

Case Report

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An esophageal neuroendocrine tumor with initial present dysphagia: A case reportSepide Shirchi¹; Alireza Kashian¹; Hossein Ghorbani²; Javad Shokri-Shirvani^{3*}¹Student Research Committee, Babol University of Medical Sciences, Babol, Iran.²Department of Pathology, Rohani Hospital, Babol University of Medical Sciences, Babol, Iran.³Department of Internal Medicine, Rohani Hospital, Babol University of Medical Sciences, Babol, Iran.***Corresponding Author: Javad Shokri-Shirvani**Department of Internal Medicine, Rohani Hospital,
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Abstract

Introduction: Neuroendocrine Neoplasms (NENs) of the esophagus are exceedingly rare, representing 1.3% of gastrointestinal NENs and 0.4%-2% of all esophageal malignancies. Esophageal NENs are classified into well-differentiated Neuroendocrine Tumors (NETs) and poorly differentiated Neuroendocrine Carcinomas (NECs). Esophageal NETs commonly present with dysphagia, weight loss, and appetite loss.

Case report: A 70-year-old male with a history of GERD presented with progressive dysphagia and weight loss. Endoscopy revealed an ulcerative lesion, which was confirmed to be a small cell neuroendocrine carcinoma through biopsy and immunohistochemistry. A PET scan indicated a stage III tumor with locoregional lymph node involvement. The patient initiated chemotherapy and, symptomatic improvement was reported after two cycles.

Conclusion: We present a case of esophageal Small Cell Neuroendocrine Carcinoma (SCNEC) characterized by initial symptoms of dysphagia and weight loss. Given the rarity of this malignancy and the absence of a well-established standard treatment and staging system for Neuroendocrine Carcinomas (NECs), the management of patients and prediction of patient prognosis pose considerable challenges.

Keywords: Neuroendocrine neoplasm; Esophageal cancer; Small cell carcinoma; Dysphagia.

Introduction

Neuroendocrine Neoplasms (NENs) of the esophagus are extremely rare, comprising 1.3% of all NENs arising from the gastrointestinal tract and between 0.4% and 2% of all malignancies of the esophagus [1,2]. The 2019 World Health Organization (WHO) Classification for the digestive system categorizes NENs into well-differentiated Neuroendocrine Tumors (NETs) and poorly differentiated Neuroendocrine Carcinomas (NECs) based on their molecular differentiation. NETs can be subdivided into three grades based on the mitotic rate and Ki-67 index, while NECs are considered high grade and can be subdivided

into Large-Cell type (LCNEC) and Small-Cell type (SCNEC) according to the nucleus/cytoplasm ratio, cell shape, chromatin, and nucleoli [3]. The most common symptom of esophageal NETs is dysphagia, followed by weight and/or appetite loss. Retrosternal and epigastric pains, odynophagia, dysphonia, dyspnea, and digestive bleeding (hematemesis and melena) have also been reported as less frequent clinical features [4]. Standardized guidelines for staging and managing esophageal NENs have not yet been described due to their rarity. This report describes a 70-year-old male diagnosed with small cell cancer of the esophagus.

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Case report

A 70-year-old male who presented with a six-month history of progressive dysphagia to solid foods associated with weight loss attended the gastroenterology clinic in September 2023. He denied retrosternal and epigastric pain, gastrointestinal bleeding, or fever. He had a history of Gastroesophageal Reflux Disease (GERD) for several years and was managed with Proton Pump Inhibitors (PPIs). The patient's past medical history, apart from GERD, was unremarkable. He also reported no use of alcohol or tobacco. On physical examination, the patient exhibited a normal head and neck and a soft, nontender, non-distended abdomen, indicating no apparent organomegaly or lymphadenopathy. The initial laboratory test results, including complete blood count, basic metabolic panel, and liver function test results, were within normal ranges. The patient underwent Esophagogastroduodenoscopy (EGD), which revealed a 1.5x1.5 cm ulcerative lesion precisely situated at the 10 cm mark from the gastroesophageal junction (Figure 1). Biopsy obtained via endoscopy demonstrated the presence of small cell neuroendocrine carcinoma. According to the Immunohistochemistry (IHC)

results, TTF1 (Transcription Termination Factor 1) exhibited positivity in a subset of neoplastic cells, while synaptophysin demonstrated strong immunoreactivity; however, no immunoreactivity was observed for chromogranin or CK5/6 (cytokeratin 5/6) (Figure 2). A Positron Emission Tomography (PET) scan indicated a hypermetabolic tumoral mass in the middle thoracic esophagus, confirming the existence of the known malignancy. Furthermore, there was locoregional lymph node involvement in the right paratracheal region (CNI), with no indication of hypermetabolic tumoral lesions in other imaged areas of the body. The involvement of locoregional lymph nodes without evidence of distant metastases confirmed stage III poorly differentiated small cell neuroendocrine carcinoma. The patient initiated chemotherapy in November 2023, during which he underwent two cycles per month. Thus far, the treatment has been well-tolerated, and the patient has reported improvement in his initial symptoms.



Figure 1: Esophagogastroduodenoscopy.

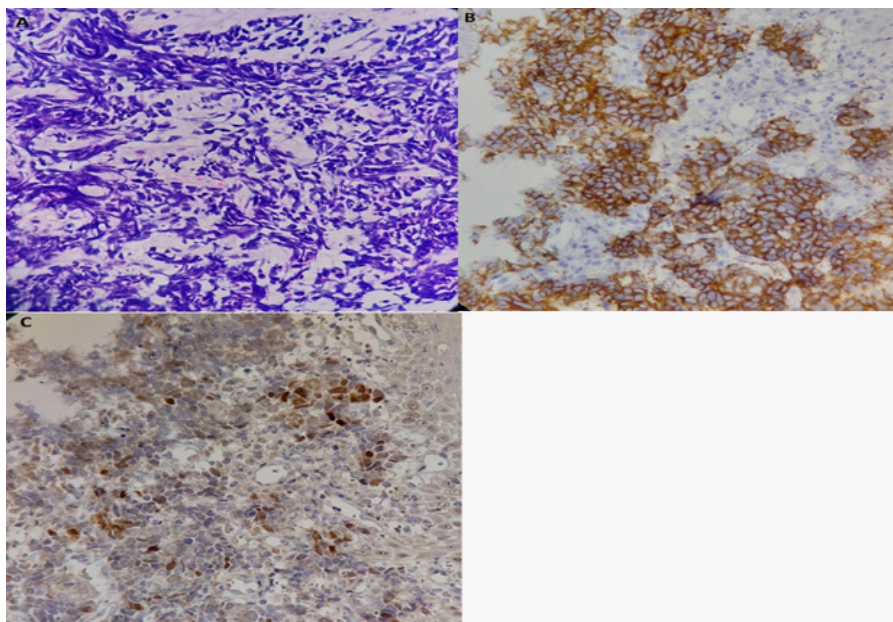


Figure 2: **A)** Sheets of small neoplastic cells with a high N/C ratio, hyperchromatic nuclei and scant eosinophilic cytoplasm associated with nuclear molding and crushing artifacts [Hematoxylin and eosin (H&E) $\times 400$] **(B)** Strong cytoplasmic synaptophysin expression in tumor cells. **(C)** Occasionally expressed nuclear TTF1 in tumor cells.

Discussion

The incidence of neuroendocrine neoplasms of the esophagus varies geographically, generally constituting a rare type of NEN. Tutsumi et al. reported that of 2957 patients, 98% had SCNEC (23% in Western countries; 77% in Eastern countries), 1.18% had LCNEC (94% in Western countries; 6% in Eastern countries) and 0.82% had carcinoid tumors (43% in Western countries; 54% in Eastern countries). Esophageal SCNEC demonstrated a predominant prevalence in men, with a mean age of 63.8 years [5]. According to Schizas et al. dysphagia remains the most prevalent presenting symptom. The most frequent endoscopic finding was a single elevated polypoid or nodular lesion [6]. In contrast, the endoscopic findings of our patient revealed an ulcer type tumor. The risk factors for esophageal Small Cell Neuroendocrine Carcinoma (SCNEC) are generally smoking and alcohol consumption, similar to those for Squamous Cell Carcinoma (SCC) [7]. However, due to its rarity and lack of adequate data, the causal relationship between these factors and SCNEC has not been strongly established. It is noteworthy that our patient was a lifelong nonsmoker and did not consume alcohol. Our patient exhibited regional lymph node involvement according to the findings from the PET scan. Based on Tutsumi et al.'s research, among 423 patients with Small Cell Esophageal Neuroendocrine Carcinoma (SCNEC), 63% were diagnosed with distant metastasis, while 22% and 15% of the patients were diagnosed with regional and localized disease, respectively. At present, there is no established standard treatment for NECs, and esophageal NENs were not included in the 8th edition of the AJCC/UICC TNM staging system [8]. This can pose a challenge in evaluating the prognosis and management of patients. Large-scale research is required to develop a standardized staging system and treatment algorithm.

Conclusion

We present a case of esophageal Small Cell Neuroendocrine Carcinoma (SCNEC) with initial symptoms of dysphagia and weight loss. The diagnostic journey revealed regional lymph node involvement, and the patient started chemotherapy two months after the initial visit. Extensive research is needed to establish a standardized staging system and treatment algorithm.

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