Primary Esophageal Small Cell Neuroendocrine Carcinoma in a Child: A Case Report with Review on Demography, Presentation, Treatment, and Survival

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Abstract

Primary gastrointestinal small cell carcinoma is reported 0.1%–1.0% of malignant gastrointestinal tumors and predominantly in the esophagus. All reported cases are in the adult population. We present a 9-year-old boy with small cell neuroendocrine carcinoma of the esophagus with mediastinal lymph node involvement, whose chief complaint was progressive dysphagia. He survived for 22 months with chemoradiation but did not have resectional surgery. Although small cell neuroendocrine carcinoma of the esophagus is extremely rare in children, it should be considered in the differential diagnosis of any undifferentiated tumor of the esophagus in any age.

Keywords: Child, esophagus, neuroendocrine tumor, small cell carcinoma

INTRODUCTION

The current incidence of neuroendocrine tumors (NETs) is about 6 in 100,000 in adults and about 2.8 per million in children. The most common locations of NETs are gastrointestinal tract and lung, but they can be seen in many organs.1 The most common organs for small cell neuroendocrine carcinoma include lung, gastrointestinal tract, genitourinary system, gynecologic organs, and head-and-neck region.2

Primary gastrointestinal small cell neuroendocrine carcinoma is reported 0.1%–1.0% of malignant gastrointestinal tumors and predominantly in the esophagus.3 All reported cases are in the adult population. The latest case of esophageal carcinoma reported in children was a 14-year-old child from Iran with squamous cell carcinoma.4

Here, we present the youngest patient with esophageal small cell neuroendocrine carcinoma up to now. There is no previous report of small cell neuroendocrine carcinoma of the esophagus in children.

CASE REPORT

A 9-year-old boy presented with progressive dysphagia from 2 months ago after obtaining patient consent. He had no heart burn or weight loss. All laboratory data were in the normal limit. In computed tomography (CT) scan, increase in esophageal thickness reported in entire of its length [Figure 1].

Upper endoscopy achieved and intraluminal polypoid mass leading to narrowing of esophageal lumen is noted. Several biopsies undertaken and prepared slides revealed neoplastic proliferation of small tumoral cells with high N/C ratio, pleomorphism, and marked mitotic activity with necrosis [Figure 2]. Furthermore, striated muscle invasion was noted. In immunohistochemistry (IHC) study, cytokeratin and...
neuron-specific enolase were positive diffusely, chromogranin, and synaptophysin focally and leukocyte common antigen and Vimentin were negative. Ki67 was positive in 50% of tumoral cells [Figure 3]. The diagnosis was high-grade small cell neuroendocrine carcinoma. Furthermore, two resected mediastinal lymph nodes were involved, and hence, the patient is categorized in the extensive stage.

The patient referred to oncologist and received standard chemotherapy and radiotherapy but not resection surgery. Unfortunately, after 22 months, he expired for the recurrence of tumor.

**Discussion**

NET according to the WHO definition reveals positive endocrine marker in IHC study, such as synaptophysin, chromogranin A, and CD56. The origin cell of NEC of the esophagus is not known, but possible origins are Merkel, stem, or Cajal cells.[5]

In the last decades, a rise in NET incidence has been occurred. The Kentucky Cancer Registry evaluating 6179 NET patients and reported increase in the incidence rate from 3.1 in 1995-7.1 in 2015 per 100 000 population in the linear pattern.[1] The incidence rate of esophageal cancer is high in Northern provinces of Iran and makes the “esophageal cancer belt” region.[2]

In various studies, the median age of the patients’ is 61, 58, 69, and 59 years at the time of diagnosis and with a male-to-female ratio of 0.46 and 3.7.[2,3,6] Furthermore, in Jeen study, 48% of patients were older than 65 and 52% were younger but all were adult with the male-to-female ratio of 1.[7] There are a few reports of esophageal carcinoma in children, but most of them are squamous cell carcinoma and some are adenocarcinoma, but there is no report of small cell neuroendocrine carcinoma of the esophagus under the age group of 18 years in the literature. The latest case reported was an 8-year-old child from India. Another reported case is esophageal squamous cell carcinoma in a 14-year-old boy.[4] Our case is the only reported small cell neuroendocrine carcinoma in children.

The most common presenting symptom in affected patients was dysphagia. Weight loss was the second common symptom. Other complaints were chest pain, hot flushes, and abdominal discomfort. Melena was reported in only one patient. No patient presented with typical carcinoid symptoms.[6,2,1] Our case presented with progressive dysphagia from 2 months ago but no weight loss or carcinoid syndrome.

The most prevalent endoscopic finding was ulcerative tumors. However, some cases had polypoid lesions and some had no specified lesions. In upper gastrointestinal series, some patients had only mucosal irregularity, whereas stenosis and filling defect were reported in others.[2] CT scan of our patient revealed esophageal thickening and in endoscopy narrowing of the esophageal lumen, and polypoid mass was noted.

Small cell neuroendocrine carcinoma of the esophagus is a rare tumor, and it makes difficult to conduct a randomized clinical trial. Thus, selecting treatment modality relies on retrospective studies.[8]

Systemic chemotherapy should always be the part of multimodality treatment. Most long-term survivors received treatment including surgery.[9] In patients with extensive disease, concurrent or sequential chemoradiation or only radiotherapy was the modalities of treatment. Surgical procedures alone can be recommended for Stage I/IIA patients.[2,7,8] A few after neoadjuvant chemoradiation or chemotherapy underwent surgery, one patient after endoscopic mucosal resection received chemoradiation.[2,7] Our patient according to lymph node involvement was not candidate for surgery and only received chemotherapy and radiotherapy.

After esophageal surgery, quality of life took a year to recover to baseline usually. Many surgically treated patients live only a few months, and their entire remaining life has low quality.[10] The median survival was reported various in studies; it is reported 16, 11, 12.5, and 13.5 months.[3,7,2,9] The median survival time was 3.53 years in Lei Ye study.[6]
The median survival of patients with limited disease was 20.5 and 17 months, whereas it was 4.5 and 8.5 months for patients with extensive disease. Survival at 1, 3, and 5 years was 65%–52.2%, 30%–15.9%, and 22%–12.2%, respectively (7.3). Our patient expired after 22 months due to infield recurrence.

Although small cell neuroendocrine carcinoma of the esophagus is extremely rare in children, it should be considered in the differential diagnosis of any undifferentiated tumor of the esophagus in any age.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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