Gastrointestinal Stromal Tumors of the Stomach with Extensive Calcification: Report of Two Cases

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Abstract

Gastrointestinal stromal tumors (GISTs) can present with focal calcification. However, the presence of extensive calcification that constitutes the major portion of a GIST is extremely rare and can be associated with diagnostic pitfalls. We herein present the first two cases of rare gastric GIST with predominantly calcified components that mimicked pancreatic solid and pseudopapillary neoplasms with extensive calcification. In patients presenting with hyper-dense, heavily calcified masses in the abdominal cavity, the possibility of GIST should be considered in the differential diagnosis. A careful search for cellular areas and the judicious application of immunostaining will thus make it possible to make a correct diagnosis.

Key words: gastrointestinal stromal tumor, stomach, extensive calcification

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Introduction

Gastrointestinal stromal tumor (GIST) is an important type of tumor arising in the gastrointestinal tract. GISTs originate from the interstitial cells of Cajal, which are pacemaker cells that regulate the autonomic motor activity in the gastrointestinal tract. The majority of GISTs arise in the stomach, followed by the small intestine, colon, esophagus, omentum and mesentery (1, 2). Focal calcifications in large GISTs are not unusual, as occasionally occurs in other tumors; most are circumscribed, mottled or patchy (1-3). However, extensive calcification of the majority of a GIST is extremely rare. Although two cases of extensively calcified GISTs of the colorectum have been reported in the literature (4, 5), to the best of our knowledge, no such cases have so far been reported in the stomach. In this report, we document the first two cases of gastric GIST with predominantly calcified components, and highlight the potential diagnostic pitfalls that may arise in association with such tumors.

Case Reports

Case 1

A 53-year-old man presented to the emergency department with acute onset of epigastric pain. Laboratory data showed no remarkable findings. A contrast-enhanced computed tomography (CECT) scan of the abdomen showed a hyper-dense, irregularly calcified mass, which was located between the liver, pancreas and stomach. The mass had areas of low attenuation suggesting necrosis (Fig. 1A) and was suspected to be an exophytic solid pseudopapillary neoplasm arising in the pancreatic body. During laparoscopic exploration, the mass was seen to arise in the lesser curvature of the stomach. The mass was resected completely via laparoscopy.

Grossly, the mass was a hard, relatively well-circumscribed and extensively calcified tumor with irregular nodularity that measured 8.0×7.5×5.0 cm. The cut surface of the tumor had yellow to white areas of calcification alternating with pink to gray areas of necrosis, with variable-sized, irregularly-shaped cystic spaces (Fig. 1B). Conventional tissue processing was carried out following treatment in decal-

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Figure 1. Imaging results and gross findings. Case 1. (A) A preoperative CECT scan showed a densely calcified abdominal mass (arrow), which was located between the left lobe of the liver, pancreas and stomach. (B) The resected mass was a relatively well-circumscribed gastric tumor measuring 8.0×7.5×5.0 cm. The cut surface of the tumor had areas of calcification alternating with areas of necrosis with variable-sized, irregular-shaped cystic spaces. Case 2. (C) A preoperative CECT scan showed a mass with an abundant calcified component, which was located near the pancreatic tail (arrow). (D) Grossly, the mass measured 6.2×5.5×4.2 cm and was a hard, well-circumscribed tumor showing irregular nodularity with a solid, yellow-to-white cut surface with extensive calcification.

cifying fluid. Histologically, the tumor tissue was predominantly composed of large areas of dystrophic calcification and coagulation necrosis (Fig. 2A). A closer examination revealed small intervening areas featuring a poorly-defined but discernable spindle cell component (Fig. 2B). The tumor cells were arranged in interlacing bundles and fascicles as well as in sheets and nests. No mitotic figures or nuclear pleomorphism were detected.

Immunohistochemical staining showed strong immunoreactivity of the lesional cells for CD117 (1:1,000, polyclonal, Dakocytomation, Glostrup, Denmark; Fig. 2C) and CD34 (1:1,500, clone QBEnd/10, Labvision, Fremont, CA, USA; Fig. 2D). There was no immunostaining for actin (1:4,000, clone 1A4, Dakocytomation, Glostrup, Denmark), S100 (1:2,000, polyclonal, Dakocytomation, Glostrup, Denmark) or desmin (1:1,000, D33, Dakocytomation, Glostrup, Denmark). A diagnosis of GIST with extensive calcification was made, and despite the absence of mitotic figures, the tumor was classified as being of low risk due to its large size (6).

Case 2

A 69-year-old woman underwent surgery due to severe epigastric pain. She had been suffering from intermittent

epigastric pain which had begun more than five years prior to admission. Her abdominal pain had worsened two months before admission. On physical examination, the patient's abdomen was slightly distended. There was no reflex rigidity, guarding or rebound tenderness. There were no specific abnormalities noted in the laboratory results. An abdominal CECT scan revealed a mass with abundant calcification near the pancreatic tail (Fig. 1C). The mass was suspected to be a pedunculated solid pseudopapillary neoplasm arising in the pancreatic tail. During laparoscopic exploration, the mass was easily removed from the pancreatic parenchyma but was connected to the posterior wall of the gastric body. Consequently, a complete tumor resection with a gastric wedge resection was performed via laparoscopy.

Grossly, the resected tumor measured 6.2×5.5×4.2 cm and was hard, well-circumscribed, and had irregular nodularity. The tumor also had a solid, gray to white cut surface with extensive calcification (Fig. 1D). Conventional tissue processing was carried out following treatment in decalcifying fluid. Histologically, the tumor exhibited extensive dystrophic calcification and had multiple areas of coagulation necrosis (Fig. 2E). Small areas of viable tumor tissue alternating with large necrotic parts revealed spindle cells ar-

Figure 2. The results of the histopathological analysis and the immunohistochemical findings. Case 1. (A) The tumor tissue was dominated by large areas of dystrophic calcification and coagulation necrosis. (B) At higher magnification, small intervening areas revealed a poorly-defined but discernable spindle cell component. Immunohistochemically, the tumor cells were strongly positive for (C) CD117 and (D) CD34. Case 2. (E) The tumor formed large dystrophic calcifications and exhibited areas of coagulation necrosis. (F) Small areas of viable tumor tissue alternating with large necrotic parts revealed spindle cells arranged in interlacing bundles. Immunostaining of the tumor tissue demonstrated strong reactivity for (G) CD117 and (H) CD34 (A, B, E and F, Hematoxylin and Eosin staining; C, D, G and H, polymer method). Original magnification, A and E, $\times 100$; B to D and F to H, $\times 400$.

ranged in interlacing bundles and fascicles (Fig. 2F). Two mitotic figures per 50 high-power fields were detected. No atypical mitosis or nuclear pleomorphism was identified.

Immunohistochemical staining of the tumor demonstrated diffusely strong immunoreactivity for CD117 (Fig. 2G) and CD34 (Fig. 2H) but negative reactivity for actin, S100 and desmin. The tumor was diagnosed to be a GIST with extensive calcification. It was classified as being of low risk because of its large size, despite the paucity of mitotic figures (6).

Discussion

Rana et al. reported an asymptomatic GIST of the sigmoid colon with extensive calcification that mimicked an inspissated intramural barium (5). On CECT, the round, hyper-dense focus extending inferiorly from the rectosigmoid colon was thought to most likely represent residual barium from a prior examination. However, after three months, repeat CT showed no interval changes. Endoscopic ultrasonography (EUS) revealed a large hypoechoic mass, which had large, shadowing calcifications and arose in the muscularis propria of the sigmoid colonic wall. After surgical resection, a histopathological examination confirmed it to be an extensively calcified GIST. Ong et al. also reported a case of heavily calcified GIST of the lower rectum presenting as a colonic submucosal nodule (4). The authors re-

ported that the gross and even initial histopathological impression of a heavily calcified colonic nodule suggested an impacted fecalith. In these patients, the diagnosis of GIST was not straightforward for two main reasons. First, GISTs arise in the colorectum in only about 5% of cases, thus making the sigmoid colon and lower rectum an unusual location. Second, the appearance of a large area of homogeneous dense calcification throughout the tumor is also unusual in GISTs. As a result, their appearances were initially identified as inspissated barium and an impacted fecalith, respectively.

In the cases described in our report, although the stomach is the most common site for GISTs, the correct diagnosis was not suggested preoperatively. The masses in the lesser sac appeared to be abutted to the stomach, liver and pancreas, thus making it difficult to determine the origins of the lesions. Furthermore, the presence of large, hyper-dense calcifications throughout the tumor made it difficult for even experienced radiologists to consider the possibility of gastric GIST. The diagnosis considered to be most likely by the radiologists was a pancreatic solid pseudopapillary neoplasm with massive calcification in both cases. However, this diagnosis was unlikely given the age of the patients.

Interestingly, a few cases of extensively calcified pancreatic solid pseudopapillary neoplasm have been recently reported in the literature (7, 8); the imaging findings presented in these reports were very similar in appearance to those

shown in our cases. Due to the similarity of these radiological findings, we suggest that GIST should therefore be included in the differential diagnosis of calcified intra-abdominal masses located near the stomach or pancreas. In addition, it is essential for radiologists and clinicians to be aware of the possibility of extensive calcification in a GIST and the characteristic imaging findings of such GISTs in order to establish the correct diagnosis.

Recent studies have shown that EUS combined with fine-needle aspiration (FNA) appears to be of great value in the evaluation of subepithelial tumors. EUS-guided FNA (EUS-FNA) is accurate and safe for the diagnosis of intramural lesions of the GI tract, especially GISTs (9, 10). Gu et al. (11) evaluated the efficacy and accuracy of EUS-FNA in the diagnosis of GIST and described its cytomorphological features. They demonstrated that when smears and cell blocks are combined with immunohistochemical staining, EUS-FNA is an accurate and efficient way of diagnosing GIST. Moreover, EUS-FNA provides abundant information on the capacity of the tumor for cellular progression. Ando et al. (9) reported that, for the diagnosis of malignant GIST, the accuracy, sensitivity and specificity of EUS-FNA with the addition of Ki-67 immunostaining were 100%, whereas the accuracy of EUS imaging alone was 78%. Okubo et al. (12) also suggested that when used with Ki-67 immunostaining, EUS-FNA indicates the prognosis of GIST and influences decisions regarding therapeutic strategies. In our cases, endoscopy and EUS-FNA were not performed because urgent surgery was mandatory due to the acute presentation.

Dystrophic calcification, in which calcium salts are deposited in degenerating tissues and cells, is seen at the sites of tissue damage, especially at sites of scarring, hemorrhage and necrosis. Previous episodes of bleeding or tumor necrosis with cystic degeneration also cause dystrophic calcification. In our cases, the GISTs underwent degenerative changes with necrosis, thus resulting in cystic degeneration and dystrophic calcification. It was extremely difficult to identify viable tumor cells in these tissues, because most of the masses were dominated by areas of necrosis and calcification. Even though the entire specimens were submitted for a histopathological examination, viable tumor tissues were found in less than 5% of the total tumor volume in both cases. When a heavily calcified specimen is decalcified as part of the tissue processing, the intervening small but informative areas of spindle cells may appear very pale with routine staining. In this situation, the true nature of the spindle cells may escape detection or may be interpreted as fibrous tissue. Therefore, when calcified nodules are encountered in the gastrointestinal tract, the possibility of a GIST should be considered. A careful search for cellular areas and the judicious application of relevant immunostaining examinations

will thus make it possible for the correct diagnosis to be made.

In summary, we herein presented the first two cases of gastric GIST with predominantly calcified components. Although there have been two previous cases of colorectal GIST with extensive calcification, to the best of our knowledge, no such cases have so far been reported in the stomach. In patients presenting with a hyper-dense, heavily calcified mass around the stomach, the possibility of a GIST should therefore be considered in the differential diagnosis.

The authors state that they have no Conflict of Interest (COI).

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