# Case Report

# Coexisting of Gastric GIST and Leiomyoma

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*A 53-years-old man presented with RUQ pain for 2 years. The CT abdomen showed two homogeneous enhancing submucosal nodules at gastric body, 1.6 cm and 1.9 cm in size at lesser and greater curvatures of stomach. The upper GI endoscope revealed two submucosal nodules at lesser and greater curvatures of gastric body without any ulcer. He was undergone explor-laparotomy and wedge resection of both lesions were performed. Pathologic examination reported gastrointestinal stromal tumor (GIST) with coexisting gastric leiomyoma. To our best knowledge, this is the first case of coexisting gastric GIST and leiomyoma.*

***Keywords:*** *GIST, Leiomyoma, Synchronous gastric tumor, Coexisting gastric tumor*

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**Case Report**

A 53-years-old male presented with right sided abdominal pain without alarm symptoms for 2 years. He was treated as having right ureteric stone but the symptoms were not relieved. He was sent to perform the CT scan of whole abdomen for re-evaluation. The CT scan showed two homogeneous enhancing submucosal nodules at gastric body about 1.6 cm and 1.9 cm in size at the lesser and greater curvatures of stomach respectively. The differential diagnosis from imaging was either small GIST or other mesenchymal tumors such as leiomyoma or nerve sheath tumor (Fig. 1A, 1B). Upper GI endoscope revealed two submucosal nodules at lesser curvature and greater curvature of gastric body without any ulcer (Fig. 2A, 2B) and thought to be gastric GIST. He was undergone explorative laparotomy and wedge resections of both lesions were performed.

Pathological examination showed two pieces of circumscribed, rubbery white-tan submucosal masses. The mass from greater curvature was measuring 2x2x2 cm. The mass from lesser curvature was 3x2x1.5 cm. No mucosal involvement identified. Their cut surfaces showed homogenous white-tan appearance (Fig. 3A, 4A). The histology of the mass from greater curvature showed fascicles of uniform spindle cells arranged in palisading pattern. The tumor nuclei were oval to short spindle shape. Pale eosinophilic and indistinct cytoplasms were noted (Fig. 3B, 3C). The mitotic count was 19/50 HPFs. The histology of the other mass from lesser curvature

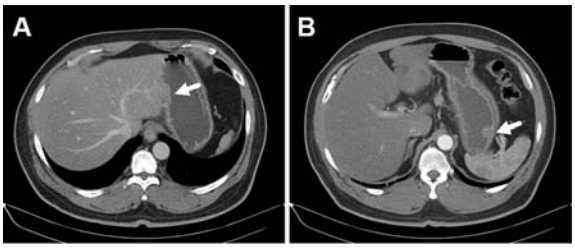


**Fig. 1** CT scan abdomen showed two homogeneous enhancing submucosal nodules at the lesser curvature (A) and the greater curvature (B).

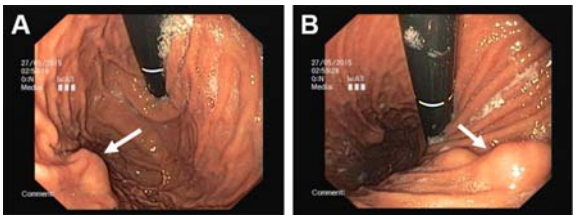


**Fig. 2** Upper GI endoscopy showed two submucosal masses at the greater curvature (A) and the lesser curvature (B).

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showed intersecting fascicles of bland spindle cells with abundant cytoplasm (Fig. 4B, 4C, 4D). The mitotic count was 0 to 1/50 HPF. There was no necrotic area identified in both tumors.

Immunohistochemistry for CD117 (c-Kit) and DOG-1 revealed strong and diffusely positive in cytoplasm of tumor from greater curvature (Fig. 3D, 3E), while showed weak positively for Cajal cells but negative staining for tumor cells from lesser curvature (Fig. 4E, 4F). Desmin, Caldesmon and smooth muscle actin (SMA) were strongly positive for tumor from lesser curvature (Fig. 4G, 4H, 4I), but SMA was negative for tumor from greater curvature (Fig. 3F). A diagnosis of gastrointestinal stromal tumor (GIST) coexisting with gastric leiomyoma was established. After recovery from operation, the patient was referred to the Oncology Department and was given adjuvant Imatinib 400 mg/day because of high risk of recurrence.

## Discussion

The most common mesenchymal tumors of GI tract is gastrointestinal stromal tumor (GIST) that occurs at stomach (50 to 60%), small intestine (30 to 40%), colon (10%), rectum (5 to 7%) and esophagus (<5%)[1,2]. GIST is originated from interstitial cells of Cajal (ICC) progenitors within the wall of the gastrointestinal tract.

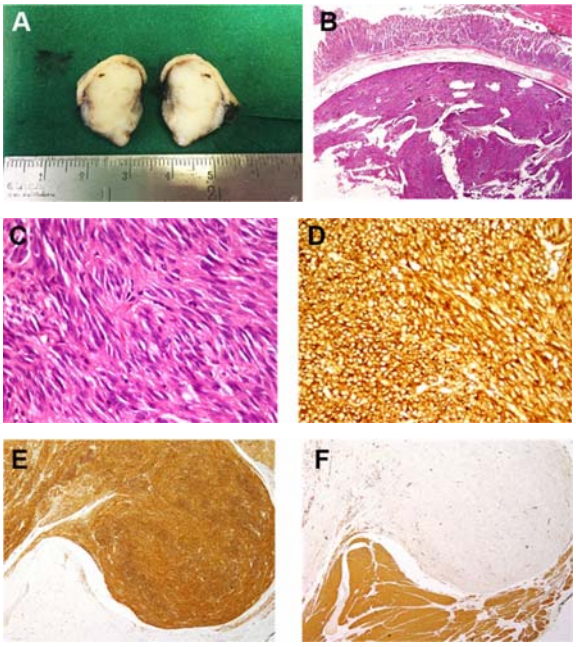


**Fig. 3** Gross and microscopic findings of the tumor from greater curvature. (A) Gross finding, (B-C) H&E stain, (D) CD-117, (E) DOG-1, (F) SMA.

Mutations of tyrosine kinase receptor (c-Kit, CD117) that make loss control of cellular growth is contributed tumor formation[3,4]. In the past before the development of imatinib, complete tumor excision is only the possible way to control disease and cure from GIST. Recurrences commonly occur and median survival rate is less than 20 months. However, the development of Imatinib (Tyrosine kinase inhibitor, TKI) in 1999 serves the new era of GIST treatment; the 5-years survival rate was more than 65% and median survival rate was between 50 to 65 months even metastasis[5,6]. The prognosis also depends on the locations of tumor; Stomach and esophageal GIST are better in overall survival rate (OS) compared to small bowel and colon GIST[6].

Incidence of GIST is between 3.2 to 7 per million. GIST often found in Asia-Pacific region. Hong Kong and Korea had high incidence of GIST around 15 to 20 per million[7]. The median age at the time of diagnosis is 63 years and less than 1% present before the age of 20[5]. GIST in young people is mostly associated with familial syndromes such as neurofibromatosis type 1, familial GIST syndrome or

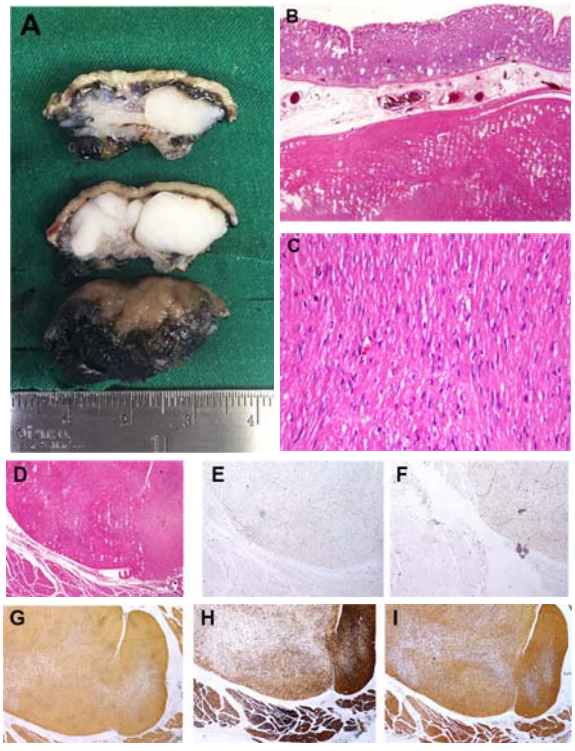


**Fig. 4** Gross and microscopic findings of the tumor from lesser curvature. (A) Gross finding, (B-D) H&E stain, (E) CD-117, (F) DOG-1, (G) Desmin, (H) Caidesmon, (I) SMA.

the Carney triad (gastric GIST, extra-adrenal paraganglioma and pulmonary chondroma). At the time of diagnosis, advance stage was detected around 20 to 30% of patients[5,6].

Clinical presentation of GIST is variable and non-specific. More than 25% of cases were incidentally found on imaging studies[8]. The tumor size was the major factor that determined clinical symptoms. In previous reports, sizes at the time of presentation were always more than 5 cm[6]. The most common clinical presentation was bleeding, abdominal pain or dyspepsia. In severe but rare cases, GIST might rupture and caused hemoperitoneum and generalized peritonitis. GIST would metastasized to liver and/or lung hematogenously. Lymph nodes metastasis could occur but not frequent and should be considered as direct tumor implantation rather than lymphatic spreading.

Diagnosis of GIST is usually obtained by computed tomography (CT). However magnetic resonance imaging (MRI) may also be used. The CT findings of GIST are typically seen as an exophytic submucosal mass confined in gastrointestinal wall. If tumor size is more than 5 cm, central necrosis can be recognized. Other imaging technique such as endoscopic ultrasonography (EUS) is an alternative modality. With upper GI endoscope, GIST can be seen as submucosal protuberance with central ulcer. Biopsy is not necessary before surgical resection, except for metastasized or unresectable cases that need tissue diagnosis for decision of other treatment modality.

Pathologic diagnoses of GISTs are based on histological appearances of the tumor and immunohistochemistry (IHC) staining. The histology subtype of GIST are divided into 1) Spindle cell GISTs (70%) which consists of ovoid to spindle nuclei and eosinophilic fibrillary cytoplasm, 2) Epithelioid GISTs (20%) which consists of sheets or nests of round cells with eosinophilic clear cytoplasm and 3) the mixed type of spindle and epithelioid cells (10%). They are generally express CD117, CD34 and DOG-1 immunohisto-chemically[15]. According to the consensus of risk classification of localized GISTs by the National Institutes of Health (NIH) in 2002[16] and The Armed Forces Institute of Pathology (AFIP)[17], the malignant potential of gastric GIST is based on tumor size and mitosis. In a very low risk group, tumor size is smaller than 2 cm and mitotic count is less than 5 per 50 high power field (HPFs). In a low risk group, tumor size is between 2 to 5 cm. and mitotic count is less than 5/50 HPFs. In an intermediate group, tumor size is between 5.1 to 10 cm and mitotic count is less than 5/50 HPFs. In a high risk group, tumor size is bigger than 10 cm and mitotic count is over 10/50 HPFs. Differential diagnoses of spindle cell GISTs includes other stromal tumors such as leiomyoma, leiomyosarcoma, schwannoma and fibromatosis[18]. For epithelioid GISTs, carcinoma and melanoma should be considered in differential diagnosis.

Gastrointestinal leiomyomas are tumors that originated from smooth muscle cells. By morphology alone, it is difficult to differentiate leiomyoma from spindle cell GISTs because both shared spindle shaped cells. In current practice, immunohistochemistry is a useful tool for providing final diagnosis. Leiomyomas are positive expression for SMA, Desmin, Caldesmon and may some positive expression for CD117 and DOG-1 in interstitial cell of Cajal[19,20]. In contrast, most of GISTs are positive expression for CD117 (94 to 98%), CD34 (60 to 80%) and DOG1 (85 to 95% in c-Kit positive GISTs and 30 to 36% in c-Kit negative GISTs). GISTs are also positive expression for SMA (30 to 40%), S100 (5%) and rarely positive expression for Desmin (2%)[21].

Our case showed two separated masses from greater and lesser curvatures, differences in histological findings and immunohistochemistry expressions (+CD117, +DOG1, -SMA) and (-CD117, -DOG1, +SMA), which are supportive evidences for diagnosis of Gastrointestinal GIST coexisting with gastric leiomyoma.

Synchronous GIST with other tumor is rarely seen. The incidence of synchronous GIST with other primary tumor is still unsettled. The etiology is also still unclear. Recently, there has been only few published studies regarding this situation. From the Polish GIST Clinical Registry, the cases of coexistence GIST with second neoplasm accounted for approximately 10%[9,10], most cases were metachronous and most of them revealed that other tumors had presented before GIST. The most common synchronous tumors with GIST are GI carcinomas and rarely lymphoma or carcinoid[11,12]. Stomach adenocarcinoma is the most common synchronous GI carcinoma[2,12-14]. This case is synchronous GIST with leiomyoma, that has not been reported in the literature.

The pathogenesis of synchronous GIST with other tumors is still unclear but it may involve common carcinogenic agent such as nitroguanidine and acetylsalicylic acid or similar in genetic defects[2,4,12-14]. We did not find any correlation of mutation between these tumors regarding PDGFRA genes by using the KIT. However, our study was performed under the

constantly budget and resource. The molecular study for this entity awaits further investigations.

**Conclusion**

The synchronous tumors with GIST may be malignancy or benign lesions such as leiomyoma or well differentiated malignant neuroendocrine tumor. Physicians should be aware of the possibility of synchronous GIST with other tumors so that the appropriate preoperative plan for surgery and adjuvant therapy can be achieved.

**What is already known on this topic?**

Synchronous GIST with other tumor is rarely seen. The incidence of synchronous GIST with other primary tumor is still unclear. The etiology is still unclear too. Recently, only few published studies deal with this situation. From the Polish GIST Clinical Registry had a coexistence GIST with second neoplasm approximately 10%, there were usually metachronous and most occurred before presentation of GIST. The Most common synchronous tumors with GIST are GI carcinomas and rarely lymphoma or carcinoid. Stomach adenocarcinoma is the most common synchronous GI carcinoma.

**What this study adds?**

This case is synchronous GIST with leiomyoma, that not report in previous study.

**Potential conflicts of interest**

None.

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## *กรณีศึกษาเนื้องอกกระเพาะอาหารชนิด GIST พบร่วมกับชนิด Leiomyoma*

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*ผู้ป่วยชายอายุ 53 ปี มาโรงพยาบาลด้วยอาการปวดท้องขวาบนมา 2 ปี การตรวจภาพรังสีช่องท้อง พบก้อนที่กระเพาะอาหาร 2 ก้อนพร้อมกัน ขนาดก้อน 1.6 เซนติเมตรและ 1.9 เซนติเมตรตามลำดับ การส่องกล้องทางเดินอาหารส่วนบนพบลักษณะก้อนอยู่ใต้ชั้นพื้นผิวหน้ากระเพาะอาหารทั้ง 2 ก้อน ผู้ป่วยได้รับการวินิจฉัยเป็นเนื้องอกชนิด GIST และได้รับการผ่าตัดก้อนออกทั้งสองก้อน ผลการตรวจทางพยาธิวิทยา พบว่าก้อนหนึ่งเป็นเนื้องอกชนิด GIST จริง ส่วนอีกก้อนหนึ่งเป็นเนื้องอกชนิด leiomyoma ซึ่งการตรวจพบลักษณะ ดังกล่าวไม่เคยมีรายงานมาก่อน กรณีศึกษานี้จึงเป็นกรณีศึกษาแรกของการตรวจพบเนื้องอกสองชนิดนี้พร้อมกัน*