DOI:10.31557/RRO.2025.11.1.41

CASE SERIES

Large Cell Neuroendocrine Carcinoma of the Stomach: A Case Series

Zahra Taheri[1], Saeed Jalili Bazel[2], Elham Samami[3], Masoumeh Gharib[4], Maryam Anvary[5], Mehdi Molavi[6], Seyedehhoda Khatibmasjedi[7], Mobina Mohammadkhani[8], Seyed Alireza Javadinia[9]

[1]Student Research Committee, Sabzevar University of Medical Sciences, Sabzevar, Iran. [2]Student Research Committee, Sabzevar University of Medical Sciences, Sabzevar, Iran. [3]University of Florida Health Cancer Center, Gainesville, FL, United States and College of Nursing, University of Florida, Gainesville, FL, United States. [4]Department of Pathology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad Iran. [5]Assistant Professor, Department of Internal Medicine, Mashhad University of Medical Sciences, Mashhad, Iran. [6]Assistant Professor, Department of Internal Medicine, Sabzevar University of Medical Sciences, Sabzevar, Iran. [7]Palliative care department, Case Western Reserve University, University Hospitals, Seidman Cancer Center, Cleveland, Ohio, USA. [8]Instructor, Iranian Research Center on Healthy Aging, Sabzevar, University of Medical Sciences, Sabzevar, Iran. [9]Assistant Professor, Non-Communicable Diseases Research Center, Sabzevar University of Medical Sciences, Sabzevar, Iran.

Abstract

Gastric large-cell neuroendocrine carcinoma (LCNEC) is a rare and highly aggressive malignancy, accounting for less than 1.5% of all gastric cancers. It is associated with a poor prognosis and may arise through distinct oncogenic pathways, including neuroendocrine cell lineage origin or transdifferentiation from gastric epithelial cells. This case series describes three patients diagnosed with gastric LCNEC. Case 1 involved an 88-year-old man who presented with weakness, lethargy, anorexia, and lower-extremity edema. Imaging revealed gastric wall thickening with suspected liver metastases. Histopathological examination confirmed poorly differentiated LCNEC. The patient received palliative radiotherapy followed by carboplatin and etoposide but developed severe pancytopenia after the first chemotherapy cycle and died four months after diagnosis. Case 2 was a 67-year-old man who presented with epigastric and flank pain. Immunohistochemical analysis demonstrated positivity for chromogranin and synaptophysin, with a Ki-67 index of 55–60%, confirming a high-grade neuroendocrine carcinoma. Despite multimodal treatment, including chemotherapy and chemoradiotherapy, he developed brain metastasis and died shortly after craniotomy. Case 3 involved a 70-year-old man with diabetes who presented with progressive dysphagia and marked weight loss. Endoscopy revealed an esophageal neuroendocrine carcinoma and a large gastric cardia mass. Immunohistochemistry showed positivity for cytokeratin, chromogranin, TTF-1, and a Ki-67 index of 70–80%. The patient received platinum-based chemotherapy followed by concurrent chemoradiotherapy. These cases highlight the highly aggressive clinical behavior of gastric LCNEC, its propensity for early metastatic dissemination, and the poor prognosis despite multimodal treatment. Early recognition and accurate histopathological diagnosis are essential for appropriate management of this uncommon malignancy.

Keywords: Gastric large-cell neuroendocrine carcinoma; Neuroendocrine neoplasms; Stomach neoplasms; Case series

Rep Radiother Oncol, **11 (1)**, 41-46

Submission Date: 05/05/2025 Acceptance Date: 07/01/2025

Introduction

Unlike gastric adenocarcinoma, which is the most common malignant tumor of the stomach, gastric neuroendocrine carcinoma is a rare and highly aggressive neoplasm [1]. Gastric large-cell neuroendocrine carcinoma (GLCNEC) represents an uncommon subtype of gastric neuroendocrine carcinoma, accounting for less than 1.5% of all gastric malignancies, and is associated with an unfavorable prognosis [2].

Corresponding Author:
Dr. Seyed Alireza Javadinia
Assistant Professor, Non-Communicable Diseases Research Center, Sabzevar University of Medical Sciences, Sabzevar, Iran.
Emails: Javadinia.alireza@gmail.com and Javadiniaa941@mums.ac.ir

Recent evidence suggests that GLCNEC may develop through at least two distinct oncogenic pathways. One pathway involves malignant transformation of neuroendocrine cells, whereas the other is thought to result from transdifferentiation of gastric epithelial cells. Genomic studies have identified recurrent alterations involving genes such as MYC, TP53, RB1, and KMT2C, supporting the molecular heterogeneity of these tumors and suggesting that pure GLCNECs are biologically distinct from conventional gastric adenocarcinomas [3, 4].

According to the World Health Organization (WHO) Classification of Digestive System Tumours, large-cell neuroendocrine carcinoma (LCNEC) is a high-grade malignant neoplasm characterized by large polygonal cells arranged in organoid, nesting, trabecular, rosette-like, or palisading patterns, with neuroendocrine differentiation confirmed by immunohistochemistry and, less commonly, electron microscopy. Compared with small-cell neuroendocrine carcinoma, LCNEC demonstrates abundant cytoplasm, vesicular nuclei, and prominent nucleoli [5].

Although the lung is the most common primary site of LCNEC, this malignancy has also been reported in the gastrointestinal tract and several other organs, including the cervix, uterus, kidney, urinary bladder, prostate, pharynx, and larynx. Regardless of the primary site, LCNEC is characterized by aggressive biological behavior, early metastatic spread, and poor clinical outcomes [6-8].

Gastric neuroendocrine neoplasms are traditionally classified into three clinicopathological subtypes. Types 1 and 2 are associated with hypergastrinemia and are frequently multifocal, whereas Type 3 tumors occur independently of serum gastrin levels and exhibit the most aggressive clinical behavior, the highest metastatic potential, and the poorest prognosis. Treatment strategies vary according to tumor type, stage, and extent of disease and may include endoscopic resection, surgery, chemotherapy, radiotherapy, or multimodal treatment [9, 10].

Given the rarity of gastric LCNEC and its highly aggressive clinical course, additional case reports and case series remain valuable for improving the current understanding of its clinicopathological characteristics, diagnostic challenges, therapeutic approaches, and clinical outcomes. Therefore, we present a case series of three patients with GLCNEC treated at our institution.

Case 1

An 88-year-old man presented with a two-week history of weakness, lethargy, and anorexia, accompanied by bilateral lower-extremity edema that had progressively worsened over the preceding month. His medical history was significant for hypothyroidism, chronic kidney disease, ischemic heart disease, benign prostatic hyperplasia, and Parkinsonism. On physical examination, he appeared pale and had weak distal pulses, bilateral 2+ pitting edema of the lower extremities, tachycardia (heart rate, 100 beats/min), blood pressure of 105/55 mmHg, and an oxygen saturation of 96% on room air. Digital rectal examination revealed no abnormalities.

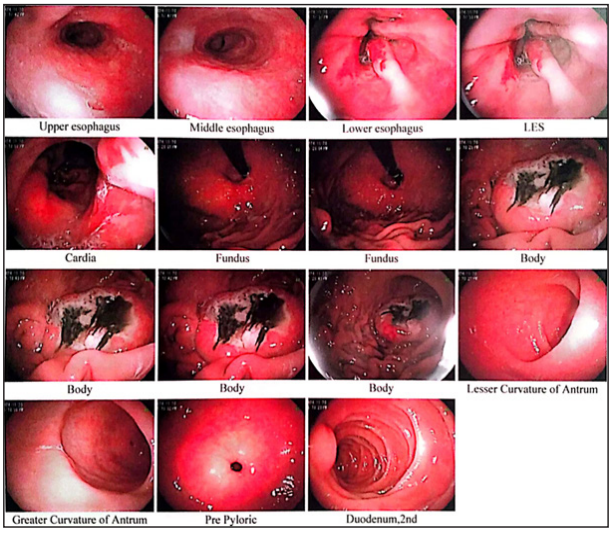

Figure 1. Endoscopy Pictures of the Case 2

Initial laboratory investigations demonstrated severe anemia with a hemoglobin level of 6.0 g/dL, necessitating packed red blood cell transfusion. Contrast-enhanced computed tomography (CT) of the abdomen and pelvis demonstrated irregular wall thickening along the greater curvature of the stomach with adjacent serosal involvement, highly suggestive of gastric malignancy. Triphasic contrast-enhanced CT of the liver revealed multiple hypovascular hepatic lesions with imaging characteristics consistent with metastatic disease (Figure 1 and 2). Upper gastrointestinal endoscopy demonstrated a large fungating ulcerative mass in the gastric body, and multiple biopsy specimens were obtained for histopathological evaluation.

The initial pathological assessment suggested a poorly differentiated adenocarcinoma because of the limited endoscopic biopsy material and extensive tumor necrosis. Owing to the unusual morphological features, additional histopathological review with an extended immunohistochemical panel was performed. Microscopic examination demonstrated a high-grade malignant neoplasm composed of large polygonal cells arranged in organoid nests and trabecular structures, exhibiting abundant eosinophilic cytoplasm, vesicular nuclei with prominent nucleoli, frequent mitotic figures, and extensive necrosis. Immunohistochemically, the tumor cells showed diffuse positivity for synaptophysin, chromogranin A, CD56, and pancytokeratin (AE1/AE3), with a markedly elevated Ki-67 proliferation index (>70%). These morphologic and immunophenotypic findings established the final diagnosis of gastric large-cell neuroendocrine carcinoma (LCNEC), WHO Grade 3. Based on the presence of hepatic metastases identified on triphasic liver CT, the disease was considered metastatic at presentation (cT4NxM1, Stage IV).

Because of persistent tumor-related gastric bleeding and the patient's poor surgical candidacy, palliative radiotherapy was administered. Following multidisciplinary team discussion, best supportive care was recommended owing to the patient's advanced age,

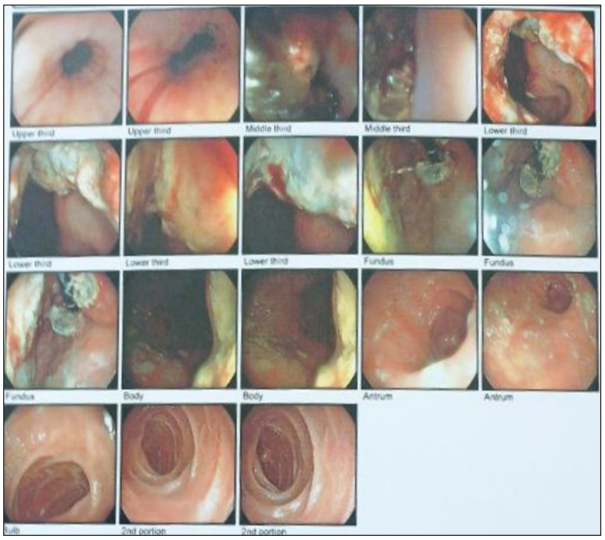

Figure 2. Endoscopy Pictures of the Case 3

multiple comorbidities, poor performance status, and metastatic disease. However, at the request of the patient's family, systemic chemotherapy consisting of carboplatin (selected instead of cisplatin because of chronic kidney disease) and etoposide was initiated.

After the first cycle of chemotherapy, the patient developed severe pancytopenia requiring hospitalization. Owing to progressive clinical deterioration and poor treatment tolerance, further anticancer treatment was discontinued, and he was transitioned to best supportive care. The patient died four months after the diagnosis.

Case 2

A 67-year-old man with a history of nephrolithiasis presented to the internal medicine clinic with epigastric and left flank pain that had developed on the day of admission. He also reported intermittent regurgitation but denied dysphagia, odynophagia, nausea, anorexia, or significant weight loss.

Abdominal ultrasonography demonstrated several hypoechoic oval lesions adjacent to the liver, suggestive of enlarged regional lymph nodes, together with multiple renal calculi measuring up to 3 mm. Contrast-enhanced abdominal CT subsequently demonstrated irregular thickening of the gastric wall with regional lymphadenopathy, without evidence of distant metastatic disease. Upper gastrointestinal endoscopy revealed an ulceroinfiltrative gastric mass, and multiple biopsy specimens were obtained.

Histopathological examination initially demonstrated a poorly differentiated high-grade malignant neoplasm. Following multidisciplinary pathological review, additional immunohistochemical studies were performed to further characterize the tumor. Microscopic examination demonstrated large polygonal tumor cells arranged in organoid nests and trabecular structures with abundant eosinophilic cytoplasm, vesicular nuclei containing prominent nucleoli, extensive geographic necrosis, and a high mitotic rate, consistent with large-cell neuroendocrine morphology. Immunohistochemically, the tumor cells showed diffuse positivity for chromogranin A, synaptophysin, CD56, and pancytokeratin (AE1/AE3), while CK7 and CK20 were negative. The Ki-67 proliferation index was approximately 55–60%. These combined morphologic and immunophenotypic findings established the diagnosis of gastric large-cell neuroendocrine carcinoma (WHO Grade 3).

The disease was staged as locally advanced without distant metastasis at presentation (cT3/4N+M0). Because the initial pathological diagnosis suggested an undifferentiated gastric carcinoma before completion of the immunohistochemical work-up, the patient initially received systemic chemotherapy consisting of paclitaxel, carboplatin, and pemetrexed. After the diagnosis was revised to LCNEC, treatment was modified to platinum-based chemotherapy with cisplatin and etoposide in accordance with current recommendations for high-grade neuroendocrine carcinomas. Following systemic treatment, the patient underwent concurrent chemoradiotherapy, and interval imaging demonstrated a marked radiological response. Consequently, total gastrectomy was planned.

Before definitive surgery, however, the patient developed new-onset generalized seizures. Brain magnetic resonance imaging demonstrated a solitary left frontal enhancing metastatic lesion. Craniotomy was performed, and histopathological examination confirmed metastatic neuroendocrine carcinoma consistent with the known gastric primary. Unfortunately, despite neurosurgical intervention and supportive management, the patient's clinical condition deteriorated rapidly, and he died two weeks after surgery.

Case 3

A 70-year-old man with a history of type 2 diabetes mellitus presented with progressive dysphagia to both solids and liquids accompanied by profound weight loss, decreasing from 70 kg to 45 kg during the preceding six months. He also reported nausea and postprandial vomiting. He was referred for upper gastrointestinal endoscopy.

Endoscopic examination demonstrated a large infiltrative ulcerative mass centered at the gastric cardia with contiguous extension into the distal esophagus. Biopsies were obtained from both the gastric and esophageal components of the lesion. Initial histopathological interpretation suggested a poorly differentiated neuroendocrine carcinoma with focal squamous differentiation because of limited biopsy material.

Following expert pathological review and additional immunohistochemical evaluation, both biopsy specimens demonstrated identical tumor morphology characterized by sheets and trabecular nests of large polygonal malignant cells with abundant eosinophilic cytoplasm, coarse chromatin, prominent nucleoli, frequent mitotic figures, and extensive tumor necrosis. Immunohistochemical analysis demonstrated diffuse positivity for pancytokeratin (AE1/AE3), chromogranin A, CD56, and focal synaptophysin expression, with a Ki-67 proliferation index of approximately 70–80%. Tumor cells also showed

TTF-1 positivity, whereas leukocyte common antigen (LCA) and CD20 were negative. Because thoracic computed tomography demonstrated no pulmonary mass or mediastinal lesion, a primary pulmonary neuroendocrine carcinoma was excluded. The identical histopathological and immunophenotypic findings in both biopsy sites supported a diagnosis of primary gastric large-cell neuroendocrine carcinoma involving the gastroesophageal junction with secondary extension into the distal esophagus, rather than synchronous primary tumors.

Contrast-enhanced abdominopelvic CT demonstrated direct extension of the primary tumor into the pancreatic body without evidence of distant metastatic disease. Whole-body PET/CT confirmed intense uptake within the primary lesion but showed no distant metastatic involvement. Accordingly, the disease was staged as locally advanced gastric LCNEC (cT4bNxM0).

The patient received three cycles of cisplatin and etoposide chemotherapy followed by concurrent chemoradiotherapy to a total dose of 50.4 Gy. Post-treatment imaging demonstrated partial radiological response with symptomatic improvement in dysphagia. Nevertheless, owing to the aggressive biological behavior of the disease, subsequent follow-up demonstrated progressive locoregional disease, and the patient was transitioned to palliative supportive care.

Discussion

Gastric large-cell neuroendocrine carcinoma (GLCNEC) is an uncommon but highly aggressive malignancy associated with an unfavorable prognosis. Owing to its rarity and the considerable histopathological overlap with other poorly differentiated gastric malignancies, including adenocarcinoma, small-cell neuroendocrine carcinoma, and undifferentiated carcinoma, establishing an accurate diagnosis on limited endoscopic biopsy specimens can be challenging. Consequently, additional well-characterized case series remain valuable for improving the understanding of its clinicopathological features, diagnostic pitfalls, and therapeutic management [2].

A notable finding in the present case series is the initial diagnostic heterogeneity observed in all three patients. The first case was initially interpreted as poorly differentiated adenocarcinoma, the second as a high-grade neuroendocrine neoplasm, and the third as small-cell neuroendocrine carcinoma with focal squamous differentiation. However, in each patient, comprehensive histopathological re-evaluation together with extended immunohistochemical analysis established the final diagnosis of gastric large-cell neuroendocrine carcinoma (WHO Grade 3). The diagnosis was based on the integration of characteristic morphological features, including large polygonal tumor cells with abundant cytoplasm, vesicular nuclei with prominent nucleoli, organoid nesting and trabecular architecture, extensive necrosis, and high mitotic activity, together with confirmation of neuroendocrine differentiation by immunohistochemistry. Diffuse expression of neuroendocrine markers, including chromogranin A, synaptophysin, and CD56, combined with cytokeratin positivity and a markedly elevated Ki-67 proliferation index, supported the diagnosis of LCNEC in all three cases. These findings emphasize that the definitive diagnosis of LCNEC should rely on the combined assessment of morphology and immunophenotype rather than on the initial biopsy interpretation alone.

The diagnostic evolution observed in our patients reflects a well-recognized limitation of endoscopic biopsy in high-grade neuroendocrine carcinomas. Small tissue samples, extensive tumor necrosis, crush artefact, intratumoral heterogeneity, and overlapping morphological features may result in an initial diagnosis of poorly differentiated adenocarcinoma or another high-grade malignant neoplasm. Therefore, whenever a poorly differentiated gastric malignancy demonstrates atypical morphological features, additional immunohistochemical evaluation using an appropriate neuroendocrine marker panel should be performed to avoid diagnostic misclassification and to guide appropriate treatment selection.

Several studies have reported gastric collision tumors composed of LCNEC and adenocarcinoma occurring within the same lesion. These tumors are believed to arise either independently from multipotent epithelial stem cells or through divergent differentiation from a common precursor cell. Regardless of the underlying mechanism, LCNEC demonstrates a significantly more aggressive biological behavior than conventional gastric adenocarcinoma, with earlier metastatic spread and poorer survival outcomes [2].

The diagnosis of LCNEC relies on the integration of histopathological morphology and immunohistochemical findings. Typical immunophenotypic features include positivity for neuroendocrine markers such as chromogranin A, synaptophysin, CD56, and pancytokeratins, together with a high Ki-67 proliferation index, although expression profiles may vary among individual tumors [11, 12]. Histologically, LCNEC is distinguished from small-cell neuroendocrine carcinoma by its larger polygonal cells, abundant cytoplasm, lower nuclear-to-cytoplasmic ratio, coarse chromatin, prominent nucleoli, and high mitotic activity [3].

Although the molecular characteristics of pulmonary LCNEC have been extensively investigated, comparatively little is known about the genomic landscape of gastrointestinal LCNEC. Recent studies have identified biomarkers such as programmed death-ligand 1 (PD-L1) expression and tumor mutational burden (TMB) as potential predictors of response to immune checkpoint inhibitors, highlighting the need for further molecular characterization of these rare tumors [6].

Several published reports have described gastric LCNEC with liver metastases at presentation. A Japanese case reported LCNEC involving both the stomach and liver, with focal alpha-fetoprotein (AFP) expression demonstrated by immunohistochemistry [13]. Similarly, Fujimura et al. described a patient with multiple liver

metastases who achieved a partial response after treatment with S-1 plus cisplatin [12]. Another report documented an initial response to platinum-based chemotherapy followed by disease progression requiring gastrectomy because of persistent tumor growth and bleeding [14].

Similarly, the patients presented in our case series demonstrated the aggressive clinical behavior of gastric neuroendocrine carcinoma. Advanced disease at presentation, early metastatic spread to the liver and brain, and poor clinical outcomes despite multimodal treatment were common findings. Although platinum-based chemotherapy remains the recommended first-line treatment for advanced high-grade neuroendocrine carcinomas, the prognosis remains poor even when chemotherapy is combined with radiotherapy and surgery [9]. These observations are consistent with previously published reports and further emphasize the aggressive nature of this uncommon malignancy.

The present study has several limitations. First, it includes only three patients from a single institution, limiting the generalizability of the findings. Second, because of the rarity of gastric LCNEC, standardized diagnostic and therapeutic approaches remain limited. Nevertheless, these cases contribute additional clinical and pathological evidence that may improve recognition of this uncommon entity and facilitate future studies.

In conclusion, gastric LCNEC is a rare but highly aggressive malignancy characterized by rapid disease progression and poor survival. Early recognition, accurate histopathological diagnosis supported by immunohistochemistry, multidisciplinary management, and the accumulation of additional well-documented cases are essential to improve diagnostic accuracy and optimize treatment strategies.

In conclusion, gastric large-cell neuroendocrine carcinoma (GLCNEC) is a rare but highly aggressive malignancy that is frequently diagnosed at an advanced stage and is associated with poor clinical outcomes. As demonstrated in our case series, the definitive diagnosis of GLCNEC may be challenging on limited endoscopic biopsy specimens because of overlapping histopathological features with poorly differentiated adenocarcinoma, other high-grade neuroendocrine neoplasms, and undifferentiated carcinomas. In all three patients, the final diagnosis of gastric large-cell neuroendocrine carcinoma (WHO Grade 3) was established through comprehensive histopathological review integrated with immunohistochemical confirmation of neuroendocrine differentiation. These cases underscore the importance of combining characteristic morphological features with an appropriate immunohistochemical panel, including neuroendocrine markers and assessment of the Ki-67 proliferation index, to achieve an accurate diagnosis.

Despite multimodal treatment incorporating platinum-based chemotherapy, radiotherapy, and surgery when feasible, gastric LCNEC demonstrated an aggressive clinical course characterized by rapid progression, early metastatic dissemination, and limited survival. Continued reporting of well-documented cases with comprehensive pathological characterization and multicentre collaborative studies is essential to improve diagnostic accuracy, refine therapeutic strategies, and enhance the understanding of this uncommon but clinically significant malignancy.

Data Availability Statement

The original contributions presented in this study are included in the article and its Supplementary Material. Further inquiries may be directed to the corresponding author.

Ethics Statement

The study protocol was approved by the Ethics Committee of Sabzevar University of Medical Sciences (Approval No. IR.MEDSAB.REC.1404.018). Written informed consent was obtained from all patients prior to publication.

Author Contributions

All authors contributed to the study conception, data collection, manuscript preparation, and approved the final version of the manuscript.

Funding

This research received no external funding.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Acknowledgements

The authors sincerely thank the staff of the Vasei Clinical Research Development Unit, Sabzevar University of Medical Sciences, for their valuable advice and guidance throughout this research.

References

1. Li Z, Ren H, Zhao L, Zhang X, Wang T, Sun C, Niu P, et al. Better Prognosis of Gastric Neuroendocrine Carcinoma Than Gastric Adenocarcinoma among Whites in the United States: A Propensity Score Matching Analysis Based on SEER. Current Oncology. 2022 07 11;29(7):4879-4892. https://doi.org/10.3390/curroncol29070387
2. Payet E, Pilco PI, Montes J, Cordero-Morales A, Savitzky MJ, Stenning-Persivale K. Collision tumour of large-cell neuroendocrine carcinoma and adenocarcinoma in the stomach: A case report. Ecancermedicalscience. 2016;10:616. https://doi.org/10.3332/ecancer.2016.616
3. Matsui K, Jin XM, Kitagawa M, Miwa A. Clinicopathologic features of neuroendocrine carcinomas of the stomach: appraisal of small cell and large cell variants. Archives of Pathology & Laboratory Medicine. 1998 Nov;122(11):1010-1017.
4. Lamberti G, Panzuto F, Pavel M, O'Toole D, Ambrosini V, Falconi M, Garcia-Carbonero R, et al. Gastric neuroendocrine neoplasms. Nature Reviews. Disease Primers. 2024 04 11;10(1):25. https://doi.org/10.1038/s41572-024-00508-y
5. Capella C. Endocrine tumours of the stomach. World Health Organization Classification of Tumours Pathology & Genetics Tumours of the Digestive System. 2000:53-7...

6. Corbett V, Arnold S, Anthony L, Chauhan A. Management of Large Cell Neuroendocrine Carcinoma. Frontiers in Oncology. 2021;11:653162. https://doi.org/10.3389/fonc.2021.653162
7. Inage T, Nakajima T, Fujiwara T, Sakairi Y, Wada H, Suzuki H, Iwata T, et al. Pathological diagnosis of pulmonary large cell neuroendocrine carcinoma by endobronchial ultrasound-guided transbronchial needle aspiration. Thoracic Cancer. 2018 02;9(2):273-277. https://doi.org/10.1111/1759-7714.12576
8. Metro G, Ricciuti B, Chiari R, Baretti M, Falcinelli L, Giannarelli D, Sidoni A, et al. Survival outcomes and incidence of brain recurrence in high-grade neuroendocrine carcinomas of the lung: Implications for clinical practice. Lung Cancer. 2016 05;95:82-87. https://doi.org/10.1016/j.lungcan.2016.03.006
9. Basuroy R, Srirajaskanthan R, Prachalias A, Quaglia A, Ramage JK. Review article: the investigation and management of gastric neuroendocrine tumours. Alimentary Pharmacology & Therapeutics. 2014 05;39(10):1071-1084. https://doi.org/10.1111/apt.12698
10. Sok C, Ajay PS, Tsagkalidis V, Kooby DA, Shah MM. Management of Gastric Neuroendocrine Tumors: A Review. Annals of Surgical Oncology. 2024 03;31(3):1509-1518. https://doi.org/10.1245/s10434-023-14712-9
11. Terada T, Maruo H. Simultaneous large cell neuroendocrine carcinoma and adenocarcinoma of the stomach. World Journal of Gastroenterology. 2011 Nov 21;17(43):4831-4834. https://doi.org/10.3748/wjg.v17.i43.4831
12. Fujimura Y, Nakahara O, Otao R, Goto H, Baba H. A case of large cell neuroendocrine carcinoma of the stomach with liver metastasis effectively treated with S-1 and CDDP combination therapy. Gan to Kagaku Ryoho. Cancer & Chemotherapy. 2014 03;41(3):369-371.
13. Takahashi K, Nihei T, Aoki Y, Konno N, Nakagawa M, Munakata A, Okawara K, et al. Rapidly progressed large cell neuroendocrine carcinoma of the stomach with an increased serum alpha fetoprotein level: a case report. Clinical Journal of Gastroenterology. 2020 04;13(2):225-232. https://doi.org/10.1007/s12328-019-01041-2
14. Fujimoto H, Ito S, Kawaguchi K, Isobe H, Urayama M, Fuse A, Ota K. [A Case of Large-Cell Neuroendocrine Carcinoma of the Stomach with Multiple Liver Metastases That Show Complete Response to Multidisciplinary Therapy]. Gan to Kagaku Ryoho. Cancer & Chemotherapy. 2019 Oct;46(10):1577-1580.