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Original Article

Metastatic Nasopharyngeal Carcinoma: Outcome from Cancer Institute, Chennai

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Abstract

Background: Optimal management of metastatic nasopharyngeal carcinoma (NPC) at presentation is debatable. The aim of this study was to investigate the treatment outcome of patients with metastatic NPC treated with concurrent chemoradiation or with radiation alone and to analyze the factors that correlate with the outcome. **Methods:** This was a retrospective study of patients with metastatic NPC treated in Cancer Institute, Chennai, from 1996 to 2015 with either chemoradiation or only radiation. Factors including age, sex, stage, treatment type, and type of metastasis were correlated with the outcome. Statistical analysis was done using SPSS version 20, and survival was estimated by Kaplan–Meier's curve. **Results:** A total of 515 patients with NPC were treated during this period, and among them, 74 patients (14%) had metastasis at the time of presentation. The median follow-up was 14 months; the median progression-free survival and overall survival (OS) were 11 months and 19 months, respectively. About 72% (n = 53) were treated with chemoradiation and the rest 28% (n = 21) were treated with radiation alone. The 3-year OS was better in patients who received chemoradiation (39%) as compared to those who received only radiation (23.8%). Patients with the bone-only site of metastasis had better survival. Among them patients with oligometastatic bone disease (1–3 sites) had a better 3-year OS (51%) as compared to multiple bone metastasis (>3) 15.8%. **Conclusion:** Chemoradiation can be an option to treat metastatic NPC. Patients with oligometastatic bone disease had better survival.

Keywords: *Chemoradiation, metastatic nasopharyngeal cancer, survival*

Introduction

Nasopharyngeal carcinoma (NPC) is a rare malignancy with the highest incidence in patients from northeast India.[1] The majority of patients in India present with locally advanced stage or with distant metastasis.[2,3] NPC is a chemotherapy and radiosensitive disease with distinct demographic, clinical, staging, and treatment options as compared to nonnasopharyngeal head-and-neck cancer.[4] In view of the paucity of randomized controlled trials in metastatic NPC, the optimal treatment is unknown. The usual practice is first-line platinum-based therapy and second-line gemcitabine- or taxane-based chemotherapy.[5] There is ongoing research with Epstein–Barr virus (EBV) such as vaccination or administration of cytotoxic T cells targeting EBV[6] and immunotherapy.[7] There is a lack of long-term outcomes of metastatic NPC from India. This study was done to compare the outcomes of patients with NPC treated with chemoradiation or radiation alone and to assess factors that correlated with the outcome.

Methods

This was a retrospective study of patients with metastatic NPC treated in Cancer Institute, Chennai, from 1996 to 2015. The diagnosis was established by biopsy of the nasopharyngeal mass. The staging investigations were contrast-enhanced computerized tomography of head and neck, chest X-ray, ultrasound of abdomen/pelvis, and bone scan. Patients were treated with palliative intent either with chemoradiation or only radiation. The chemotherapy regimen concurrent with radiation was either cisplatin and 5-fluorouracil or only cisplatin. Patients were reassessed after completion of chemoradiation or only radiation. Zoledronic acid 4 mg intravenously every month for 2 years was administered for patients with bone metastasis. After completion of treatment,

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patients were evaluated monthly for the first 6 months, 2 monthly until 2nd year, 3 monthly in the 3rd year, and 6 monthly thereafter. During the first follow-up, patients underwent clinical examination, nasopharyngoscopy, and biopsy, if any residual disease. Further investigations during the follow-up were nasopharyngoscopy, chest X-ray, ultrasound abdomen/pelvis every year, and bone scan, if symptomatic.

Progression-free survival (PFS) was calculated from the date of diagnosis to date of progression or date of the last follow-up. Overall survival (OS) was calculated from the date of diagnosis to date of death or date of the last follow-up. Survival was estimated by the Kaplan–Meier method. The Cox regression model was used to assess prognostic factors. $P < 0.05$ was considered statistically significant, and statistical analysis was performed using SPSS version 20 (IBM corporation, New York, USA).

Results

A total of 74 patients were included in this analysis, with a median follow-up of 14 months. The median age was 42 years (range: 9–77 years). Fifty-five patients (74%) were male and 19 (26%) were female. The most common symptom at presentation was a lump in the neck (78%) followed by a nasal block (18%). The histology was the World Health Organization (WHO) Type 2 in 93% and WHO Type 1 or 3 in 7%. T Stage was T1–T2 (57%) and T3–T4 (43%). N stage was N 0–1 (24%) and N 2–3 (76%). The sites of metastasis were bone only in 95% (n = 70) and 5% (n = 4) had visceral metastasis [Table 1].

A total of 72% (n = 53) were treated with concurrent chemoradiation. The radiation schedule was 2 Gy per fraction per day to a total dose of 66–70 Gy. The chemotherapy schedule concurrent with radiation was cisplatin 70 mg/m^2 on day 1 and 5-fluorouracil 325 mg/m^2/day from day 1 to day 3 every 3 weekly for 3 cycles (70%), cisplatin 70 mg/m^2 every 3 weekly for 3 weeks (23%), and weekly cisplatin 40 mg/m^2 for 6 cycles (7%). A total of 28% (n = 21) received only radiation to locoregional sites. Complete response in the locoregional site was 87% in patients who received chemoradiation and 48% in those who received only radiation.

Table 1: Baseline characteristics

Variable	*n* (%)
Median age (years) (range)	42 (9-77)
Male	55 (74)
Female	19 (26)
Symptom at presentation	
Lump in the neck	58 (78)
Nasal block	13 (18)
Others	3 (4)
Histology	
WHO Type 2	69 (93)
WHO Type (1 or 3)	5 (7)
T stage	
T1-T2	42 (57)
T3-T4	32 (43)
N stage	
N0-N1	18 (24)
N2-N3	56 (76)
Site of metastasis	
Bone only	70 (95)
Visceral	4 (5)

The median PFS was 11 months (range 1–201 months), and the 3-year PFS was better in patients who received chemoradiation (35%) as compared to only radiation (19%). The median OS was 19 months (range 1–201 months), and the 3-year OS rate was 36%. The median OS for patients with bony only metastasis and visceral metastasis was 23 months and 4 months, respectively.

The factors included in the univariate analysis [Table 2] were age, sex, histology, stage, number of sites of bone metastasis, and treatment modality. Univariate analysis showed that type of treatment (chemoradiation) and oligometastatic bone-only disease correlated with improved outcome. Multivariate analysis [Table 3] showed that patients with extensive bone metastasis >3 correlated with poor outcome (hazard ratio-2.03, confidence interval 1.10–3.74, P = 0.022). Figures 1 and 2 show the Kaplan–Meier curve for type of treatment and bone metastasis, respectively.

Discussion

Nasopharyngeal cancer has a higher incidence of metastasis at presentation than nonnasopharyngeal head-and-neck cancers.[8-11] In our study, 14.3% of carcinoma of nasopharynx presented with metastasis at presentation. Bone was the most common site (95%) of distant metastasis in our patients. A study from China also reported bone (75%) as the most common site of metastasis.[12]

It is debatable to consider chemoradiation or radiation alone for the treatment of metastatic NPC. A Japanese study[13]

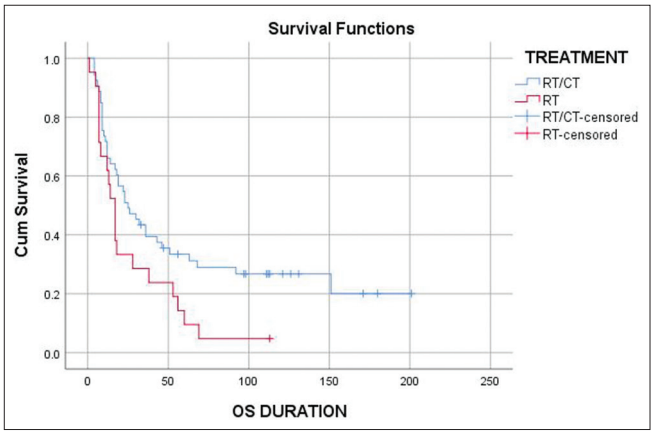

Figure 1: Kaplan–Meier curve of treatment modality. Blue line - Chemoradiation; Red line - Radiation only

Table 2: Univariate analysis

Variable	*n*	Median survival (months)	3-year OS (%)	HR	CI	*P*
Age						
<42	36	26	44.4	1.00*	0.81-2.29	0.233
>42	38	18	34.2	1.36		
Sex						
Male	55	19	38.2	1.00*	0.59-1.87	0.857
Female	19	22	31.6	1.05		
Histology						
WHO Type 2	69	19	36.2	1.00*	0.17-1.75	0.309
WHO Type (1/3)	5	36	40	0.54		
T stage						
T1-T2	42	19	34.7	1.00*	0.45-1.30	0.332
T3-T4	32	23	38.7	0.76		
N stage						
N0-N1	18	23	50	1.00*	0.68-2.30	0.457
N2-N3	56	18	35.7	1.25		
Treatment modality						
Chemoradiation	53	25	39.5	1.00*	1.02-3.06	0.039
Radiation only	21	17	23.8	1.77		
Type of metastasis						
Oligometastasis	51	36	51	1.00*	1.30-4.14	0.004
Multiple metastasis	19	13	15.8	2.32		

HR – Hazard ratio; CI – Confidence interval; OS – Overall survival

Table 3: Multivariate analysis

Variable	HR	CI	*P*
Treatment modality			
Chemoradiation	1.00*	0.84-2.77	0.161
Radiation only	1.53		
Type of metastasis			
Oligometastasis	1.00*	1.10-3.74	0.022
Extensive metastasis	2.03		

HR – Hazard ratio; CI – Confidence interval

showed incorporating radiation in advanced NPC improved the outcome. The National Comprehensive Cancer Network Guidelines recommend concurrent chemoradiation as an option in metastatic NPC.

The median survival of bone-only metastasis was 23 months, whereas, in visceral metastasis, it was 4 months. Consideration to participate in a clinical trial should be strongly recommended in patients with NPC with visceral metastasis.

The majority (72%) of our patients were treated with concurrent chemoradiation with 5-fluorouracil and cisplatin. A meta-analysis of palliative chemotherapy in metastatic NPC showed that the triplet regimen improved response but failed to improve survival and had more toxicity.[14] Among the doublet regimens, the taxane–platinum combination had the best efficacy followed by gemcitabine platinum and then 5-fluorouracil and platinum.[14] Patients who cannot tolerate cisplatin can be considered for carboplatin-based chemotherapy.[15]

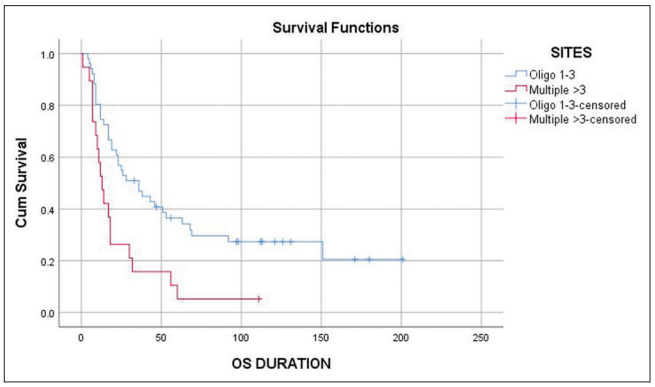

Figure 2: Kaplan–Meier curve showing type of metastasis. Blue line - Oligometastasis; Red line - Multiple metastasis

In one study, Yeh *et al*.[13] showed that median and 2 years' OS of metastatic NPC were 9.7 months and 14%, respectively. In our study, the median survival and 2 years' OS was 19 months and 45.9%, respectively, and patients treated with concurrent chemoradiation had a better median OS (25 months). Bouaouina *et al*.[16] showed that cisplatin-based chemoradiation with curative dose improved survival. A case series from Memorial Sloan Kettering Cancer Center[17] also showed that patients treated with chemoradiation had a long-term survival.

A Chinese study[18] showed that patients with >3 metastatic bone lesions have poor OS as compared to patients with <3 bone lesions. Our study also showed that patients with oligometastatic bone disease (1–3 lesions) had a better survival rate as compared to those with multiple bone metastases.

The limitations of this study are the retrospective nature, nonrandomized study, small sample size, physician discretion on type of treatment, lack of EBV testing in tumor, and plasma EBV for surveillance.

Conclusion

Chemoradiation can be an option to treat metastatic NPC. Patients with bone-only oligometastasis (<3 bone lesions) had improved survival.

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Conflicts of interest

There are no conflicts of interest.

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