumoral necrosis and age of the patient were suggested as criteria for the disease prognosis [10]. Although many of duodenal GISTs extend from submucosal or muscularispropria to external aspects (58 tumors out of 156 duodenal GISTs), most of them comprise a gross ulceration of the mucosa with a component that bulged underneath the mucosa coincidentally, which helps in the detection of the tumor upon endoscopic examination [7]. Tumors with a size larger than 5 cm have poor prognosis resulting decreased survival rate and increased chances of metastasis. At time of diagnosis, approximately 20% - 50% of the patients already have metastasis, most likely in the liver and/or the peritoneum. Metastasis can be found very rarely in the lymph nodes; therefore, surgery does not have to be that radical [11] [12]. However, the mitotic activity remains one of the strongest prognostic factors for GIST [13]. The tumor presented in our case belongs to the category determined by size between 2 - 5 cm and a mitotic count < 5/50 HPF, which is classified as "low risk".

The clinical presentations of duodenal GIST are highly variable according to their size and the existence of mucosal ulceration. According to the previous report, duodenal GISTs most commonly present GI bleeding, epigastric pain, palpable mass, and intestinal obstruction [7]. Small tumors, especially which are not accompanied by mucosal ulceration, are usually incidental findings upon operation, endoscopy or imaging studies for other reasons. The tumor size of our patient was not so large so, he didn't have any such peculiar features suggestive of GIST.

Diagnosis of GISTs can be done with upper gastrointestinal endoscopy [11]. Endoscopic appearance of duodenal GISTs is as smooth submucosal bulge with ulceration; this examination is often performed for nonspecific complaints or gastrointestinal bleeding. Endoscopic ultrasound can provide information about the intramural or extramural origin of tumor and even about the layer of origin of the intramural mass [14]. However, the final diagnosis is confirmed by biopsy [11] [15] [16], which is often performed in a CT or ultrasound setting. Other diagnostic modalities which have become the best choice for assessment of the primary lesion and detection of metastasis include CT scan and magnetic resonance imaging (MRI) [17]. In a CT scan, the features of GISTs vary greatly, depending on the size and aggressiveness of the tumor mass and the time of presentation during the course of the disease. Primary GISTs typically presents with large, enhancing masses on contrast-enhanced CT scans and are often heterogeneous with central low density due to necrosis, hemorrhage or cystic degeneration. Usually in case of duodenal GIST, CT scan shows the tumor mass at the site of the duodenum and head of the pancreas which make it unreliable in diagnosing the origin of the mass. Thus, on various occurrence the mass was misdiagnosed as arising from the head of the pancreas [17] [18]. On the contrary, large tumors tend to have central necrosis and cavitations, as well as heterogeneous enhancement [19]. Depending on tumor necrosis, hemorrhage and cavitation MRI findings of GISTs are extremley variable, which can affect signal

intensity [20] [21]. Usually, on T1 weighted images the solid portion of GIST shows low signal intensity and on T2 weighted image high signal intensity and are enhanced after gadolinium administration [21]. Lymphadenopathy is unusual with GISTs and, if present, should raise an alternative diagnosis of lymphoma or adenocarcinoma [22]. Similarly, our case had been misdiagnosed as carcinoma of head of pancreas in accordance to the findings of CT scan. In MRI T1weighted images show low signal intensity solid component and the enhancement is usually present peripherally in larger lesions. T2 weighted images show high signal intensity solid component.

The treatment of GIST depends upon localization and the size of the tumor. Resection of the tumor with primary closure can be performed for smaller lesions if the resulting lumen is adequate and the ampulla of Vater can be preserved. Segmental duodenectomy with duodenojejunostomy can be performed for larger tumors located in the infraampullary portion. When the duodenal GISTs are located at the second portion of the duodenum, major resection via a pancreatico duodenectomy or a pancreas sparing duodenectomy is indicated. Various techniques of limited resection for duodenal GISTs have been implemented, depending on the site and the size of the tumors. The resection needs to be with a tumor free margin and a safety clearance of at least 1cm, to be considered as potentially curative [15] [16]. The outcome depends on the pathological features of the tumor and the nature of surgical resection whether it is complete or not. Large tumors with high mitotic counts act much worse than small tumors with low mitotic counts. Chance of recurrence is higher in tumors which are not completely resected or with a positive microscopic margin.

Adjuvant therapy with Imatinib has been recommended in patients with locally advanced or metastatic or substantial risk of relapse (Tumor size > 10 cm, mitotic count > 10/50 HPF, and tumor rupture). Risk of relapse is increased in large tumors, increased mitotic activity and resection with positive margins. Adjuvant therapy with Imatinib has been shown to increase the relapse-free survival but not the overall survival [24] [25] [26]. Imatinib is a signal transduction inhibitor that especially inhibits the binding of adenosine triphosphate to tyrosine kinase which includes PDGFRA and the c-Kit receptor expressed in GISTs [18] [27]. Recently sunitinib malate, an oral receptor tyrosine kinase inhibitor, was approved for the treatment of GISTs for those who are intolerance to imatinib. Sunitinib inhibits platelet-derived growth factor receptors and vascular endothelial growth factor receptors, which play key roles in tumor angiogenesis and tumor cell proliferation. In case of development of sunitinib resistance, a novel drug namely Regorafenib has come to practice, which is an oral multikinase inhibitor that blocks the activity of multiple protein kinases, including those involved in the regulation of tumour angiogenesis, oncogenesis and the tumor microenvironment [28]. Regarding the prognosis of malignancy, Miettinen et al. classified by the amount of mitosis per 50HPF the size and origin of the tumour [23] (Table 1). In this case adjuvant treatment is not necessary, as our patient was classified as "low risk" duodenal GIST.

4. Conclusions

We report a case of a rare duodenal GIST mimicking pancreatic head tumor, treated successfully by wedge resection. The patient has been doing well without recurrence since surgery, and we will continue to monitor him with a strict follow-up schedule.

Duodenal GISTs are mesenchymal neoplasm of the gastrointestinal tract, which can be difficult to differentiate from the pancreas head mass because of its anatomical proximity. It should be suspected in any patient with a duodenal wall mass. It is usually asymptomatic when small in size and can progress to a larger size before being symptomatic. Surgical management is the primary modality of the treatment. There is more than one surgical approach available, but the absolute requirement is complete surgical excision.

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflicts of Interest

No conflicts of interest.

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Abbreviations

GIST: Gastrointestinal stromal tumor CT: Computed tomography MPR: Multiplanar reformations BP: Blood pressure MRI: Magnetic resonance imaging CEA: Carcinoembryonic antigen Ca-19.9: Carbohydrate antigen 19.9 GI: Gastrointestinal