A large gastric splenosis mimicking gastrointestinal stromal tumor: A case report and literature review

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Abstract. Splenosis pertains to the phenomenon wherein a segment of the spleen undergoes detachment and becomes embedded in other anatomical regions subsequent to traumatic rupture or therapeutic resection, and then progressively establishing blood circulation to foster the regeneration of splenic tissue. Existing literature posits that splenosis predominantly manifests within the confines of the abdominal and pelvic cavities. The objective of the current study was to present an uncommon case involving the occurrence of splenosis within the gastric myometrium, thereby contributing to the current knowledge regarding splenosis. A 16-year-old female sought medical assistance owing to recurrent abdominal pain persisting for a duration of six months, and had a history of splenectomy two years prior. Gastroscopy, endoscopic ultrasound and computed tomography (CT) examination collectively identified a lesion in the submucosal prominence of the fundus of the stomach. Initial considerations based on imaging examinations leaned towards a gastrointestinal stromal tumor. Consequently, an endoscopic resection was undertaken. Remarkably, the pathological findings and histochemistry concurred with the alterations associated with ectopic spleen implantation, leading to a stable postoperative course. In conclusion, splenosis denotes the implantation of a segment of the spleen into extraneous anatomical sites, attributable to traumatic rupture or therapeutic resection. The preoperative diagnosis of splenosis can pose a challenge, potentially culminating in unnecessary radical clinical interventions. Therefore, the acquisition of a comprehensive medical history, with a particular focus on surgical and trauma events, emerges as pivotal for an accurate diagnosis. In light of novel diagnostic modalities, the non-invasive technology of nuclear medicine can efficaciously visualize ectopic splenic tissue, thereby averting superfluous surgical procedures. It is both feasible and imperative to implement individualized treatment strategies for patients afflicted with splenosis.

Introduction

Various forms of ectopic splenic tissue exist, encompassing splenosis, accessory spleen, wandering spleen and polysplenism (1-3). Splenosis is the primary focus of this paper. Splenosis denotes the detachment and embedding of a segment of the spleen in various anatomical sites subsequent to traumatic rupture or therapeutic resection (2). The disseminated spleen tissue can be propagated through various means, such as direct dissemination or via splenic venous blood (3-5). This process leads to the gradual establishment of blood circulation and subsequent regeneration of splenic tissue. Statistically, the likelihood of splenic implantation resulting from splenic trauma or rupture post-splenectomy is ~67%, with 16-17% of patients undergoing elective splenectomy for hematological disease (6). This implantation, when observed elsewhere months or years later, is often misinterpreted as a tumor (7). The present study reported a rare case of splenosis located on the gastric wall in a female patient. Initially, gastrointestinal stromal tumor (GIST) was considered based on imaging findings. The patient exhibited clinical symptoms and presented with a sizable tumor, prompting the decision to perform a comprehensive endoscopic resection for tumor removal. Unexpectedly, the histopathological diagnosis post-resection revealed splenosis. In terms of splenosis treatment, surgical resection remains the primary therapeutic option for symptomatic or large lesions. However, an asymptomatic splenosis should not receive any treatment, including surgical intervention (8-10). Asymptomatic splenosis misdiagnosed as tumors can lead to unnecessary surgery, and real diseases may be overlooked due to misdiagnosis (11). Recent studies propose that spleen imaging using Tc-99m sulphur colloid scanning and Tc-99m tagged heat-damaged autologous red blood cells (99mTc-DRBC) serves as the ‘gold standard’ for diagnosing ectopic splenic tissue (12,13). The objective of the present study was to augment the diagnostic accuracy of splenosis.
within the context of the novel diagnostic modality. Clinicians should aim to individualize treatment approaches for patients afflicted with splenosis, thereby averting unnecessary clinical interventions.

Case report

A 16-year-old female patient presented at the Zunyi Medical University Hospital (Zunyi, China) with persistent abdominal pain spanning six months in November 2019. The patient’s medical history included thalassemia, and the patient had undergone laparoscopic splenectomy two years prior at Kunming Children's Hospital (Kunming, China) due to hypersplenism. The postoperative recovery was uneventful, evidenced by multiple scattered 1 cm-sized old surgical scars on the abdominal wall during physical examination. Upon admission, biochemical analysis revealed abnormal values in the following parameters: Decreased hemoglobin (74 g/dl; normal: 114-154 g/l), elevated white blood cells (12.51x10⁹/l; normal: 3.5-9.5x10⁹/l), increased total bilirubin (34.2 µmol/l; normal: 5.1-19.8 µmol/l), slightly elevated direct bilirubin (8.3 µmol/l; normal: 0-6.84 µmol/l) and slightly increased indirect bilirubin (25.9 µmol/l; normal: 0.0-17.0 µmol/l). Other laboratory indicators, including renal routine and serum tumor markers, fell within the normal reference range. Endoscopic ultrasound (EUS) examination for upper abdominal discomfort revealed a well-defined microhypoechoic mass at the bulge of the gastric fundus, measuring ~5.9x5.1 cm and originating from the fourth layer with uniform echo (Fig. 1). As indicated in Fig. 2, abdominal computed tomography (CT) confirmed a round-like mass shadow with a smooth edge in the stomach cavity, measuring ~5.7x5.1 cm, and located close to the back wall of the fundus and stomach, displaying an unclear boundary with the gastric wall. The contrast-enhanced scan depicted slightly uniform enhancement in the arterial phase, further enhancement in the venous phase and attenuation in the delayed phase. Initial considerations based on these imaging findings leaned towards a GIST. Preoperative magnetic resonance imaging (MRI) and positron emission tomography-CT scans were recommended to the patient and the patient’s family in order to further determine the best treatment plan; however, they refused the examination for financial reasons.

Most patients presented at the hospital with upper abdominal discomfort and pain, while 33% of patients were asymptomatic and their splenosis was discovered incidentally during physical examinations. With the exception of one patient without a history of splenectomy, the remaining patients had undergone splenectomy due to spleen rupture resulting from trauma, blood diseases or other conditions. The predominant site of gastrosplenic implantation was the fundus of the stomach, followed by the body of the stomach, antrum, gastroesophageal junction and pylorus. Tumor foci were predominantly solid, round or oval, with a minority exhibiting irregular or lobulated shapes, and diameters ranging from 0.4 to 6 cm. During gastroscopy, the lesions typically manifested as smooth submucosal protuberant lesions, with only one case displaying multi-strip protuberant lesions. These terms were employed individually with the Boolean operator ‘AND’ or ‘OR’. A systematic search yielded an initial 251 articles. Following the exclusion of duplicates and irrelevant articles, 21 articles were ultimately considered for inclusion in this study. A detailed flow chart of the literature screening process is presented in Fig. S1. The first author, publication year and country of each case, along with the patient's age, gender, main clinical symptoms, medical history, lesion size and findings from gastroscopic, ultrasonic and CT imaging, were meticulously recorded, as depicted in Table I (4,6,14-31). Through a systematic search, a total of 22 cases of gastric splenosis and intragastric splenosis were definitively confirmed from the published literature. Including the patient of the present study, the literature review comprised 23 patients for statistical analysis, including 16 males and 8 females, with the median age of 46.8 years. The majority of cases were reported in China (50%), followed by the US (12.5%) and Italy (12.5%). The detailed characteristics of gender, medical history, lesion size, location and CT findings of the 23 patients are illustrated in Fig. 4.

Most patients presented at the hospital with upper abdominal discomfort and pain, while 33% of patients were asymptomatic and their splenosis was discovered incidentally during physical examinations. With the exception of one patient without a history of splenectomy, the remaining patients had undergone splenectomy due to spleen rupture resulting from trauma, blood diseases or other conditions. The predominant site of gastrosplenic implantation was the fundus of the stomach, followed by the body of the stomach, antrum, gastroesophageal junction and pylorus. Tumor foci were predominantly solid, round or oval, with a minority exhibiting irregular or lobulated shapes, and diameters ranging from 0.4 to 6 cm. During gastroscopy, the lesions typically manifested as smooth submucosal protuberant lesions, with only one case displaying multi-strip protuberant lesions resembling varicose veins (14). EUS revealed that the lesions generally exhibited low echo, high echo or medium-low echo, maintaining a uniform echo pattern. Calcifications were observed in certain cases, predominantly in round, oval or...
Splenosis manifests as the autologous implantation of splenic tissue following splenic trauma or resection procedures (5). The disseminated spleen tissue can be propagated through various means, such as direct dissemination or via splenic venous blood. Direct dissemination commonly results in implantation in the splenic hilum, pancreas, omentum, pelvic organs and the serosal layer of the intestinal wall. Transsplenic vein blood dissemination may lead to implantation in the liver, pancreas, stomach, small intestine and, in rare instances, breast and brain tissue (32-34). The splenic pulp primarily disseminates in the abdominal cavity or other organs through the circulation. The vascular network and lymphoid tissue of the regenerated spleen tissue undergo adjustments, with undifferentiated reticular cells and fibrous tissue-forming scaffolds. Subsequent differentiation results in the formation of endothelial sinuses, capillaries and lymphocytes, ultimately constituting splenic tissue (35,36). The blood supply is maintained by several small vessels in the surrounding tissues rather than the splenic arteries (37). Debris can be implanted in the body cavity or any other part, gradually establishing blood circulation supply for the development and regeneration of spleen tissue. In the 1980s, Chatterjee et al (38) transplanted spleen tissue slices of rats and rabbits into subcutaneous sites and muscle, achieving a success rate of >90% in the operation, indicating the strong regenerative capacity of spleen tissue. Pathological features typically include a complete fibrous envelope, absence of splenic hilum, muscle and elastic fiber
components, predominantly red pulp, imperfect white pulp, abnormal vascular structure and the absence of the ‘portal’ vascular structure of the splenic hilum, which contains hematin (36,39). The patient reported in the present study had a history of laparoscopic splenectomy. Given that laparoscopic splenectomy at times involves the removal of a sample after the spleen has ruptured in the abdominal cavity, this procedure may result in implantation in the stomach through direct or hematogenous dissemination. Pathological examination of the resected lesion revealed visible red and white pulp, with the structure of the white pulp being imperfect and the absence of a splenic hilum, consistent with the diagnosis of splenosis.

Regarding imaging examinations, the density and enhancement pattern of splenosis observed on CT and MRI were akin to those of a normal spleen. On a contrast-enhanced CT scan, the lesion exhibited uniform enhancement in the three stages: Prominent enhancement in the arterial stage, sustained enhancement in the portal vein stage and a slight decrease in the delayed stage. Splenosis can manifest in various organs, such as the lung, pancreas, liver, kidney and gastrointestinal tract, necessitating differentiation from the primary tumor organ (40,41). On contrast-enhanced CT scans, splenosis often lacks the speck enhancement characteristic of normal splenic tissue in the arterial stage. This enhancement pattern may be confused with the imaging features of GIST, leading to potential misdiagnosis (15). Furthermore, careful attention must be given to distinguishing splenosis from accessory spleen. The key distinction lies in the fact that splenosis is supplied by the implant organ without the splenic hilum, whereas accessory spleen receives its blood supply from the splenic vessel. Occasionally, splenosis is erroneously diagnosed as a malignant tumor (42). For instance, in a case reported by Ksiażynia (43) in 2011, a 54-year-old woman with a history of splenectomy exhibited multiple abdominal nodules in areas such as the ileum, greater omentum and uterus, raising suspicions of disseminated malignant tumors. However, histological examination revealed a typical spleen structure, leading to the diagnosis of abdominal splenosis. In the case reported in the present study, the CT plain scan displayed a uniformly, slightly enhanced round soft tissue density image in the arterial phase, continued enhancement in the venous phase and weakened enhancement in the delayed phase. Of note, the patient had undergone splenectomy, and the contrast with the enhancement pattern of a normal spleen was absent. The arterial phase imaging features of gastric splenosis often overlap with those of GISTs, posing challenges in their differentiation (6).

The presence of splenosis as a tumor may result in unnecessary surgical intervention, potentially leading to the oversight of the actual underlying condition due to misdiagnosis. This may significantly heighten patient anxiety and psychological stress (33), underscoring the crucial importance of accurately diagnosing splenosis. The rapid advancement in medical examination technology has contributed to an increased occurrence and detection of this disease (44). Spleen imaging using Tc-99m sulphur colloid scanning and Tc-99m-tagged heat-damaged autologous red blood cells (99mTc-DRBC) serve as the ‘gold standard’ for diagnosing ectopic splenic tissue (45). The fundamental principles underlying the noninvasive Tc-99m sulphur colloid scanning and 99mTc-DRBC in the diagnosis of splenosis are outlined as follows: The spleen has a role in phagocytosing foreign bodies in the blood and destroying senescent red blood cells. Following the introduction of the former radioactive colloid into the body, ~5-10% of colloidal particles are engulfed by mononuclear macrophages in the spleen, inducing spleen development. As for the latter, upon passing through the spleen, ~90% of radionuclide-labelled denatured red blood cells are intercepted and phagocytosed by macrophages in the medullary cord. These cells selectively remain in the spleen, thus revealing the location, size, morphology and function of the spleen. Consequently, ectopic splenic tissue can be more effectively displayed irrespective of its location, even detecting small splenic nodules that may be overlooked by CT. This imaging approach is highly specific and non-invasive (12,13). In addition, a recent study (40) has constructed a deeply comprehensive Cancer Serum Protein Atlas to improve the sensitivity and specificity of multican addendum.
<table>
<thead>
<tr>
<th>Author/s, year</th>
<th>Country</th>
<th>Sex</th>
<th>Age, years</th>
<th>Splenectomy</th>
<th>Presentation</th>
<th>Location</th>
<th>Size (cm)</th>
<th>Endoscopy</th>
<th>Ultrasound</th>
<th>CT</th>
<th>Follow-up</th>
<th>Refs.</th>
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<td>Fujita et al., 2020</td>
<td>Japan</td>
<td>M</td>
<td>47</td>
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<td>Well-marginated and enhanced rounded mass</td>
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<td>Wang et al., 2016</td>
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<td>Gastric fundus</td>
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<td>Duodenal bulb</td>
<td>6.1x3.6</td>
<td>-</td>
<td>-</td>
<td>Irregular soft tissue density and slight inhomogeneous enhancement</td>
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<td>Location</td>
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<td>Gastric body</td>
<td>2.2x1.5</td>
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<td>Hypoechoic</td>
<td>Sub-serosal ovoid mass</td>
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<td>Falk et al., 2009</td>
<td>Ireland</td>
<td>F</td>
<td>64</td>
<td>Y (pancreatic cystadenoma)</td>
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<td>Gastric cardia</td>
<td>4.3 in diameter</td>
<td>Smooth submucosal mass</td>
<td>Hypoechoic</td>
<td>-</td>
<td>-</td>
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<td>Submucosal mass</td>
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<td>67</td>
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<td>Gastric body</td>
<td>-</td>
<td>Smooth bulge</td>
<td>-</td>
<td>Well-marginated and enhanced ovoid mass</td>
<td>-</td>
<td>(31)</td>
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</table>

M, male; F, female; Y, yes; N, no.
detection and classification based on mass spectrometry. The plasma metabolic fingerprint of patients with gastric cancer was obtained by the nanoparticle-enhanced laser desorption/ionisation mass spectrometry technique and the diagnostic and prognostic model was established (41). Furthermore, the application of nanomaterials in assisted metabolic analysis and in vitro diagnosis was advanced (42). These new diagnostic methods help to improve the efficiency of cancer diagnosis and treatment and have a positive impact.

Concerning splenosis treatment, surgical resection remains the primary therapeutic option for symptomatic or large lesions, particularly in cases where symptoms such as intestinal obstruction, bleeding, abdominal pain or hemoptysis are evident. In such instances, surgical intervention is deemed necessary and should be promptly performed (37). However, it is well-documented that ectopic splenic tissue possesses certain compensatory and proliferative properties, exerting extensive immune functions in hematopoiesis and red blood cell clearance. This capability may reduce the incidence of fulminant infection (46). Consequently, asymptomatic splenosis should, in principle, not be treated, including surgical intervention (8–10). Furthermore, certain scholars argue that splenectomy serves as a therapeutic measure for patients with blood disorders and splenosis may result in the partial restoration of splenic function, potentially leading to disease recurrence. The question of whether surgical resection is necessary for patients with blood diseases remains controversial (47,48). In the case of a patient with thalassemia and hypersplenism who underwent laparoscopic splenectomy, the hemoglobin level was 90 g/l post-surgery. Two years later, upon hospitalization due to abdominal pain, the hemoglobin level was found to be 74 g/l. Following the excision of the gastric splenosis lesion, the hemoglobin level increased to 91 g/l two months after surgery. Therefore, it is thought that splenosis may contribute to the partial recovery of spleen function and potentially lead to disease recurrence.

In summary, splenic rupture resulting from splenic trauma frequently occurs during splenectomy, leading to the autologous implantation of fragmented splenic tissue. This implantation, when observed elsewhere months or years later, is often misinterpreted as a tumor. Hence, meticulous attention to the collection of medical history, particularly the details of splenic rupture and splenectomy, is imperative for the accurate diagnosis of ectopic spleen. When identification proves challenging, the application of Tc-99m tagged heat-damaged autologous red blood cells ($^{99m}$Tc-DRBC) and Tc-99m sulphur colloidal noninvasive nuclear medicine technology can enhance the visualization of ectopic spleen tissue, thereby improving the diagnostic accuracy for gastric splenosis diseases. For patients with confirmed splenosis, particularly those exhibiting symptoms and a history of blood disorders, individualized treatment is not only feasible but also necessary.

Figure 4. Bar chart indicating the sex, medical history, lesion size, location and CT imaging findings of the 24 adult patients analyzed.
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Availability of data and materials

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Authors’ contributions

XH and GH conceived and designed the study. XL acquired the data and performed the literature review. JC and PW analyzed and interpreted the data and critically revised the manuscript. BZ acquired the scanning images and managed the patient. XH and XL checked and confirmed the authenticity of all the raw data. All authors contributed to the article and have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from both parents of the patient to publish this case report.

Competing interests

The authors declare that they have no competing interests.

References


