Osteosarcoma of head and neck: A retrospective study on prognostic factors from a single institute database

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SUMMARY

Background: Osteosarcoma is a common bone malignancy occurring infrequently in head and neck region, the NCDB database of osteosarcoma suggests that the survival and prognosis of the head and neck osteosarcomas lie midway among other sites of occurrence, poorest survival is pelvic region and best is upper extremity. The influence of other prognostic factors independently effecting survival and recurrence are not studied widely because of scarce data even in databases. More over; these database are underrepresent eastern population. The authors institute treated around 160 head and neck osteosarcomas (HNOS) from 2007 to 2013 which were evaluated retrospectively for prognostic factors effecting survival and recurrence in specific population.

Patients and method: The historical records of patients treated for head and neck osteosarcomas from 2007 to 2013 were charted. The clinical and pathological factors affecting the local recurrence (LR), overall survival (OS), disease free survival (DFS), metastasis (MT) were analyzed in univariate and multivariate cox regression model for survival.

Results: A total of 160 HNOS patients were treated in the given time period, and 137 patients with follow up were analyzed. The median period of follow up was 3.067 ± 0.356 years for the alive patients. In the multivariate cox regression model for OS; surgical margin ($p = 0.000$) was most significant, histological grade was borderline ($p = 0.062$). For LR: surgical margin ($p = 0.002$), histological subtype ($p = 0.048$) and histological grade ($p = 0.024$). For MT; surgical margin ($p = 0.000$) was the significant factor.

Conclusion: Histological grade and unclear margins are the significant independent prognostic factors effecting disease outcome of HNOS.

Introduction

Osteosarcoma is a common neoplasm of the bones, effecting infrequently in the head and neck region, Osteosarcoma occurs in two peaks of life, first peak is during adolescence and the second peak in older adulthood. Skeleton of the extremities are most often involved by this tumor and only 8% are reported in skull and jaw [1].

The treatment protocols of osteosarcoma is based on the large trials or meta-analysis which are conducted for the limbs and the trunk, notably many of these studies have omitted head and neck region due to complexities of treatment in these sites [3], moreover; head and neck osteosarcomas have not showed a similar pattern of demographic presentations of the other sites of the body, the mean age of diagnosis of head and neck osteosarcoma is 30 years of age while children and adolescents are most often affected for other sites [5]. The survival outcomes of osteosarcoma among various sites and age groups vary drastically and because of these differences, the treatment protocols of other sites are not applicable in head and neck sites.

Thus, current concepts of managing the osteosarcoma of head and neck (HNOS) is based on multiple retrospective studies consisting of limited number of patients which does not represent the global population, Kassir et al. [2] contributed to a meta-analysis of 173

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patients illustrating the survival status and prognostic factors effecting HNOs. The national cancer database report on osteosarcoma of head and neck in 2003 had elaborated many factors influencing survival and specifically highlighted the need of initial surgery [4], both these studies stress on importance of initial surgery for better outcome however; either of them don't represent eastern population.

The authors institute experiences a fairly high number of patients with osteosarcoma of head and neck for multivariate analysis, a retrospective study is conducted to understand the prognostic factors and the results are discussed with the previous studies.

Patients and methods

The records of all the patients treated for osterosarcoma of head and neck form 2007 to 2013 were retrieved, patients were charted for recurrence and survival, the prognostic and demographic factors such as age, gender, site of the tumor, size of the tumor, histological subtype, grade of tumor, therapeutic regimen were analyzed in a univariate model for locoregional recurrence (LR), overall survival (OS), disease free survival (DFS), distant metastasis (MT); further a multivariate cox regression was performed for overall survival (OS). Locoregional recurrence (LR). K M graph was made for all the significant factors effecting survival or DFS.

Statistical methodology

Descriptive statistics were derived for parameters such as age and gender. Univariate analysis was carried out by using either chi-square test or fisher's exact test as appropriate. Univariate Log-rank test was also carried out to find the association between various factors and LR, OS, DFS status. Factors that were associated with the outcome with a p-value of <1.000 in the univariate analysis were considered for multivariable cox proportional hazards model. Kaplan–Meier survival curves were drawn to study the survival distributions. All statistical analysis was performed by using SPSS version 17.0 for Windows (Chicago, IL). A p-value of less than 0.05 was considered to be statistically significant.

Results

There were a total of 160 patients treated with head and neck osteosarcoma in the given time period.

The records of all the patients were retrieved for information on follow up and survival. 23(14.3%) patients did not show continued follow up and could not be recalled. Table 1 shows the demographic distribution of all the patients treated in the given time period.

A total of 137 patients contained follow up information who were analyzed for this study. The median period of follow up was 3.067 ± 0.356 years for the alive patients.

A total of 89(65%) patients had survived by the time of study and 48(35%) had died of disease specific causes, the DSS in the study is same as OS. 26(19%) patients had LR, 26(19%) patients had reported MT.

All of 137 patients were charted for factors influencing LR, DFS, and OS, MT. Table 1 shows the univariate analysis of all the factors analyzed in the study for LR, DFS, MT and OS.

Maxillary and skull base tumors often showed metastasis to that of mandibular tumors (p = 0.015). Patients who did not undergo surgery as an initial therapy often showed metastasis (p = 0.002), patients with unclear margins often showed metastasis (p = 0.002), patients without initial surgical treatment (p = 0.05) and positive margins (p = 0.001) died more often. Surgical margin was the only significant factor effecting DFS (p = 0.002).

Table 1
Demographic and prognostic factors of the patients with HNOS treated from 2007 to 2013 including the patients lost in follow up.

	Follow up N	All N
Age (years)		
⩽30	43	55
31–60	75	85
>60	19	20
Gender		
Male	62	71
Female	75	89
Site		
Maxilla and skull base	58	64
Mandibular	79	96
Initial surgery		
Yes	81	98
No	56	62
Histological subtype		
Conventional	93	109
Secondary	22	24
Small cell	2	3
Telangiectatic	2	3
High grade surface	2	2
Low grade central	6	6
Periosteal	2	2
Parosteal	0	1
Unknown	8	10
Grade		
I (well differentiated)	8	8
II (median differentiated)	0	1
III (poorly differentiated)	121	141
Unknown	8	10
Size (cm)		
⩽4	92	103
>4	45	57
Surgical margin		
Clear	130	152
Unclear	7	8
Therapy given		
Surgery only	57	–
Surgery + chemo	11	–
Surgery + chemo + Radio	19	–
Surgery + Radio	50	–

In the multivariate cox regression model for OS; surgical margin, histological grade were the significant factors (Table 3).

In the multivariate cox regression model for LS; surgical margin, histological subtype and histological grade were the significant factors (Table 4).

In the multivariate cox regression model for MT; surgical margin was the significant factor, there was non-significant but a trend of higher metastasis in maxillary and skull base tumors (Table 5).

The 5-year overall survival rate was 56.0% for the patients with HNOS between 2007 and 2013 (Fig. 1 and Table 6), the prognostic factors significantly effecting 5 year survival rate were, weather; surgery was the initial therapy (p = 0.041), the surgical margin (p = 0.001), and site (p = 0.043). The surgery alone vs surgery and chemotherapy group showed borderline significance (p = 0.08). Fig. 1 illustrates disease free survival and overall survival of the cohort, Fig. 2 illustrates the survival of patients according to therapy given, Fig. 3 illustrates the survival of patients with various histological grade of tumor.

Table 7 describes the total number of the patients treated in each year along with the number of patients lost in follow up from one to seven years.

Out of 7 patients with positive margins; 4 patients received radiotherapy and one patient received chemotherapy and one did