**INTRODUCTION**

- Squamous cell carcinoma and adenocarcinoma represent the majority of esophageal cancer cases.
- Esophageal neuroendocrine carcinomas are exceedingly rare but are important to recognize given an increasing incidence.
- Neuroendocrine tumors (NET), defined as epithelial neoplasms with predominant neuroendocrine differentiation, can occur anywhere along the gastrointestinal tract. Primary tumor locations include stomach, pancreas, and large bowel.
- Patients typically present with dysphagia, anorexia and weight loss; chest pain is infrequently reported.
- The World Health Organization (WHO) classifies neuroendocrine tumors as:
  - Well differentiated: show a solid, trabecular, gyriform, or glandular pattern; with fairly uniform nuclei, salt-and-pepper chromatin, and finely granular cytoplasm
  - Poorly differentiated: tend to resemble small cell or large cell neuroendocrine carcinoma of the lung
- The majority of cases are non-functioning while approximately 25 percent are hormonally active. The secretary product varies based on the location of the tumor.
- Well differentiated tumors have a 67% prognosis at 5 years, while the poorly differentiated group typically has a rapid clinical decline within months to years.

**CASE PRESENTATION**

**HP:**
- A 68 year-old male with history of GERD presented with worsening liquid and solid food dysphagia.
- The dysphagia started with solid food and progressed to liquids over the course of several months.
- His past medical history was otherwise unremarkable: specifically, he denied prior tobacco or alcohol abuse and reported no prior endoscopic evaluation for symptoms.

**ROS:**
- Positive: unintentional 5 pound weight loss
- Negative: denied fever, chills, night sweats, nausea, vomiting, abdominal pain, or change in bowels

**Physical Exam Findings:**
- Vitalis: BP 134/76, HR 76, RR 16, Temp 98.9
- General: ill appearing without acute distress
- Cardopulmonary exam: RRR, no murmur or rub, CTA bilaterally
- Abdomen: distended, non-tender, positive bowel sounds, no organomegaly

**Laboratory Studies**
- WBC 10.4, Hgb 13, Platelets 418
- Na 145, K 3.7, Cl - 95, CO2 41, BUN 16, Cr 1.26
- Albumin 4.7; calcium 9
- AST 19, ALT 8 Alk phos 140, total bilirubin 0.4
- He underwent neoadjuvant chemotherapy and radiation followed by transhiatal esophagectomy and cervical primary anastomosis.
- His postoperative course was complicated by functional pyloric obstruction from his vagotomy causing abdominal pain and dysphagia.
- Upper endoscopy with dilatation and botulinum injection provided temporizing relief until planned surgical pyloromyotomy.
- His symptoms of dysphagia, nausea, and vomiting improved but his renal function continued to decline.
- Palliative care was consulted for goals of care and the patient and family elected to proceed with symptomatic management.
- He was discharged home with hospice where he expired soon after from worsening renal function.

**HOSPITAL COURSE**

- The patient was admitted for evaluation of increasing dysphagia, unintentional weight loss and IVF in the setting of an acute kidney injury.
- EGD demonstrated a fungating ulcerated mass located in the middle third of the esophagus along with erythema next to the gastro-esophageal junction, suggestive of Barrett’s esophagus.
- Final pathology results for the mass revealed an infiltrating high-grade epithelial neoplasm, consistent with high-grade neuroendocrine carcinoma, large cell type.
- The immunostains for synaptophysin and vimentin were positive type.

**DISCUSSION**

- Esophageal carcinoma is the 6th leading cause of cancer-related mortality worldwide; US data reports 16,000 new cases annually, and 14,000 deaths.
- Male predominance, usually fifth to sixth decade
- NET Foregut (stomach, duodenum, bronchus, thymus) tumors:  
  - Associated with secretory products: 5-hydroxytryptophan, histamine, and multiple polypeptides
  - Rarely present with carcinoid syndrome
- WHO classification of NET tumor grade is based on expression of Ki-67 (3) and Mitotic count (count per high power field)
  - Well differentiated: low grade <3%
  - Intermediate: 3-20%
  - Poorly differentiated: High grade: >20%
- Forcut NETs can have metastatic spread to the bone.
- **TREATMENT**
  - Treatment of poorly differentiated (high grade) NET is similar to small cell lung cancer
  - Early-stage disease treatment: maximal resection followed by 4-6 rounds of etoposide + platinum drug
  - Extra-pulmonary, poorly differentiated NETs suggest a lower frequency of central nervous metastases compared with pulmonary small cell lung cancer therefore prophylactic cranial irradiation is not pursued.
  - Well-differentiated NETs are indolent and patients can often be effectively managed with expectant observation and serial imaging using triple-phase contrast enhanced CT scanning or MRI

**TAKE HOME POINTS**

- While Esophageal NETs are increasing in incidence overall, the diagnosis remains rare as overall GI NETs occur in 3.5 cases per 100,000 people.
- The clinical presentation of esophageal NETs is essentially identical to squamous cell carcinoma and adenocarcinoma because the tumor is rarely hormonally active.
- Well-differentiated tumors are often indolent and can be effectively managed with expectant observation. In contrast, poorly differentiated tumors are associated with poor progression despite aggressive medical intervention.

**REFERENCES**


**Neuroendocrine Carcinoma: An Uncommon Cause of Dysphagia**

Jay Anderson DO
Department of Internal Medicine; Riverside Methodist Hospital, Columbus, Ohio