Limited Stage Small Cell Carcinoma of the Anal Canal: A Case Report and Review of the Literature

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Abstract

Extrapulmonary small cell carcinoma is a rare disease entity of epithelial origin accounting for less than 0.2% of all colorectal malignancies. Herein we describe a case report of a patient with small cell carcinoma of the anal canal treated with concurrent platinum-etoposide based chemoradiotherapy followed by prophylactic cranial irradiation. We examine the limited prior literature for this rare histology of anal cancer, placing the presented case in the context of the < 20 prior published cases in the English literature. Due to limited data no firm conclusions can be drawn, however our case and literature review highlights promising disease outcomes for a paradigm of concurrent platinum-etoposide chemotherapy and local irradiation followed by prophylactic cranial irradiation.

Introduction

Extrapulmonary small cell carcinoma is a rare disease entity of epithelial origin, accounting for less than 1.0% of all gastrointestinal malignancies and 0.2% of all colorectal malignancies [1]. The most common location for extrapulmonary small cell carcinoma of the gastrointestinal tract is the esophagus, accounting for approximately ½ of reported cases [1]. Small cell carcinoma of the anal canal is exceedingly rare, with only 19 reported cases in the English literature; as such there is limited data to guide management [2-8]. Herein we report a case of limited stage extrapulmonary small cell carcinoma of the anal canal treated with concurrent chemo-radiotherapy followed by prophylactic cranial irradiation and examine treatment outcomes for the limited reported literature on extrapulmonary small cell carcinoma of the anus.

Case Report

A 55 year-old white male with no prior history of malignancy presented with a 3-month history of rectal pain and hematochezia. Further workup including digital rectal examination followed by rigid proctoscopy and colonoscopy showed a 3-4cm mass on the anterior anal wall 1cm from the anal verge. Biopsy revealed a solid malignant tumor with extensive necrosis and a high Ki 67 index of 90%. Immunohistochemistry staining was positive for CK 7, CK 56, synatophysin, and weakly positive for p63. Immunohistochemistry staining was negative for p40, CK 5/6, CK 20, and HPV. Morphology was consistent with small cell carcinoma of the anal canal. Further staging including PET/CT and brain MRI was negative for metastatic disease, consistent with limited stage extrapulmonary small cell carcinoma of the anus.

Extrapolating from treatment paradigms for limited stage small cell lung cancer, the patient received concurrent cisplatin (80 mg/m² day 1) and etoposide 100 mg/m² (day 1, day 2, and day 3) every 3 weeks for 6 total cycles plus intensity-modulated radiotherapy to the entire mesorectum from the anal verge to the recto-sigmoid junction, inguinal lymph nodes, and pelvic lymph nodes to 45 Gy in 25 fractions plus boost to the gross disease for an additional 14.4 Gy in 8 fractions. He tolerated chemoradiotherapy well without any grade 3+ toxicity. Restaging physical exam, PET/CT, and brain MRI showed complete response. Thus he received prophylactic cranial irradiation to 25 Gy in 10 fractions. He is now 21 months from initial diagnosis with no evidence of recurrent disease or major treatment related toxicity.

Discussion

Extrapulmonary small cell carcinoma of the anal canal is a rare disease entity with 19 reported cases in the English literature [2–8]. Similar to pulmonary small cell carcinoma where 5% to 7% of patients present with extensive stage disease, many of the reported cases were of patients with distant metastases at presentation [2–4]. Table 1 summarizes the 12 reported cases of limited stage small cell carcinoma of the anal canal treated with definitive intent [2, 5–8]. Due to its rare nature it remains difficult to draw firm conclusions regarding treatment recommendations.

Table 1: Summary of Treatment Outcomes for Reported Cases of Limited Stage Small Cell Carcinoma of the Anus.

<table>
<thead>
<tr>
<th>N</th>
<th>Treatment</th>
<th>PCI</th>
<th>Disease Status</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 APR, 1 RT</td>
<td>-</td>
<td>Median time to recurrence 6 months (7/8 recurred)</td>
<td>Median 0–6 months, 1 patient 5 years</td>
<td></td>
</tr>
<tr>
<td>1 Sequential CRT</td>
<td>-</td>
<td>Died of DM</td>
<td>12 months</td>
<td></td>
</tr>
<tr>
<td>1 APR followed salvage CRT</td>
<td>-</td>
<td>Complete with local and distant failure</td>
<td>5 months</td>
<td></td>
</tr>
<tr>
<td>1 Concurrent CRT</td>
<td>-</td>
<td>Died of DM</td>
<td>12 months</td>
<td></td>
</tr>
<tr>
<td>1 Concurrent CRT</td>
<td>yes</td>
<td>NED</td>
<td>2 months</td>
<td></td>
</tr>
<tr>
<td>1 Concurrent CRT</td>
<td>yes</td>
<td>NED</td>
<td>21 months</td>
<td></td>
</tr>
</tbody>
</table>


In the largest series of anal canal small cell carcinoma, 88% of 8 definitively treated limited stage patients underwent abdominopereineal resection with dismal outcomes including a 6-month median survival and a 4-month median time to recurrence [2]. The authors concluded that surgery was a “gross failure.” These results however, may speak to the systemic nature of small cell carcinoma of the anal canal at diagnosis, rather than the inability of definitive local therapy contributing to curability [1–2]. However, one long-term survivor after abdominopereineal resection has been reported in a patient with a T1N0 lesion. Similar promising outcomes have been seen for surgical resection in the rare clinical scenario of completed resected early-stage T1-2N0 small cell carcinoma of the lung [9]. None-the-less, similar to treatment paradigms in squamous cell carcinoma of the anal canal it appears that an organ preserving approach of concurrent chemotherapy and radiation with surgery reserved for salvage seems most prudent. Consistent with prior recommendations from large series of extrapulmonary small cell cancer, the treatment of limited stage small cell carcinoma with concurrent platinum-etoposide chemotherapy and local radiotherapy were applied to our patient, recognizing that small cell carcinomas are commonly radiosensitive tumors with a high propensity for distant failure especially in the extra pulmonary setting [10].

The unique part of our case was both the excellent clinical outcome with the patient having no evidence-of-disease 21-months from diagnosis, and the application of the prophylactic cranial irradiation. Due to a high propensity for brain metastases, approaching 70% in autopsy series, prophylactic cranial irradiation has been studied in small cell lung cancer showing a decrease in the incidence of brain metastases and a significant improvement in overall survival of 5.4% [11]. Multiple recent series in extra pulmonary small cell carcinoma have questioned the role of prophylactic cranial irradiation especially for non-genitourinary and non-head-and-neck sub-sites where the risk of brain metastases appears to be lower than pulmonary small cell, which is on the order of 15–20% [12–14]. Others have argued that cases such as ours, where patients with limited stage extra pulmonary small cell carcinoma disease have a complete response to chemo-radiotherapy, prophylactic cranial irradiation may still have a role, as median survival after intracranial relapse are dismal at 2-months. Thus even small absolute improvements can potentially improve outcomes with an estimated number need to treat of 13 [15].

Conclusion

Due to the low overall incidence of anal small cell carcinoma (< 20 published cases in the English literature) no firm conclusions regarding optimal management can be drawn. The reported case herein adds to a limited body of literature examining small cell carcinoma of the anal canal with promising disease outcomes for a paradigm of concurrent platinum-etoposide chemotherapy and local irradiation followed by prophylactic cranial irradiation.

References


