



THE DUODENAL GIST CONUNDRUM – NAVIGATING THE CHALLENGES OF EARLY DETECTION AND EFFECTIVE MANAGEMENT

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ABSTRACT

GISTs are rare mesenchymal tumors arising from the Interstitial Cells of Cajal, the pacemaker cell of the GIT due to mutations in the c-KIT, PDGFR- or wild type mutations and are more common in the stomach(50%). The behaviour of GISTs vary widely based on their size, mitotic rate and location. Small bowel GISTs(25% incidence) metastasize early and tend to have poor prognosis. Duodenal GISTs are less frequently encountered and their management poses difficulty owing to their complex anatomy. Here, we encountered 2 such cases each posing diagnostic difficulty by imaging and required different strategy for management though situated in the same location. To diagnose GISTs, high index of suspicion is required and early decision-making is necessary to prevent metastasis especially in duodenal GISTs.

KEYWORDS : GIST, duodenum, imatinib, c-KIT, pancreaticoduodenectomy

INTRODUCTION:

Gastrointestinal Stromal Tumors are uncommon tumors of the gastrointestinal tract representing only 1-2% of all GI malignancies[1]. The peak incidence is thought to be 60yrs in 60% of patients. They are thought to arise from myenteric Interstitial cells of Cajal, responsible for neuromediation and intestinal pacemaking or their precursor cells, thus can be found anywhere along the GIT. They arise from the submucosa within the muscularis propria or subserosa. c-KIT (75-80%) and PDGFR- (10%) are the two mutations associated with GIST. Those without the above 2 mutations have "wild type GIST" thought to arise from downstream mutations of SDH, BRAF, IGF-1 and are found among children. They are more common in stomach (50-60%) than in any other place like small bowel(25-30%), colon and rectum (5%), oesophagus(1%). The clinical behaviour and prognosis of duodenal GISTs is highly variable and depends greatly on their size, mitotic rate and location. GISTs can become quite large before symptoms develop and small bowel GISTs tend to metastasize earlier than Gastric GISTs. Most GISTs, about 5-10% occurs familial (Type 1 neurofibromatosis and Carney triad). Most common presentation is abdominal pain, bleeding while many are asymptomatic with incidental diagnosis.

Case 1:

A 54 year old female who had complaints of vague upper abdominal pain for past 1 month, incidentally diagnosed to have duodenal GIST on imaging. CECT had revealed a 3.5*4cm lesion in 2nd part of duodenum with central necrotic component. CT guided biopsy revealed a spindle cell neoplasm. This case was presented in multidisciplinary team & surgery was advised as the lesion was less than 5cm radiologically. We did a Whipple's pancreaticoduodenectomy for the same. HPE showed spindle cell type of Gastrointestinal stromal tumour of size 5.5*5*2.5cm with low grade neoplasm, mitotic activity of <5/50hpf, necrosis<5%, and moderate risk of 4.5%, pT2.Ki67-7% , CD117-positive in 90% tumor cells. Though a low grade neoplasm, moderate risk of 4.5% was there, hence adjuvant chemotherapy initiated T.Imatinib 400mg OD was started and advised to continue for 2 years.

Fig 1: Endoscopic image of duodenal GIST showing growth in submucosal region with normal duodenal mucosal folds.**Fig 2:** CT Image showing hypodense mass in second part of duodenum with central necrotic component. **Fig 3:** MRI image of same patient showing T1 hypointense peripheral part and

hyperintense central component of GIST

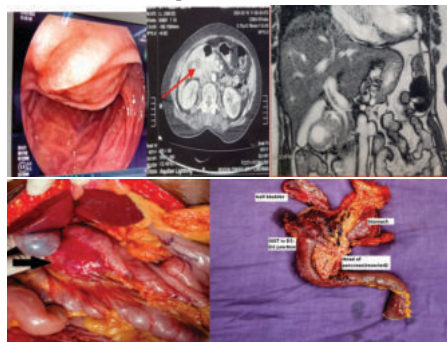


Fig 4: Intraoperative image of Duodenal GIST. **Fig 5:** Post-operative resected specimen of Whipple's pancreaticoduodenectomy

NCCN guidelines for treatment of duodenal GIST has insufficient data regarding the recurrence rate of intermediate sized(5-10cm) GISTs

Case 2:

A 36yr old male came with c/o abdomen pain and distension for past 20 days. On examination he had a distended abdomen with tenderness in right hypochondrium. CECT revealed a well defined lobulated exophytic lesion 9.2*9.0*10cm lesion in duodenum causing luminal narrowing, with vivid enhancement with central necrosis and specks of calcification along with hypodense lesion of size 12*11.2*9.2 in VIII lobe of liver s/o metastasis.MRCP - 12*11.2*9.9cm T1 hypointense, T2 hyperintense lesion in segment 5,6,7,8 of liver with peripheral enhancement-p/o cystic metastasis. Another lesion of size 1.6cm*1.6cm enhancement during arterial phase and washout in venous phase-p/o metastasis



Fig 6: CT image at the level of 2nd part of duodenum showing GIST with central necrotic component

MRCP with contrast- Cystic metastasis with rim enhancement in liver. We did a CT guided biopsy to confirm the diagnosis of GIST, it confirmed the possibility of GIST with CD117 strong positivity, risk assessment could not be done as it was a small biopsy. He was started on T. Imatinib 400mg OD after multidisciplinary tumor board discussion. 6 months after chemotherapy, patient had reduction in symptoms and is on continuous followup.



Fig 7: A small Duodenal GIST causing huge metastasis in liver. The larger metastatic lesion draws our attention which can be confused with hydatid cyst which has similar features radiologically.

DISCUSSION:

Duodenal GIST have uncertain malignant potential and they are usually asymptomatic or present with bleeding and pain. We often find difficult to diagnose GISTs in uncommon locations and patients often present with non-specific and vague clinical symptoms. They are often mistaken for pancreatic head neuroendocrine tumors[4]. The incidence of duodenal GISTs is highest in D2, followed by D3, D1 and D4 [5]. There is wide variation in the radiological appearance of these tumors, hence radiological diagnosis becomes challenging too[1]. Incidence of diagnosing GIST in asymptomatic patients range from 5-40%[2]. One of the patient in our study had GIST in her 50's and the other patient was very young in early 30s. Both of them had non specific vague symptoms like dyspepsia and abdomen distension. EUS guided FNAC is recommended for lesions of stomach and duodenum. In a study conducted by Sepe et al., the diagnostic accuracy of EUS- FNAC is high in Gastric GISTs vs duodenal GISTs(84.4% vs 0%) as none of the duodenal FNAC yielded a diagnostic cytology[3]. This limitation was influenced by size, location and layer of origin of tumor[2] however further studies reveal that EUS-FNAC is superior to CT or MRI in diagnosing GISTs of duodenum or stomach. The European Society for Medical Oncology and European References for Adult Rare Solid Tumors suggest follow-up of patients whose duodenal lesions are less than 2cm, but excision or biopsy is indicated for those with >2cm. Surgery is the mainstay of treatment in GISTs and they provide complete cure although risk of recurrence depends on the mitotic rate of the tumor. The anatomical complexity of the location makes it difficult to choose between surgery and neoadjuvant therapy when the literatures suggest neoadjuvant chemotherapy for inaccessible locations of the GIST. Surgery can be performed safely in these patients, provided adequate surgical margin can be achieved[2]. Laparoscopic approaches can be carried out too with good oncological outcomes in experienced hands. But open surgery provides important access for safety and oncological outcome especially in major resection and reconstruction procedures[3]. The risk of incomplete resection and pseudocapsule rupture precludes the resection of GISTs by endoscopic methods[3]. Both the patients in our study showed CD117 and CD 34 strong positivity, absence of which could indicate poor response to chemotherapy. The first patient had low malignant potential, moderate risk for recurrence, and the second patient who presented with hepatic metastasis had

high risk of recurrence based on core biopsy. Though the risk of metastasis depends on the site of the tumor some reported high incidence of malignant potential for tumors located in the ileum.

The standard treatment for resectable tumors is complete surgical excision with adequate margins and there is no need for lymphadenectomy in these cases as these mesenchymal tumors rarely metastasize via lymphatic route. Their main mode of metastasis is by hematogenous route to the liver (50%), more commonly in small bowel GISTs. Local recurrence occurs in those tumors with positive R1 margin and 100% in case of tumor rupture or spillage [2]. The decision for surgery should be individualized and adjuvant therapy with imatinib mesylate, a tyrosine kinase inhibitor is indicated based on the risk of recurrence.

Surgical procedures vary from wedge resection to pancreaticoduodenectomy for larger infiltrating tumors. Duodenal wedge resection can be performed when the tumor is located on the wall at least 2cm away from the ampulla. Limited resections have been advocated for small tumors not infiltrating the surrounding structures and when the ampulla of Vater can be preserved[3,4]. Segmental duodenectomy with end to end or side to end duodenojejunal anastomosis for large tumors located below the ampulla of Vater in D3 or D4 parts[4]. In those tumors involving the ampulla, pancreaticoduodenectomy or pylorus preserving pancreaticoduodenectomy can be done. In a study, patients with Pancreaticoduodenectomy had a higher incidence of mitotic count > 5/50 high power fields, a higher incidence of tumors located at D2, a larger tumor size > 5 cm and an increased recurrence rate than those who underwent Limited Resection[5]. According to the National Cancer Database, most of the resected D-GIST patients did not receive adjuvant systemic therapy with only 31.3% in the Pancreaticoduodenectomy group vs 21.5% in the Limited Resection group. This data may explain the reason neoadjuvant and adjuvant systemic therapy was not associated with improved Overall survival[5]. As recommended by the National Comprehensive Cancer Network and European Society for Medical Oncology-European Reference Network for Rare Adult Solid Cancers guidelines of resected D-GIST, the intermediate risk group should receive adjuvant Imatinib Mesylate for at least 1 year, and the high-risk group should receive treatment for at least 3 years. The surgical approach for D-GISTs located at D1 and D2 proximal to the ampulla is distal gastroduodenectomy with Billroth II or Roux-en-Y gastroduodenostomy anastomosis.[4,5]

CONCLUSION:

Duodenal GISTs have uncertain malignant potential and vary widely in their behaviour and clinical presentation. Small bowel GISTs pose diagnostic difficulty and hence require a high degree of suspicion. Once diagnosed, next challenge comes to us in deciding the best treatment for the patient in terms of neoadjuvant or upfront early surgery which would otherwise be difficult after chemotherapy as it induces a desmoplastic reaction. Due to the complex anatomy of the duodenum, wedge resection, limited resection, segmental duodenectomy are not always feasible especially for tumors larger than 3cm or when it involves the ampulla of Vater. Though surgical resection offers excellent post-operative recovery, it should be weighed against the risks when performed in anatomically complicated locations like the duodenum.

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