Mixed adenoneuroendocrine carcinoma (MANEC) of the gastroesophageal junction: a case report and review of the literature

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ABSTRACT

Esophageal cancer is the fourth most common neoplasm of the gastrointestinal tract. It is responsible for 1.7% of all deaths related with cancer. The two main types of esophageal cancer are squamous cell carcinoma and adenocarcinoma. Other types of esophageal cancer are uncommon. We present a 57-year-old man admitted to the hospital with nausea and vomiting due to a high-grade malignant mixed adenoneuroendocrine carcinoma of the gastroesophageal junction. The patient underwent Ivor-Lewis esophagectomy and adjuvant chemoradiotherapy. At 8-month follow-up he was alive without evidence of recurrence.


INTRODUCTION

Mixed exocrine-neuroendocrine carcinomas, now renamed by the 2010 World Health Organization (WHO) classification as mixed adenoneuroendocrine carcinomas (MANECs) are uncommon tumors (1). They are by definition neoplasms in which each component represents at least 30% of the lesion. MANECs have different morphological features ranging and degrees of differentiation (well to poorly differentiated neoplasm). These tumors have non-specific symptoms and are mainly diagnosed histopathologically and immunohistochemically after surgery. To date, the optimal management strategy is unknown and no therapeutic strategies are recommended, although taking into account the more aggressive component of MANECs seems reasonable.

CASE REPORT

A 57-year-old male was admitted to our department with nausea, vomiting, dysphagia and weight loss. Physical examination and laboratory markers were unremarkable. Upper endoscopy revealed an ulcerative and stenotic mass arising from the mucosa of the gastroesophageal junction. It was initially biopsied and diagnosed as large cell neuroendocrine carcinoma with a Ki-67 proliferation rate of > 95%. Subsequently, regional disease was confirmed by computed tomography and Ivor-Lewis esophagectomy was performed. On histopathological examination the neoplasm showed two distinct components with an abrupt transition. On the one hand, a poorly differentiated adenocarcinoma with some isolated ring cells. On the other hand, a neuroendocrine carcinoma with small cell component arranged in cords was observed (Fig. 1). The neoplasm involved all layers of the gastrointestinal wall, invaded perineural and lymphovascular tissue and infiltrated up to 14 regional lymph nodes (pT3N3M0 stage III-B according to the 7th edition of the American Joint Committee on Cancer TNM classification). On immunohistochemical study, it presented a strong immunexpression of synaptophysin and isolated positivity for chromogranin in the neuroendocrine component (Fig. 2), while a strong immunexpression of periodic acid-Schiff (PAS) was observed in the adenocarcinoma component. In both cases, a high Ki-67 proliferation rate (> 60%) and a strikingly positivity for citokeratin-7 and E-cadherin was detected. Therefore, according to the current WHO criteria the final pathological diagnosis was high-grade malignant MANEC of the gastroesophageal junction.

DISCUSSION

Esophageal cancer is the fourth most common tumor of the gastrointestinal tract, and it is responsible for 1.7% of all cancer-related deaths. It is usually three to four times more common among men than among women. The two
in the literature as a case report. They are, by definition, neoplasms in which each component (exocrine and neuroendocrine differentiation) represents at least 30% of the lesion, and have usually different morphological features ranging and degrees of differentiation (well to poorly differentiated). The first description was published by Cordier in 1924 (3). Since then, several cases have been reported using different names. In 2000 the WHO classification defined them as mixed exocrine-endocrine carcinomas, and renamed them as mixed adenoneuroendocrine carcinomas (MANECs) ten years later (4). However, this classification did not contemplate subcategories assessing the grade of malignancy of each component, which helps to improve and standardize therapeutic protocols. Thus, in 2012, Rose et al. (5) stratified gastrointestinal MANECs in different prognostic categories: a) High-grade malignant MANECs (adenomatous or carcinomatous component and a poorly differentiated neuroendocrine carcinoma); b) Intermediate grade malignant MANECs (adenomatous or carcinomatous component with different degrees of differentiation, and differentiated neuroendocrine tumor or amphicrine carcinoma); and c) Mixed adenoneuroendocrine tumor (adenoma and well differentiated neuroendocrine tumor). Because MANECs neoplasms are rare entities, to date few aspects are known about their clinical presentation, histogenesis or treatment. No specific symptoms or carcinoid syndrome have been reported in the literature and little is known about their origin, although most authors admit this could be in a multi-potent stem cell with bidirectional differentiation (6-8). Diagnosis is mainly based on the neoplasm architecture, completed by the immunostains with specific neuroendocrine markers (chromogranin, synaptophysin, CD56 or neuron-specific enolase) combined with the markers on non-endocrine differentiation (9). To date, the optimal management strategy is unknown and no therapeutic strategies are recommended, although it seems reasonable to take into account the more aggressive component of MANECs (10). According to the 2010 WHO classification, surgery seems to be the treatment of choice, and adjuvant chemotherapy can be administered after surgery, although there is insufficient evidence about its effectiveness.

In conclusion, we report an uncommon case of high-grade mixed adenoneuroendocrine carcinoma of the gastroesophageal junction, categorized by the 2010 WHO classification as MANEC. Because of its uncommon presentation, to date little is known about the optimal management strategy and more studies are needed to recommend new therapeutic strategies.

REFERENCES