

Primary extragastrointestinal stromal tumor arising In the pancreas: report of a case

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Abstract: Primary extra-gastrointestinal stromal tumor (EGISTs) arising in the pancreas is extremely rare: only 32 cases have previously been reported in the English literature.

We report a further case of EGIST of the pancreas. A 49 -year-old woman presented with abdominal pain localized in the right hypochondrium.

Magnetic resonance imaging (MRI) showed well-demarcated, heterogeneous solid-cystic mass of pancreatic head measured 25mm without invasion of the surrounding tissues. Subtle but distinct flat plane was noted between the mass and pancreatic tissue. At laparotomy, a well-demarcated nodule was identified in the head of the pancreas; no attach with the duodenal wall was found. Careful enucleation of the tumor was successfully performed. Histopathology and immunohistochemical examination confirmed the final diagnosis of EGIST of the pancreas (CD117+), with one mitosis per 50 high-power fields. EGIST with low risk of malignancy has been placed. She did not receive any adjuvant therapy after surgery; 9 months later she is in good general condition and there is no evidence of recurrent disease.

EGIST was introduced into the literature in the last decade.

We are limited to the case reports that have been published to date. Nonetheless, additional research of more cases with longer follow-up is needed before drawing definitive conclusions.

Keywords: Gastrointestinal stromal tumour, extragastrointestinal, pancreas.

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I. Background:

Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the gastrointestinal tract, with an annual incidence of 10 to 20 per million [1]. The disease originates from neoplastic transformation of the interstitial cells of Cajal (ICC) or their precursors in the GI (gastrointestinal) tract [2].

Although GISTs can be diagnosed in all sites of the GI tract, from the esophagus to the anus. The most common sites are stomach (60%), small intestine (30%), rectum (5%), and esophagus (<5%) [1, 2]. These tumors could arise from the omentum, mesentery, gallbladder, and retro peritoneum, adjacent, but separate from the stomach and the intestine. But display no connection to the wall or the serosal surface of the viscera [2] in this case the neoplasm is defined as 'extra-gastrointestinal stromal tumors (EGISTs) [3].

The pancreas is rarely the site of origin, and according to our knowledge, 32 cases of pancreatic EGISTs have been reported to date [1, 2, 4]. We report a case of pancreatic EGIST which was diagnosed based on histopathological and immunohistochemical findings.

The morphological, histopathological, immunohistochemical and molecular profiles of EGISTs are similar to those of GISTs [5, 6].

II. Case report:

A 49 -year-old woman presented with abdominal pain localized in the right hypochondrium. There was no history of vomiting, gastrointestinal bleeding, jaundice, anorexia, or weight loss. Laboratory findings, including serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9), were within normal limits. Abdominal ultrasonography revealed a solid, hyper vascular nodule in the head of the pancreas, measuring 36 mm.

Magnetic resonance imaging (MRI) (Figure 1) showed well-demarcated, heterogeneous solid-cystic mass of pancreatic head measured 25mm without invasion of the surrounding tissues. Subtle but distinct flat plane was noted between the mass and pancreatic tissue. The common bile duct and major pancreatic duct diameter was normal size. No regional lymphadenopathy, ascites, or metastases were seen and there was no

obvious lesion in the stomach or small intestine. The initial diagnosis was a solid pseudopapillary tumor or serous cystic neoplasm of the pancreas.

At laparotomy, a well-demarcated nodule was identified in the head of the pancreas; no attachment with the duodenal wall was found. Careful enucleation of the tumor was successfully performed. Pancreatic capsule was closed with absorbable stitches. The postoperative course was uneventful, and the patient was discharged 8 days after surgery. Macroscopic examination showed a 24 mm well defined, ovoid mass.

Microscopically, the tumor was composed of spindle-shaped cells, with focal nuclear palisading tumor (Figure 2). The mitotic count was 4 mitoses/50 high power fields (HPFs). Immunohistochemical examination showed neoplastic cells diffusely positive for C-kit (Figure 3), focally positive for CD34 (Figure 4), while cells were negative for desmin and PS100, Ki67 (<5%).

A diagnosis of pancreatic EGIST with low risk of malignancy has been placed, pT2N0M0, stage I according to TNM (AJCC) classification.

She did not receive any adjuvant therapy after surgery; 9 months later she is in good general condition and there is no evidence of recurrent disease.

III. Discussion:

GISTs represent 0.1%-3% of all GI tumors and 80% of GI mesenchymal tumors [2].

In fact, the most selective immunohistochemical markers differentiating GISTs from true smooth muscle tumors is the expression of the c-Kit kinase receptor tyrosine in 95% of GISTs [1].

"EGIST" was initially reported by Reith et al [7] in 2000 to define stromal tumors originating from outside of GI tract. EGISTs represent 5%-10% of all GISTs [2, 6, 8].

In 2004, Yamamoto et al [9] reported that EGISTs show similar KIT mutations of typical GISTs suggesting that these tumors have a similar origin. However, at present the origin of EGISTs was a subject for debate [1, 6].

Some authors consider that GISTs and EGISTs arise from the common precursor cell of ICCs and the smooth muscle cells of the gut, which may account for their growth within and outside the gastrointestinal tract [1, 2, 6]. On the other hand, others authors suggest that EGISTs are in fact mural GISTs with extensive extramural growth, resulting in eventual loss of their connection with the gut wall [1, 6].

Pancreatic EGISTs are often symptomatic [8] and diagnosis may even be found fortuitously by radiological examination [2] the clinical presentation of EGISTs is variable, depending on the location and size of the tumors. The most frequent clinical symptoms are: abdominal pain, abdominal distension and weight loss [8].

Our patient presented with postprandial abdominal discomfort.

From literature review of pancreatic GISTs reported by Akbulut S et al, the studies involved 30 patients with pancreatic GIST: mean age was 55 years (range 30-84 years), tumor size was obtained from 28 cases (mean 114.4 ± 78.6 mm; range 20-350 mm). Equal distribution between female and male [2]. Other published reports [8, 10], including the present case, revealed a distinct female predominance.

As evidenced in the literature review, about (48%) of tumors occurred in the head of the pancreas [1]. EGIST rarely involved the entire pancreas [1, 11].

A similar finding of small solid tumor in the uncinate process of the pancreas was reported by Yan et al [12] and Beltrame et al [1].

In 50% of the reported cases, radiologic features showed heterogeneously mass (necrotic areas) or solid-cystic appearance; thus can mimic cystic neoplasm of the pancreas [1].

The surgical procedure depends on pancreatic EGIST localization. Standard treatment for primary GIST is complete resection with microscopically clean (R0) margins [2, 8, 10].

Duodenum-preserving pancreatic head resection may be performed for small tumors, low-grade tumors, or patients who cannot tolerate the Whipple procedure [2].

Various surgical procedures have been reported, such as pancreaticoduodenectomy (PD) and local resection (LR), some author reported that enucleation suggested that it was an adequate operation especially for small tumor with low risk of malignancy [1].

Nevertheless, radical surgical treatment is indicated to prevent local and/or distant metastases [2].

Lymphatic spread of GISTs is uncommon; therefore, a systematic lymph node dissection is not a standard surgical management [1].

In the literature, nine and seven of the 30 patients underwent distal pancreatectomy with splenectomy, and the Whipple procedure, respectively [2].

In our case, we performed a simple tumor's enucleation because it was small and encapsulated. Furthermore after discussion with oncologists, the small size of the lesion and the low-risk according to previously reported prognostic criteria, suggested that it was an adequate operation, as reported in a recent study [1].

The advent of target therapy: Imatinib (Gleevec), which is an inhibitor of the tyrosine kinase activity of c-Kit, changed the treatment of this disease. However, the role of Imatinib in the treatment of EGISTs is not clarified [10].

Disease recurrence following surgery was reported in only 6 patients of the 30 pancreatic GISTs [2]. This suggests that pancreatic GISTs follow a more benign course than EGISTs arising at other sites [10].

Conclusions:

EGIST was introduced into the literature in the last decade [10].

We are limited to the case reports that have been published to date. Nonetheless, additional research of more cases with longer follow-up is needed before drawing definitive conclusions.

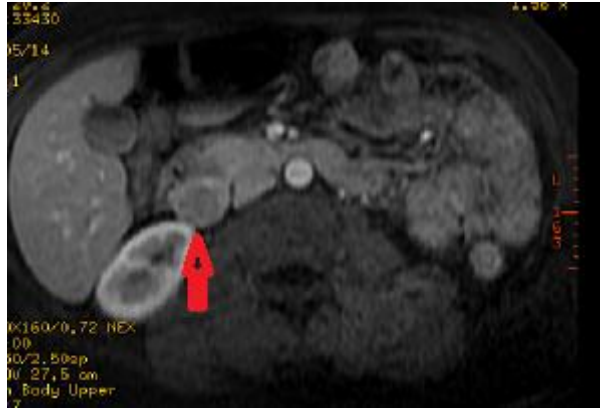


Figure 1: Magnetic resonance imaging (MRI) showed well-demarcated, heterogeneous solid-cystic mass of pancreatic head measured 25mm without invasion of the surrounding tissues. Subtle but distinct flat plane was noted between the mass and pancreatic tissue.

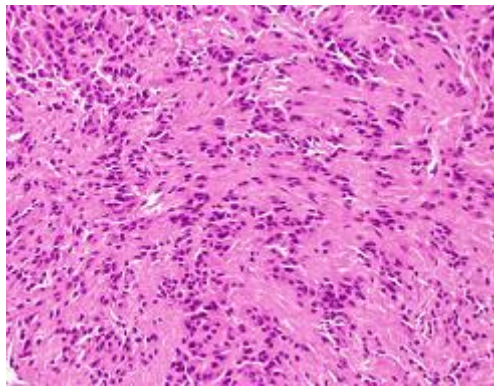


Figure 2: spindle-shaped cells, with focal nuclear palisading tumour

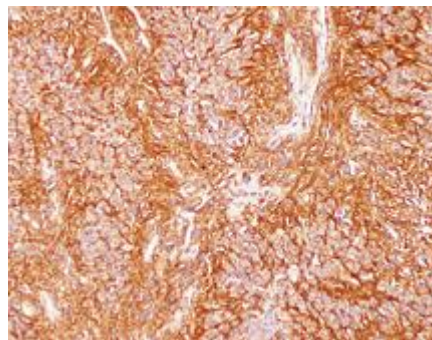


Figure 3: Immunohistochemical findings for c-KIT: strong and diffuse cytoplasmic immunoreactivity.

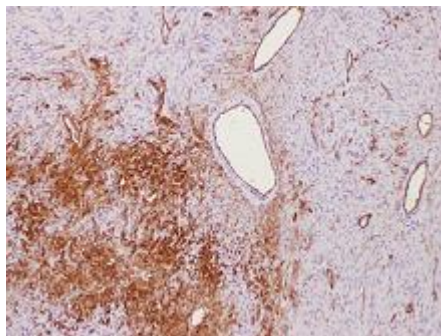


Figure 4:Immunostain for CD34, focal immunoreactivity.

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