Large Cell Neuroendocrine Carcinoma of the Esophagus: A case report

Said Sharawi M.D., Adarsh Sidda M.D., Toni Pacioles M.D.

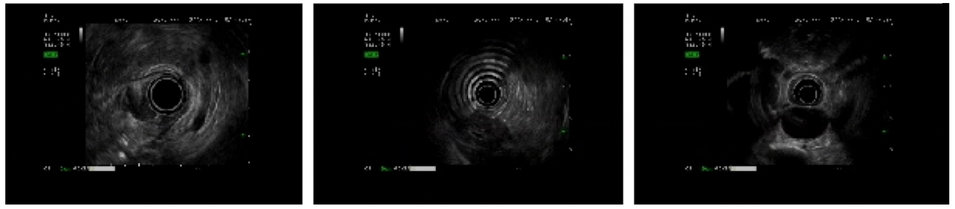
Marshall University Joan C. Edwards School of Medicine, Department of Internal Medicine

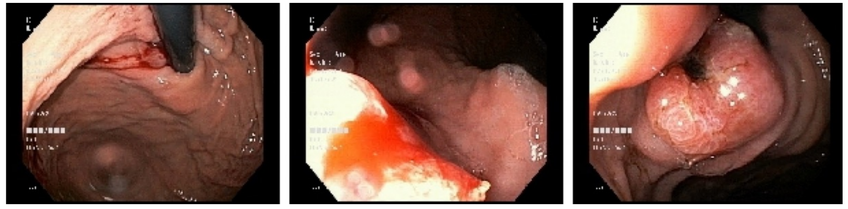
Introduction

Large cell neuro-endocrine carcinomas (NECs) of the esophagus are rare, high-grade tumors with poor long-term prognosis. They are aggressive and metastasize easily compared to adenocarcinomas. Here we present a case of large cell NEC of the esophagus who initially presented with respiratory failure.

Case Description

A 70-year-old male presented to ER with acute respiratory failure requiring intubation with mechanical ventilation. His hospital course was complicated by renal failure and gastrointestinal (GI) bleeding. To evaluate this GI bleed, patient underwent esophagogastroduodenoscopy and colonoscopy which showed a 3 cm ulcerated nonobstructive mass at the gastroesophageal junction which was biopsied. Pathology showed a poorly differentiated NEC, large cell type with a Ki-67 >80%. Immunohistochemistry showed positive CK7, synaptophysin, chromogranin and patchy CD 56+ cells. CK20 was negative. PET scan showed extensive mediastinal lymphadenopathy and right-sided eighth rib metastasis without primary lung lesion. Patient was started on carboplatin, etoposide, and atezolizumab and is currently under treatment.





Discussion

Neuroendocrine tumors are poorly differentiated, high-grade malignant neoplasms diffusely expressing the general markers of neuroendocrine differentiation (synaptophysin, faint or focal staining for chromogranin A) with marked nuclear atypia, multifocal necrosis and a high number of mitoses (>20 per 10 high-power fields). Large cell NECs of the esophagus are extremely rare subtype originating from Merkel cells. These cells are mostly concentrated in the mid-esophagus but may also arise from endocrine cells in the esophageal cardiac glands present in the distal esophagus. 2017 WHO classification divides these neoplasms into well differentiated (grade 1, 2 or 3) or poorly differentiated NEC's (small or large cell) based on tumor's Ki67% values, grading and mitotic index. Large-cell tumors also consist of cells with solid nests or acinar structures, and a low nuclear/cytoplasm ratio. Pathology is the gold standard for establishing diagnosis. Immunohistochemistry staining for NECs is usually negative for p40, p63, CK5/6 while squamous cell carcinomas express them. Compared to NECs, adenocarcinomas typically express napsin A while former do not. Though robust survival data is lacking, prognosis is usually poor, with a 2-year survival of < 20% and a median overall survival of 5 months. There is no established treatment for NEC.

References

1. Yao, JC, Hassan, M, Phan, A. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. J Clin Oncol 2008; 26: 3063–3072.

2. GIOVANNINI, M. (1995). Métastases hépatiques multiples d'une tumeur indifférenciée. Hépato-Gastro & Oncologie Digestive, 2(6), 571-5.

3. Okubo, Y, Yokose, T, Motohashi, O. Duodenal rare neuroendocrine tumor: clinicopathological characteristics of patients with gangliocytic paraganglioma. Gastroenterol Res Pract 2016; 2016: 5257312.

4.Travis, W. D., Linnoila, R. I., Tsokos, M. G., Hitchcock, C. L., Cutler Jr, G. B., Nieman, L., ... & Doppman, J. (1991). Neuroendocrine tumors of the lung with proposed criteria for large-cell neuroendocrine carcinoma. An ultrastructural, immunohistochemical, and flow cytometric study of 35 cases. The American journal of surgical pathology, 15(6), 529-553.

5.Travis, W. D., Gal, A. A., Colby, T. V., Klimstra, D. S., Falk, R., & Koss, M. N. (1998). Reproducibility of neuroendocrine lung tumor classification. Human pathology, 29(3), 272-279.

6. Bosman FT, Carneiro F, Hruban RH, Theise ND. WHO classification of tumours of the digestive system. CAB Direct. 2010;417

7. Kuriry, H., & Swied, A. M. (2015). Large-cell neuroendocrine carcinoma of the esophagus: a case from Saudi Arabia. Case reports in gastroenterology, 9(3), 327-334.

8. Wilson, C. I., Summerall, J., Willis, I., Lubin, J., & Inchausti, B. C. (2000). Esophageal collision tumor (large cell neuroendocrine carcinoma and papillary carcinoma) arising in a Barrett esophagus. Archives of pathology & laboratory medicine, 124(3), 411-415.

9. Ma, Z., Cai, H., & Cui, Y. (2017). Progress in the treatment of esophageal neuroendocrine carcinoma. Tumor Biology, 39(6), 1010428317711313.

10. Deng, H. Y., Ni, P. Z., Wang, Y. C., Wang, W. P., & Chen, L. Q. (2016). Neuroendocrine carcinoma of the esophagus: clinical characteristics and prognostic evaluation of 49 cases with surgical resection. Journal of thoracic disease, 8(6), 1250.