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ABDOMINAL IMAGING

PICTORIAL ESSAY

A pictorial review on clinicopathologic and radiologic features of duodenal gastrointestinal stromal tumors

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ABSTRACT

Duodenal gastrointestinal stromal tumors (GISTs) are rare, and studies on their management are not sufficient. Owing to the complex anatomy of the duodenum and pancreatic head, GISTs can be misdiagnosed as pancreatic head tumors. Surgical resection is the first treatment for localized duodenal GISTs; thus, noninvasive imaging is important for the diagnosis and treatment of GISTs. Computed tomography, magnetic resonance imaging and endoscopic ultrasonography findings can be helpful for the diagnosis of duodenal GISTs and can help differentiate GISTs from other adjacent tumors.

Periampullary neoplasms are tumors occurring in the duodenum, distal common bile duct, ampulla of Vater and pancreas. These tumors show similar clinical presentations but they have different outcomes. Duodenal gastrointestinal stromal tumors (GISTs) show different clinical presentations, according to their size and origin (1). Most common symptoms are gastrointestinal bleeding and abdominal pain. In general, primary duodenal GISTs present as large, well-defined masses with variable degree of enhancement on computed tomography (CT). They show low signal intensity on T1-weighted images and high signal intensity on T2-weighted images with enhancement on magnetic resonance imaging (MRI). Endoscopic ultrasonography (EUS)-guided fine needle aspiration cytology is also helpful in the diagnosis of duodenal GISTs (2).

In this review, we discussed the clinical and radiologic findings of the duodenal GISTs and other periampullary lesions to differentiate GISTs from their mimickers. In addition, we have reviewed the management and outcomes of duodenal GISTs.

Anatomy of the periampullary region

Periampullary lesions include four structures adjacent to major papilla of duodenum, ampulla of Vater, common bile duct, pancreas, and duodenum. Periampullary neoplasms are the tumors occurring in this area. These tumors are located closely and their clinical presentations are similar, so it is hard to know the origin of tumors.

These tumors also have similar therapeutic approaches such as pylorus-preserving pancreaticoduodenectomy. However, their outcomes vary according to the type of tumors (3).

Clinicopathologic findings of duodenal GISTs

GISTs are rare tumors with incidence rate of 1.5 cases per 100 000 persons per year (4). GISTs are typically submucosal tumors originating in muscularis propria layer. GISTs are closely related to the interstitial cells of Cajal, which compose the structure within the gastrointestinal tract between the bowel wall and smooth muscle. Microscopic appearance of GIST usually shows spindle cells and less commonly, epithelioid cells. GISTs have been reported to show positive staining for CD117 (c-KIT protein) in immunohistochemistry (5). Some factors affecting prognosis of GISTs are tumor size, mitotic count, anatomical location, and KIT mutation (1, 5). The tissue stains positive for CD117 and CD34 in immunohistochemistry because of proto-oncogene product of c-KIT. Most of the malignant GISTs have a KIT mutation, which is inhibited by imatinib (Fig. 1) (1, 5).

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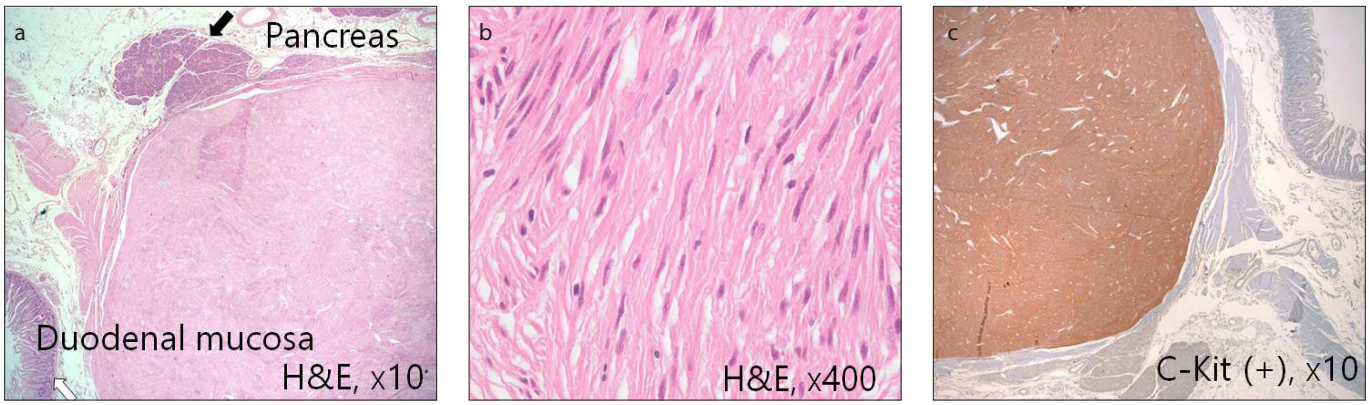

Figure 1. a–c. Immunohistology of a small duodenal gastrointestinal stromal tumor (GIST) (1.8×1.3 cm) in a 62-year-old woman. The patient had pylorus-preserving pancreaticoduodenectomy and biopsy from obtained specimen proved it to be a duodenal GIST. Low-power photomicrograph **(a)** (original magnification, ×10; hematoxylin-eosin stain) shows a well-circumscribed tumor at ampullary region (duodenum mucosa, *white arrow*; pancreas parenchyme, *black arrow*). Photomicrograph **(b)** (original magnification, ×400; hematoxylin-eosin stain) demonstrates that the tumor is composed of spindle cells with absent mitotic activity. Photomicrograph **(c)** (original magnification, ×10; immunohistochemical stain for c-KIT) shows brown staining of the tumor, suggesting strong positivity for c-KIT.

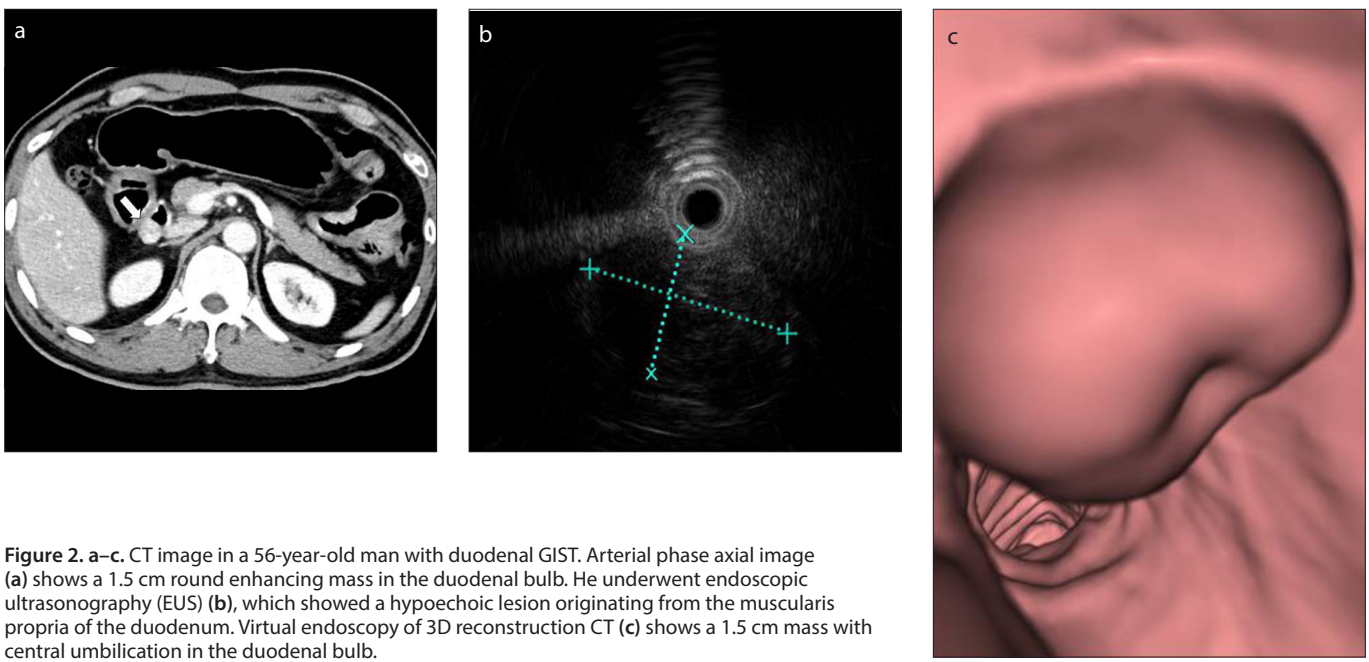

Figure 2. a–c. CT image in a 56-year-old man with duodenal GIST. Arterial phase axial image **(a)** shows a 1.5 cm round enhancing mass in the duodenal bulb. He underwent endoscopic ultrasonography (EUS) **(b)**, which showed a hypoechoic lesion originating from the muscularis propria of the duodenum. Virtual endoscopy of 3D reconstruction CT **(c)** shows a 1.5 cm mass with central umbilication in the duodenal bulb.

Main points

- Large duodenal GISTs have irregular lobulated margin, mucosal ulcer, central necrosis, and cavitations showing heterogeneous enhancement on CT and MRI, while small duodenal GISTs show well-defined and homogeneous masses with moderate enhancement.
- Duodenal GISTs have prominent arterial blood supply and draining vessels visible on CT and MRI, which can aid in differential diagnosis from other periampullary tumors and some benign lesions.
- Surgical R0 resection with clear margin is the desired treatment of GIST, but unresectable or metastatic GISTs may be treated by targeted therapy with imatinib mesylate to shrink the tumor.

GISTs can occur anywhere in the gastrointestinal tract. However, the most common reported location is stomach, at about 60% (1). The incidence in small intestine is about 20%–30%, and it is rare in the duodenum (5%). Duodenal GIST accounts for 10%–30% of all malignant tumors of the duodenum (1).

Duodenal GISTs show various clinical presentations, according to their size and origin. Most patients have symptoms of gastrointestinal bleeding and abdominal pain, however, they can also be asymptomatic, especially for the small GISTs. Other rare symptoms include back pain, jaundice and bowel obstruction (1, 6). Ulceration and gas are relatively common features of duodenal GISTs, especially in large tumors (6).

Radiologic findings of duodenal GISTs

CT and MRI are the most useful imaging techniques. Radiologic findings of duodenal GISTs, usually vary from small homogeneous mass to large necrotic mass. Primary duodenal GISTs usually show large, well-defined mass with irregular lobulated margin and heterogeneous enhancement in CT images. As they are originated from the deep muscularis propria, GISTs show exophytic or intramural mass. Duodenal GISTs may show a central umbilication or ulceration of the overlying mucosa (Fig. 2). Duodenal GISTs are known to be most common in the second part. Small tumors appear as

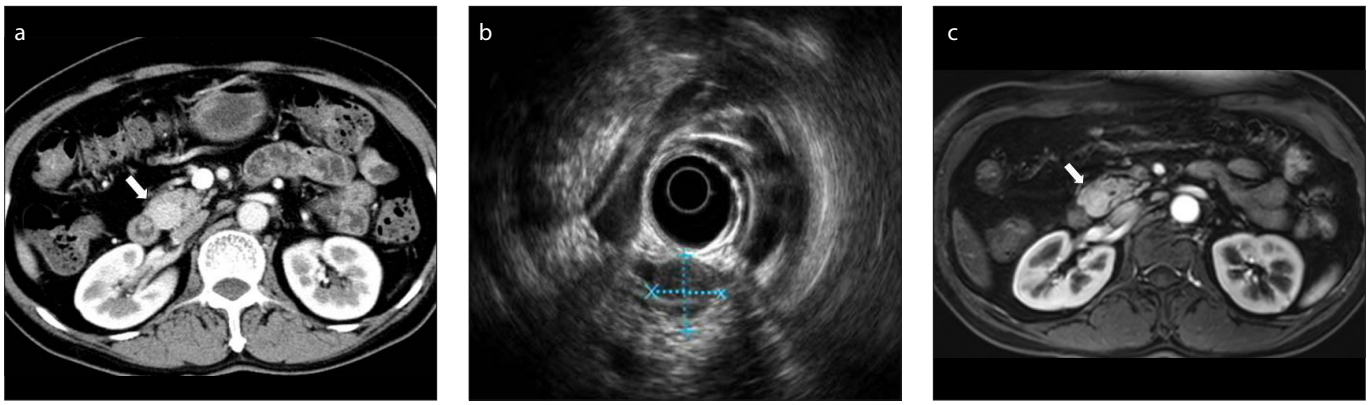

Figure 3. a–e. A 63-year-old woman with small duodenal GIST. Portal phase axial image of contrast-enhanced CT **(a)** shows a 1.9 cm round enhancing mass *(arrow)* in the second part of the duodenum, adjacent to the pancreas. EUS **(b)** shows a 1.9 cm hypoechoic lesion with irregular margins originating from the muscularis propria of the duodenum and internal color flow. Contrast-enhanced MRI also shows a 1.9 cm round enhancing mass in the second part of the duodenum on arterial phase (**c**, *arrow*), which shows low signal intensity on T1-weighted image (**d**, *arrow*) and high signal intensity on T2-weighted image (**e**, *arrow*). This was a hypervascular tumor that needed differentiation between duodenal GIST and pancreatic neuroendocrine tumor. It was proven to be an ampullary GIST in biopsy.

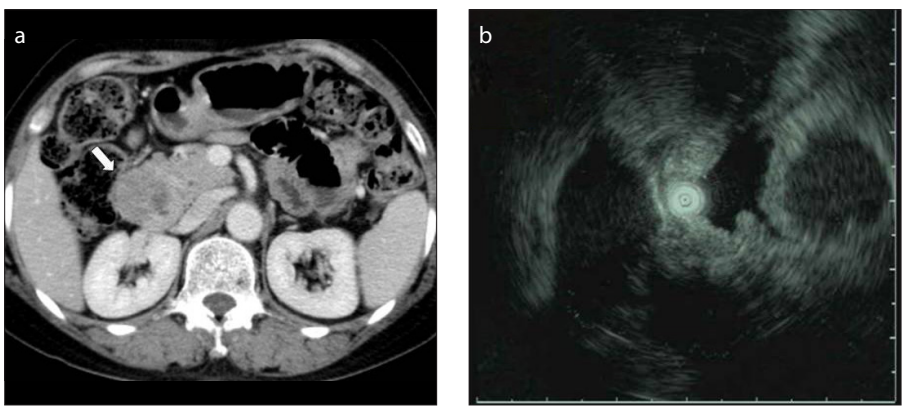

Figure 4. a, b. CT and EUS images in a 59-year-old woman with large duodenal GIST. Arterial phase axial image **(a)** and arterial phase coronal image of contrast-enhanced CT shows a 4.0 cm well-defined lobulated, heterogeneous enhancing mass *(arrow)* at anterolateral wall of the second part of the duodenum invading the pancreas head. Note the central hypodense portion within the mass suggesting central necrosis. She underwent EUS **(b)** to reveal a bulge in the second part of the duodenum, which showed a heterogeneous hypoechoic lesion with irregular margins, originating in muscularis propria. It was proven to be a duodenal GIST in biopsy.

well-defined, homogeneous masses with moderate contrast enhancement (Fig. 3). However, large tumors have irregular lobulated margin, mucosal ulcer, central necrosis, and cavitations showing heterogeneous enhancement (Figs. 4, 5) (8).

Some characteristic CT findings of duodenal GISTs have been reported. Lee et al. (6) reported that duodenal GISTs have prominent arterial blood supply and draining vessels. Blood supply is helpful to find the origin of tumor. Superior pancreaticoduodenal artery and superior mesenteric artery supply blood in duodenal GISTs, and they are drained to portal venous trunk and superior mesenteric vein (Fig. 6).

MRI findings vary according to tumor necrosis, hemorrhage and cavitation. Usually, GISTs show low signal intensity on T1-weighted images and high signal intensity on T2-weighted images with enhancement (1, 3). Depending on the time of hemorrhage with the mass, GISTs show variable signal intensity on T1- and T2-weighted images.

EUS images show homogeneous and hypoechoic mass occurring in the duodenum. Also, it is possible to do EUS-guided fine needle aspiration (FNA) and the cytology from this study helps to diagnose the GIST.

Barium study shows well-defined submucosal masses in the duodenum with or without ulceration. It can help to evaluate tumor location and ulceration. It can show extrinsic compression of duodenum by mass as focal collection of barium.

Differential diagnosis of duodenal GISTs with other periampullary lesions

It is important to differentiate duodenal GISTs from other periampullary tumors and some benign lesions (3).

Duodenal adenocarcinoma

Duodenal adenocarcinomas show pol-

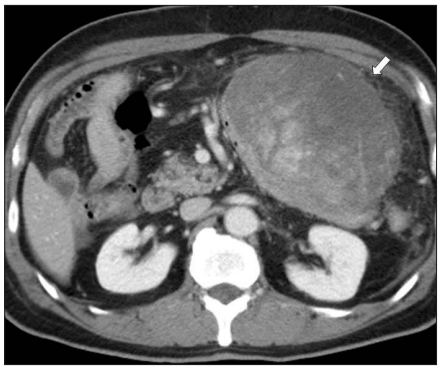

Figure 5. CT image in a 66-year-old man with a large duodenal GIST. Portal phase axial image CT shows a 13.8 cm well-defined, lobulated, heterogeneous enhancing mass *(arrow)* abutting jejunum with peritoneal infiltration. Central hypodense portion within the mass suggests central necrosis. It was proven to be a duodenal GIST in biopsy.

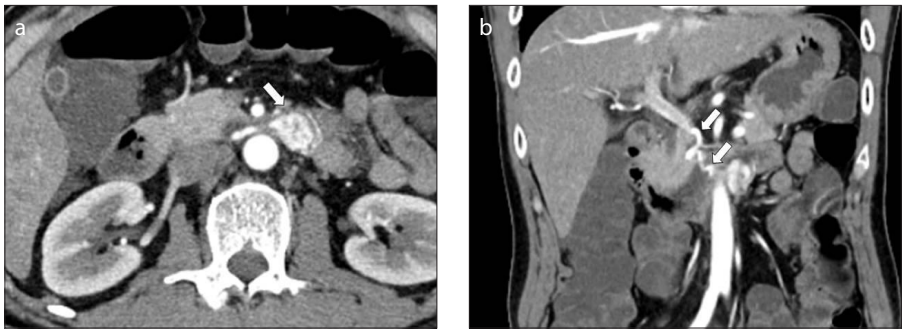

Figure 6. a, b. CT images in a 49-year-old man with duodenal GIST. Arterial phase axial image **(a)** shows a 2.8 cm hypervascular mass *(arrow)* with draining veins, which eventually drained into superior mesenteric vein, arising from the fourth part of the duodenum on coronal image **(b** , *arrows*).

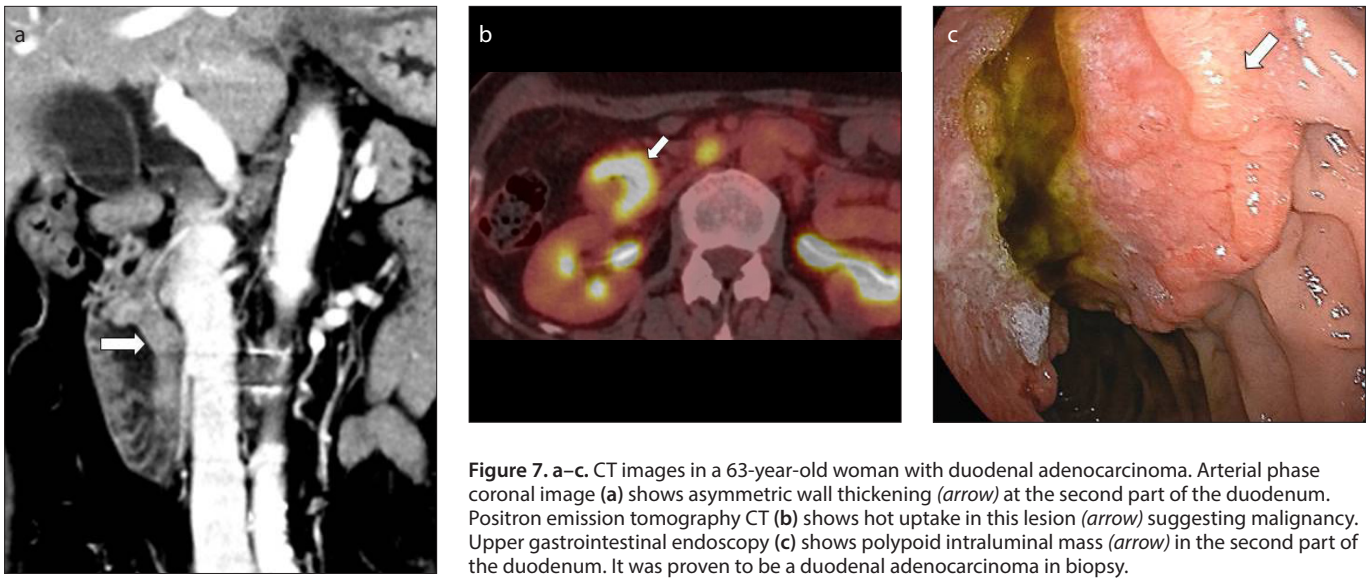

Figure 7. a–c. CT images in a 63-year-old woman with duodenal adenocarcinoma. Arterial phase coronal image **(a)** shows asymmetric wall thickening *(arrow)* at the second part of the duodenum. Positron emission tomography CT **(b)** shows hot uptake in this lesion *(arrow)* suggesting malignancy. Upper gastrointestinal endoscopy **(c)** shows polypoid intraluminal mass *(arrow)* in the second part of the duodenum. It was proven to be a duodenal adenocarcinoma in biopsy.

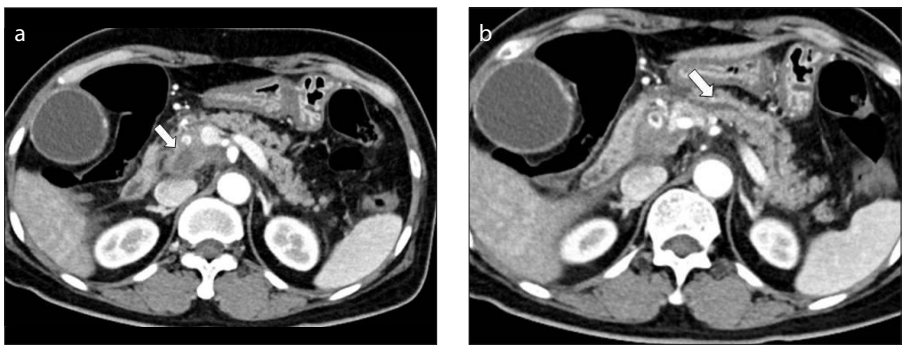

Figure 8. a, b. CT images in a 63-year-old woman with pancreatic adenocarcinoma. Arterial phase axial image **(a)** shows a 2.0 cm ill-defined poorly enhancing mass *(arrow)* with dilatation of upstream pancreatic duct on arterial phase axial image **(b**, *arrow***)**. It was proven to be a pancreatic adenocarcinoma in biopsy.

ypoid or intraluminal masses with eccentric wall thickening compared with duodenal GIST. Duodenal adenocarcinoma is relatively hypovascular (Fig. 7). As already stated, duodenal GISTs have more prominent blood supply with draining veins and it helps to differentiate them from duodenal adenocarcinomas (7).

Pancreatic head adenocarcinomas

Pancreatic adenocarcinomas show hypoattenuating masses but some of them show isoattenuation compared to pancreatic parenchyma in small tumors (8). They may show cystic or necrotic features. Pancreatic adenocarcinomas are more hypovascular than normal pancreas and heterogeneously enhanced with progressive delayed enhancement pattern. They also present with dilated pancreatic duct and common bile duct. Duodenal GISTs show more vascularity than pancreatic adenocarcinomas. In addition, duodenal GISTs have softer texture, so biliary obstruction is rare. Duodenal GISTs may show ulceration, gas, and cavity but pancreatic head adenocarcinomas do not show these features (Fig. 8) (8).

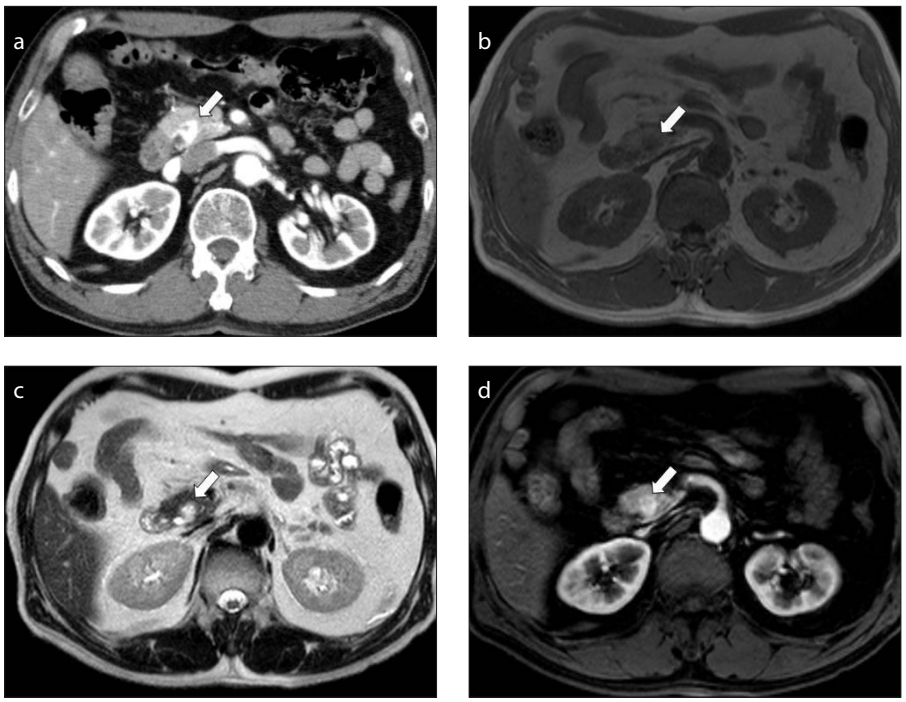

Figure 9. a-d. CT and MRI images in a 76-year-old man with pancreatic neuroendocrine tumor. Arterial phase axial CT image **(a)** shows a 1.5 cm well-defined, enhancing mass *(arrow)* in the uncinate process of pancreas. The lesion shows low signal intensity on T1-weighted image **(b)**, high signal intensity on T2-weighted image **(c)** with arterial enhancement on arterial phase axial MRI **(d)**. It was proven to be pancreatic neuroendocrine tumor in biopsy.

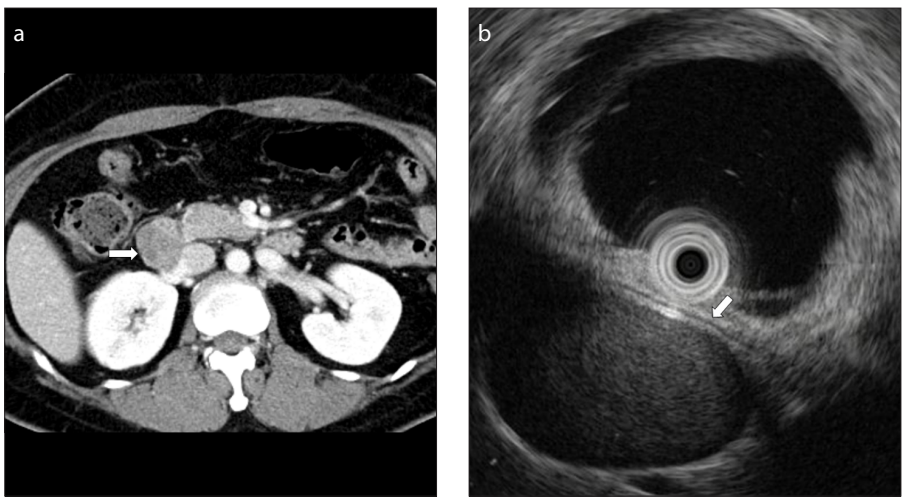

Figure 10. a, b. CT image in a 48-year-old woman with duodenal leiomyoma. Portal phase axial image **(a)** shows a 3.0 cm well-defined, ovoid, homogeneously enhancing mass *(arrow)* abutting the second part of the duodenum. EUS **(b)** shows a homogeneous hypoechoic mass *(arrow)* thought to be originated from the fourth part of the duodenum. It was proven to be a duodenal leiomyoma in biopsy.

Pancreatic head neuroendocrine tumors

Duodenal GISTs and pancreatic head neuroendocrine tumors (NETs) are hypervascular tumors showing strong enhancement at the arterial phase. It is difficult to differentiate duodenal GISTs from pancreatic head NETs when they grow outwards from duodenum towards the pancreatic head. Pancreatic NETs show low signal intensity on T1-weighted images and high signal intensity on T2-weighted images along with enhancement on MRI (Fig. 9). Duodenal GISTs are larger than pancreatic head NETs. Additionally, necrosis or cystic degeneration is more often in duodenal GISTs than pancreatic head NETs. Also, pancreatic head NETs show higher enhancement than duodenal GISTs on MRI (3).

Other duodenal malignancies

Duodenal lymphoma shows circumferential wall thickening or aneurysmal dilatation of duodenum, with abdominal lymphadenopathy. Lymphadenopathy is the key clue to differentiate the lymphoma from GISTs (7).

Duodenal metastasis from a distant site is rare. However, metastases from primary tumors of melanoma, lung cancer, renal cell carcinoma, and seminoma have been reported (9). The most frequent metastatic site is duodenal bulb or the second part of the duodenum. Duodenal metastasis usually shows periduodenal lymph nodes, which can be useful to differentiate them from duodenal GISTs (9).

Leiomyoma

Leiomyoma usually shows well-circumscribed, ovoid, homogeneously enhancing mass in submucosal layer with exophytic appearance (Fig. 10). Leiomyomas show low signal intensity on T2-weighted images with homogeneous enhancement, while GISTs show high signal intensity on T2-weighted images with heterogeneous enhancement, especially when they have necrosis (10).

Paragangliomas

Paragangliomas are clusters of neuroendocrine cells and rare tumors, which can also occur in the duodenum. They can occur in external, intramural, or intraluminal locations. Paragangliomas are usually found within the adrenal medulla with small collections in the paravertebral space. They are typically located in the second or third part of the duodenum. Paragangliomas usually show soft tissue attenuation with homogeneous enhancement on both CT and MRI (11). However, they can appear as heterogenous enhancing masses due to hemorrhage and necrosis (Fig. 11).

Other benign lesions

Adenoma

Duodenal adenoma shows variable attenuation and enhancement patterns. Duodenal adenoma is usually flat or sessile and occurs in the second part of the duodenum (Fig. 12). Duodenal adenoma usually does not show extraduodenal extension or metastatic disease (12).

Brunner's gland hamartoma

Brunner's gland hamartoma shows massive enlargement of a single gland, which

Figure 11. CT image in an 80-year-old woman with duodenal paraganglioma. Portal phase axial image shows a 3.7 cm well-defined, exophytic growing, heterogeneously enhancing mass *(arrow)* in distal duodenum around left paraaortic area. It was proven to be a duodenal paraganglioma in biopsy. The imaging finding is atypical of paraganglioma as it usually presents as a homogeneous enhancing mass.

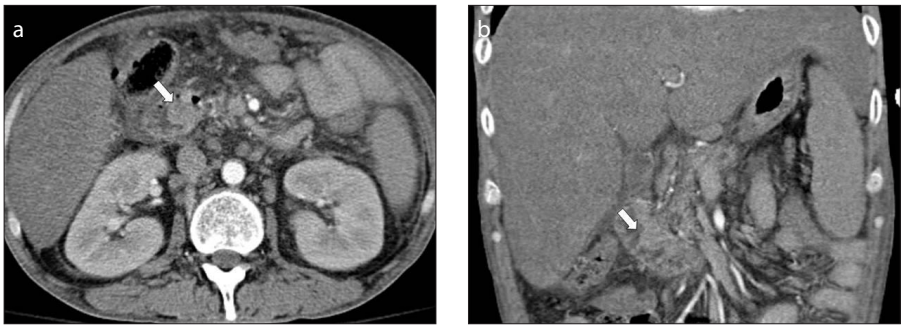

Figure 12. a, b. CT image in a 54-year-old woman with duodenal adenoma. Portal phase axial **(a)** and coronal **(b)** CT images show a 1.7 cm circumferential wall thickening of ampulla of Vater of duodenum *(arrow)*. It was proven to be a duodenal adenoma in biopsy.

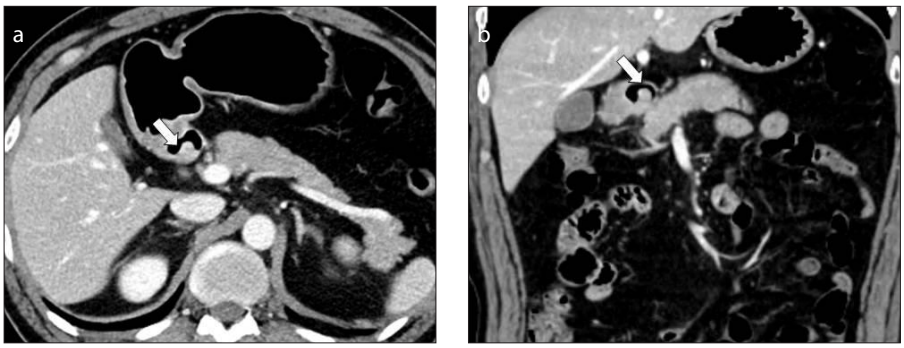

Figure 13. a, b. CT image in a 46-year-old man with Brunner gland adenoma. Portal phase axial **(a)** and coronal **(b)** CT images show a 1.6 cm endoluminal protruding mass *(arrow)* in the duodenal bulb with homogeneous enhancement. It was proven to be a Brunner gland adenoma in biopsy.

is greater than 5 mm (13). Brunner's gland hamartoma shows variable attenuation with homogeneous enhancement pattern on CT (Fig. 13). The homogeneous pattern correlates with histologic findings of glandular proliferation. However, multiple cysts within the hamartoma can lead to enhanced heterogeneity (13).

Lymph nodes

Enlarged lymph nodes in periampullary region such as tuberculous lymphadenopathy and Castleman disease can be misdiagnosed as duodenal GISTs (Fig. 14). Localized Castleman disease shows a solitary, well-defined mass with enhancement on CT, which is similar to CT findings of duodenal GISTs.

Aneurysm

Some aneurysms around the duodenum can mimic hypervascular tumor in the periampullary region. Pancreaticoduodenal artery or splenic artery aneurysms can mimic hypervascular tumors in periampullary region including GISTs (15).

They may have wall calcifications in the mass due to vascular calcifications. The connection to vascular structure is key clue to differentiate from other periampullary tumors. Doppler US, MRI, and angiography can be helpful to find the aneurysms (Fig. 15).

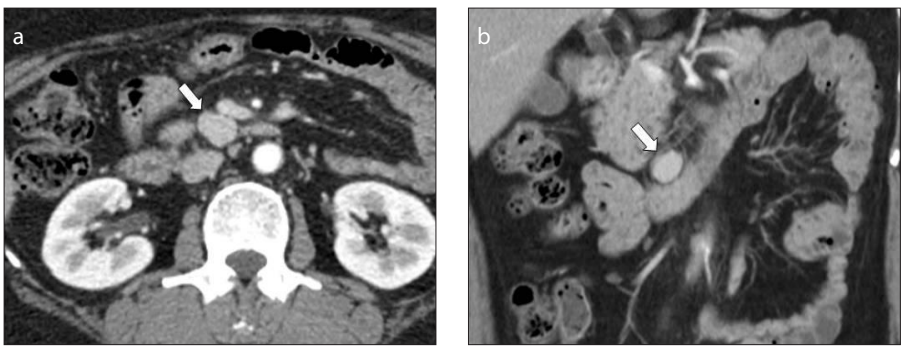

Figure 14. a, b. CT image in a 49-year-old woman with Castleman's disease. Portal phase axial **(a)** and coronal **(b)** CT images show a 1.9 cm ovoid homogeneous enhancing lesion *(arrow)* in precaval space. It shows preservation of the fat plane between the mass and the duodenum, which is indicative of an extramural subepithelial mass. It was proven to be the Castleman's disease, hyaline vascular type, in biopsy.

Management and outcomes of duodenal GISTs

Gastrointestinal endoscopy may be helpful for the tumors located in the stomach or proximal duodenum. However, GISTs of the distal duodenum are hard to detect by gastrointestinal endoscopy, so CT and MRI are the best imaging modalities to assess the primary lesion and detect metastases.

Treatment of GISTs varies according to tumor size, location and growth pattern. Surgical R0 resection with clear margin is the only curative treatment for duodenal GISTs, and it can achieve high survival rates. Indications of surgery include symptomatic GISTs more than 2 cm with high risk features, such as irregular margins, ulceration, internal heterogeneity, and increasing tumor size (1, 14). Operative methods include wedge resection, segmental resection such as duodenal transaction with Roux-Y or Billroth II gastrojujunostomy (G-J), end-to-end duodenoduodenostomy (D-D), pancreaticoduodenectomy (PD), and Whipple procedure with pancreatojejunostomy (1, 14). Careful follow-up and targeted therapy with imatinib mesylate (Glivec) is needed if the resection margin is positive.

GISTs that are unresectable due to large size or difficult location may be treated by targeted therapy with imatinib mesylate to shrink the tumor, followed by surgery. Met-

Figure 15. a–c. CT image and angiography in a 41-year-old man with pancreaticoduodenal artery aneurysm. Arterial phase axial image **(a)** shows a 2.0 cm hypervascular lesion *(arrow)* medial to pancreas uncinate process with suspicious communication with vessel posterior inferior pancreatoduodenal artery from superior mesenteric artery. Angiograph **(b)** shows an aneurysm of pancreaticoduodenal artery *(arrow)* and post-embolization angiograph **(c)** shows microcoils *(arrow)* placed in the aneurysm of pancreaticoduodenal artery.

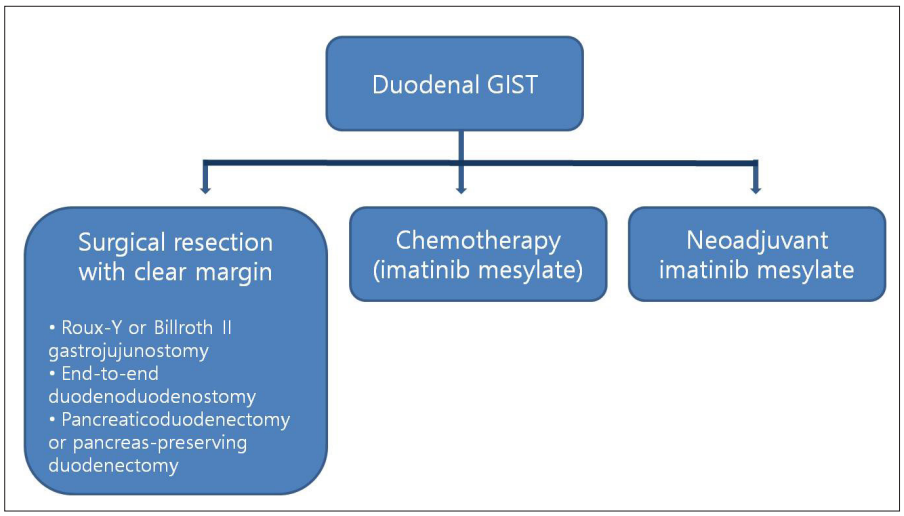

Figure 16. Flow chart of management of duodenal GIST. Duodenal GIST can be cured by surgical resection with clear margin. Chemotherapy and neoadjuvant imatinib mesylate helps to treat GISTs.

astatic or recurrent GISTs can be treated by targeted therapy with imatinib mesylate. Sunitinib is useful, if the tumor grows during imatinib mesylate therapy or if there is high possibility of side effects. Further, as already reviewed, KIT mutations have malignant potential so they should be treated with neoadjuvant therapy (Fig. 16) (14).

Conclusion

CT, MRI, and EUS are useful noninvasive imaging modalities for differential diagnosis and treatment of duodenal GISTs. Surgical resection with clear margin is the desired treatment. However, neoadjuvant chemotherapy is helpful to reduce tumor size and treat GISTs, which are unresectable, metastatic, or recurrent. Owing to the complex anatomy of the duodenum, radiologists should be familiar with imaging features of duodenal GISTs to differentiate them from other adjacent tumors.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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