Case Report

A Rare Case of Esophageal Neuroendocrinal Carcinoma

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Introduction

Neuroendocrinal neoplasms of the digestive tract are well-known entities of disease but remain a relatively rare phenomenon. These tumors lack a specific symptom pattern, creating a diagnostic clinical challenge. Various tools must be implemented. A combination of imaging studies, endoscopic procedures, and histopathological analysis will accurately identify a neuroendocrine tumor. Cell-specific markers are particularly important. These tumor markers classify the neuroendocrine cell of origin. Herein, we present a case of a 41-year-old male diagnosed with an esophageal neuroendocrinal carcinoma who underwent an upper endoscopy due to progressive dysphagia. Our patient was treated with neoadjuvant chemotherapy(carboplatin/etoposide) followed by a distal esophagectomy. Post-operative complications of an anastomotic leak wound dehiscence, and stricture formation required multiple endoscopic wound vacuum and dilation procedures.

Case Presentation

A 41-year-old male with no significant past medical history presents to the Gastroenterologist with symptoms of progressive dysphagia to both solids and liquids. His social history includes a 15-year

smoking history, social alcohol use, and no long-term illicit drug use. Progressive dysphagia, with this age-related alarm symptom, prompted the Gastroenterologist to perform an endoscopic evaluation. Endoscopic results showcased a large, fungating ulcerative mass in the lower third of the esophagus at the gastroesophageal junction and the cardia of the stomach.

This 33-centimeter mass partially obstructed and circumferentially involved one-half of the lumen. Non-erosive gastritis was observed, along with a normally examined duodenum. Biopsies were taken using the cold forceps technique and sent for histopathological analysis. He was instructed to use pantoprazole 40mg oral daily and to sustain a full liquid diet for one week. CT scan of the chest, abdomen, and pelvis with contrast was ordered as well. The pathological report identified a high-grade malignant neoplasm, consistent with a poorly differentiated neuroendocrine tumor of the lower third of the esophagus, cardia, and fundus of the stomach. Immunochemical stains show the tumor to be positive for OSCAR keratin, synaptophysin, and chromogranin.

The tumor was negative for CAM5.2, CK18, and 4A4/p63 markers. Ki-67 stain showed a labeling index >80% and an expression of Rb was retained. Immunostains of AE1/AE3, CD45, and S100 were also negative on these tumor cells. The report concluded that with these staining results and tumor morphology, this tumor is most consistent with a poorly differentiated neuroendocrine carcinoma with a closer relation to the large cell subtype. A second pathologist review proceeded to agree with these findings. The mass appeared to involve all wall layers from the mucosa through the serosa(T3) and two malignant lymph nodes adjacent to the gastroesophageal junction measuring 9mm and 16mm were hypoechoic and well demarcated. CT scan results showed no extra serosal extension, an 11mm celiac axis lymph node, no mediastinal lymphadenopathy or masses, and a 24mm liver lobe lesion. The hepatic lesion was identified as a posterior hemangioma of the right lobe of the liver. An MRI showed no brain metastasis.

The patient was then started on a chemotherapy combination of carboplatin and etoposide. Two cycles were administered followed by a PET scan, which was again followed with two more cycles of chemotherapy. A partial distal esophagectomy with esophagogastrostomy was then performed. Post-surgical complications ensued. An anastomotic leak and dehiscence required multiple endoscopic vacuums assisted therapeutic procedures. The patient also developed peri splenic ascites. Ascitic fluid culture grew E. Coli. It was treated with drainage and the appropriate targeted antibiotic medications. Our patient continued to complain of dysphagia due to an esophageal stricture at the anastomotic site. Multiple dilation therapies relieved his symptoms. Our patient continues to be closely monitored for local recurrence and distant metastasis.

Image -1

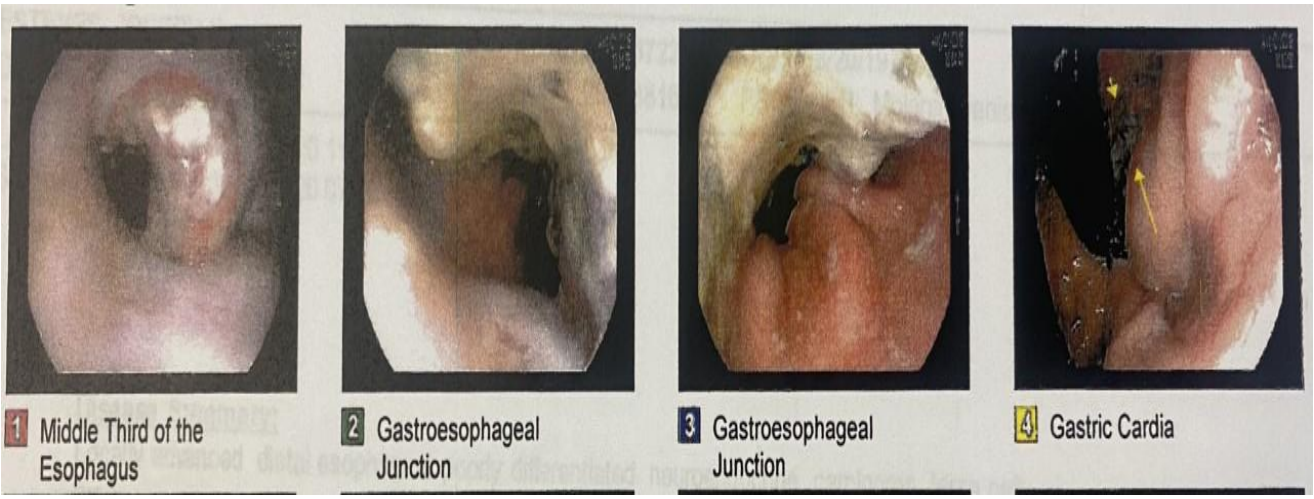
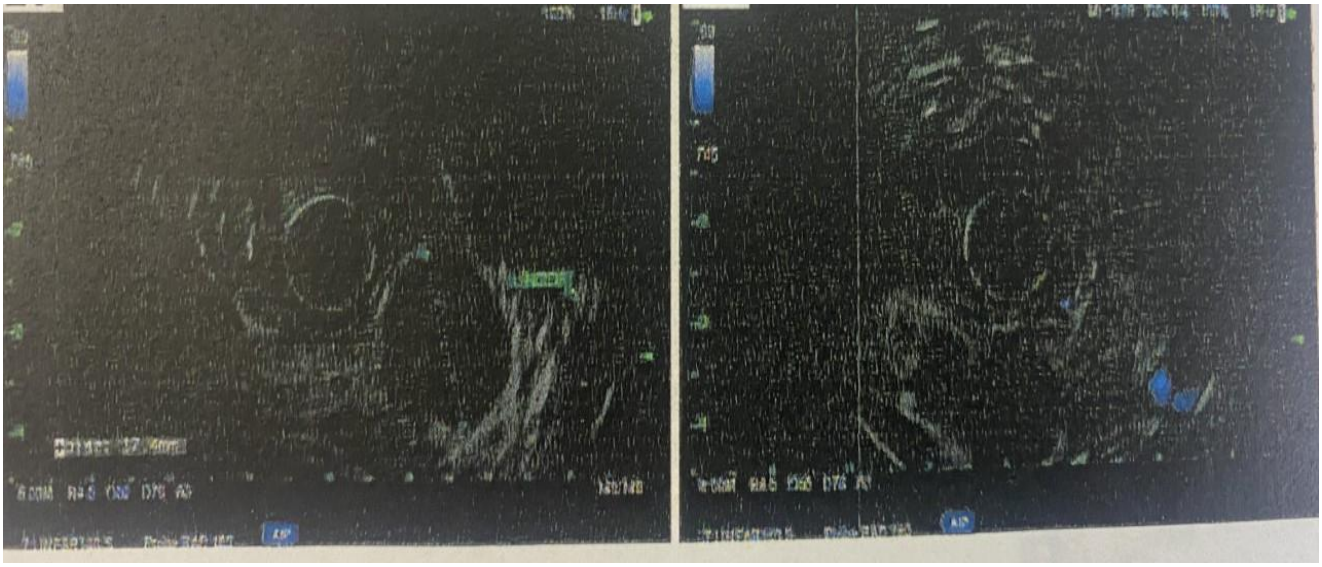


Image - 2



Discussion

Esophageal cancer (Ca) considers one of the top 10 common cancer and leading of death worldwide **(**1**)**, as per American cancer society, in 2020 there was 18440 cases of esophageal CA with Male: Female ratio of 3.5:1 and 16170 expected death cases **(**2**)**. The most common types are consistent with mainly squamous cell carcinoma and adenocarcinoma which represented around 95 % of all esophageal CA **(**3**)** but another kind of cancer can also be originated from the esophagus including neuroendocrinal tumor which considers rare. in the last few years clinicians and pathologists have been facing difficulties in

classifying neuroendocrinal neoplasms; given this complexity and confusion; an organ-specific system has been widely used **(**4**)**. Despite the annual incidence rate of NEN arising from the digestive system is rising in the united states recently but still consider relatively rare with 3.56 per 100,000 population **(**5**)**. Further classification using proliferative rate and local advance is also used dividing the NEN namely into two categories; well-differentiated tumor traditionally called carcinoid neoplasm **(**6**)** and poorly-differentiated tumor that consists of small cell or large cell **(**7**)**.

NEN of the esophageal and gastric cardia consider very rare and usually presented with vague symptoms including chest pain, loss of appetites, weight loss, and dysphagia are commonly reported with a tendency to affect men above the age of 60 years **(**8**)**. The risk factor of these neoplasms is still not well documented but some literature has reported smoking, gastroesophageal reflux disease, or Barrett metaplasia possibly associated with esophageal NECs **(**9**)**. Also, as a transformation from a well-differentiated into poorly differentiated phenotype is uncommon, the presence of a well-differentiated neuroendocrine tumor (NET) is not a risk factor for (NEC). Given the aggressiveness of NEC, more than newly diagnosed case has already distant metastatic disease **(**10 11**)**.

The cell of origin of these neoplasms is not identified but some studies indicate that Kulchitsky cells in the epithelium, which function as amine uptake and decarboxylation cells could be precursor cell of origin **(**12**)**. As pathology and immunohistochemistry are used also to classified this neoplasm by using mitotic count and Ki-67 index into G1, G2, G3, G3 considers as poorly differentiated with mitotic count > 20/10 HPF and > 20% Ki-67 index **(**13 14**)**. the cell tumor usually exhibits essential neuroendocrine markers and potent immunoreactivity to both synaptophysin and chromogranin A **(**15**)** and other less important markers such as CD56, protein gene product 9.5 is also identified. contrast-enhanced CT scan or magnetic resonance imaging (MRI) is the preferred diagnostic workup to show the extent of the disease and if it's NEC, PET-CT is also advised. without forget to mentioned that esophageal NEN requires a EUS (endoscopic ultrasound) for more accurate local staging as lymph node metastases are common **(**16 17**)**.

As brain metastasis is rare the brain MRI of benefits once patient complains of neurological symptoms **(**18**)**. staging system of NENs is still controversial but until now the best practice to follow The World Health Organization (WHO) recommended to use tumor, node, metastases (TNM)-based system as is used by the American Joint Committee on Cancer (AJCC) **(**19 20**)**. Due to a small number of the esophageal NEN and absence of multicentric large studies; the universal recommendation and specific guideline is lack. giving this fact most of the recommendation rising from small studies including case reports and series **(**17**)**. surgical resection and chemotherapy consider the best approach and as NEN is

relatively chemotherapy responsive platinum-based chemotherapy represents the backbone of treatment **(**14**)** which is usually used as neoadjuvant therapy with 4-6 cycle etoposide plus a platinum drug (cisplatin or carboplatin) **(**21**)**.

In contrast, the esophageal NEC consider an exception to this recommendation where most experts preferred using chemoradiotherapy rather than surgery plus chemotherapy supported by multiple studies and even these approaches show better survival **(**22 17 23 24**)**. Partial or complete esophageal resection also carries the risk of procedure-specific complications including but not limited to anastomotic leak, conduit ischemia, anastomotic stricture, chylothorax, hiatal hernia. An anastomotic leak can occur 5-40 % post esophageal resection25 and a risk factor for developing it included obesity, coronary disease, hypertension, diabetes, use of steroid, smoking, procedure duration greater than 5 hours **(**26**)**. Managing this complication could be done by surgical re-exploration **(27)** or endoscopic stenting/transluminal vacuum therapy/ percutaneous endoscopic jejunostomy is widely an acceptable option **(**28 29**)**.

Conclusion

Esophageal neuroendocrinal neoplasms are rare in relation to the more common gastrointestinal tumors arising from this location. The treatment and prognostic challenges are astounding. This is due to the lack of specific protocol guidelines, recommendations, and systematic algorithms. Management centers around chemotherapeutic treatment, in conjunction with surgical procedures. Generally, the prognosis and median survival for these neuroendocrinal tumors remain to be poor. Gastroenterologists are facing an immense obstacle. A recent increase in this subtype of esophageal carcinomas is being observed in our patient population. It is imperative that we conduct a large-scale multicenter clinical study to better understand this gastrointestinal disease entity.

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