Original Article
Characteristics of clinic, CT and immunohistochemistry in duodenal gastrointestinal stromal tumors

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Abstract: Objective: To investigate the characteristics of clinic, CT and immunohistochemistry in duodenal gastrointestinal stromal tumors (GISTs), and to identify the evaluation in predicting prognosis for patients with duodenal GISTs. Methods: Retrospectively analyzed the characteristics of clinic, CT imaging and pathological data in 11 patients with duodenal GISTs confirmed by operation and pathology. Results: 6 patients were with gastrointestinal hemorrhage (54.5%), 2 were with pain in upper abdomen (18.2%), and 3 were with tumor by physical examination (27.3%). There were 7 patients with tumor in the descending part of duodenum, 3 were in the horizontal part of duodenum, and one was in the rising part of duodenum. 8 patients were with extra cavity growing and 3 were transmural growing. The maximum diameter was between 1.7 and 14 cm, average 6.9 cm. There were 3 lesions appearing round or oval in shape, and 8 irregular or lobular shapes. After enhancement, 4 cases appeared significantly homogeneous enhancement, while 7 cases appeared significantly heterogeneous enhancement with necrosis. The results of immunohistochemistry showed that there were 8 cases with differentiating to smooth muscle (72.7%), 2 cases lacking of differentiated characteristics (18.2%), and 1 with differentiating to nerve (9.1%). Conclusions: GISTs appeared the characteristics of CT image and clinic and pathology, which helped to increase the diagnostic accuracy of GISTs.

Keywords: Duodenal gastrointestinal stromal tumors, clinical characteristics, tomography, X-ray, immunohistochemistry

Introduction
GISTs independently originate from gastrointestinal tract, which is the most common mesenchymal tumor with spontaneous differentiation. GISTs happen in the whole digestive system from esophagus to anus, including omentum, mesangium, peritoneum, retroperitoneal space and so on. Most of GISTs generated in gastro (60%~70%) and intestine (25%~35%) [1], while less generated in duodenum, which was 10%~20% in intestinal stromal tumor [2] and 3%~5% in all GISTs [3]. However, there were fewer researches on duodenal GISTs. We retrospectively analyzed the characteristics of clinic, CT imaging and pathological data in 11 patients, from January 2000 to December 2013, with duodenal GISTs in order to enhance the acknowledgements and increase the diagnostic accuracy of GISTs.

Materials and methods

Clinical data
The 11 patients, 6 males and 5 females, aging from 36 to 81, average age 61.7, with duodenal GISTs were confirmed by operation and pathology. All the patients were received plain CT scan and enhanced scan.

CT examination methods
With GE Light Speed and Bright Speed 16 rows spiral CT scanner. The patients were fasting for 6 h. Orally took warm water 500~1000 ml before 30 min of examination and scanning. Scanning parameters: tube voltage 140 kV, tube current 220 mA, slice thickness 5 mm, plain scan and dual phase enhanced scan were carried on. Nonionic contrast agent (iohexol 300 mgI/ml, 1.5 ml/kg, with injection rate of 3
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ml/s) was injected through vein. The arterial phased and portal vein phased scans were carried after 30 s and 60 s. Maximum intensity projection (MIP), multi-planar reconstruction (MPR) and other after-treatments were carried in some scanning images of patients in AW4.3 and AW4.4 workstations.

Analysis of CT images, observation and judging criteria

All the CT images were analyzed and recorded separately by 2 senior attending physicians according to previously confirming observation content and criteria. The results were confirmed when the two physicians obtained consistency after discussions. The observation content included the position, size, morphology, edge, growth pattern, enhancing level, necrosis level and so on. The positions of lesion included duodenal bulb, descending parts, horizontal part and ascending portion. Took the surgical results as the final evidences when there were unclear portions in CT images. Tumor size was confirmed according to the longest diameter on the largest cross section. The tumor morphology included regular (round or oval) and irregular (lobular). According to the CT image, we divided the tumors, with or without invasion, into two kinds, one was with clear border (without infiltration) and the other was with unclear border (with infiltration). The growth pattern included endogenous growth (the tumors grew to intra cavity), exogenesis growth (the tumors grew to extra cavity) and transmural growth (the tumors grew to intra cavity and extra cavity). The tumors included with obvious necrosis and without obvious necrosis. Enhancement level included slight enhancement (CT value increased < 20 HU), moderate enhancement (CT value increased between 20 to 40 HU) and obvious enhancement (CT value increased > 40 HU).

Immunohistochemical classification

According to Erlandson [4] et al. the immunohistochemical classification of duodenal GISTs included the following 4: ① differentiating to smooth muscle; ② differentiating to nerve; ③ bi-differentiating to smooth muscle and nerve; ④ lacking of differentiated characteristics. The results were confirmed as differentiating to smooth muscle if Actin, Desmin and SMA were positive, while differentiating to nerve if S-100 and NSE were positive. If Actin/Desmin/SMA and S-100/NES were both positive, then the results were confirmed as bi-differentiating to smooth muscle and nerve, while that mentioned above were both negative but positive Vimentin, then the results were confirmed as lacking of differentiated characteristics.

Results

Clinical data

There were 6 patients with gastrointestinal bleeding (54.5%), which was the most common clinically manifestation. The course of these 6 was from 2 days to 2 weeks. 5 of them were with recurrent melena, 1 of them was with
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melena and hematemesis, 4 of them were with combining with severe anemia (hemoglobin < 5.5 g/L). 2 of the 11 were with dull pain in the abdomen (18.2%), with the course of half month and a month. One of them, which was with longer course, was with progressive whites and yellowing skin. 3 patients with duodenal GISTs were discovered accidentally for routine examination and hospitalization for diabetes mellitus (27.3%).

CT images

The position and size of the lesions: the 11 patients were all with the single lesion. 7 of them were with the lesion generating in the descending part of duodenum (63.6%), 3 were in the horizontal part (27.3%), and 1 was in the ascending part (9.1%). The maximum diameter was 1.7 cm~14 cm, average 6.9 cm.

The morphology and edge: there were 3 lesions with regular morphology, clear edge and diameter < 4.0 cm (Figure 1); 8 lesions were with irregular or lobular morphology (Figure 2), including 5 of them with clear edge (Figure 3) and 3 with unclear edge for adhesion to the around (Figure 4).

Growth pattern: 8 lesions were exogenesis growth (72.7%), including 4 in the anterior wall of duodenal descending part projecting to the right peritoneal (Figure 3), 1 in the ascending part extending to left retroperitoneal and peritoneal (Figure 4), and 3 in horizontal part including 2 generating to the retroperitoneal (Figure 2) and 1 projecting into pancreatic head (Figure 5). 3 lesions were transmural growth (27.3%), locating in the medial wall of duodenal descending part and projecting into intestinal cavity (Figure 1), which might be related to the restricted development space of the lesions.

Enhancement and necrosis: all the lesions appeared obvious enhancement in arterial and venous phase (100%). The CT value was 40 HU~100 HU higher than plain scan. Peak attenuation (PA) was in late arterial phase and early venous phase, including 4 appearing obviously homogeneous enhancement (Figures 1 and 5) and 7 obviously heterogeneous enhancement (Figures 2-4). 5 lesions with diameter above 8.0 cm all appeared widely and obviously internal necrosis, and cystic and solid changes (Figures 2 and 3). 2 of the 5, with diameter of 8.0 cm and 14.0 cm separately, appeared unequal gas and formed into the plane of gas-liquid (Figure 4).

The relationship between the lesions and the adjacent intestine and duct: partial of duodenal intestine in lesion showed unclear compressed, deformed and displaced morphology. However, we observed in 4 patients that the duodenal mucosa cling to lesion extended and elongated due to the traction of being suppressed by the development and enlargement of extraduodenal masses, which led to the potential expansion but not the coarctation of regional intestinal cavity (Figures 1 and 3). 2 of the 4 were led to obstructive bile duct dilation locating in distal common bile duct being compressed by lesion around the duodenal papilla. 1 case appeared
clinically that skin and sclera were stained yellow progressively (Figure 5). 1 case was with increase of hemobilirubin.

Results of operation and pathology

11 patients were received resection. All the lesions were pathologically diagnosed as GISTs after operation. 11 appeared positive CD117 and 8 appeared positive CD34. According to the immunohistochemistry, we typed into 4 including 8 differentiating to smooth muscles (72.7%), lacking of differentiated characteristics (18.2%) and differentiating to nerve (9.1%), without di-differentiation.

Discussion

Clinical characteristics

Duodenal GISTs were more common in older people and less in those before 40, without significant difference in sex. The pathogenic sites mainly included the descending and horizontal part of duodenum, less in duodenal bulb and ascending part. In our study, the minimum age of onset was 36, while the others were above 48, including 6 patients above 60 (54.5%, 6/11). The proportion of male and female was 1.2: 1 (6/5). 90.9% lesions generated in the duodenal descending part (63.6%) and horizontal part (27.3%), which were consistent with previous researches [3, 5, 6].

Duodenal GISTs lacked of specifically clinical symptoms and signs. Our study and the researches at home and abroad showed [7, 8] that the symptom of gastrointestinal bleeding (black stool/hematemesis) combining with blood loss and anemia was the most common, indicating the lesion coming from gastrointestinal but lack of specificity. The cause of bleeding was that mucosa side was easily involved by lesion and formed into ulcer. For duodenal GISTs were mainly exogenous, there was less intestinal obstruction clinically [6]. Although 6 lesions were with the diameter above 5 cm in our study, there was no digestive intestinal obstruction. 1 patient among the 11 appeared stromal tumor in horizontal part (Figure 2) with the diameter of 13 cm, which obviously compressed and pushed duodenal intestine in the narrow space of the posterior to mesenteric vessels but without any obstructions. Therefore, we considered that without digestive tract obstruction was the importantly clinical feature.

However, when the lesion appeared around duodenal papilla, distal common bile duct was easily compressed, which induced bile duct obstruction [9]. In our study, there were 2 patients belonged to the situation mentioned above. One of them was with the diameter of 1.7 cm (Figure 5) but compressed common bile duct early and induced progressive jaundice, which was misdiagnosed as islet cell tumors with abundant blood supply in pancreatic head until the operation.

20%~30% of the cases with GISTs were without any symptoms, while they were accidently discovered in physical examination or operation for other diseases. There were 3 patients (27.3%) in our study belonged to the situation...
mentioned above. 2 of them had huge tumors with the diameter of 12 cm and 13 cm separately and extensive necrosis in the anterior wall of descending part and ascending part. But there was no obvious symptom in clinic (Figure 4), so we presumed that when the tumor generated to serosal surface and projected into abdominal cavity, or when there was enough for the generation, there was less symptoms being induced for being uneasy to compress the adjacent organs.

CT image features

Previous researches [6, 10] and our results showed that the CT image of duodenal GISTs contained the common characteristics of GIST: the smaller lesion was clear and regular without internal necrosis or local cerebral mild necrosis. As the enlarging and malignant degree increasing of the tumor, the profile became irregular or lobular with obviously internal necrosis, cystic solid masses and slight infiltration to the around. When the inner connected to intestinal cavity, the gas would go into the lesion.

In our study, there was obvious strengthening after enhancing the substantive part of arterial and venous phases. CT value increased above 40 HU, mainly about 100 HU, comparing with plain scan, which was usually strengthened in late arterial phase. Previous researches also showed related results [10]. The duodenal GISTs were different from the stromal tumors in the other digestive tract, significantly [11]. Otherwise, we observed that by the traction of the enlarging tumor, the mucosa layer in the intestinal wall of duodenum, which was adjacent to lesion, gradually extended (Figures 1, 3). The results showed that the lumen in the lesion enlarged potentially but not became narrow, the same phenomenon to the stromal tumors observed in esophagus.

That mentioned above might be the reason why there was less digestive tract obstruction in GISTs, which were fewer reported in previous researches. We considered this as the characteristics of the submucosal stromal tumors, which was different from other gastrointestinal lesions and needed further researches. For the position, size, morphology, edge, density, invasion and metastasis of tumor could not be observed by CT directly, we need to improve the ability of location and qualitative analysis by means of reconstruction technique, which is convenient, noninvasive and helpful to clinical treatment. Therefore, reconstruction technique has become the most effective and main examination method to observe and diagnose GISTs.

Immunohistochemical characteristics

For the single (muscle-derived or neurogenic) or double (muscle-derived and neurogenic) differentiation ability in interstitial cells of Cajal (ICC) or mesoblastic-Interstitial stem cell, the tumor has 4 differentiated forms including differentiating to smooth muscles, nerve, both smooth muscles and nerve, and lacking to differentiated characteristics [12]. In the observation of the differentiation in 165 patients with GIST, Hurlimann [13] et al. found that 29.7% of the tumors differentiated to smooth muscles, 10.9% to nerve, 3% to both smooth muscles and nerve, and 15.2% lacked of differentiated characteristics.

In our previous study, we observed the immunohistochemistry of 85 patients with GISTs [11] and found that 30.6% of the tumors differentiated to smooth muscles, 23.5% to nerve, 11.8% to both, and 34.1% lacked of differentiated characteristics, closed to the results of Hurliman [13] et al. In this study, the ratio of differentiating to smooth muscles, the expression rate of muscle-derived marker was higher than the distribution ratio of other parts in digestive tract (8/11, 72.7%), closed to previous researches [14, 15]. We need further researches to investigate the meaning of expression rate in muscle-derived marker of duodenal GISTs and the relationship to the abundant blood supply and characteristics of easy liquefaction and necrosis.

Diagnosis

The partial and exogenous tumor generating in duodenal wall was with the round or irregular-lobular shape, clear profile, significant homogeneous or heterogeneous enhancement after strengthening, easy liquefaction and necrosis. Even the huge tumor was without duodenal obstruction but with gastrointestinal bleeding and abdominal pain and discomfort. Obstructive jaundice was induced when the tumor compressed the ampulla around the duodenal papilla, which belonged to the clinical charac-
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Duodenal adenocarcinoma, as the poor blood supply lesion, was easy to infiltrate along the intestinal wall irregularly and annularly, and led to intestinal cavity coarctation and obstruction. Pancreatic head carcinoma, also as the poor blood supply lesion, was easy to infiltrate the adjacent structure and induce unclear edge of lesion. Lymphoma was with wide intestinal wall, homogeneous and annular thickening, and slight or mild strengthening. Duodenal adenoma, as the soft tissue nodules, projected into intestinal cavity with slightly or mildly homogeneous strengthen. Duodenal tuberculosis was partially intestinal cavity irregularly and narrowly with peripheral structure cohesion or multiple-annular strengthening lymph but without obvious soft tissue mass.

However, when the stromal tumors generated in the inner side of the duodenum and was closed to pancreatic head, it was easy to mix the significantly strengthened characteristics and the abundant blood supplying neuroendocrine tumors from pancreatic head [16]. In our study, one patient was misdiagnosed for this reason. Otherwise, it was difficult to identify the duodenal GISTs and the abundant blood supply tumor, which generated around duodenum and was closed to duodenal GISTs including smooth muscle tumor, nerve tumor and malignant fibrous histiocytoma. The final confirmation still dependence on histopathology and immunohistochemistry.

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Disclosure of conflict of interest

None.

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