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Poorly Differentiated Gastric Adenocarcinoma Mimicking Spindle Cell Tumor: Case Report

Lam Lek Man[1,#], Chan Chong Man[1,#], Ao Ieong Kam Lok[1], Chan Kin Iong[1], Yu Hon Ho[1,*]

[1]Macau Kiang Wu Hospital, Macau, 999078, China
[#]These Authors Contributed Equally to This Work and Share First Authorship
**Corresponding author*

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Abstract: Endoscopic procedures combined with imaging modalities such as computer tomography can differentiate gastric cancer from gastric submucosal tumors. However, due to lack of typical endoscopic manifestations, small proportion of gastric cancers are easily misdiagnosed as submucosal tumors. Here we present a rare case of poorly differentiated gastric adenocarcinoma that was initially misdiagnosed as a spindle cell tumor.

1. Introduction

Gastric cancer arises from the neoplastic transformation of glandular epithelial cells lining the gastric mucosa. It accounts for around 1.2 million new cases globally per year, particularly China where nearly half of all cases occur. [1]However, the detection rate of early gastric cancer remains relatively low, around 20% in China. [2]Poorly differentiated gastric adenocarcinoma have the worst prognosis. [3]The overall survival of advanced gastric adenocarcinoma was only 3 to 5 months without treatment. [4]The widespread endoscopic screening has led to a significant rise in diagnosed cases of gastric submucosal tumors (SMTs) - protruding lesion originating from the muscularis mucosae, submucosal tissue, or muscularis propria. Most SMTs such as leiomyomas, lipomas, and schwannomas are benign. However, neuroendocrine tumors (NETs) and gastrointestinal stromal tumors (GISTs) carry a potential risk of malignancy. [5, 6].

Poorly differentiated gastric adenocarcinoma represents a particularly aggressive histological subtype characterized by rapid progression, early metastasis, and minimal glandular formation. Its nonspecific endoscopic features and deep mucosal or submucosal origin can obscure timely recognition, resulting in a diagnostic challenge. This is further complicated when such lesions mimic submucosal tumors (SMTs), such as gastrointestinal stromal tumors (GISTs), which are generally benign but share overlapping endoscopic and imaging features.[7]

The incidence of gastric cancers mimicking SMTs is relatively rare, reported in only 0.1–0.6% of resected cases, but these lesions often evade detection due to the preservation of normal-appearing mucosa and subepithelial growth patterns.[8] These tumors may be falsely classified as GISTs or leiomyomas on imaging, especially when conventional endoscopic biopsies yield non-diagnostic samples. Therefore, a high index of suspicion and integration of advanced diagnostic modalities are

critical for accurate diagnosis.

2. Case Report

A 65-year-old male with a past medical history of vitiligo presented with upper abdominal fullness for three weeks and emesis for a week, with an unintentional weight reduction of 3 kg within a month. There was no malignant family history. Laboratory tests showed negative tumor markers, but elevated serum ferritin at 1296μg/L. Abdominal computed tomography (CT) revealed significant fluid retention within the stomach and localized nodular thickening of the gastric wall at the antrum and pyloric region, raising suspicion for a submucosal tumor (Figure 1 (A)).

Gastroscopy showed a 2.5 cm mass on the greater curvature of the prepyloric region, with a central depression that could not be clearly visualized (Figure 1 (B-D)). Endoscopic ultrasound (EUS) showed a heterogeneously hypoechoic lesion measuring 28.9 ×17.7 mm, protruding into the lumen and penetrating the muscularis propria. The serosa was not involved(Figure 1 (E&F)). Color Doppler imaging showed vascular signals. No enlarged perigastric lymph nodes or peritoneal fluid were observed.

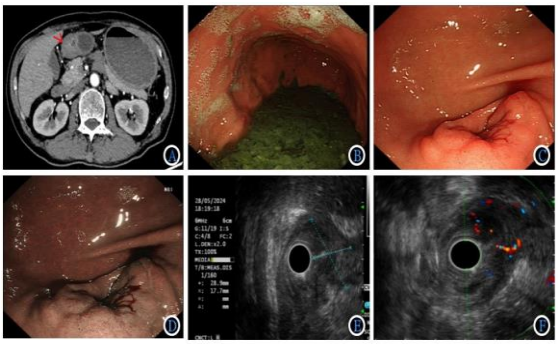

Figure 1 A: Abdominal computed tomography (CT) reveals wall thickening involving the gastric antrum and pyloric region (arrow), suggestive of a submucosal tumor. B: Significant fluid retention within the stomach. C&D: Gastroscopy showing a 2.5 cm mass at the greater curvature with the central depressed area was not clearly visualized. E: EUS showing a hypoechoic lesion measuring approximately 28.9×17.7 mm, protruding into the gastric lumen and infiltrating the muscularis propria. The serosal layer was not involved. F: Color Doppler imaging demonstrated punctate internal vascular signals.

Histopathological examination of the lesion biopsy yielded negative results, however, EUS-guided fine needle aspiration (FNA) demonstrated spindle cell morphology. Comprehensive evaluation of radiological and histopathological findings established gastrointestinal stromal tumor (GIST) as the primary diagnostic consideration. Following multidisciplinary discussion, surgical treatment was recommended. The surgical procedure was performed under general endotracheal anesthesia, consisting of laparoscopic distal gastrectomy with Billroth II reconstruction. Intraoperative exploration identified a well-circumscribed 3×3 cm tumor localized to the muscularis propria along the lesser curvature of the gastric antrum. Adhesions were noted between the gastric wall and the pancreas. Intraoperatively, frozen section suggested a spindle cell tumor, with differential diagnosis including GIST, leiomyoma, and schwannoma.

Grossly, A gastric specimen measuring 5x4x3 cm was received. On sectioning, a well-circumscribed, solid, gray-white mass measuring approximately 3x2x2cm was identified (Figure 2 (A)). Microscopically, the tumor in the gastric antrum consisted of pleomorphic tumor cells distributed diffusely and invaded the full thickness of the gastric wall (Figure 2 (B)). Only focal mucosal involvement was noted (Figure 2 (C)). The cells were variably short spindle-shaped or

epithelioid with marked nuclear dysplasia. The initial impression was a malignant mesenchymal tumor of stromal or smooth muscle origin. Immunohistochemistry is useful in differential diagnosis in the gastric tumor. CK and CK7 were strongly stained in all tumor cells (Figure 2 (D)). CEA and CK20 were only stained in the focal area of tumor cells, while smooth muscle ACTIN, DOG-1, CD117, S-100, CD34 were negative in all pathological sections(Figure 2 (E&F)). The final diagnosis was poorly differentiated gastric adenocarcinoma.

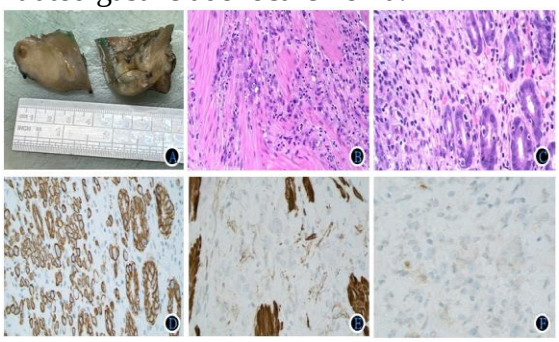

Figure 2 A: Resection specimen demonstrated a 3x2x2cm well-circumscribed, solid, gray-white mass in the muscular layer of the stomach. B: The tumor cells predominantly show infiltrative growth within the muscular layer (HE, original magnification x100). C: Focal infiltration of tumor cells in the mucosa (HE, original magnification x200). D: Immunohistochemistry showing diffuse positivity for CK. E&F: Immunohistochemistry showing negative staining for Actin (E) and DOG-1 (F).

3. Discussion

Clinically, both gastric adenocarcinoma and submucosal tumors (SMTs) can present with similar symptoms, including abdominal pain, distension, bleeding, and obstruction, making diagnosis challenging. In this case, unlike most advanced-stage gastric cancers, the tumor markers were negative, and the mucosal surface appeared normal. The lesion was characterized by localized wall thickening. The lesion was covered by non-neoplastic tissue arising from reactive hyperplasia of the muscularis propria and submucosa, resulting in an extremely low diagnostic yield for endoscopic biopsies, which may easily lead to a misdiagnosis of SMT. The diagnostic performance of EUS-FNA for submucosal tumors is size-dependent, with sensitivity rates of 71-86% for lesions <4 cm lesions compared to 95-100% for lesions >4 cm, reflecting the technical advantages in sampling larger masses. [9] Therefore, in patients with small SMT-like lesions who also present with obstructive symptoms or unexplained weight loss, the possibility of malignancy should be considered. Given the limitations of EUS-FNA in evaluating lesions <4 cm, more aggressive tissue acquisition strategies when SMT-like lesions demonstrate atypical features such as rapid growth, central ulceration, or unresolving symptoms. Methods including mucosal incision-assisted biopsy (MIAB), endoscopic submucosal dissection (ESD), or laparoscopic and endoscopic cooperative surgery (LECS) may be warranted for diagnostic confirmation. [10]

Moreover, additional diagnostic tools such as PET/CT may be beneficial for assessing the nature of the lesion and evaluating systemic involvement. Circulating cell-free DNA (cfDNA) - based liquid biopsy acts as a new non-invasive modality for gastric cancer detection, demonstrating superior diagnostic potential compared to conventional serum tumor biomarkers. [11] Multidisciplinary team (MDT) evaluation should be emphasized to minimize the risk of misdiagnosis.

In this case, the intraoperative frozen section and H&E findings initially supported a spindle cell tumor, this lesion resembled a mesenchymal tumor, leading to diagnostic confusion. The gastric

mucosa appeared smooth with no ulceration or overt mass formation, which is atypical for conventional gastric adenocarcinoma. Both frozen and histological sections were dominated by a reactive stromal and smooth muscle background, with scattered, inconspicuous tumor cells infiltration. These tumor cells were small and did not form glandular or typical cancerous structures. This case highlights the limitations of FNA in detecting poorly differentiated or atypical adenocarcinomas. The diagnostic yield of FNA cytology varies significantly by tumor type, demonstrating approximately 78% sensitivity for GISTs[12], and typically exceeding 80% for adenocarcinomas[13], and it is significantly influenced by tumor size, morphological features, and anatomical layer of origin. Pathology reports should clearly indicate when a sample is "non-diagnostic" or "unsatisfactory" and recommend repeat biopsy when necessary. Intraoperatively, increased sampling during frozen section and adjunctive cytology techniques. For resected specimens, extensive tissue sampling is essential to uncover diagnostic clues. Ultimately, accurate diagnosis relies on a combination of histological examination and immunohistochemistry.

4. Conclusion

This case highlights the risk of diagnostic pitfalls when gastric adenocarcinoma presents with spindle cell morphology. In this case, first of all, the tumor's lack of ulceration, minimal mucosal disruption, and muscularis-based growth pattern made it indistinguishable from benign SMTs on initial imaging and endoscopy. This atypical presentation is not unique; multiple reports document similar pitfalls where adenocarcinomas mimic SMTs, delaying definitive diagnosis and treatment. [14] Secondly, both intraoperative and frozen sections suggested a spindle cell tumor, leading initially to a misdiagnosis. The tumor infiltrated the muscularis propria and was interspersed with hypertrophic smooth muscle bundles, mimicking a mesenchymal lesion. Only after broad sampling of the resected specimen and immunohistochemistry (CK and CK7 positivity) was the diagnosis of poorly differentiated adenocarcinoma confirmed.

Furthermore, in cases with high suspicion of malignancy despite inconclusive biopsy, surgical resection may be warranted. Intraoperative frozen section analysis can offer rapid preliminary diagnosis, but as illustrated in this case, its utility is constrained by limited sampling and tumor heterogeneity. Definitive diagnosis often relies on extensive post-operative histologic sampling and immunohistochemistry.

Clinicians should maintain a high level of suspicion when evaluating SMT-like lesions that exhibit unusual clinical or imaging characteristics. Multidisciplinary team evaluation, thorough histopathological examination, and appropriate use of immunohistochemical panels are key to avoiding misdiagnosis and ensuring timely surgical intervention.

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