

Non melanoma skin cancers: a retrospective study in department of radiation oncology, Mashhad, Iran

Kazem Anvari, MD
Sare Hosseini, MD
Mehdi Seilanian Toussi, MD
Saeede Afifi, MD

Solid Tumor Treatment Research Center, Omid Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

*Corresponding Author:
Sare Hosseini, MD
Solid Tumor Treatment Research Center, Omid Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
Email: hosseinis@mums.ac.ir*

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Background: Non melanoma skin cancer (NMSC) is the most common cancer worldwide. In most cases, the general outlook is excellent; however, local recurrence or metastasis can occur. In this study, we investigated possible tumor and host characteristics affecting the treatment outcome in our department of radiation oncology.

Method: We retrospectively studied cases with non melanoma skin cancer (NMSC) who were consecutively referred to department of radiation oncology in Omid and Ghaem Hospitals between 1997 and 2007. The effect of the patients' characteristics (age, sex), tumor characteristics (histology, size, location), and treatment modalities on prognosis were evaluated.

Result: We studied 426 patients with a median age of 65 (range: 14 to 102) and a male to female ratio of 1.4:1. Pathologic review showed 72% of the patients had basal cell carcinoma (BCC) and 28% had squamous cell carcinoma (SCC) with a 5-year event free survival of $87\pm 3\%$ and $67\pm 8\%$, respectively ($p < 0.001$). The local recurrence rate was higher in cases with scalp lesions (35%). The patients who underwent combined modality treatment experienced significantly more instances of failure as compared to those receiving radiotherapy alone (5-year event free survival of $81\pm 6\%$ vs. $84\pm 6\%$, $p=0.04$) which reflects the higher number of cases with adverse features including larger lesions and/or a positive surgical margin in this group. Sex, age, and multifocality were not significant predictors of prognosis.

Conclusion: SCC histology and scalp location were predictive of higher rates of treatment failure in patients with NMSC. There was no correlation between age, sex, multifocality and overall outcome. The higher rate of recurrence in cases receiving combined modality treatment is most probably due to the high number of tumors with adverse prognostic features in these cases.

Keywords: local recurrence, metastasis, non-melanoma skin cancer, prognostic factors, radiotherapy, radiation oncology, surgery

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INTRODUCTION

Non melanoma skin cancers (NMSC), which mostly include basal cell and squamous cell carcinoma (BCC, SCC), are the most common

human cancers in the world¹. Most of the lesions develop on sun-exposed sites. Although metastasis is very rare, these malignancies are able to invade underlying soft tissues, bone, and cartilage if left untreated². As compared to sun-related skin cancers,

SCCs that also occur on burn scars or develop secondary to underlying chronic inflammation or immunosuppressive diseases tend to be more aggressive with a higher tendency for distant metastasis³. Ten-year survival rates of less than 10% have been reported in patients with metastatic cutaneous SCC⁴. Metastatic BCC is extremely rare with a generally poor prognosis with an average survival of 8 to 10 months⁵. As compared to BCC, metastasis occurs much more frequently in cutaneous SCC, especially in non-sun related cases^{5,6}.

Although most NMSC cases are treated successfully by complete excision or radiation therapy, there is still a lifelong risk of recurrence or rarely metastasis which depends on multiple prognostic factors. According to the results of previous trials, several factors including the pathological subtype, location and tumor size, feature of tumor borders, whether the tumor is primary or recurrent, and the underlying factor for tumor development affect prognosis^{7,8}.

According to the Iranian cancer registry report in 2008, skin cancer ranks first among five most common cancers in Iran⁹. The purpose of this study was to determine the epidemiological features and overall outcome in patients with non melanoma skin cancer (NMSC) who were referred to our institute department of radiation oncology in the Northeast of Iran.

PATIENTS AND METHODS

This retrospective study was performed using hospital based data. All patients with pathological diagnosis of NMSC who were referred to Omid and Ghaem Radiation Oncology Department from 1997 to 2007 were reviewed. Demographic data including age and sex as well as the lesion location and tumor characteristics were obtained from medical records. We confined our statistical analysis to patients with SCC or BCC. For patients who had both

SCC and BCC, any event was considered for the specific histological subtype. Disease free survival was calculated using the Kaplan-Meier method by measuring the interval between pathological diagnosis and disease recurrence/ metastases or the last visit without the disease evidence.

We used SPSS V.17 for statistical analysis. We utilized log-rank test to compare survival curves and chi-square test to compare recurrence rates between groups. P-values less than 0.05 were considered significant.

RESULTS

Among 470 patients with the diagnosis of NMSC, 420 cases with sufficient medical records were eligible for enrolling in this study. Histologic examination revealed that 293 (72%) had BCC and 114 (28%) had SCC. Moreover, 401 (94%) lesions were located on sun exposed areas. Burning scar was the underlying disease in 3 cases of SCC on the extremities of whom 2 experienced local recurrence. Eleven patients had a history of scalp radiation for the treatment of tinea capitis in childhood. Most patients with SCC and BCC (323, 77%) had a single lesion. The median age at diagnosis was 65 years (range: 14-102) with a male to female ratio of 1.4:1. The largest and smallest lesions were 10×9 cm on the scalp and 0.5×0.5 cm on the cheek, respectively. Among patients with SCC and BCC, with a median follow-up duration of 20 months (range: 3 to 168 months), 40 events including 27 local recurrences and 13 metastases were recorded. The 5-year event free survival for patients with SCC and BCC was (67±8%) and (87±3%), respectively (P value < 0.001). As shown in Table 1, patients with scalp tumors experienced a higher rate of recurrence. In comparison with those receiving radiotherapy alone, patients undergoing combined modality treatments or surgery experienced higher rates of treatment failure with significantly lower event free survival rates (P= 0.04). Age, sex, and

Table 1. Five-year event-free survival rates according to the tumor location

Tumor location	patients, n	Event, n (%)	Five-year event-free survival% ±SD	P-value
Face	103	10 (9.7)	76±8	0.013
Eyelid & canthus	45	7 (15.5)	81±9	
Scalp	83	14 (16.8)	64±9	
Nose	120	6 (5)	94±3	
Ear	38	0 (0)		
Other	31	3 (9.6)	81±12	

the number of lesions had no significant effect on the recurrence rate (Table 2).

DISCUSSION

In a review of 420 patients with NMSC, we found that patients with BCC had a significantly lower recurrence rate than those with SCC of the skin. In addition, patients with scalp lesions experienced significantly higher rates of recurrence as compared to other locations. The patients who received radiotherapy alone had the best overall outcome when compared to other treatment modalities. Age, sex, and the number of lesions were not significant predictors of the recurrence rate.

In a review of multiple studies on SCC of the skin, ear, and lip since 1940, Rowe et al showed that the following variables were correlated with local recurrence and metastatic rates: 1) treatment modality, 2) prior treatment, 3) location, 4) size, 5) depth, 6) histologic differentiation, and 7) perineural involvement. Mohs micrographic surgery was associated with a lower number of local recurrences as compared to conventional excision, especially in larger, deeper, and poorly differentiated SCC tumors⁷.

In our institute, conventional excision is the usual method of surgery with or without radiotherapy. Patients with an uncertain or positive margin following surgery receive postsurgical radiation therapy. In our series, those who received radiotherapy alone had better outcomes as compared to cases receiving combined surgery followed by radiotherapy. This finding can be explained by the fact that combined modality is more commonly

performed for tumors with less favorable features including larger and deeper lesions with positive or close margins. The failure rates were the highest among patients who underwent surgery alone. Considering the fact that our study was hospital/department based and performed retrospectively, we cannot compare the effectiveness of different treatment modalities precisely.

According to the existing data, SCC of the midface and lip are especially prone to higher local recurrence and lower 10-year disease free survival^{10,11}. In BCC, migration along the perichondrium, facial and tarsal plates accounts for the higher recurrence rates in tumors involving the eyelid, nose, and scalp¹². We found higher rates of local recurrence on the scalp. This can be explained by the difficulty of adequate surgical margin in some cases, especially in large and deep lesions. Compatible with previous studies^{13,14}, we could not find any correlation between age, sex, tumor multifocality, and overall outcome. The local control rates in our cases with NMSC were satisfactory, especially in BCC patients. Even in patients with unfavorable features who needed the combined treatment modality (surgery plus radiotherapy), only 12 out of 128 (9.3%) experienced recurrence.

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Table 2. Demographic and clinical characteristics of the patients

	Patients, n	Event, n (%)	Five-year event free survival% \pm SD	P. value
Age				
\leq 66 years	210	24 (11)	84 \pm 4	0.2
>66 year	210	16 (7.6)	79 \pm 6	
Gender				
Male	250	24 (9.6)	80 \pm 4	0.8
Female	170	16 (9.4)	84 \pm 5	
Number of lesions				
Single	323	28 (8.6)	83 \pm 3	0.2
Multiple	97	12 (12.3)	79 \pm 7	
Treatment modality				
Surgery alone	82	11 (13)	74 \pm 9	0.04
Radiotherapy alone	196	16 (8)	84 \pm 4	
Surgery with adjuvant radiotherapy	128	12 (9)	81 \pm 6	

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