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SMALL CELL CARCINOMA OF THE HEAD AND NECK: A TERTIARY CARE HOSPITAL FROM CHENNAI EXPERIENCE AND REVIEW OF LITERATURE

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ABSTRACT **AIM:** To analyze retrospectively the experience and outcome in the treatment of small cell neuroendocrine carcinoma of head and neck at our center.

METHODS AND MATERIALS: A total of 12 patients had reported with small cell neuroendocrine carcinoma of head and neck to Government Royapettah hospital, Chennai from the year 2016 to 2018. Of these, 3 had tumor in paranasal sinus, 1in nasal cavity, 3 in nasaopharynx, 1 in retromolar trigone, 1 in larynx,1 in floor of mouth,2 in salivary gland. Radiotherapy was given as local treatment to all patients either with curative intent or palliative intent with or without chemotherapy. 8 out of 12 patients were treated with curative intent and four patients treated with palliative intent in view of upfront bone metastasis

RESULTS: Of the 12 patients 7 were men and 5 were women. The median age at presentation was 41 years (Range 10-70 years). Of the 12 patients, 8 had died after the median follow up of 8 months. The four patients who were alive were followed for a median of 37months. The 2 year disease free survival and 2 year overall survival of patients treated with curative intent were 37.5% and 60% respectively. Two patients developed bone metastasis, two patients developed lung metastasis, 1 patient developed liver and bone metastasis and all died within year of completion of treatment. All four patients treated with palliative intent died within a year due to progression of metastasis.

CONCLUSION: Concurrent chemo radiation is a reasonable alternative to surgery for patient with small cell neuroendocrine carcinoma of the head and neck. Patients who had complete response after completion of treatment did better irrespective of the site of the treatment. More effective systemic therapy is needed as most patients had local and distant failure.

KEYWORDS : Small cell carcinoma, head & neck, radiotherapy, chemotherapy

BACKGROUND:

Small cell carcinoma of the head and neck is a rare neuroendocrine tumor caries aggressive clinical behavior with poor prognosis(1,2). It constitutes <0.5% of head and neck malignancies. It has propensity for distant metastasis despite aggressive treatment(2,3). The management of small cell carcinoma is multimodality treatment which includes various combinations of surgery, chemotherapy and radiation therapy(10). There are no definite treatment guidelines in view of rarity of disease.

AIM:

The purpose of the study was to analyze the patients of small cell carcinoma of head and neck treated at a tertiary cancer hospital, Government Royapettah hospital, Chennai treated with radiation therapy as a part from 2016 to 2018.

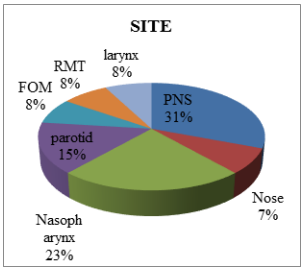
MATERIALS AND METHODS:

Twelve patients diagnosed as small cell carcinoma of head and neck involving nasal cavity, paranasal sinuses, nasopharynx, salivary gland, larynx, floor of mouth and retromolar trigone treated at a tertiary cancer hospital, Government Royapettah hospital, Chennai from the period of January 2016 to December 2018 were analyzed retrospectively. Case details collected from from case record, chemotherapy chart, radiotherapy chart and investigations were reviewed to collect data concerning age, sex, habits, comorbids, disease site, TNM stage, radiotherapy dose/fractionation, chemotherapy details, surgery details if any, toxicity, response, site of failure and survival status for patients treated with small cell carcinoma of head and neck. Radiotherapy was given to all patients either with curative intent or palliative intent with or without chemotherapy. 8 out of 12 patients were treated with curative intent and four patients treated with palliative intent in view of upfront bone metastasis.

Of 8 patients treated with curative intent seven patients received platinum based chemotherapy along with radiation therapy followed by addition of etoposide and cisplatin based on general condition. 1 patient did not receive chemotherapy in view of poor general condition. Radiation therapy is given with 6MV photons with 2Gy daily/fraction to total dose of 60-66Gy. Of four patients treated with palliative intent received concurrent chemo radiation with cisplatin. No patients were lost to follow up.

RESULTS:

Fig. 1- Site distribution



Of 12 patients treated seven patients were women and 5 were men. The age group among patients ranges between 10 to 64 years. Of these 12 patients, 3 had tumor in paranasal sinus, 1 in nasal cavity, 3 in nasaopharynx,1 in retromolar trigone,1 in larynx, 1 in floor of mouth, 2 in salivary gland. 92% of patients have stage III and stage IV carcinoma (Fig-1).

The patient characteristics, disease status, treatment received, response, failure rate and survival are summarized (Table 1 and 2).

Table 1: Patients Characteristics Treated With Curative Intent

S.No	Age Sex	Site	Stage	Radiation dose (Gy)	Chemotherapy	Resp Onse	LF	RF	DF	DFS (months)	OS (months)
1	20/M	PNS	T4aN0M0	60	EP	CR	-	-	-	36	36
2	22/F	PNS	T4aN0M0	54	CDDP EP	PR	yes	-	bone	3	12

3	17/F	Nose	T4bN1M0	62	CDDP CDDP+5FU	CR	-	-	-	38	38
4	10/F	Nasopharynx	T2N2M0	62	CDDP +5FU CDDP	CR	-	-	-	42	42
5	46/F	Larynx	T2N0M0	66	CDDP VP16	CR	-	-	lung	6	8
6	42/F	parotid	T4aN1M0	60	CDDP	CR	-	yes	-	2	36
7	64/M	Nasopharynx	T3N2M0	60	CDDP	CR	-	yes	lung	2	6
8	19/M	Nasopharynx	T4bN2M0	60	CDDP+5FU	CR	-	-	Liver, bone	6	8

PNS- Paranasal sinuses; C- curative; P-palliative, CDDP= cisplatin, EP- Etoposide + cisplatin, 5FU- 5- flurouracil, VP 16- Etoposide, CR-complete response, PR- partial response, LF- local failure, RF- regional failure, DF- Distant failure, DFS- disease free survival, OS- Overall survival.

Table 2: Patients Characteristics Treated With Palliative Intent

S.No	Age Sex	Site	Stage	RT(GY)	Chemo	Response	LF	RF	DF	DFS(months)	OS (months)
1	56/F	PNS	T4aN1M1	54	CDDP	PR	yes	-	bone	-	14
2	38/F	RMT	T2N2M1	10	EP	Progressive	-	-	Marrow	-	5
3	24/M	Parotid	T4aN0M1	60	CDDP+VP16	Progressive	-	-	Bone, brain	-	8
4	53/M	FOM	T2N1M1	54	-	PR	-	-	bone	-	10

PNS- Paranasal sinuses; C- curative; P-palliative, CDDP= cisplatin, EP- Etoposide + cisplatin, 5FU- 5- flurouracil, VP 16- Etoposide, CR-complete response, PR- partial response, LF- local failure, RF-regional failure, DF- Distant failure, DFS- disease free survival, OS0-Overall survival, FOM- floor of mouth.

Of the 12 patients, 8 had died after the median follow up of 8 months. The 4 patients who were alive were followed for a median of 37months. Of 8 patients treated with curative intent, seven patients received concurrent chemo radiation and 1 patient received only radiotherapy followed by surgery. The 2 year disease free survival and 2 year overall survival of patients treated with curative intent were 37.5% and 50% respectively.1 patient failed regionally underwent salvage neck dissection and survived till now (36 months). Two patients developed bone metastasis, two patients developed lung metastasis, 1 patient developed liver and bone metastasis and all died within year of completion of treatment. All patients except one received chemotherapy as a part of treatment. Among six patients who achieved complete response after treatment 66% patients has two year survival rate.

Among patient treated with palliative intent all four patients has bone metastasis at presentation. Of these three patients received chemotherapy along with radiation therapy and one patient received only radiation therapy as he was medically unfit for chemotherapy. One patient progressed to bone marrow before completion of treatment and radiation therapy not contemplated. One patient developed brain metastasis after completion of 6 months of treatment. All four patients treated with palliative intent died within a year due to progression of metastasis.

DISCUSSION:

In 1972, Olofsson and Van Norstrand reported first case of small cell carcinoma of head and neck and involved the larynx(4). Extra pulmonary site constitutes 2-2.5% of all small cell carcinoma. Small cell neuroendocrine carcinoma diagnosed on the basis of morphology of cells along with immunohistochemical studies. As it has high propensity of disseminated disease, complete metastatic investigations is essential before starting treatment(2,3).

Small cell carcinoma of head and neck are most commonly treated with concurrent chemoradiation. According to Moisa et al (5) based on the report in his series 59% percent of patients presented with cervical lymphadenopathy. In our study 58% of patients have cervical lymphadenopathy at diagnosis. It is well known that small cell carcinoma is known for hematogenous spread. Aguilar et al (6) reported that incidence of distant metastasis at diagnosis was 17% and subsequent distant metastasis was 21%. In our study 50% of patients developed distant metastasis after concurrent chemoradiation.

Comparative studies with other universities summarized (Table 3).

Table 3: Comparative Studies (8,9)

S. No	Study	Total Patients	Outcome
1	University of Florida(1989-2001)	6	3 year DFS- 17% Rest patients develop regional and distant metastasis.
2	University of Miami(1987-2007)	12	1 year DFS 71% & 2 year DFS 44%. 8 patients died after median survival of 13 months.
3	Goverment Royapettah hospital (2016-2018)	12	2 years DFS 37.5% & 2year OS 50%. Except 4 patients all developed distant metastasis at presentation or after treatment

Local recurrences are less common than distant metastasis. This may be due to death from high distance metastasis before time evident for local recurrence. This also indicates increased response to radiotherapy in locally and need for aggressive systemic therapy during and after radiation therapy.

Chemotherapy common used were same as that of used in small cell lung cancer(7). Of these cisplatin and etoposide can be used concurrently with radiation therapy. Despite aggressive treatment of small cell carcinoma of head and neck all the series and study reported higher failure rates with 5 year survival rate less than 5%.

CONCLUSION:

Concurrent chemo radiation is a reasonable alternative to surgery for patient with small cell neuroendocrine carcinoma of the head and neck. Patients who had complete response after completion of treatment did better irrespective of the site of the treatment. More effective systemic therapy is needed as most patients had local and distant failure. Routine use of chemotherapy post chemoradiation improves locoregional control and also decreases distant failure.

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