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Histopathologic Surprise Of Primary Gastric Small Cell Neuroendocrine Carcinoma - A Rare Case Report

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Abstract:
Primary gastric small cell neuroendocrine carcinomas (GSCNEC) are extremely rare, highly aggressive tumours with early and widespread metastasis and poor overall prognosis. Only a few hundred cases were reported in literature. It is usually challenging to confirm the histological diagnosis from a preoperative endoscopic sample. Here, we report a case of 45-year-old male who had upper abdomen pain, weight loss, along with signs of gastric outlet obstruction. Preoperative endoscopic biopsy revealed poorly differentiated carcinoma. He underwent subtotal gastrectomy with D2 lymphadenectomy. Postoperative histopathological examination revealed small cell neuroendocrine carcinoma of the antropyloric region and synaptophysin was positive in more than 90 % of the tumour cells with Ki 67 index of 80%. For locoregional nonmetastatic GSCNEC, aggressive curative surgery can be considered a standard treatment with adjuvant chemotherapy.

Key Word: *Primary gastric small cell carcinoma, small cell neuroendocrine carcinoma, Gastric cancer, Neuroendocrine tumours, carcinoma stomach*

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I. Introduction

In the gastrointestinal system, small cell neuroendocrine carcinomas are uncommon[1]. The most frequent site is the esophagus (53.3%), accompanied by the stomach (11.0%) as well as colorectum (20.3%)[2]. Of all cases of gastric cancer, less than 0.1% are primary gastric small cell neuroendocrine carcinomas (GSCNEC). It has aggressive biological behavior and, even in its early stages, frequently spreads to the liver and lymph nodes.[3] They are more common in men (5.4:1 ratio)[4] and typically appear beyond the age of 60. Particularly when it is advanced, the prognosis for GSCNEC is poorer than that of gastric adenocarcinoma, with a median survival period of nine to twelve months.[5] There is currently no documented conventional treatment plan for GSCNEC due to its exceptional rarity.

II. Case Report

A 45-year-old male with no comorbidities or previous surgery, presented with upper abdominal pain for 1 month, associated with vomiting after food intake for two weeks and significant loss of weight. He was not a smoker but an occasional alcoholic. He had no history of any malignancy in the family. Clinical examination was normal. The lab tests' outcomes remained within the typical range. Upon evaluation, Upper gastrointestinal (UGI) scopy showed circumferential ulceroproliferative growth in the antropyloric region (Figure 1) with scope not passed beyond. Multiple biopsy specimens were obtained. Histopathology revealed poorly differentiated carcinoma (Figure 2) characterized by submucosal neoplasm composed of cells with scant cytoplasm, nuclear pleomorphism, and hyperchromasia. Contrast-enhanced CT of the abdomen with oral contrast revealed circumferential thickening of the antropyloric region for a length of 4 cm (Figure 3) and thickness of 1 cm, with few perigastric nodes, the largest measuring 1.5 *1 cm. Computed tomography of the chest revealed no metastasis. The cardiac and pulmonary evaluation were done and the patient was optimized. Multidisciplinary team (MDT) discussion was done. He underwent open subtotal gastrectomy with D2 lymphadenectomy. Intraoperatively, he had 5*5 cm hard growth involving the antropyloric region (Figure 4,5) with suprapyloric

and infrapyloric nodes. No liver, omental, or peritoneal metastases were noted.

Histopathological examination revealed small cell neuroendocrine carcinoma (Grade 3) of the antropyloric region (Figure 6) with all margins free from the tumour and the presence of lymphovascular invasion was noted. 14 out of 19 lymph nodes retrieved were positive for malignancy. Pathological staging was pT4a N3a Mx and group staging was IIIB. Immunohistochemistry (IHC) showed that synaptophysin was positive in more than 90 % of the tumour cells (Figure 7) with Ki67 index of 80% (Figure 8). On the tenth postoperative day, the patient was discharged following an uneventful course. A multidisciplinary team discussion was made. Since post-operative HPE revealed small-cell neuroendocrine carcinoma, PET CT was done to rule out metastases, which turned out to be negative. He was started on cisplatin and etoposide and doing well on regular follow-up.

III. Discussion

Primary GSCNEC was first reported in 1976.[4,6] There have only been a few hundred primary GSCNEC cases since, mostly in Asian populations.[4,7-9] The lack of prospective and randomized clinical trials due to the disease's rarity has prevented the establishment of comprehensive and explicit treatment guidelines for GSCNEC. However, because of similarities between small-cell lung carcinoma (SCLC) as well as primary GSCNEC in terms of their clinical course, molecular biology, and histology, the same therapeutic approaches are used for both conditions.[2,4]

In terms of clinical presentation, GSCNEC is usually indistinguishable from other gastric cancer histologic categories. The majority of individuals present with weight loss, anemia, dysphagia, as well as epigastric discomfort. GSCNEC has propensity spread to spread to the liver, then to the bones, as well as bone marrow, and it is a form of non-functioning neuroendocrine tumour that lead to their delayed diagnosis.[2] GSCNEC has a reduced preoperative diagnosis rate in endoscopy, most likely due to the small amount of tissue biopsied, the high proportion of cases with composite histology, along the frequent crush effect in the biopsy material.[4] According to Tanemura et al., only 18% of individuals suffering from GSCNEC had an appropriate preoperative diagnosis; 35% of cases were misdiagnosed as common type gastric cancer, 18% as malignant lymphoma, and 18% as undifferentiated carcinoma.[10]

There are two histologic subtypes of GSCNEC: mixed and pure.[6,11] The diagnosis is made by immunohistochemical staining using certain markers (CD56, synaptophysin, and chromogranin).[2,6] The Veterans' Administration Lung Study Group (VALSG) system along with TNM system are the two staging systems in practice.[2,4,11] The TNM staging system is the same as the one employed in gastric cancer.

Surgery is typically done for individuals with GSCNEC who do not have distant metastasis, even though there is currently no clear standard treatment plan.[4] In their retrospective investigation, Ishida et al. found that curative surgery was an independent prognostic factor.[12] Kubota et al. reported critical survival factors are lymph node metastasis and lymphovascular invasion.[13]

The chosen treatment strategy affects the survival of patients. The survival rate for individuals who underwent curative surgery was 6 times higher than that for individuals who did not (46.45 and 7.65 months, respectively)[4,14,15]; additionally, post-operative chemotherapy patients had a two fold greater survival time (48.50 months compared to 19.00 months).[16] With 1, 2, as well as 5-year survival rates of 66.75, 37.13, as well as 20.10%, respectively, those suffering from GSCNEC had median overall survival duration of 18.50 months.[14,17] For locoregional nonmetastatic GSCNEC, curative surgery can therefore be considered a routine treatment.[4,16]

For both early and metastatic disease, platinum-based chemotherapy serves as the cornerstone of treatment.[18] Another first-line treatment option is cisplatin with irinotecan.[19] While concurrent or sequential chemoradiotherapy has been associated with positive results, there is currently little information available concerning the effect of radiotherapy.

IV. Conclusion

The prognosis for GSCNEC, an uncommon aggressive cancer, is not promising. For this disease, a multimodal therapy approach and a careful assessment of every individual's condition by the MDT are highly advised. The MDT must decide on the best plan of action for each case and critically assess the function and order of local treatments (such as radiotherapy or surgery) given either alone or in conjunction with chemotherapy.Considering that there are currently no prospective randomized investigations and that the only data accessible are from treated individuals, this is especially crucial. Aggressive curative surgery combined with adjuvant chemotherapy can be considered a standard treatment for individuals with locoregional non-metastatic GSCNEC.

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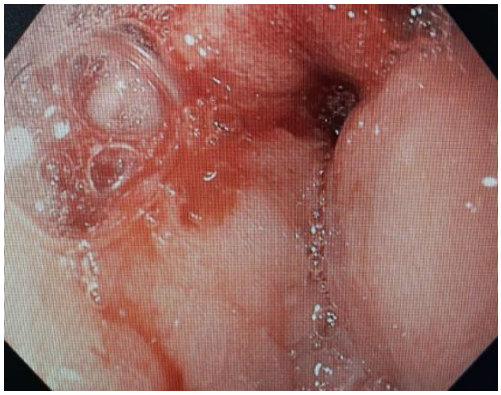

Figure 1 Shows Narrowed Pylorus In Upper GI Endoscopy

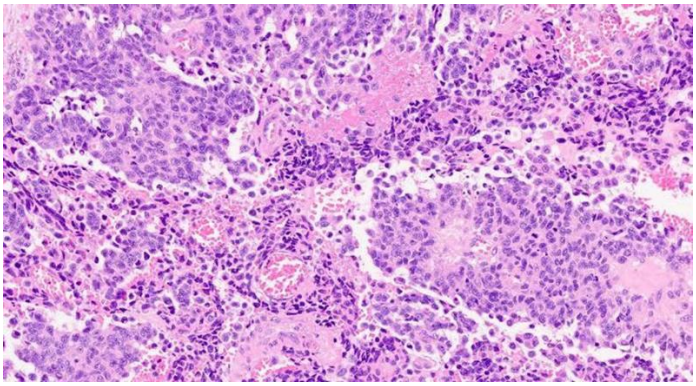

Figure 2 Shows Poorly Differentiated Carcinoma - Cells With Scant Cytoplasm, Nuclear Pleomorphism, And Hyperchromasia.

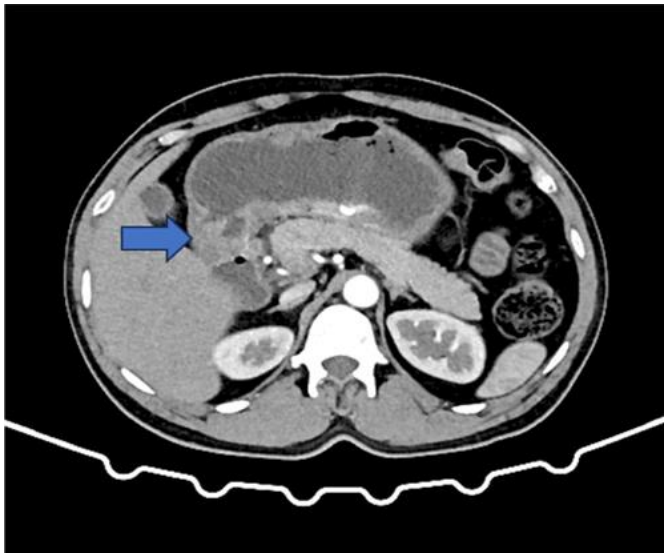

Figure 3 Showing Circumferential Thickening In Antropyloric Region, Marked By Arrow.

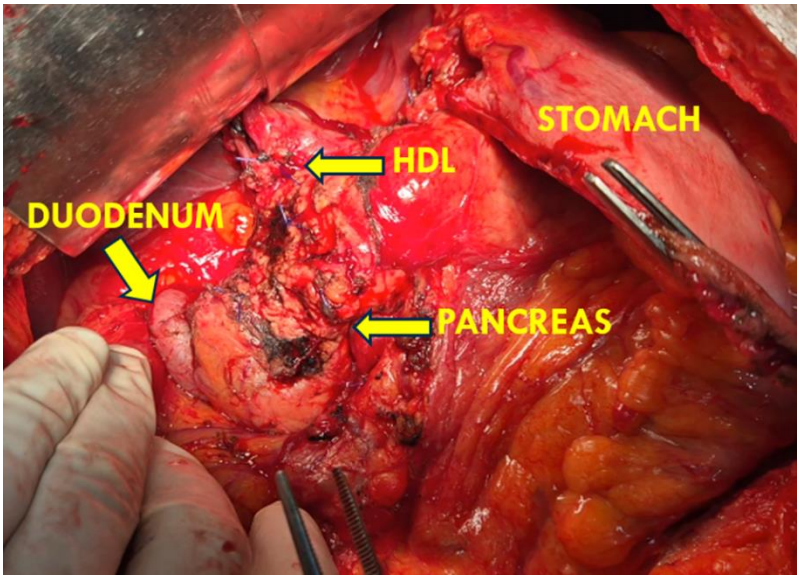

Figure 4 Shows Operative Bed After Removing The Specimen

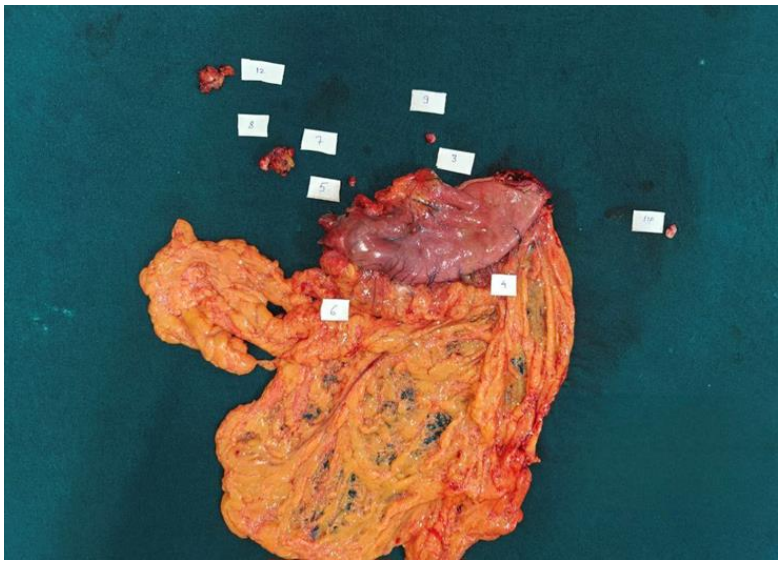

Figure 5 Shows Post Post-Operative Specimen

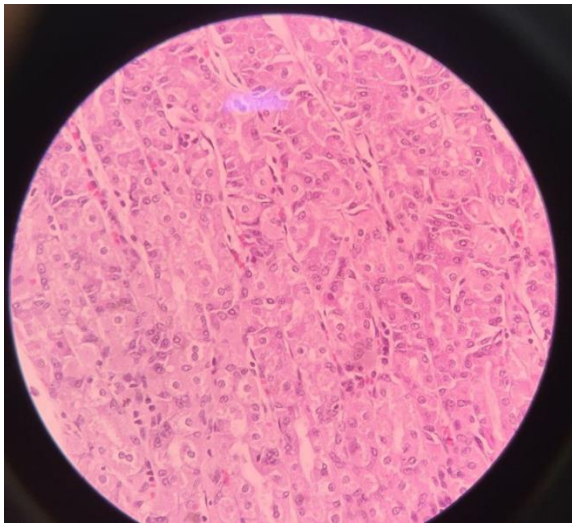

Figure 6 Shows Neoplasm Arranged In An Organoid Pattern And In Trabeculae. The Cells Are Small To Medium-Sized With Round Nucleus, Having Stippled Chromatin.

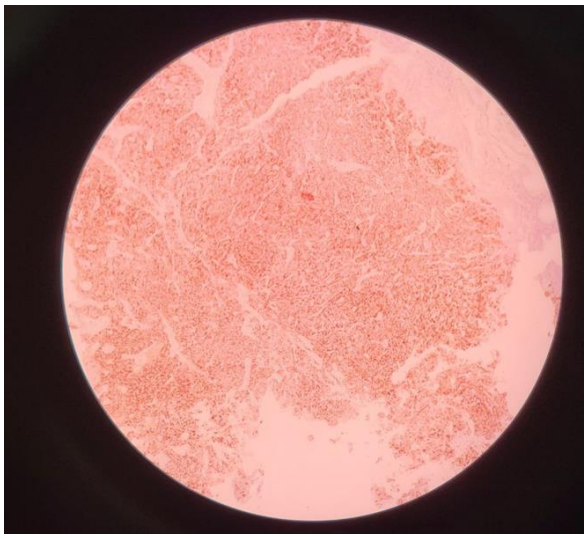

Figure 7 Shows Immunohistochemistry- Synaptophysin - Diffuse Cytoplasmic Positivity For Synaptophsin In All Tumor Cells.

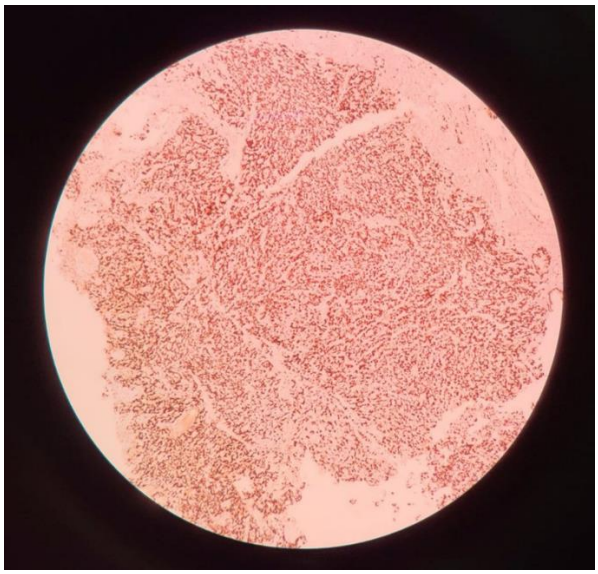

Figure 8 Shows Ki 67 Nuclear Positivity In Tumour Cells