The Journal of Laryngology & Otology (2015), ***129*** (Suppl. S2), *S83–S85*.

doi:10.1017/S002221511400245X

Extrapulmonary small cell carcinoma in head and neck

R YASUMATSU, T NAKASHIMA, M YAMAUCHI, S TOH, S KOMUNE

Department of Otorhinolaryngology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Abstract

Purpose: The management of extrapulmonary small cell carcinoma has not been standardised to date. This study reviewed the clinical course, management and survival outcomes of patients with extrapulmonary small cell carcinoma in the head and neck region.

Methods: Nine patients with extrapulmonary small cell carcinoma in the head and neck were included in this study.

Results: Five patients received radical surgery followed by adjuvant chemotherapy or radiotherapy or both. Two other patients were treated with chemotherapy consisting of CPT11 plus cisplatin or CPT11 plus cisplatin plus VP-16 three times. Two other patients received chemoradiotherapy consisting of S-1 or CPT11 plus cisplatin. The median overall survival was 14.5 months, with a three-year survival rate of 23.7 per cent.

Conclusions: The prognosis of extrapulmonary small cell carcinoma is generally poor. Further prospective multicentre studies are required for better understanding of disease entities and response to treatment modalities.

Key words: Extrapulmonary Small-Cell Carcinoma; Head and Neck; Treatment

Introduction

Extrapulmonary small cell carcinoma is a heterogeneous group of cancers accounting for 2–4 per cent of all small cell carcinomas and 0.1–0.4 per cent of all cancers.[1,2] According to the National Comprehensive Cancer Network (NCCN), the most common extrapulmonary sites of origin, in order of decreasing frequency, are the cervix, oesophagus, head and neck, colon and prostate. In the head and neck region, the larynx is the most common site affected by extrapulmonary small cell carcinoma.[3]

The clinical course of these tumours is known to be aggressive in general, with early dissemination and frequent recurrences.[4,5] Although chemotherapy seems to be an effective therapeutic modality as in small cell lung cancer, surgery and radiation therapy may also play an important role depending on the stage or primary site.[5]

The management of extrapulmonary small cell carcinoma has not been standardised to date, but is, by medical consensus, similar to that of small cell lung cancer because of their similar clinicopathological features.[6] This study reviewed the clinical course, management and survival outcomes of patients with extrapulmonary small cell carcinoma in the head and neck region.

Patients and methods

Between 1995 and 2010, nine patients with extrapulmonary small cell carcinoma in the head and neck were treated at Kyushu University Hospital. The data for the nine patients, consisting of seven males and two females, were analysed. The subjects' ages ranged from 53 to 82 years, with a median age of 64 years. The following clinical data were collected from the medical records of the nine patients: age and gender, primary sites, treatment modalities and clinical response, time to progression and overall survival rate.

Results

In the nine patients studied, two cases of extrapulmonary small cell carcinoma were detected in the larynx, two in the sinonasal region, two in the nasopharynx, one in the oropharynx, one in the hypopharynx and one in the external auditory canal. All patients had locoregional disease at the time of first diagnosis. They were treated with a variety of therapeutic modalities, including chemotherapy. Five patients received radical surgery followed by adjuvant chemotherapy or radiotherapy or both. Two other patients were treated with chemotherapy consisting of CPT11 plus cisplatin (CDDP) or CDDP plus VP-16 three times. Two other patients received chemo-radiotherapy consisting of S-1 or CDDP. Their total radiotherapy dose was 70.2 Gy. Stage, primary, treatment modalities and outcome are summarised in Table I. The outcomes of the nine patients were as follows: four died of cancer,

TABLE I
CLINICOPATHOLOGICAL CHARACTERISTICS AND CLINICAL COURSE IN NINE PATIENTS WITH EXTRAPULMONARY SMALL CELL CARCINOMA

Age	Gender	Primary site	TNM	Treatment	Radiation dose (Gv)	Chemotherapy	Follow-up periods (month)	Status
66	M	Sinonasal	$T^3N^0M^0$	ORC	30	CDDP,VP16	18.2	Died of other disease
68	M	Sinonasal	$T^3N^0M^0$	ORC	60	CDDP	6	Died of disease
52	M	Nasopharynx	$T^3N^0M^0$	RC	70	CDDP,PEP	12	Died of disease
54	M	Nasopharynx	$T^2N^0M^0$	RC	70	CDDP,VP16	41	Died of other disease
65	M	Oropharynx	$T^2N^{2b}M^0$	RC	65.4	CDDP,CPT-11	21	Died of disease
61	F	Hypopharynx	$T^3N^{2b}M^0$	RC	65.4	CDDP,VP16	11	No evidence of disease
57	M	Larynx	$T^{4a}N^1M^0$	ORC	27	CDDP,VP16	20	No evidence of disease
82	M	Larynx	$T^{4a}N^{2c}M^0$	ORC	50	CDDP,VP16	15	Died of disease
79	F	External auditory canal	$T^3N^0M^0$	ORC	60	S1	5	No evidence of disease

TNM = tumour-node-metatasis; ORC = operation + radiation + chemotherapy; RC = radiation + chemotherapy; CDDP = cisplatin; PEP = pepleomycin; VP16 = etoposide; CPT11 = :irinotecan; S1 = tegafur, gimeracil, oteracil potassium

two died of other diseases, and three showed no evidence of disease after treatment. The median overall survival was 14.5 months (range 2.6–41.0 months), with a three-year survival rate of 23.7 per cent (Figure 1).

Discussion

The vast majority of small cell carcinomas develop from the lung, but only 2.5–4 per cent of all small cell carcinomas are present at extrapulmonary sites.[1,2] The primary site of occurrence of extrapulmonary small cell carcinoma has been described as being in a variety of organs and regions, such as the head and neck, oesophagus, stomach, pancreas, gallbladder, uterine cervix, kidney, urinary bladder and prostate.[7] Although extrapulmonary small cell carcinoma is rare, the clinical course of the tumour in patients with extrapulmonary small cell carcinoma, is generally aggressive and often recurrent.[4] The optimal therapeutic strategy of extrapulmonary small cell carcinoma is still unknown. In addition, extrapulmonary small cell carcinoma is a difficult to treat cancer with early sensitivity to chemotherapy but a poor overall prognosis. As extrapulmonary small cell carcinoma does not have a proven algorithm for treatment, it has generally been treated in a similar fashion to small cell carcinoma of the lung via systemic chemotherapy. These two diseases are separate clinical entities and risk factors for development of extrapulmonary small cell carcinoma may not apply for pulmonary small cell carcinomas. different strategies are needed.

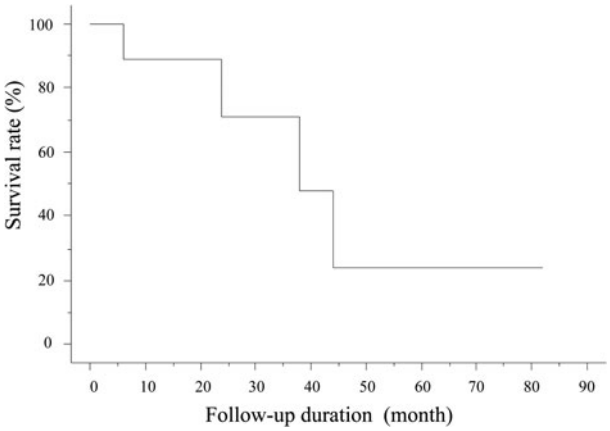

FIG. 1
The three-year disease-free survival time.

- **This study reviewed the clinical course, management and survival outcomes of patients with extrapulmonary small cell carcinoma in the head and neck region**
- **Nine patients with extrapulmonary small cell carcinoma in the head and neck treated at Kyushu University Hospital were included in this study**
- **The median overall survival was 14.5 months, with a three-year survival rate of 23.7 per cent**

Multimodality therapy has become increasingly applied, including chemotherapy, radiotherapy and possibly surgery depending on the extent of disease or primary site.[8] For the majority of patients with first diagnosed extrapulmonary small cell carcinoma, radical surgery or definite radiotherapy has been frequently employed.[9] In this study, five of nine patients underwent radical surgery. Previous reports indicated that the combination of radiotherapy with surgical extirpation was associated with significantly improved ten-year survival for extrapulmonary small cell carcinoma of all sites.[10] No significant reduction in mortality was observed for head and neck extrapulmonary small cell carcinomas for combination therapy. The chemotherapeutic regimen of EPSCC is similar to those utilised in small cell lung

https://doi.org/10.1017/S002221511400245X Published online by Cambridge University Press

cancer, and the combination of etoposide and cisplatin is the first line treatment with a response rate of 69 per cent.[5] The most common regimens used in our study were also the combination of etoposide-CDDP.

However, the prognosis of extrapulmonary small cell carcinoma is generally poor with a five-year survival of 13 per cent and a median survival from diagnosis of 14.5 months, which has also been shown to be partially dependent on the primary disease site.[11,12] Our study has several limitations related to the retrospective design and the small number of patients. However, our results showed that overall three-year tumour-free actuarial survival rate after treatment was 23.7 per cent, and this result closely resembles other reports.[12,13] Further prospective multicentre studies are required for better understanding of disease entities and response to treatment modalities.

References

1 van der Heijden HF, Heijdra YF. Extrapulmonary small cell carcinoma. *South Med J* 2005;**98**:345–9
2 Walenkamp AM, Sonke GS, Sleijfer DT. Clinical and therapeutic aspects of extrapulmonary small cell carcinoma. *Cancer Treat Rev* 2009;**35**:228–36
3 Ferlito A. Diagnosis and treatment of small cell carcinoma of the larynx: a critical review. *Ann Otol Rhinol Laryngol* 1986;**95**: 590–600
4 Remick SC, Ruckdeschel JC. Extrapulmonary and pulmonary small-cell carcinoma: tumor biology, therapy, and outcome. *Med Pediatr Oncol* 1992;**20**:89–99
5 Lo Re G, Canzonieri V, Veronesi A, Dal Bo V, Barzan L, Zancanaro C, *et al*. Extrapulmonary small cell carcinoma: a single-institution experience and review of the literature. *Ann Oncol* 1994;**5**:909–13
6 Brennan SM, Gregory DL, Stillie A, Herschtal A, Mac Manus M, Ball DL. Should extrapulmonary small cell cancer be managed like small cell lung cancer? *Cancer* 2010;**116**: 888–895
7 Cicin I, Karagol H, Uzunoglu S, Uygun K, Usta U, Kocak Z *et al*. Extrapulmonary small-cell carcinoma compared with small-cell lung carcinoma: a retrospective single-center study. *Cancer* 2007;**110**:1068–76
8 Weng CT, Chu PY, Liu MT, Chen MK. Small cell carcinoma of the head and neck: a single institution's experience and review of the literature. *J Otolaryngol Head Neck Surg* 2008;**37**: 788–793
9 Haider K, Shahid RK, Finch D, Sami A, Ahmad I, Yadav S *et al*. Extrapulmonary small cell cancer: a Canadian province's experience. *Cancer* 2006;**107**:2262–9
10 Grossman RA, Pedroso FE, Byrne MM, Koniaris LG, Misra S. Does surgery or radiation therapy impact survival for patients with extrapulmonary small cell cancers? *J Surg Oncol* 2011; **104**:604–12
11 Weiss MD, deFries HO, Taxy JB, Braine H. Primary small cell carcinoma of the paranasal sinuses. *Arch Otolaryngol* 1983;**109**: 341–3
12 Kim KO, Lee HY, Chun SH, Shin SJ, Kim MK, Lee KH *et al*. Clinical overview of extrapulmonary small cell carcinoma. *J Korean Med Sci* 2006;**21**:833–7
13 Ochsenreither S, Marnitz-Schultze S, Schneider A, Koehler C, Daum S, Loddenkemper C *et al*. Extrapulmonary small cell carcinoma (EPSCC): 10 years' multi-disciplinary experience at Charite. *Anticancer Res* 2009;**29**:3411–15

Address for correspondence:
Ryuji Yasumatsu,
Department of Otorhinolaryngology,
Graduate School of Medical Sciences,
Kyushu University,
3-1-1 Maidashi,
Higashi-ku,
Fukuoka 812-8582, Japan

Fax: + 81926425685
E-mail: yasuryuj@qent.med.kyushu-u.ac.jp

Competing interests: None declared

https://doi.org/10.1017/S002221511400245X Published online by Cambridge University Press