

CASE REPORTS

The Retroperitoneal Gastrointestinal Stromal Tumor, Simulating a Cystic Pancreatic Neoplasia. A Case Report.

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Abstract

Introduction: Gastrointestinal stromal tumors (GISTs) are rare mesenchymal tumors that can arise anywhere within the gastrointestinal tract. Approximately 70 % are in the Stomach, representing 1 – 3 % of all gastrointestinal malign neoplasms. GISTs originate from the Cajal interstitial cells or their stem cell precursors within the myenteric plexus of the muscularis propria.

Histologically, GIST presents three different architectural patterns: a. composed of epithelioid cells embedded in a thin reticular stroma; b. by spindle cells with a fascicular or storiform arrangement immersed in a thin reticular stroma focally myxoid, and c. the mixed forme.

This study describes a 72-year-old man who, in the computed tomography, presented a gross appearance as pancreatic cystic neoplasia. Clinicians should be aware that this condition might be mistaken for a primary pancreatic malignancy.

The diagnostic Workup includes endoscopy with ultrasonography, cross-sectional imaging studies, and histopathological examination.

Conclusions: The reported case illustrates that the retroperitoneum might be the place of initial presentation of a cystic gastric GIST and that only an accurate pathological evaluation can establish the diagnosis and origin. Clinicians must know this condition might be mistaken for a primary pancreatic malignancy. Early surgical resection is the gold standard of treatment for primary GIST.

Keywords: GIST, retroperitoneal, stromal tumor, CD117.

Introduction

GISTs represent a distinct biological subset of mesenchymal tumors of the gastrointestinal tract, originating from interstitial Cajal cells or their stem cell precursors. [1, 2, 3]

The neoplastic cells are characterized by spindle or epithelioid aspects, or mixed and occasionally pleomorphic

cells, and by the immunohistochemical expression of c-KIT (CD117), which is a glycoprotein as a receptor of the Growth Factor of staminal cells. Mutations of c-KIT occur preferentially in malignant GISTs [2, 3, 5, 7] and lead to constitutional activation of tyrosine kinase function, which causes cellular proliferation and resistance to apoptosis. GISTs, which encompass most tumors previously classified as gastric and intestinal smooth muscle tumors, are typically present in adults over 50 years (Median age 50 - 60 years) and only exceptionally in children. [1, 2, 4, 5].

The great majority of GISTs occur in the Stomach (70 %) or small intestine (20 %), while the esophagus, colon, appendix, and anus are rarely affected.

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GISTs generally occur in the submucosa (60 %), less commonly intramural (10 %) or subserosal (30 %), where they can grow as a pedunculated mass in the retroperitoneal space. [1, 2, 5, 6, 7]. The specific identification of GIST has become more critical after the availability of a KIT-selective tyrosine kinase inhibitor, imatinib mesylate (STI571), in treating unresectable and metastatic tumors. [1, 5, 6, 8]

Herein, we describe a retroperitoneal GIST, macroscopically evident as a large cystic pancreatic mass, simulating a cystic pancreatic neoplasia. We speculated about the origin of such neoplasm, suggesting a subserosal GIST.

Case Report

A 72-year-old (S. F) man presented with upper abdominal discomfort, pain, and dyspnea. Physical examination revealed a palpable indolent mass. Serum markers were notable only for an elevation of CA125. Ultrasonography evidenced a cystic mass of 180 x 135 mm. Computed tomography of the abdomen, obtained after intravenous administration of contrast material, revealed a mass with a mean diameter of 18 cm, with a central cystic degeneration and an irregular thick-walled mass that showed intense enhancement (Fig. 1A).

The mass was located back to the posterior wall of the Stomach and adherent in limited areas to the posterior gastric wall. It was not separated from the pancreas. There was neither retroperitoneal pathological lymphadenopathy nor ascitic fluid.

The intervention showed a cystic mass that filled the epiploon retroactivity, displacing the Stomach and the omentum (Fig. 1B). The anterior wall of the cyst mass was easily separated from

the omentum. At the same time, it was firmly adherent to a little area of the gastric posterior wall. The posterior wall of the cyst, which appeared englobed into the pancreatic head, was gently cleaved from the pancreatic parenchyma. Finally, a distal gastrectomy was performed.

The histological report was of a gastrointestinal stromal tumor (GIST) in mixed form with epithelioid cells and spindle cells.

Two months later, hepatic metastases were diagnosed, and the patient was enrolled for a cycle with

STI571. A partial objective response was obtained a year after the initial diagnosis.

Pathology Findings

At the gross examination, the mass of GIST was 18 cm in diameter. The external surface appeared glistening and smooth without papillary projections. The lumen contained a dirty liquid. The cystic wall was firm, whitish, 3 - 4 cm thick, and showed irregular, yellowish, and brown, solid flat nodules projecting into the cystic cavity. The excised lesions were subjected to formalin (10 %) fixation and delivered to the Department of Pathology, followed by histopathological examination, immunohistochemical staining of CD117, CD34, S-100, SMA, vimentine and Ki-67 was performed. The mitotic index was calculated under 10 / 50 high-power field.

In the histological examination, two different architectural patterns were evident: the bulk of the mass was composed of epithelioid cells embedded in a thin reticular stroma. Such cells formed thick digitations in the lumen, simulating a papillary pattern. The remaining neoplasia comprised spindle cells with a fascicular or storiform arrangement immersed in a thin reticular stroma focally myxoid. (Fig. 2A and 2B).

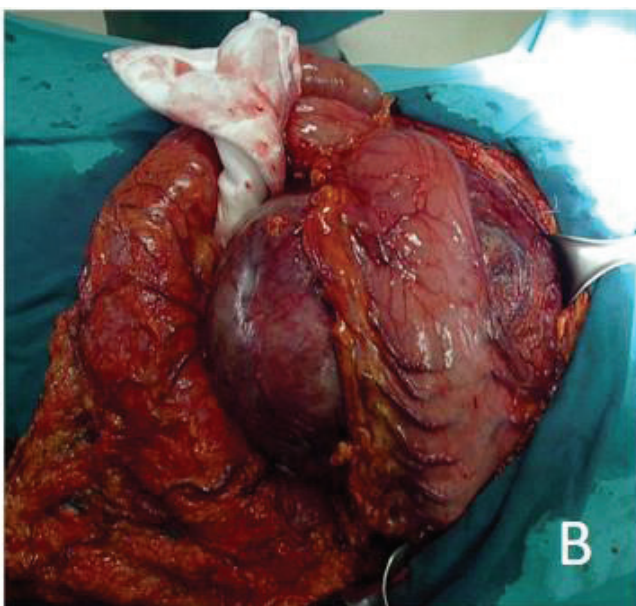
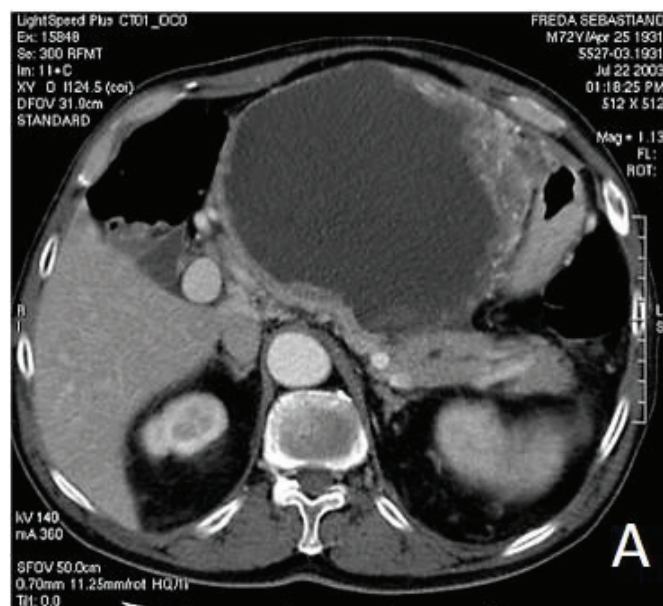


Figure 1A. In the computed tomography, the mass was located back to the posterior wall of the Stomach and was not separated from the pancreas.

Figure 1B. The tumor filled the epiploon retrocavity, displacing the Stomach and the omentum.

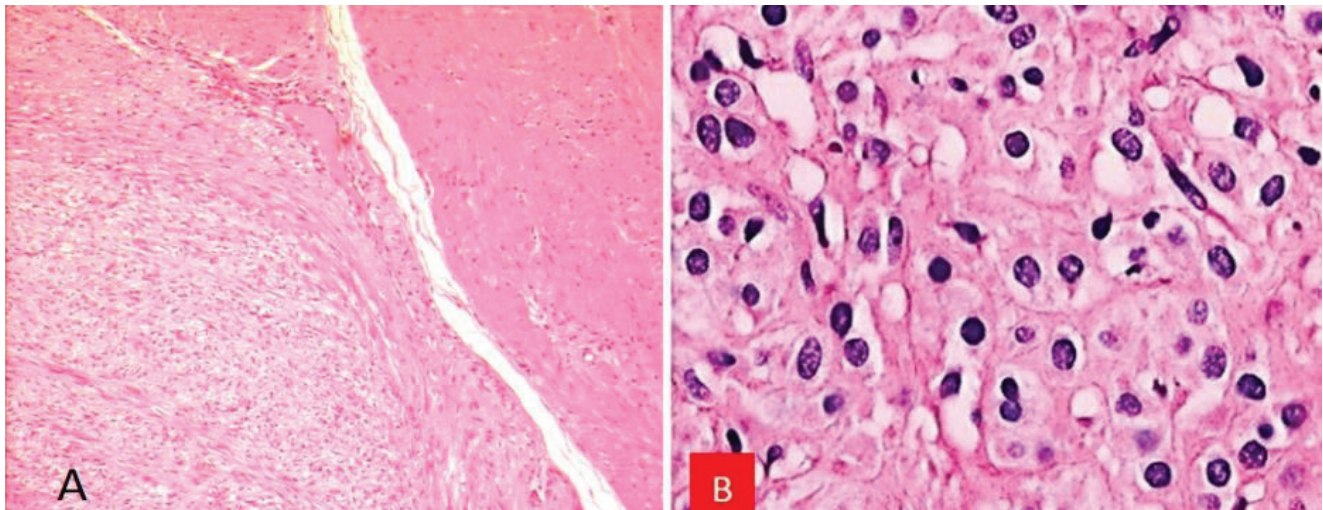


Figure 2 A. (Hematoxylin—Eosin / X 10): This is a neoplastic growth pattern characterized by interlacing bundles of spindle cells in a fascicular or storiform arrangement.

Figure 2 B. (Hematoxylin—Eosin / X 200): The mass comprised epithelioid cells embedded in a thin reticular stroma with focal mitotic activity.

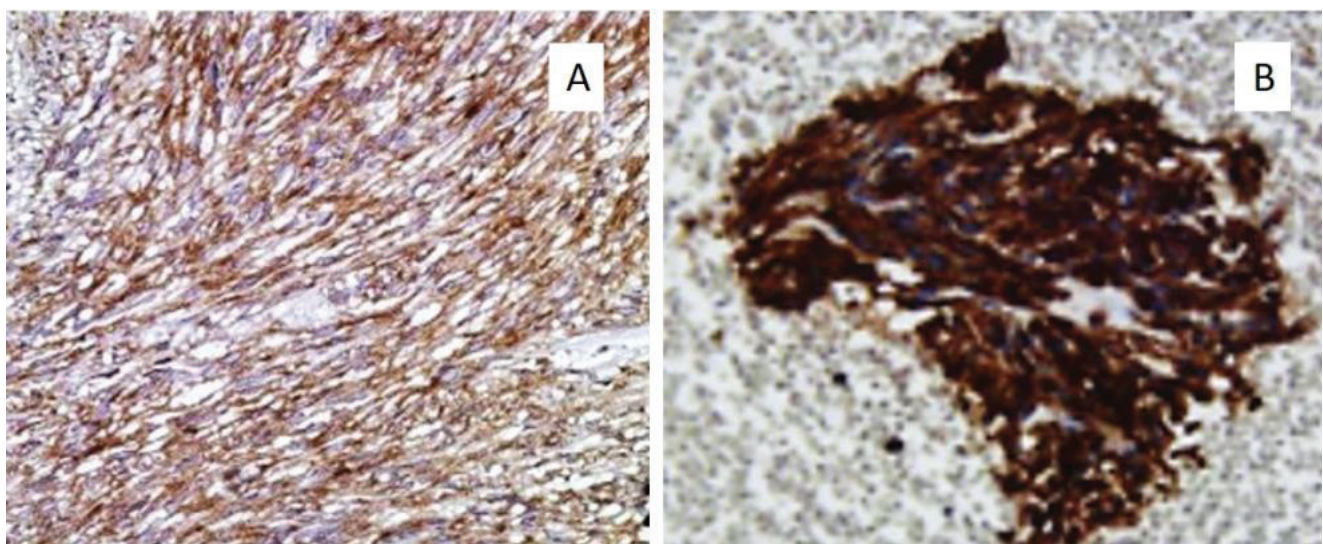


Figure 3 A. Immunohistochemical analysis revealed an intense, granular surface and cytoplasmic c-Kit positivity.(X 10)

Figure 3 B. Cytology: intensive immunoreactivity for vimentin of neoplastic cells. (X 200)

No whorled extracellular collagen fibers designated as skeinoid fibers were seen.

A thick fibrous capsule separated the neoplastic cells from the pancreatic parenchyma. In a

limited area, the neoplasia infiltrated the gastric wall. The mitotic index was > 15 mitoses in the ten hpf, indicating a high risk of aggressive behavior. Mild nuclear atypia and focal cell cytoplasmic vacuolizations were appreciated. (Fig. 2B). Areas of coagulative necrosis were present (Fig. 2A). The neoplastic cells were separated from the pancreatic parenchyma by a thick fibrous capsule. In a limited area, the neoplasia infiltrated the gastric wall.

Immunohistochemical analysis revealed an intense, granular surface and cytoplasmic c-Kit positivity (Fig.

3A). CD34 expression was also solid and diffuse. The cytologic examination of neoplastic cells showed intensive immunoreactivity for vimentin (Fig. 3B). A high percentage of proliferative neoplastic cells evidenced Ki-67 $> 20\%$ expression. In the immunohistochemical examination for smooth muscle, actin was expressed only weakly and focally, but in neuroendocrine markers, cytokeratins, S-100, caldesmon, and desmin expression were absent.

The molecular characterization showed unusual genetic alterations (the internal repeat of codon 502 and 503 in exon 9 of the KIT gene and the KIT exon nine single nucleotide substitution c.1427G-T).

The morphology and the immunohistochemical features suggested a diagnosis of retroperitoneal GIST.

Discussion

Herein, we describe a gastrointestinal stromal tumor masquerading as a pancreatic cystic neoplasia. While the cystic feature is well documented, the interest of this case was the radiological and gross features that strongly suggest a pancreatic origin. Generally, the gross pathology features of GIST are solid or partially cystic [1, 2, 3, 4]. In our case, the gross pathology was of a large cystic mass. The rapid growth of the neoplasm could explain the central necrosis and the cystic feature.

The histological and immunohistochemical features show spindle and epithelioid cells and striking cytoplasmic and membrane CD117 positivity, respectively. [2, 5, 6, 8] Such data satisfy the two absolute requirements of the definition of GISTs. Positivity for CD34 was also concurrent with the diagnosis. [2, 7, 8]

GISTs have many different pathways of differentiation. [1, 2, 3, 9, 10] The focal smooth muscle actin expression and the absence of Schwannian/glia differentiation, demonstrated by the absence of the S-100 and GFA expression, indicated a differentiation toward smooth muscle cells. Furthermore, the large size and the high mitotic index suggested a high risk of malignant behavior. [1, 2, 3]

Differential diagnosis included first a primitive pancreatic cystic lesion, but a pancreatic pseudocyst which presents a fibrous hypocellular wall, pancreatic cystic or intraductal papillary-mucinous neoplasms that show an epithelial glandular component of the cyst lining and a solid pseudopapillary tumor formed by characteristic papillae of uniform oval cells were discarded. [11, 12]

Second, we excluded retroperitoneal mesenchymal hyperplasia or neoplasia: the intra-abdominal fibromatosis is characterized by a spatially homogeneous proliferation of wavy spindle cells without atypia, associated with collagen deposition (often the keloidal type) and a c-KIT positivity in 75 % of cases, but the pattern of growth is usually infiltrative and diffuse; peritoneal solitary fibrous tumor shares CD34 positivity with GIST, but lacks c-KIT expression. Finally, smooth muscle tumors, GI-schwannomas, and undifferentiated sarcomas share some histological features with GISTs, but all lack c-KIT expression. [13, 14, 17, 18]

As stated by the histotype, another intriguing aspect was the origin of the tumor: a retroperitoneal, pancreatic primitive or metastatic, and gastric subserosal origin were considered. Retroperitoneal or omental GISTs have been well documented and are called extra-gastrointestinal GISTs (EGISTs).

Exceptionally, EGISTs have also been reported in organs such as the gallbladder. Until now, there is only one report of a primitive pancreatic GIST, and Cajal cells have not yet been documented in the pancreas differently from the gallbladder, bladder, and ureter. [10, 11, 16, 19]

Thus, the existence of true pancreatic GIST should be confirmed over a more extensive series and prompt an investigation of the cell of origin. In a recent review about the

frequency of secondary pancreatic tumors, three metastatic GIST (7, 9 % in autopsy series) have been reported [19], but our patient was negative for other gastrointestinal neoplasia. Thus, we excluded a metastatic GIST. [15, 16]

Finally, we considered the origin of a pedunculated gastric subserosal GIST. The evidence of the relationship with the muscular wall supports this hypothesis. This specimen is referred to as having a limited diameter but firm adhesion with the posterior gastric wall, and the remainder of the gastrectomy specimen was uninvolved. On the contrary, it was separated from the pancreatic parenchyma by a fibrous capsule.

Conclusions

The reported case illustrates that the retroperitoneum might be the place of initial presentation of a cystic gastric GIST and that only an accurate pathological evaluation can establish the diagnosis and origin. Clinicians must know this condition might be mistaken for a primary pancreatic malignancy. Early surgical resection is the gold standard of treatment for primary GIST.

COI Statement:

This paper has not been submitted in parallel. It has not been presented fully or partially at a meeting or podium or congress. It has not been published nor submitted for consideration beforehand.

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