Composite Glandular and Neuroendocrine Carcinoma of the Stomach—Two Case Reports

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Abstract

Introduction: Neuroendocrine tumors develop throughout gastrointestinal tract. The concurrence of mixed adenocarcinoma and neuroendocrine tumor together in the stomach is rare.

Case Report: We report two cases of poorly differentiated carcinoma stomach with neuroendocrine component. These patients underwent radical total gastrectomy with D2 lymph node dissection followed by adjuvant chemotherapy. They are asymptomatic and disease free on follow-up.

Conclusion: Combination of neuroendocrine tumours and adenocarcinoma stomach a rare entity. Pre operative diagnosis with endoscopic biopsy is difficult. However, if there is a suspicion based on endoscopic biopsy, and then Immunohistochemical staining for neuroendocrine tumor markers may help in establishing preoperative diagnosis.

Keywords: Stomach; Neuroendocrine cell carcinomas; Adenocarcinoma; Composite tumour

Introduction

Neuroendocrine tumors of the gastrointestinal tract is rare, they account less than 1% of GI malignancies [1]. The combination of both adenocarcinoma and neuroendocrine tumor together in the gastrointestinal tract is very rare. Gastric neuroendocrine carcinoma arises predominantly from endocrine precursor cells that develop in the preceding adenocarcinoma component. Immunohistochemical staining of the tumor cells are positive for one of the neuroendocrine tumor markers such as chromogranin A, synaptophysin. Adenocarcinoma with neuroendocrine tumors have poor prognosis due to high proliferating biological behavior. Here we report a case of carcinoma stomach, histologically showed poorly differentiated adenocarcinoma with concurrence of neuroendocrine tumor.

Case Report 1

A 57-year-old man presented with abdominal pain and melaena for six months. He had decreased appetite and significant weight loss. He had normal bowel habits. He was a reformed smoker. He was on regular medications for hypertension. Clinical examination was unremarkable. Blood investigations were normal. Oesophago gastroduodenoscopy showed an ulcer proliferative growth in the body along the lesser curve of the stomach, duodenum was normal (Figure 1). HPE of the biopsy was poorly differentiated adenocarcinoma. Contrast enhanced computed tomography of the abdomen and pelvis showed a large, exophytic lesion involving hepatoduodenal ligament, no metastasis to the liver. He underwent total gastrectomy with D2 lymph nodal dissection and Roux-en-Y anastomosis.

The histopathological examination of the surgical specimen showed poorly differentiated mixed adenocarcinoma infiltrating the muscularis propria (Figure 2). Two out of fifteen nodes had metastatic tumor. Tumor cells were synaptophysin positive, focal faint positive for chromogranin and CD 56 (Figure 3). MIB proliferative index was about 50-60%. He received six cycles adjuvant chemotherapy. He was asymptomatic and disease free on follow-up of two years.

Case Report 2

A 42-year-old man was evaluated for upper abdominal pain and loss of appetite for duration of three months. He had had significant weight loss and a few episodes of non bilious vomiting. He had no known co-morbidities. Clinical examination was normal except for visible gastric peristalsis. He was found to have ulcerative growth in the antrum and scope could not be negotiated into the duodenum (Figure 4). Histopathological examination revealed poorly differentiated adenocarcinoma. There were no liver metastases or ascites on CECT of the abdomen. A D2-sub-total gastrectomy was done with Roux-en-Y anastomosis.

Figure 1: CT image showing irregular nodular thickening of the posterior wall of the body of the stomach along the lesser curvature.
Most gastric endocrine cell tumors arise in the setting of hypergastrinemia causing the patient to present with peptic ulcer disease or chronic gastritis [2]. Tumours from the pylorus and antrum may present with symptoms of gastric outlet obstruction.

The biological behaviour of mixed adenocarcinoma of the stomach is significantly more aggressive than that of gastric adenocarcinoma [7]. Therefore preoperative diagnosis may help in assessing prognosis and planning appropriate treatment. These tumors are usually reported as poorly differentiated or undifferentiated tumors on endoscopic biopsy. Therefore appropriate immunohistochemistry may be performed in suspicious cases, in order to achieve a preoperative diagnosis [8].

The histological origin of these composite tumors is unclear. It has been postulated that signet-ring cell carcinomas originate from the gradual dedifferentiation from enterochromaffin-like (ECL) cells through signet ring cells with endocrine immunoreactivity [9]. There are two other hypotheses have been proposed, the first suggesting coincidental neoplastic changes in two different cell types and the second proposing...
Composite neuroendocrine carcinomas with adenocarcinomas in the stomach can be diagnosed if at least one of the neuroendocrine markers, such as chromogranin A, synaptophysin, andNSE, has a positive reaction in the immunohistochemical staining of the neuroendocrine carcinoma component [11]. In our case, the neuroendocrine carcinoma had a strong positive response to synaptophysin positive, focal faint positive for chromogranin and CD 56. MIB proliferative index was about 50-60%.

**Treatment**

Treatment of composite tumors of adenocarcinoma with neuroendocrine cancers that occur in the stomach is radical surgical resection with D2 lymph node dissection and Roux-en-Y anastomosis including the tumours which are less than 2 cm. There is no role for endoscopic resection unlike smaller neuroendocrine tumours of the stomach. In patients with locally advanced adenocarcinoma with type 2 NETs of the stomach secondary to ZES/MEN I syndrome, neo-adjuvant chemotherapy including somatostatin analogs can be initiated for tumor regression [12]. In cases of solitary liver metastasis, radical gastrectomy with hepatectomy is effective treatment [13]. An early metastasis to lymph nodes and liver associated with neuroendocrine tumors due to their aggressive biological behavior. Intensive chemotherapeutic regimens, including cisplatin, doxorubicin, and vincristine can be administered. The adjuvant chemotherapy after gastrectomy has significantly reduced liver and lung metastasis [14]. In patients with multiple metastases confined to liver who are well preserved, and have a patent portal vein, Hepatic arterial embolization is recommended as a palliative option [15].

**Prognosis**

Because of uncertain histopathogenesis and rare occurrence, the clinical behavior and prognosis of composite tumors is still unclear, but Volante et al. [7] reported that the clinical behavior of composite carcinomas depends on the adenocarcinomatous component if the associated endocrine component is well-differentiated and upon the neuroendocrine component if it is poorly-differentiated. Adenocarcinoma with an endocrine component is more aggressive than ordinary adenocarcinoma [8].

**Conclusion**

Combination of neuroendocrine tumours and adenocarcinoma of the stomach is a rare entity. Pre operative diagnosis with endoscopic biopsy is difficult due to focal lesions. Immunohistochemical staining is advised in poorly differentiated adenocarcinoma of the stomach. Neuroendocrine tumors associated with poor prognosis due to high proliferative behaviour.

**References**


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