

Case Report

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

Melvin Deutsch^{1*} MD and John A Vargo¹ MD, Mohammed Islam² MD MS and Sherif Rizk³ MD

¹University of Pittsburgh Cancer Institute, Department of Radiation Oncology, USA

²Medical Oncology, USA

³General Surgery, Pittsburgh PA, USA

*Corresponding author: Dr. Melvin Deutsch MD, University of Pittsburgh Medical Center Shadyside, Department of Radiation Oncology, 5230 Centre Ave, Pittsburgh PA, 15238, USA, Tel: 412-623-6720; Fax: 412-623-6725; Email: deutschm@upmc.edu

Received: 07-11-2014

Accepted: 07-17-2014

Published: 07-21-2014

Copyright: © 2014 Melvin

Abstract

Extrapulmonary small cell carcinoma is a rare disease entity of epithelial origin accounting for less than 0.2% of all colorectal malignancies. Here-in 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.

Keywords: Small Cell Carcinoma; Anal Canal; 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, synaptophysin, 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 45Gy in 25 fractions plus boost to the gross disease for an additional 14.4Gy in 8 fractions. He tolerated chemo-radiotherapy well without any grade 3+ toxicity. Restaging physical exam, PET/CT, and brain MRI showed complete response. Thus he received prophylactic cranial irradiation to 25Gy 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 $\frac{2}{3}$ to $\frac{3}{4}$ 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.

	N	Treatment	PCI	Disease Status	Survival
Boman <i>et al</i> [2]	8	7 APR, 1 RT	-	Median time to recurrence 4-months (7/8 recurred)	Median 6-months, 1 patient 5-years
Doddi <i>et al</i> [5]	1	Sequential CRT	no	Died of DM	18-months
Nakahara <i>et al</i> [6]	1	APR followed salvage CRT	-	Suicide with local and distant failure	3-months
Eberhardt <i>et al</i> [7]	1	Concurrent CRT	no	Died of DM	10-months
Marcus <i>et al</i> [8]	1	Concurrent CRT	no	NED	5-months
Present Case	1	Concurrent CRT	yes	NED	21-months

PCI = prophylactic cranial irradiation. N = number of patients. CRT = chemo-radiotherapy. RT = radiotherapy. APR = abdominal perineal resection. NED = no-evidence-of-disease. DM = distant metastases.

In the largest series of anal canal small cell carcinoma, 88% of 8 definitively treated limited stage patients underwent abdominal perineal 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 abdominal perineal 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.

Conflict of interest

Acute or potential conflict of interest does not exist.

References

- Brenner B, Tang LH, Klimstra DS, Kelsen DP. Small cell carcinoma of the gastrointestinal tract: a review. *J Clin Oncol* 2004, 22: 2730-2739.
- Boman BA, Moertel CG, O'Connell MJ. Carcinoma of the anal canal: a clinical and pathologic study of 188 cases. *Cancer* 1984, 54: 114-125.

3. Alcindor T, Tosikyan A, Voung T, Marcus V. Small cell anal carcinoma and AIDS: case report and review of the literature. *Int J of Colorectal Dis.* 2008, 23: 135-136.
4. Meyer A, Bruns F, Richter K, Grunwald V, Karstens JH. Small cell cancer of the anal canal-case report of a rare tumor. *Anticancer Res.* 2007, 27: 1047-1050.
5. Doddi S, Singhal T, De Silva C et al. Small cell carcinoma of the anus: a case report. *Cases J.* 2009, 24: 93-96.
6. Nakahara H, Moriya Y, Shinkai T, Hirota T. Small cell carcinoma of the anus in the HIV carrier: report of a case. *Surg Today.* 1993, 23: 85-88.
7. Eberhart JM, Brown K, Lo S, Nagda S, Yong S. Extrapulmonary small cell carcinoma of the anal canal: a case report and review of the literature. *Case Reports in Medicine.* 2012: 341432.
8. Marcus DM, Edgar MA, Hawk NN, Sullivan PS, Stapleford LJ. Small cell carcinoma of the anus in the setting of prior squamous dysplasia and carcinoma in situ. *J Gastrointest Oncol.* 2013, 4: E1-4.
9. Varlotto JM, Recht A, Flickinger JC et al. Lobectomy lead to optimal survival in early-stage small cell lung cancer: a retrospective analysis. *J Thorac Cardiovasc Surg.* 2011, 142: 538-546.
10. Brenner SM, Gregory DL, Stillie A et al. Should extrapulmonary small cell cancer be managed like small cell lung cancer? *Cancer.* 2010, 116: 888-895.
11. Auperin A, Arriagade R, Pignon JP et al. Prophylactic cranial irradiation for patients with small-cell lung cancer in complete remission. *Prophylactic Cranial Irradiation Overview Collaborative Group.* *N Engl J Med.* 1999, 12: 476-484.
12. Soto DE, Eisbruch A. Limited stage extrapulmonary small cell carcinoma: outcomes after modern chemotherapy and radiotherapy. *Cancer J.* 2007, 13: 243-246.
13. Yazici O, Ozdemir NY, Sendur MA, Aksoy S, Zengin N. Current approaches for prophylactic cranial irradiation in extrapulmonary small cell carcinoma. *Curr Med Res Opin.* 2014, 30(7): 1327-1336.
14. Muller AC, Gani C, Weinmann M et al. Limited disease of extra-pulmonary small cell carcinoma: impact of local treatment nodal status, role of prophylactic cranial irradiation. *Strahlenther Onkol.* 2012, 188: 269-273.
15. Eckert F, Gani C, Bamberg M, Muller AC. Cerebellar metastases in extrapulmonary small cell carcinoma: implication for the use of prophylactic cranial irradiation. *Strahlenther Onkol.* 2012, 188: 478-482.