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Epigastric Pain and Dysphagia in a 36-Year-Old Man Due to Primary Esophageal Small Cell Carcinoma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 Parisa Aijaz
E 2 Muhammad Ahsen Niazi
AF 3 Harleen Kaur Chela
DF 3 Kamran Zahid
AEF 3 Ebubekir Daglilar

1 Department of Internal Medicine, Charleston Area Medical Center, Charleston, WV, USA
2 Department of Internal Medicine, Dow Medical College, Karachi, Pakistan
3 Department of Gastroenterology, Charleston Area Medical Center, Charleston, WV, USA

Corresponding Author: Parisa Aijaz, e-mail: Parisa.aijaz@gmail.com
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Patient: Male, 36-year-old
Final Diagnosis: Primary small cell carcinoma of the esophagus
Symptoms: Dysphagia • epigastric pain
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology • Oncology

Objective: Rare disease

Background: Small cell carcinoma is an aggressive malignant neuroendocrine tumor that most commonly occurs in the lung. Primary small cell carcinoma of the esophagus (PSCCE) is rare and is an aggressive malignancy with poor prognosis and no clear management guidelines. This report describes the case of a 36-year-old man presenting with epigastric pain, dysphagia, and melena due to a primary esophageal small cell carcinoma.

Case Report: A 36-year-old presented to the Emergency Department (ED) with epigastric pain associated with food intake. Initial workup was unremarkable, and a presumed clinical diagnosis of reflux esophagitis and peptic strictures was made, prompting empiric treatment with anti-secretory therapies. Despite these therapies, he presented to the emergency room with progressively worsening dysphagia. Endoscopic examination (EGD) revealed a large necrotic mass, and computed tomography (CT) imaging revealed liver metastasis. Biopsies from both the liver and esophageal masses confirmed small cell carcinoma. His clinical course was complicated by a broncho-esophageal fistula, leading to massive hemoptysis, necessitating intubation. Unfortunately, his condition deteriorated rapidly, and he chose to pursue hospice care. He died 3 months after his initial presentation.

Conclusions: This report has presented a rare case of primary esophageal small cell carcinoma and our approach to management. We highlight the importance of early diagnosis, supported by histopathology, and the need for management guidelines.

Keywords: Carcinoma, Small Cell • Case Reports • Esophageal Neoplasms

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Introduction

Primary esophageal small cell carcinomas (PSCCE) are rare, accounting for only 0.1-2.8% of all esophageal cancers worldwide [1-3]. In the United States, the reported incidence is approximately 0.5-0.8% [4,5]. Patients usually present with progressive dysphagia and weight loss [6]. Diagnosis is made by gastroscopic biopsy and subsequent immunohistochemistry [7]. Management consists of surgical esophagectomy in limited disease [8,9] and systemic chemotherapy in metastatic disease [10]. Few cases of PSSCE have been reported in the literature [11-13]. This report describes the case of a 36-year-old man presenting with epigastric pain, dysphagia, and melena due to a primary esophageal small cell carcinoma.

Case Report

Our patient was a 36-year-old man with no pertinent past medical history. He presented to the Emergency Department (ED) with dull epigastric pain that was worse with meals and was associated with a sensation of food being stuck in the middle of his chest. Computed tomography (CT) of the abdomen was unremarkable and he was discharged with proton pump inhibitors and an outpatient gastroenterology referral. At his outpatient gastroenterology appointment, he reported progressively worsening epigastric pain, dysphagia, decreased appetite, weight loss, and dark tarry stools. He denied smoking, alcohol consumption, and gastroesophageal reflux disease (GERD). He was scheduled for a diagnostic upper endoscopy (EGD) but presented to the ED again with worsening symptoms. CT abdomen in the ED reported lymphadenopathy (LAD) in the gastrohepatic space and multiple liver lesions. These were new findings compared to a CT abdomen a week prior (**Figure 1**). EGD at this time revealed an 8-cm friable necrotic mass in the lower esophagus, obstructing three-fourths of the lumen (**Figure 2A**). Ulcerations with a sinus tract at the base were noted. A biopsy was obtained and the procedure was aborted to evaluate the patient for a possible tracheaesophageal fistula, which was then ruled out with a negative CT chest. The pathology results revealed round cells with scant cytoplasm and atypical nuclei, immuno-stains were diffusely positive for synaptophysin (**Figure 3**), and the Ki-67 index was >90%. A biopsy of the liver masses (**Figure 4**) was also obtained, which reported similar histologic findings to the primary esophageal mass. We did not identify a lung mass on imaging, which made it less likely that a primary lung mass was invading the esophagus and nearby structures. Acknowledging this and the presence of a large esophageal mass, we diagnosed the patient with stage IV primary esophageal small cell carcinoma (PSCC). A palliative esophageal stent was placed (**Figure 2B**), and he was discharged home. Ten days after discharge, the patient returned with intractable hemoptysis and was intubated for airway protection. Bronchoscopy revealed a broncho-esophageal fistula caused by direct tumor invasion. His condition deteriorated rapidly, and he opted for palliative care and was transferred to inpatient hospice. He died 3 months after his initial presentation.

Discussion

We present a 36-year-old man who presented with progressive dysphagia and was diagnosed with stage IV primary small

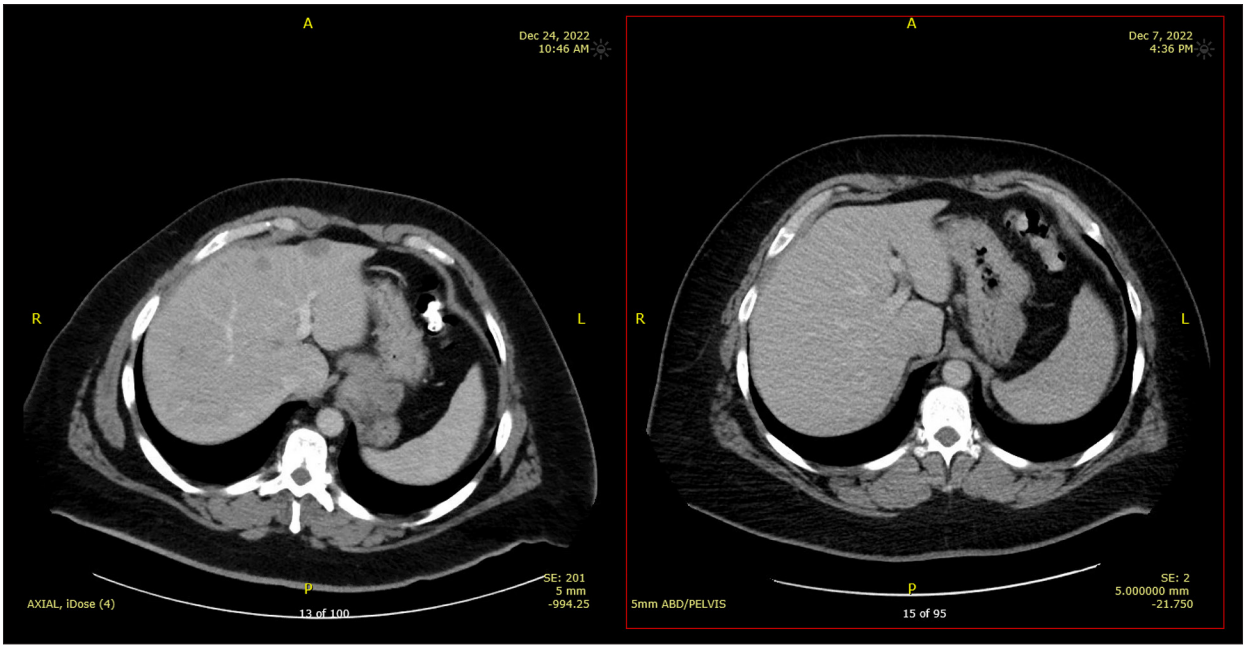

Figure 1. Computed tomography (CT) abdomen exhibiting new liver metastasis (L) compared to CT abdomen 1 week prior (R).

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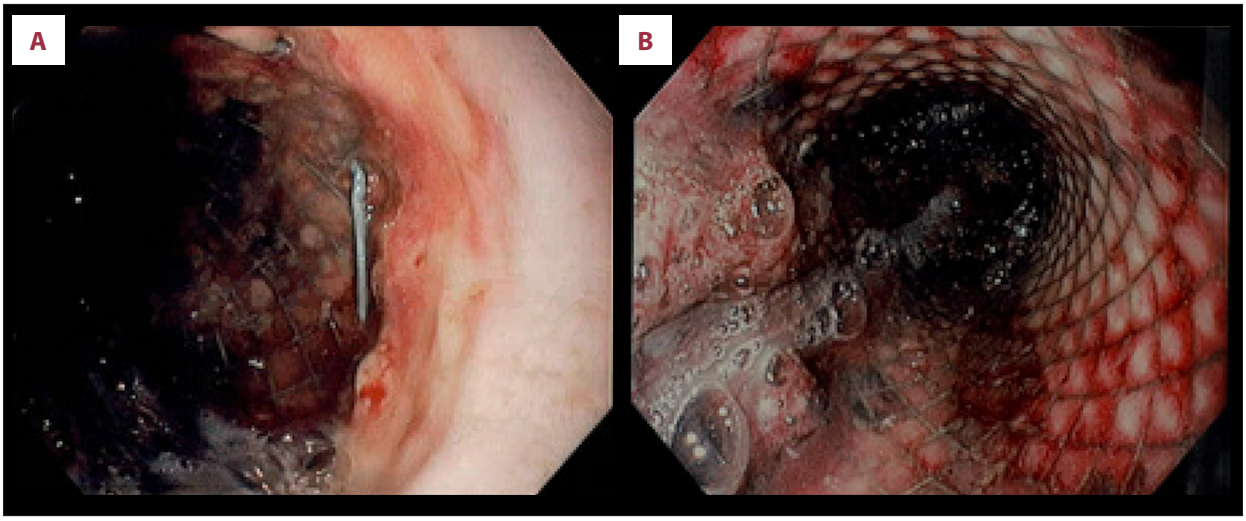

Figure 2. (**A**) An 8-cm friable necrotic mass seen in the lower esophagus during endoscopic evaluation, obstructing three-fourths of the lumen. (**B**) An esophageal stent placed via upper endoscopy with palliative intent for dysphagia symptom relief.

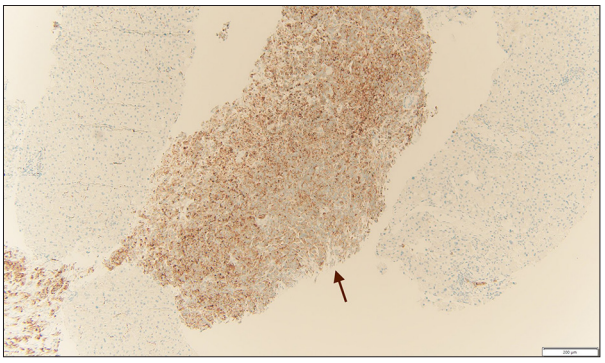

Figure 3. Photomicrograph of the immunohistochemistry for synaptophysin, a neuroendocrine marker, of a small cell carcinoma of the esophagus in a 36-year-old man. The immunohistochemistry for synaptophysin shows positive (brown) immunostaining of the malignant small cells.

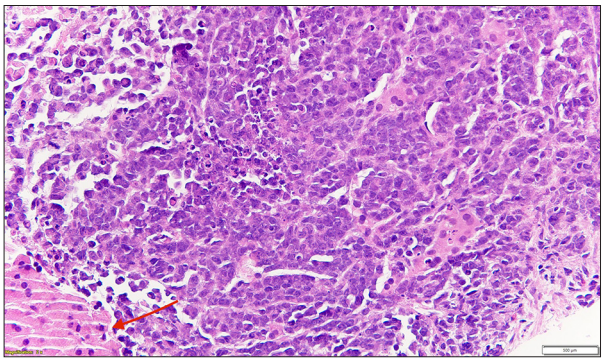

Figure 4. Photomicrograph of the diagnostic histopathology of a small cell carcinoma of the esophagus in a 36-year-old man. The histology shows atypical small cells with little cytoplasm and multiple mitoses arranged in cords and nests. No squamous or glandular differentiation is seen. Hematoxylin and eosin (H&E).

cell carcinoma of the esophagus (PSCCE). He had no discernible risk factors and no known family history of malignancy. We highlight the importance of keeping a high index of suspicion for underlying malignancy in patients presenting with progressively worsening dysphagia, even in young patients who lack obvious risk factors and do not fit the expected demographic profile.

Esophageal small cell carcinoma is rare, accounting for only 0.1-2.8% of all esophageal cancers worldwide [1-3]. The reported incidence in the United States is approximately 0.5-0.8% [4,5]. It is more common in men, with a prevalence of 1.5-3 times higher compared to women [6,14,15]. A meta-analysis conducted by Al Mansoor et al indicated that 61.3% of patients diagnosed with PSCCE were male [16]. The average age at diagnosis is 57-63.8 years [6,14,15]. Our patient was a 36-year-old man and is one of the youngest reported cases of PSCCE.

Smoking and alcohol consumption are commonly associated risk factors for esophageal cancer [16]. However, our patient did not report exposure to either of these nor did he have any other identifiable risk factors or a family history of cancer.

Patients with PSCCE typically present with progressive dysphagia, odynophagia, weight loss, and, occasionally, right upper-quadrant pain, hematemesis, sore throat, and cough [6]. Our patient presented similarly, with epigastric discomfort and progressive dysphagia.

Diagnosis of PSCCE is usually confirmed with gastroscopic biopsy and immunohistochemistry [7]. PSCCE predominantly

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occurs in the middle to lower esophagus, which aligns with our patient's presentation [6,16]. The average tumor size is 6.1 cm, with most tumors being less than 10 cm at the time of diagnosis [15]. Histologically, most of these tumors are characterized as pure small-cell carcinomas, although some exhibit mixed morphologies with squamous cell carcinoma [16]. Characteristic cytologic features include small blue cells with very scant cytoplasm [17], as seen in our case. High Ki-67 expression (>50%) is highly characteristic of small cell cancers, whereas other cancers exhibit a Ki067 expression of <25% [18]. This aligns with our findings, as our patient had a very high Ki-67 index of >90%.

PSCCE is an aggressive malignancy, with the liver being the most common site for metastasis, and approximately 50% of patients present with metastatic disease at the time of diagnosis, such as our patient [1,19]. Given the rarity of small cell carcinoma of the esophagus (PSCCE), there have been no established treatment guidelines or clinical trials. However, this tumor shares similar characteristics with small cell carcinoma of the lung, and treatment strategies have been adapted from the treatment protocols of small cell lung cancer [5]. Systemic chemotherapy is considered the cornerstone of PSCCE treatment [10]. Retrospective studies have indicated that surgical esophagectomy offers the best overall survival in patients with limited disease [8,9], while a multidisciplinary approach combining surgery, chemotherapy, and radiation therapy is considered for cases with metastatic disease. It is important to note that surgery has not been shown to have a proven benefit in patients with metastatic disease [19].

Al Mansoor et al reported that 2 significant prognostic factors for small cell carcinoma of the esophagus (PSCCE) are age, with patients younger than 50 having better median survival (MS), and disease stage, which can be categorized as limited or extensive [16]. The overall median survival for PSCCE typically falls within the range of 14-28 months [7]. In cases with metastasis to lymph nodes, the median survival is approximately 17.8 months. For individuals with limited disease and no lymph node metastasis, the median survival significantly improves to around 44.9 months [20]. The 5-year survival rate for PSCCE varies depending on the disease stage, with patients having limited disease showing more promising outcomes. Hou X et al found a 5-year survival rate of 38% in patients with limited disease who underwent a combination of surgery, chemotherapy, and radiation [14]. However, patients who underwent surgery alone or received chemotherapy and radiation without surgery exhibited a 0% survival rate, emphasizing the potential benefit of a multidisciplinary approach for limited disease [14]. A study by Lu et al reported a median overall survival of 11.1 months and a 5-year survival rate of 7.9% [6]. For limited diseases treated with systemic therapies, the median survival was 16.8 months, while local surgery resulted in a median survival of 10.1 months [6]. In cases of extensive disease, systemic treatment yielded a median survival of 7.4 months, while chemotherapy or radiation alone resulted in a median survival of 5.8 months [6].

Conclusions

This report has presented a rare case of primary esophageal small cell carcinoma and our approach to management. The report highlights the importance of early diagnosis, supported by histopathology, and the need for management guidelines.

Department and Institution Where Work Was Done

Department of Gastroenterology, Charleston Area Medical Center, Charleston, WV, USA.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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