The annual incidence of gastrointestinal stromal tumor (GIST) is 13.74 per million population in Taiwan. About 10-30% of GISTs have malignant behaviors including invasion and metastases. Although one case of primary esophageal stromal tumor with direct invasion into the lung parenchyma has been reported, rarely has a gastric stromal tumor been documented to extend into mediastinum and thoracic cavity. We report an extremely rare case of primary gastric stromal tumor with extension into mediastinum and thoracic cavity and suspicious invasion of lung, presenting predominantly with respiratory symptoms.

GISTs are mesenchymal tumors of the gastrointestinal tract. In the present classification, they account for approximately 80% of GI mesenchymal tumors [1]. GISTs can occur anywhere in the gastrointestinal tract. About 50-70% of GISTs occur in the stomach, 33% in the small bowel, 5-15% in the rectocolon, and only 1-5% in the esophagus [2]. Originally, GISTs were thought to be either muscle or nerve tumors. Recent research points to GISTs starting in cells found in the walls of the GI tract, called interstitial cells of Cajal [3]. They are typically defined as tumors whose behavior is driven by mutations in the kit gene or PDGFRA gene, and may or may not stain positively for Kit protein [4, 5].

About 10-30% of GISTs have malignant behavior [6]. The tumor can directly invade adjacent structures in the abdomen. The most common sites of spread are the liver and the peritoneum. The lung is usually not a primary site of GIST metastasis. Although primary esophageal stromal tumor with direct invasion into the lung parenchyma has been reported [7], rarely has a gastric stromal tumor been documented to extend into mediastinum and thoracic cavity. Herein, we report a case of primary gastric stromal tumor with extension into mediastinum...
and thoracic cavity and suspicious invasion of lung parenchyma.

**CASE REPORT**

A 26-year-old woman with a history of scalp neurofibroma post excision presented to a local medical doctor with complaints of cough with sputum for 2-3 weeks. Due to worsening symptoms with presence of dyspnea and mild chest pain, she visited the chest department of our hospital for help. There was no history of pulmonary disease. She was a non-smoker.

On examination, decreased breath sound with dull chest percussion was noted over the patient’s left chest. The rest of the physical examination was unremarkable. No prominent palpable abdominal mass was noted. Laboratory investigations revealed mild anemia (Hb: 11g/dL) and markedly raised D-dimer level (3682 ng/mL) and platelet count (478,000/μL). Total leucocyte count (10,300/μL) was elevated, with neutrophilic predominance (84%).

Chest radiograph (posteroanterior view) showed a huge soft tissue mass in the left perihilar region with mediastinal deviation to the right and left side pleural effusion (Fig. 1). Under the suspicion of lung cancer, the patient underwent a chest CT scan. The CT study revealed a huge exophytic gastric submucosal tumor with internal necrosis and extension into the lower mediastinum and the left lower thoracic cavity. Furthermore, invasions of pericardium and lung parenchyma are also suspected. After contrast administration, the lesion showed heterogeneous enhancement. Massive pleural effusion with collapse of left lung was also noted (Fig. 2). Finally, ultrasonography-guided biopsy was performed for histopathologic diagnosis.

Histologically, H&E section showed hypercellularity of spindle cells arranging in fascicles with hyperchromatic nuclei, moderate nuclear

![Image](image1.png)

**Figure 1.** Chest radiograph (posteroanterior view) showed a huge soft tissue mass in the left perihilar region with mediastinal deviation to the right and massive left side pleural effusion.

![Image](image2.png)

**Figure 2.** Axial (a, b) and coronal (c) contrast-enhanced computed tomographic (CT) image depicts a huge exophytic gastric submucosal tumor with internal necrosis, extension into the lower mediastinum, and invasion of the left lower lung. Massive pleural effusion with collapse of left lung was also noted.
pleomorphism, and indistinct cellular borders (Fig. 3). Several foci of tumor necrosis and 7 mitotic counts per 50 high power fields are presented. The tumor cells are CD117 (-), CD34 (+), desmin (-) and S100 (focally weak positive). The immunophenotype is compatible with GIST.

**DISCUSSION**

GIST is a relatively uncommon type of gastrointestinal tumors. In general, they constitute only 1% of all malignant tumors of the GI tract and rank a distant third in prevalence behind adenocarcinomas and lymphomas. Based on data from a Swedish epidemiology study, approximately 4,500-6,000 cases of GIST are diagnosed every year in the United States. In Taiwan, the annual incidence of GIST is 13.74 per million population [5, 8]. There is a peak incidence of GISTs in the sixth-seventh decade of life, although pediatric cases have rarely been reported [4]. The incidence of GISTs is approximately equal in males and females. Some studies show a slight preponderance in men [9]. In this report, the patient is a 26-year-old female.

The patient presented predominantly with respiratory symptoms, not like the usual symptoms of GISTs that confined in the GI tract. In combination with radiographic findings, lung cancer was highly suspected initially. After chest CT study, a huge exophytic submucosal tumor from the stomach was noted with extension into the mediastinum and left lower thoracic cavity. Invasions of pericardium and lung parenchyma are also suspected. Although radiologic exophytic gastric submucosal tumor may suggest GIST, biopsy is the only way to make a definite diagnosis, as for most types of tumors. After ultrasonography-guided biopsy, the final diagnosis was malignant GIST, based on microscopic and immunohistochemical findings.

The term GIST was introduced by Mazur and Clark in 1983 [10]. Previously, these tumors were classified as gastric or intestinal smooth muscle tumors. With the advent of immunohistochemical staining techniques, they are now recognized as a distinct group of mesenchymal tumors. GISTs do not possess the ultrastructural and immunohistochemical features characteristic of smooth muscle differentiation, as are seen in leiomyomas and leiomyosarcomas [10]. Furthermore, GISTs have been demonstrated originated from the interstitial cells of Cajal [3], the pacemaker cells that regulate peristalsis of the digestive tract. On the molecular-genetic level, GIST is frequently associated with mutations in the kit gene, and less commonly with mutations in a related gene called PDGFRA. The encoded proteins of these genes (kit and PDGFRA) act as tyrosine kinase receptors. Mutations of these genes lead to continuous growth and division of tumor cells. Most GISTs express Kit (95%), CD34 (70%), and heavy caldesmon (80%), whereas 25% are positive for smooth muscle actin.

**Figure 3. a.** Photomicrograph (original magnification, x400; hematoxylin-eosin stain) shows hypercellularity of fascicular spindle cells. Note the hyperchromasia and pleomorphism of nuclei. **b.** Immunohistochemistry for CD 34 demonstrates positive.
and less than 5% for desmin [4]. In our patient, the immunohistochemical stainings of the biopsy specimen showed positive for CD34 and S100 (focally weak positive), but negative for Kit or desmin. It was not similar to the usual appearances of GISTs.

Most GISTs are sporadic, and their cause is unknown. In rare cases, people have a more greater probability of developing GIST than the general population. Neurofibromatosis 1 (NF1) is a disease caused by a mutation at the NF1 gene characterized by pigmentation abnormalities such as café au lait spots, multiple neurofibromas, and a predisposition to various cancers. In 2004, Kinoshita et al first published that mutations in the NF1-gene might be involved in the pathogenesis of GIST in NF1 patients [11]. More recently, Maertens et al confirmed some people with NF1 also develop GISTs [12]. The incidence of GIST among NF1 patients varies from 3.9% to 25%, while the overall ratio of NF1 in GIST patients counts up to 6% [13]. GIST in NF1 predominantly involves the small intestine including the duodenum. While in two thirds of the patients, the tumors often occur in multiples [13]. In our patient, who had a past history of scalp neurofibroma, the GIST occurred solitary and involved the stomach, similar to the appearances of GISTs that occur in the general population. Also, GISTs in NF1 usually have not shown mutations in the kit gene or the PDGFRα gene; that means, they have the normal or "wild type" kit and PDGFRα genes [12]. In the presented case, the immunohistochemical staining of the biopsy specimen showed negative for Kit (CD117) but focally weak positive for S100, similar to the appearance of GIST that occurs in NF1.

About 10-30% of GISTs have malignant behavior [1]. Several studies used tumor size and mitotic rate to assess the malignant potential of these tumors. Mitotic rate greater than 5 per 10 high-power fields (HPFs) or size larger than 5 cm was predictive of malignancy [14]. Malignant GIST means it can metastasize to other parts of the body, commonly to the abdominal cavity and liver, rarely to bones, soft tissues, and skin, and extremely rarely to lymph nodes and lungs [4]. For patients with GIST, surgery is the standard for treatment and offers the only chance for cure. Recently, treatment targeted toward inhibiting the mutant kit gene by imatinib mesylate, a tyrosine kinase-inhibitor [5, 15]. It is highly effective in the treatment of both chronic myeloid leukemia and GISTs [16]. It is a newer agent for targeted oncologic therapy now widely used for metastatic and unresectable GISTs [4, 5]. During hospitalization, the patient’s surgeon has suggested cytoreduction surgery or targeted therapy to the patient, but she and her family refused. The patient finally expired 3 months after diagnosis.

In summary, GISTs rarely metastasize to lung. Direct invasion into lung by GIST is much rarer than metastasis to lung. Although primary esophageal stromal tumor with direct invasion into the lung parenchyma has been reported by Papaspyros and Papagiannopoulos in 2008 [7], rarely has a gastric stromal tumor been documented to extend into mediastinum and thoracic cavity. Herein, we report an extremely rare case of gastric stromal tumor with extension into mediastinum and thoracic cavity and suspicious invasion of lung, presenting predominately with respiratory symptoms.  

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胃間質瘤延伸入縱膈腔和胸腔：病例報告

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佑民醫院 影像醫學科\textsuperscript{1}
彰化基督教醫院 影像醫學部\textsuperscript{2}，病理科\textsuperscript{3}
彰化基督教醫院二林分院 放射科\textsuperscript{4}

在台灣，胃腸道間質瘤每年的發生率約為每百萬人 13.74 例。約百分之十到三十的胃腸道
間質瘤會有惡性的表現，包括局部侵犯及遠端轉移。雖然食道發生的間質瘤直接侵犯到肺部曾
有一個案被報導，但罕有胃部發生的間質瘤被報導會延伸入縱膈腔和胸腔。在此，我們報告一
極為罕見之案例：胃部發生的間質瘤延伸入縱膈腔和胸腔並疑似侵犯肺部，患者主要以呼吸症
狀來表現。