REVIEW

2066  Tumor circulome in the liquid biopsies for digestive tract cancer diagnosis and prognosis

2081  Isoflavones and inflammatory bowel disease
Wu ZY, Sang LX, Chang B

MINIREVIEWS

2092  Cytapheresis for pyoderma gangrenosum associated with inflammatory bowel disease: A review of current status
Tominaga K, Kamimura K, Sato H, Ko M, Kawata Y, Mizusawa T, Yokoyama J, Terai S

2102  Altered physiology of mesenchymal stem cells in the pathogenesis of adolescent idiopathic scoliosis
Ko DS, Kim YH, Goh TS, Lee JS

2111  Association between liver targeted antiviral therapy in colorectal cancer and survival benefits: An appraisal
Wang Q, Yu CR

2116  Peroral endoscopic myotomy for management of gastrointestinal motility disorder

ORIGINAL ARTICLE

Case Control Study

2127  Clinical prediction of complicated appendicitis: A case-control study utilizing logistic regression

2137  Clinical application of ultrasound-guided selective proximal and distal brachial plexus block in rapid rehabilitation surgery for hand trauma
Zhang J, Li M, Jia HB, Zhang L

2144  High flux hemodialysis in elderly patients with chronic kidney failure
Xue HY, Duan B, Li ZJ, Du P

2150  Determination of vitamin D and analysis of risk factors for osteoporosis in patients with chronic pain
Duan BL, Mao YR, Xue LQ, Yu QY, Liu MY

Retrospective Study

2162  Differences in parents of pediatric liver transplantation and chronic liver disease patients
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2173</td>
<td>Epidemiological investigation of <em>Helicobacter pylori</em> infection in elderly people in Beijing</td>
<td>Zhu HM, Li BY, Tang Z, She J, Liang XY, Dong LK, Zhang M</td>
</tr>
<tr>
<td>2181</td>
<td>Application of a pre-filled tissue expander for preventing soft tissue incarceration during tibial distraction osteogenesis</td>
<td>Chen H, Teng X, Hu XH, Cheng L, Du WL, Shen YM</td>
</tr>
<tr>
<td>2201</td>
<td>Choice and management of negative pressure drainage in anterior cervical surgery</td>
<td>Su QH, Zhu K, Li YC, Chen T, Zhang Y, Tan J, Guo S</td>
</tr>
<tr>
<td>2210</td>
<td>Risk scores, prevention, and treatment of maternal venous thromboembolism</td>
<td>Zhang W, Shen J, Sun JL</td>
</tr>
<tr>
<td>2219</td>
<td>Role of Hiraoka's transurethral detachment of the prostate combined with biopsy of the peripheral zone during the same session in patients with repeated negative biopsies in the diagnosis of prostate cancer</td>
<td>Pan CY, Wu B, Yao ZC, Zhu XQ, Jiang YZ, Bai S</td>
</tr>
<tr>
<td>2227</td>
<td>Efficacy of thoracoscopic anatomical segmentectomy for small pulmonary nodules</td>
<td>Li H, Liu Y, Ling BC, Hu B</td>
</tr>
</tbody>
</table>

**Observational Study**

2235 | Attitudes, awareness, and knowledge levels of the Turkish adult population toward organ donation: Study of a nationwide survey | Akbulut S, Ozer A, Gokce A, Demyati K, Saritas H, Yilmaz S                                         |

2246 | Metabolic biomarkers and long-term blood pressure variability in military young male adults     | Lin YK, Liu PY, Fan CH, Tsai KZ, Lin YP, Lee JM, Lee JT, Lin GM                                     |

2255 | Cytokines predict virological response in chronic hepatitis B patients receiving peginterferon alfa-2a therapy | Fu WK, Cao J, Mi NN, Huang CF, Gao L, Zhang JD, Yue P, Bai B, Lin YY, Meng WB                        |

**SYSTEMATIC REVIEWS**

2266 | Utilising digital health to improve medication-related quality of care for hypertensive patients: An integrative literature review | Wechkunanukul K, Parajuli DR, Hamiduzzaman M                                                       |

**META-ANALYSIS**

2280 | Role of IL-17 gene polymorphisms in osteoarthritis: A meta-analysis based on observational studies | Yang HY, Liu YZ, Zhou XD, Huang Y, Xu NW                                                           |
CASE REPORT

2294 Various diagnostic possibilities for zygomatic arch pain: Seven case reports and review of literature
Park S, Park JW

2305 Extensive multifocal and pleomorphic pulmonary lesions in Waldenström macroglobulinemia: A case report
Zhao DF, Ning HY, Cen J, Liu Y, Qian LR, Han ZH, Shen JL

2312 Lung cancer from a focal bulla into thin-walled adenocarcinoma with ground glass opacity — an observation for more than 10 years: A case report

2318 Pyogenic discitis with an epidural abscess after cervical analgesic discography: A case report
Wu B, He X, Peng BG

2325 Clinical characteristics, diagnosis, and treatment of COVID-19: A case report
He YF, Lian SJ, Dong YC

2332 Paraplegia after transcatheter artery chemoembolization in a child with clear cell sarcoma of the kidney: A case report
Cai JB, He M, Wang FL, Xiong JN, Mao JQ, Guan ZH, Li LJ, Wang JH

2339 Macrophage activation syndrome as a complication of dermatomyositis: A case report
Zhu DX, Qiao JJ, Fang H

2345 Serial computed tomographic findings and specific clinical features of pediatric COVID-19 pneumonia: A case report
Chen X, Zou XJ, Xu Z

2350 Myxofibrosarcoma of the scalp with difficult preoperative diagnosis: A case report and review of the literature
Ke XT, Yu XF, Liu JY, Huang F, Chen MG, Lai QQ

2359 Endoscopic pedicle flap grafting in the treatment of esophageal fistulas: A case report
Zhang YH, Du J, Li CH, Hu B

2364 Hemophagocytic syndrome as a complication of acute pancreatitis: A case report
Han CQ, Xie XR, Zhang Q, Ding Z, Hou XH

2374 Reduced delay in diagnosis of odontogenic keratocysts with malignant transformation: A case report
Luo XJ, Cheng ML, Huang CM, Zhao XP

2380 Gastric pyloric gland adenoma resembling a submucosal tumor: A case report
Min CC, Wu J, Hou F, Mao T, Li XY, Ding XL, Liu H

2387 Ataxia-telangiectasia complicated with Hodgkin's lymphoma: A case report
Li XL, Wang YL
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>2392</td>
<td>Uterine incision dehiscence 3 mo after cesarean section causing massive bleeding: A case report</td>
<td>Zhang Y, Ma NY, Pang XA</td>
</tr>
<tr>
<td>2406</td>
<td>LETTER TO THE EDITOR: Macrophage activation syndrome as an initial presentation of systemic lupus erythematosus</td>
<td>Shi LJ, Guo Q, Li SG</td>
</tr>
</tbody>
</table>
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A gastric pyloric gland adenoma resembling a submucosal tumor: A case report

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Abstract

BACKGROUND

Pyloric gland adenoma (PGA) is a recently described and rare tumor. Submucosal tumor (SMT)-like PGA is more difficult to diagnose and differentiate from other submucosal lesions.

CASE SUMMARY

We present the case of a 69-year-old man with a 10 mm SMT-like elevated lesion with an opening in the upper part of the gastric body, referred to our hospital for further endoscopic treatment. Magnifying endoscopy with narrow-band imaging, endoscopic ultrasonography, and complete endoscopic submucosal dissection were performed on the patient. Histopathological findings revealed tightly packed tubular glands lined with cuboidal or columnar cells that had round-to-oval nuclei containing occasional prominent nucleoli and an eosinophilic cytoplasm similar to that in non-neoplastic gastric pyloric glands. Additionally, immunohistochemical analysis showed positive staining for both mucin 5AC and mucin 6. Therefore, we arrived at the final diagnosis of gastric PGA. Although there was no apparent malignant component in this tumor, PGA has been considered a precancerous disease with a high risk of transformation into adenocarcinoma.

CONCLUSION

PGA should be considered when detecting gastric SMT-like lesions. Physicians and pathologists should focus on PGA due to its malignant potential.

Key Words: Pyloric gland adenoma; Submucosal tumor; Endoscopic submucosal dissection; Case report
A 69-year-old Chinese man presented to our hospital for evaluation and management of an epigastric distention for over a year. He had a history of hypertension for 10 years and was ingesting oral telmisartan 80 mg every day regularly. His blood pressure was controlled and relatively stable. He had no history of surgery and allergic drugs.

Physical examination upon admission
Physical examination revealed that he was 170 cm in height and 73 kg in weight, with a blood pressure of 127/92 mmHg and pulse rate of 67 beats per minute. There were no signs of endogenous polyp-like hyperplastic changes in the stomach. Physical examination upon admission revealed a 10 mm tumor-like elevated lesion located in the upper part of the gastric body. Preoperative diagnosis is difficult because of the generally deep location of the tumor. Endoscopic ultrasound and endoscopic submucosal dissection were performed in this patient. The histopathological and immunohistochemistry investigations resulted in the diagnosis of pyloric gland adenoma.
no other obvious abnormalities during physical examination.

**Laboratory examinations**

After admission, the patient underwent thorough evaluations including routine investigations of the blood, urine, feces and occult blood, blood biochemistry, and common serum tumor markers such as carcinoembryonic antigen, carbohydrate antigen 19-9, alpha-fetoprotein, and carbohydrate antigen 724. No significant abnormalities were recorded in these investigations.

**Imaging examinations**

Upper gastrointestinal endoscopy revealed non-atrophic gastritis without *Helicobacter pylori* (*H. pylori*) infection in the background mucosa. An SMT-like elevated lesion with a diameter of 10 mm was located at the posterior wall of the upper part of the gastric body, with an opening on the surface of the tumor (Figure 1A). Next, magnifying endoscopy with narrow-band imaging (ME-NBI) revealed a regular surface microstructure and microvascular pattern (Figure 1B). Additionally, ME-NBI revealed that the orifice showed dilated glandular duct arising from the deeper mucosa.

Endoscopic ultrasound (EUS, 20 MHz; Olympus, Tokyo, Japan) revealed a 10.6 mm × 5.5 mm equal echoic mass with several cysts located in the submucosal layer with an intact muscularis (Figure 1C). The biopsy results indicated chronic non-atrophic, *H. pylori*-negative gastritis.

**FINAL DIAGNOSIS**

According to the endoscopic performance and histopathologic examination, the patient was diagnosed with PGA.

**TREATMENT**

On the basis of the examination results, the diagnosis of SMT-like tumor in the upper part of the gastric body was uncertain. Diagnostic ESD was performed on the patient to confirm the diagnosis. An elevated tumor measuring 13 mm × 10 mm was identified in the ESD specimen with white mucus oozing out from the opening in the middle when squeezed (Figure 1D). In routine hematoxylin and eosin staining, the low-magnification view revealed that the lesion was located in the submucosal layer, showing a nodular appearance with clear boundaries and increasing number of glands in the lamina propria of the orifice (white arrow) (Figure 2A). The high-magnification view showed that some glandular cavity was irregular, with cystic expansion (orange arrow) and interstitial edema (Figure 2B). The tumor consisted of mucus-rich packed tubular glands lined with cuboidal or low columnar epithelial cells containing an eosinophilic cytoplasm and round nuclei, similar to that in pyloric glands (Figure 2C). There was slight epithelial dysplasia in some areas. Additionally, immunohistochemical staining demonstrated positivity for both mucin 6 (MUC6) and MUC5AC but negativity for MUC4 and p53, and the Ki-67 labeling index was about 2% (Figure 2C-F). According to the above histologic results, we finally made a diagnosis of PGA. Adenocarcinoma components were not identified in the ESD specimen. The horizontal and vertical margin were negative, resulting in complete and curative resection.

**OUTCOME AND FOLLOW-UP**

The lesion was removed completely by ESD. However, the patient will need to undergo a regular gastroscopy follow-up after surgery.

**DISCUSSION**

PGA is an uncommon neoplasm that has been gradually recognized in the past few decades. Since Elster first described PGA in a book chapter in 1976, similar lesions were subsequently reported in some cases and small series of clinical studies. The
Figure 1  Endoscopic findings. A: A 10 mm submucosal tumor-like elevated lesion with an opening in the posterior wall of the upper part of the gastric body was observed by white light endoscopy; B: A regular microvascular pattern was observed using magnifying endoscopy with narrow-band imaging (magnification: × 40); C: Isoechoic mass (10.6 mm × 5.5 mm) with multiple cysts could be observed in the submucosal layer with intact muscularis using endoscopic ultrasound; D: An elevated tumor measuring 13 mm × 10 mm with oozing white mucus could be observed in the endoscopic submucosal dissection specimen.

majority of reports on PGA are published by other nations, with a lack of awareness in China.

Previous studies have shown that PGAs occur more frequently in older women⁸,¹⁴. Vieth et al⁸, in one of the largest studies with 90 PGA patients, reported a 2.5:1 ratio for women to men with an average age of 73 years. The predilection site for PGA is the corpus/fundus (64%) of the stomach, followed by cardia (8%), antrum (7%) and intermediate zone (5%), and others occurred in the extra-gastric sites, similar to observations of Choi et al¹⁰. PGAs present with large lesions at the time of diagnosis, with an average size of 1.6-2.3 cm reported in multiple case reports and clinical studies⁸-¹⁰,¹². In our study, the patient was an elderly man with PGA of 10 mm diameter localized in the upper part of the gastric body near the cardia. Predominantly, PGAs appear as a polypoid lesion or mass⁹-¹², but it may also present as flat lesion⁹ or ulcer¹⁰. We reported an unusual case of PGA mimicking an SMT with an orifice on the surface of the lesion. Similarly, Yamamoto et al⁹ reported a flat lesion with two openings at the greater curvature of the upper gastric body. Considering the possible deeper depth of the SMT-like lesion, we did not obtain its biopsy. But biopsy specimen from the orifice of the SMT may contribute to diagnosis. The performance of EUS is important in the diagnosis of an SMT-like lesion. To date, limited information is available on the EUS characteristics of the PGAs. Moreover, PGAs are usually located in the mucosal or submucosal layer in EUS. In the EUS by Yamamoto et al⁹, multiple large cysts were found in the second and third layers and the intact fourth layer⁹. Whereas, in our case, EUS for the patient showed an isoechoic nodule with several cysts located in the submucosal layer.

The predisposing factors of PGAs have remained unclear. Eighteen cases (34%) of PGAs presented mainly with atrophic autoimmune gastritis (AIG), and they were also positive for H. pylori gastritis (30%). Moreover, only 3.8% cases have been reported with a normal gastric mucosa⁸. However, a controversy exists with regards to the background mucosa, where 22.4% of the PGAs developed with AIG background, while normal mucosa was seen in 35.8% cases⁹. The predominance of AIG in older women contributes to the frequent occurrence of PGA in these women⁹. In our study, the biopsy from the antrum indicated chronic non-atrophic gastritis without infection of H. pylori; however, its relationship with the background mucosa and underlying mechanism need to be further explored.
Furthermore, EUS revealed a few cysts within the equivalent echogenic mass located in the submucosal layer in our patient. Therefore, PGA should be distinguished from gastritis cystica profundal (GCP), which is a rare lesion of the stomach, characterized by polypoid cystic ectasia of benign gastric glands invading the submucosa. It associates with chronic inflammation and ischemia and is observed primarily in patients who have undergone gastrectomy\(^{[17]}\). The most frequent EUS feature of GCP was multiple anechoic cysts in the submucosal layer, as reported earlier\(^{[18,19]}\). However, we did not find any component of the GCP. There was an opening on the mucosal surface of the PGA that ought to be differentiated from the gastric ectopic pancreas. A dimple or umbilical opening can be observed in some heterotopic pancreases. Anechoic duct-like structure or rare cyst cavity structure can be detected within the hypoechoic mass located in the deep mucosal and submucosal layers by EUS\(^{[20]}\). The majority of heterotopic pancreas cases are located at the gastric antrum. No ectopic pancreatic tissues were identified in the resected specimen by ESD. Additionally, clinicians should differentiate it from other submucosal lesions such as the gastric neuroendocrine tumors\(^{[21]}\) and SMT-like gastric adenocarcinoma\(^{[22,23]}\).

Next, it was difficult to make an initial diagnosis of PGA due to the SMT-like appearance of the tumor, and an ESD was performed for final confirmation.
Histopathological findings revealed mucus-rich pyloric glands lined with cuboidal or low columnar epithelial cells. Additionally, immunohistochemical staining was performed for MUC6 (specific for PGA) and MUC5AC (present in luminal foveolar type epithelium) to confirm the diagnosis of PGA. The gastric type adenoma that needed to be differentiated from PGA is foveolar-type adenoma, which is immunohistochemically positive for MUC5AC but negative for MUC6.

PGAs are considered at a high risk of malignant transformation\cite{10,13,14}, and have been divided into three categories: Viz, without conventional histologic dysplasia; low-grade dysplasia (LGD); and high-grade dysplasia (HGD)\cite{14}. In a recent multicenter clinicopathologic study with 67 gastric PGA cases, lesions with HGD or adenocarcinoma were found to have larger mean size (3.5 cm) than LGD cases (1.5 cm) ($P < 0.001$)\cite{10}. They concluded that the risk of developing HGD or adenocarcinoma was directly associated with the size of the lesion, presence of AIG, tubulovillous architecture, and mixed type (co-expression of both MUC6 and MUC5AC in deeper glands with MUC6 expression ranging from 20% to > 90% of the neoplastic glands)\cite{10}. An immunohistochemical analysis of the gastric PGAs indicated higher nuclear expression of p53 in PGAs with adenocarcinoma (82.1%) than those without adenocarcinoma (59.3%)\cite{13}, suggesting that nuclear p53 may correlate with high-risk PGAs. In our study, the PGA ought to be classified as mixed type. The relatively small diameter without expression of p53 may be responsible for the lack of conventional hyperplasia histologically. Regardless of the presence of hyperplasia, all PGAs represent at least LGD, even in cases without noticeable conventional histologic dysplasia\cite{10}. Taken together, the patient in our study would need to be followed-up regularly.

Furthermore, in our case, the SMT-like lesion was located in the upper part of the gastric body. We performed ME-NBI and EUS for the patient, but failed to obtain the biopsy of the tumor. Moreover, we could not distinguish it from other SMTs and make an accurate preoperative diagnosis. Therefore, we subsequently performed the diagnostic ESD for this patient, with confirmed diagnosis using histopathological and IHC analysis. Additionally, the resected specimen did not show signs of malignancy. Although the overall recurrence rate of PGAs was very low\cite{10}, regular follow-up with periodic gastroscopic surveillance should be suggested.

CONCLUSION

We present a case of PGA with SMT-like appearance, located in the upper part of the gastric body. It poses difficulty in distinguishing from other submucosal lesions. Deeper biopsies using larger forceps or even EUS-guided fine needle aspiration may improve the clinical diagnosis. ESD was subsequently performed to confirm the final diagnosis. It is recommended that all PGAs be completely removed if possible, particularly when they are large or show high-grade features\cite{10}. Clinicians and pathologists should pay close attention to PGAs owing to their potential to transform to adenocarcinoma. The patient needs to be followed up with regular gastroscopy observation.

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