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Case report

Mixed Neuroendocrine-Non-neuroendocrine Neoplasm (MiNEN) of the Esophagus: A Case Report

Domingo Cristina G — Cancer Institute, St. Luke's Medical Center - Global City, Philippines.
Cornelio Gerardo H — Cancer Institute, St. Luke's Medical Center - Global City, Philippines.

Esophageal cancer incidence rates have been increasing over the past years and survival rates remain low. According to the Global Cancer Observatory, 3.1% of new cancer cases consists of esophageal cancer and 5.5% of deaths was due to esophageal cancer. Histologic classification comprises of either squamous cell carcinoma (SCC) or Adenocarcinoma. Other types are reported to be uncommon. We present a case of 33-year old male admitted due to progressive dysphagia. He underwent esophagogastric resection and histopathologic studies revealed a mixed neuroendocrine- non-neuroendocrine tumor. He received adjuvant chemotherapy. On mid-cycle evaluation, the patient showed no evidence of disease recurrence.

Introduction

Mixed Neuroendocrine- Non-neuroendocrine Neoplasm (MiNEN) is a rare cancer of the gastro-entero- pancreatic tract (GEP). In 2017, the WHO defined MiNEN as one of the classification of tumors of endocrine organs. Current data shows that it has an aggressive behavior and majority of the non-neuroendocrine component is of adenocarcinoma histology [1]. They are usually treated based on their non-nueroendocrine component or neuroendocrine component [2]. Preoperative diagnosis of MiNEN is a challenge and it is only diagnosed post- operatively with the addition of immunohistochemistry [3]. There are limited studies in the optimal treatment of MiNEN. We present a case of a patient who underwent esophagogastric resection whose final histopathology revealed MiNEN.

Case Report

A 33-year old previously healthy male initially presenting with a 3-month history of dysphagia to solid food consulted at a private hospital where an esophagogastroduodenoscopy was done.Adistal esophageal mass and a gastric cardia mass were biopsied, which showed esophageal adenocarcinoma. Fluorodeoxyglucose (FDG)-positron emission tomography (PET) scan as metastatic work-up was unremarkable. An esophagogastric resection with esophago- jejunostomy was done. Operative findings showed a 3x6 cm ulcerating mass at the gastroesophageal junction with several lymph nodes identified in the periaortic area. Histopathology revealed a mixed neuroendocrine- non-neuroendocrine neoplasm (MiNEN) of the distal esophagus comprising of moderately differentiated adenocarcinoma and well-differentiated Grade 3 neuroendocrine tumor. Twelve lymph nodes were negative for metastasis. Immunohistochemical stains were positive for chromogranin and synaptophysin. The patient was staged as stage IIB (pT3N0M0) based on the American Joint Committee on Cancer 8th edition (AJCC). He underwent 6 cycles of systemic adjuvant chemotherapy with Oxaliplatin, Folinic acid, and 5- Fluorouracil (FOLFOX). On re-evaluation post 3rd cycle, computerized tomography (CT) scans of the chest and abdomen did not show disease recurrence. FDG-PET scan post 6th cycle showed diffuse hypermetabolic activity in

the esophagojejunostomy, where recurrent disease was not ruled out. The patient has not followed up due to the corona virus disease (COVID-19) pandemic.

Discussion

Esophageal cancer incidence rates have been increasing over the past years and survival rates remain low. According to the Global Cancer Observatory, 3.1% of new cancer cases consists of esophageal cancer and 5.5% of deaths was due to esophageal cancer [4]. Histologic classification comprises of either squamous cell carcinoma (SCC) or Adenocarcinoma. Squamous cell carcinoma has become less common, while adenocarcinoma has been increasing. Other types are reported to be uncommon. In 2010, WHO classified mixed neoplasms from the GEP containing a neuroendocrine and an exocrine component, each representing 30% of the tumor, as mixed adeno-neuroendocrine carcinomas (MANECs). The WHO renamed MANECs as MiNEN to substitute the words exocrine and cancer into non-neuroendocrine and neoplasm in 2017, respectively [1]. These changes in terminology was made to encompass the variability and consider the heterogeneity of the disease. The 2008 Surveillance of Rare Cancers in Europe registry showed that the incidence of MiNENs was less than 0.01/100,000 cases per annum, emphasizing the rarity of the disease. Hence, most data is derived from case reports or small retrospective studies [1]. In the systematic review of Frizziero, et al. in 2020, the site of origin of tumor were as follows: appendix (60.3%), colon-rectum (14.5%), stomach (6.7%), esophagus/esophagogastric junction (5.9%), pancreas (3.7%), biliary tract (1.6%), small bowel (<1%), anus (<1%), and liver (<1%). In addition to this, the study also showed the histology of the non-neuroendocrine component: adenocarcinoma (92.2%), squamous (2.5%), hepatocellular carcinoma (<1%), and a mixture of adenocarcinoma and squamous cell carcinoma (<1%).

The pre-operative diagnosis of MiNEN is a challenge, and the diagnosis is usually post-operative with the aid of immunohistochemical methods. In the systematic review of Frizziero, et al., the initial diagnosis from the first sample collected were as follows: suspicion of MiNEN (36.1%), adenocarcinoma (36.1%), poorly differentiated neuroendocrine carcinoma (21.3%), and well-differentiated neuroendocrine tumor (6.6%) [1].

The treatment of choice for most cases in the systematic review is surgery for potentially curable cases. The choice of chemotherapy is most often based on the recommended clinical practice guidelines for adenocarcinoma from the same site of origin. Our patient received treatment based on the adenocarcinoma component of his neoplasm. There is no consensus for the choice of adjuvant systemic chemotherapy [3].

In conclusion, MiNEN is a group of rare heterogenous neoplasms. There is paucity of data on the optimal treatment due to the rarity of the disease and low incidence. More studies are needed to establish the standard of care for these patients. A multi-disciplinary approach may be of benefit in these cases.

Conflict of Interest

There are no conflicts of interest.

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