Mixed Small Cell Carcinoma and Adenocarcinoma of the Esophagus: A Case Report

Tasneem Dawood1*, Muhammad Nauman Zahir2, Bilal Mazhar Qureshi3, Zeeshan Uddin4, Yasmin Abdul Rashid1, Adnan Abdul Jabbar2

Abstract

Background: Small cell carcinoma is an aggressive malignant tumor characterized by small-sized cells with scant cytoplasm, nuclei with finely granular chromatin and absent nucleoli, and a high mitotic count. The most common site is the lung which comprises 10-15 percent of all lung cancers. Rare sites of small cell carcinoma include the uterus, cervix, prostate, larynx, sweat glands, and gastrointestinal tract. No matter the site, it is an aggressive disease and is usually associated with a poor prognosis.

Case Summary: We report the case of a 31-year-old gentleman, diagnosed with mixed small cell carcinoma and adenocarcinoma of the esophagus. He presented to our clinic with complaints of progressive dysphagia, cough, and weight loss for the last 6 months. An initial endoscopic biopsy was done, it was suspicious of mixed small cell carcinoma and adenocarcinoma of the esophagus which was reconfirmed by our histopathologist. MRI brain was negative. He was treated aggressively with Cisplatin and Etoposide-based concurrent chemo-radiation. He received 4 cycles of chemotherapy and 28 fractions of radiation sandwiched between cycles 2 and 4 of chemotherapy. He has been on surveillance since April 2019 and his most recent scan and upper GI endoscopy from May 2019 confirm that the disease is in remission.

Conclusion: Mixed Small cell carcinoma and adenocarcinoma of the esophagus is an extremely unique, aggressive, and swiftly progressive disease, prone to distant metastasis and poor prognosis if left untreated. Treatment should be aggressive and commenced as soon as possible. Multi-modality management should be considered the current standard of care, to achieve both local and distant disease control.

Keywords: Chemoradiation; Multi-Modality; Small Cell

Introduction

Esophageal carcinoma is the eighth most common cancer worldwide. It is mainly characterized by two histological subtypes: namely squamous cell carcinoma and adenocarcinoma. Small cell carcinoma of the esophagus is a rare histological subtype accounting for only 1-2.8% of all esophageal cancers [1]. It is a highly aggressive disease with a high risk of distant metastasis and a poor prognosis. The median survival is usually less than a year. The recurrence rate is very high even in patients with early-stage disease [1]. Mixed small cell and adenocarcinoma of the esophagus are exceedingly rare [2]. Small cell carcinoma also known as oat cell carcinoma is a neuroendocrine carcinoma that exhibits aggressive behavior, rapid proliferation, and high...
rates of distant metastasis. It is frequently associated with paraneoplastic syndromes such as hypercalcemia, Lambert Eaton syndrome, SIADH, sub-acute cerebellar degeneration, limbic encephalopathy, and acromegaly [3]. The site of small cell carcinoma is usually the lung. Extrapulmonary small cell carcinoma comprises less than 5% of cases and is rarely seen in sites such as the salivary glands, larynx, pharynx, cervix, prostate, breast, and gastrointestinal tract [4]. A combined modality approach is usually used for treatment including chemotherapy and radiation based on studies on small cell carcinoma of the lung [5]. Small Cell carcinoma of the lung is divided into limited stage and extensive stage. The limited stage is defined as disease that is limited to the ipsilateral hem thorax and regional lymph nodes and can be encompassed in a safe radiotherapy field. Extensive stage (ES) disease is defined as disease with distant metastases, malignant pericardial or pleural effusions, and/or contralateral supraclavicular and contralateral hilar lymph node involvement [6]. For Limited stage disease of the lung, some patients are candidates for lobectomy with mediastinal sampling or dissection. If surgery demonstrates mediastinal nodal involvement, adjuvant chemoradiation is indicated. If they are not surgical candidates, stereotactic ablative body therapy (SABR) may be offered. Adjuvant cisplatin-based systemic therapy typically follows both local approaches. The rest of the limited-stage patients are usually treated with concurrent chemotherapy and radiation. The chemotherapeutic agents used are cisplatin and etoposide are the current standard of care [6]. The mainstay of therapy for ES SCLC is systemic therapy. It is a fundamental part of management, as these tumors have a high proliferative index and respond well to aggressive treatment. Radiotherapy alone as a treatment modality is usually not helpful [5]. Here we report the case of a young male diagnosed with mixed small cell carcinoma and adenocarcinoma of the esophagus and how he was managed using a multimodality approach.

Case Report

A 31-year-old young gentleman, who had a history of occasional cigarette smoking with no other significant past medical history, presented to the clinic in January 2019 with complaints of dysphagia along with chest tightness, epigastric burning, and loss of appetite and weight loss over the last 4-5 months. His Upper GI endoscopy was done outside our institute in December 2018 which revealed a 3 cm ulcerated semi-circumferential mass extending from 38 cm to 41 cm to the gastroesophageal junction along with mild pan gastritis. The biopsy of the esophageal mass was taken. The biopsy was reviewed again at our institute, and it showed esophageal mucosal fragments involved by an invasive tumor composed of partly crushed small round to oval cells arranged in sheets and clusters. Individual cells show scant cytoplasm and nuclear hyperchromasia. Focally the tumor cells are forming...

Figure 1: Esophageal biopsy showing mixed small cell carcinoma (→) and adenocarcinoma (↑). Normal stratified squamous epithelium of esophagus is present in the center (H&E, 4X).

Figure 2: Esophageal biopsy showing cell carcinoma component (A), composed of sheets of undifferentiated small cells with hyperchromatic nuclei and nuclear molding. Adenocarcinoma component (B) is composed of complex glands lined by neoplastic cells and lumina showing secretion (H&E, 20X).

Figure 3: Immunohistochemical stain synaptophysin on the esophageal biopsy showing positivity in small cell carcinoma component (→), consistent with neuroendocrine differentiation. The adenocarcinoma component (↑) is negative for this marker. (4X).
Discussion

Squamous cell carcinoma (SCC) and adenocarcinoma account for 95 percent of histological subtypes of esophageal cancer. Primary small cell carcinoma of the esophagus is a rare disease accounting for 1-2.8 of esophageal cancer. It is a very aggressive disease and is notorious for early distant metastasis and poor prognosis. Small cell carcinoma of the esophagus can cause early dissemination and usually has a median survival of less than a year. It even has a high recurrence rate [1]. Small cell carcinoma is histologically thought to develop from neuroendocrine Kulchitsky cells and is composed of sheets of small, round to spindled cells with dark nuclei, scarce cytoplasm, and fine, granular (“salt and pepper”) nuclear chromatin with indefinite nucleoli [7]. Small cell carcinoma accounts for 14-15% of lung cancers [8]. Extra pulmonary small cell carcinomas (ESCCs) are very rare; these tumors have been described most frequently in the urinary bladder, prostate, esophagus, stomach, colon and rectum, gallbladder, larynx, salivary glands, cervix, and skin. In addition, small cell carcinoma will occasionally present with metastatic disease, and a primary site cannot be identified (small cell carcinoma of unknown primary) [9].

Primary small cell carcinoma of the esophagus has similar findings on endoscopy and radiology as the other subtypes. But usually presents with rapid dysphagia and weight loss in the early days. This subtype is mostly seen in men with a male-to-female ratio reported as 2:1. It is usually observed between the fourth and the seventh decades. Major symptoms include progressive dysphagia, retrosternal pain, cough, and rapid weight loss. Rarely, hoarseness and upper gastrointestinal tract bleeding have also been reported as the primary symptoms. It is usually seen in the distal or middle esophagus. Sites of distant spread include liver, lung, and bones [5]. There are 2 viewpoints regarding the pathogenesis of primary small cell carcinoma of the esophagus, one is that it arises from neuroendocrine cells of the submucosal gland or stratum basale, and the major precursor from the APUD cells is the amine precursor uptake decarboxylase cells. Since these cells are abundant in the distal esophagus, the lesion usually arises in the middle or distal esophagus. The second is that the biphasic neoplasm originates from pluripotential stem cells of the endoderm that can be partially differentiated into the squamous cell, neuroendocrine cell, or glandular cell because of the stimulation of different carcinogenic agents [5].

We could not find any cases reported yet, regarding mixed small cell carcinoma and adenocarcinoma of the Esophagus. Most of the cases reported include mixed small cell and squamous cell carcinoma of the esophagus [11,12]. No standard of care has been established because of the rarity of the disease. The significance of surgery is still controversial [5]. Some reports have stressed that surgery should be avoided for patients with advanced disease [13]. Conversely, some authors think surgery remains the primary method in patients with localized disease [14]. In recent reports, regimens including cisplatin and etoposide have achieved better response and radiotherapy is also effective [14]. Several cases suggested that the patients were treated with surgical resection, radiotherapy, and chemotherapy in combination may result in survival benefits [15]. Nonetheless, individualized treatment should be considered for all patients, based on clinical features, pathologic diagnosis, the grading and staging classification, patient characteristics, logistics, and availability of surgical expertise as incomplete surgery or recovery might delay chemoradiation which has proven to be effective for locoregional and distant control of disease [16].

Conclusion

Primary mixed small cell carcinoma and adenocarcinoma of the esophagus is an extremely rare disease with high risk of early dissemination and poor prognosis if left untreated. It should be dealt with aggressively and treatment decisions should be made early. These cases should be discussed in a multidisciplinary meeting and a plan should be made personalized to each patient. Treatment should be aggressive and started early. Multi-modality management should be considered the current standard of care in such patients to help achieve, both local and distant disease control. These patients need a close follow-up post-treatment because of the aggressive nature of the disease and the high risk of recurrence.

Conflicts of Interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

References