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MAST CELL'S PARTICIPATION IN CLINICOPATHOLOGIC OUTCOME OF CANCERS: A COMPARATIVE STUDY BETWEEN INTRA ORAL AND LOWER LIP SQUAMOUS CELL CARCINOMA

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ABSTRACT

Background: Squamous cell carcinoma is the most common oral cancer, representing approximately 94% of all oral malignancies. This study was aimed to compare of mast cell density in lower lip and intra oral Squamous cell carcinoma and also evaluate this density in central and marginal zones of these tumors.

Methods: In this cross-sectional study, 30 formalin fixed paraffin embedded tissue samples were investigated with diagnosis of well-differentiated intra oral SCC and 20 of the lower lip ones. 4 micron sections were prepared from each block in order to toluidine blue staining. Mast cells

densities were evaluated in both marginal and central areas of tumor by X400 magnifications under light microscope. Finally, results were analyzed statistically and p value of lower than 0.05 was set as significant.

Results: Mast cell densities in both marginal and central areas of tumor were significantly higher in SCC of lower lip vs. intra oral ones. (P=0.01) Also, these densities were significantly higher in central vs. marginal area at both location of tumor. (P<0.01)

Conclusion: It seems corresponding to better prognosis of lower lip SCCs vs. intraoral ones increased density of mast cells in lower lip SCCs resulting in this study, reflects inhibitory effect of these cells through tumorogenesis process.

Keywords: SCC, lower lip, Intraoral, Mast cell

INTRODUCTION

Squamous cell carcinoma (SCC) is a malignant tumor of squamous cells. This lesion is the most common oral cancers which consists 94 % of all malignancy in oral cavity. This tumor reveals great capacity of invasion and metastasis [1]. Oral tumorogenesis involves some of separate genetics contingencies that result in aggressive cancer. Every mutation causes unsteady reproduction of cells and generates cell mass. [2] Lower lip SCC usually demonstrated slower growth rate resulting better prognosis than upper lip in a way that the survival rate of 5 year patients is more than 90 percent. Tongue SCC is the most common intra oral malignancies excluding lip area. It often has aggressive manner, usually has no symptom whether in the final stage.[3]

Mast cells are ovate to round cells which has 20 to 30 micrometer diameter and contain 0,2-0,5 micrometer basophilic secretory granules. This secretory cell is widespread around vascular and lymphatic vessels, nerve bundles. It is detectable throughout the body but has more intensity in skin, digestion mucus and respiratory system. The role of these cells is obvious in the host defensive mechanisms which react to increase allergy, acute and chronic inflammation, stimulation of T cells and defense against parasites. [4-8]

Mast cells have been deleted at marginal zone of some malignancies. The increased density of these cells has been reported with colorectal neoplasms, skin cancers, lung adenocarcinoma and breast carcinoma. By then, following activation of mast cells and releasing their mediators, an increasing in reproduction of tumor cells and also vascularization occur, while repressing mast

cells pharmacologic activity restrain this effect. [9-14]

Roche WR demonstrated that injection of mast cell suspension cause tumor progression but decreased number of tissue mast cells led to tumor suppression. [7] Also, Ionov ID reported that, inhibition of mast cell degranulation resulted in tumor suppression. [8] Even though, a notable study of breast revealed that, heparin released from mast cells inhibit clonogenic growth of cancer cells.[12]

So, due to this paradoxical effect, also respect to different clinical behavior in lower lip and intra oral SCC and presence and importance of mast cells around malignancies, this study was scheduled to compare between the density of mast cells in lower lip SCC and these intraoral tumors and evaluate this density in central and marginal areas of tumor.

MATERIAL AND METHOD:

This cross sectional study was conducted by accumulation of pathologic samples with definite diagnosis of well-differentiated SCC in lower lip and intraoral region at Pathology department of Shahid Beheshti University of medical sciences, Taleghani hospital. 30 samples of intraoral SCC and 20 of lower lip ones with enough tissue were chosen and studied. Information related to age and sex was also registered. From each block, 2 sections of 4 micron were provided; the former for hematoxilin- eosin (H&E) staining in order to elementary assessing of tumor cells and the later for Toluidine-blue staining related to mast cell density evaluation.

At the next step, slides were studied by 2 observers using an Olympus microscope under 400 times magnification. Mast cells were counted separately in 10 randomly fields of central tumor area and 10 randomly fields in marginal region of tumor. (Fig 1,2)

Finally, T-statistical test of independent data (T-test) were used to compare the mast cell densities in 2 areas. Also, Paired T-test was applied to compare the difference between densities in two central and marginal areas of tumor and Multivariable linear regression method- backward type was utilized for assessment of simultaneous effect of age, sex and location of tumor. P value of lower than 0.05 was considered significant.

RESULTS:

The age average of related samples in this study was 61.1 years old but more important, as shown in table 1, the least mast cell density reported by first observer in central area of lower lip SCC was 38, the highest density of same observer in central area of this tumor was 145 and also, the average

density of mentioned areas were 85 and 90, respectively. (table1)

Statistical analysis in respect to compare mast cell densities in 2 considered areas and also comparison between central and marginal areas are described as below:

There is a significant statistical difference between mast cell densities in central area of lower lip and intraoral SCC, also in marginal tumor area of both sites. That is, in both central and marginal tumor area, density of mast cells in lower lip is significantly higher than density of these cells in intraoral SCCs. (table2)

Respect to compare mast cell densities between central and marginal tumor areas in both locations, we have found not only a high correlation between densities in two areas, but also a significant statistical difference between them. That is, in most of densities, those related to marginal area is lower than central part. (table3)

Also, in order to consider the effect of age and sex through density of mast cells, we used linear regression analysis. By then, there was no correlation between age and sex with density of mast cells.

Table 1: Count of mast cell densities in intraoral and lower lip SCCs at central and marginal areas for both observers.

Location of tumor		Minimum of mast cell density	Maximum of mast cell density	Average of mast cell density	Standard deviation
Lower lip	M.C.C 1*	38	145	85.90	32.972
	M.C.C 2	34	143	81.60	32.362
	Margin 1	27	132	70.30	29.824
	Margin 2*	26	118	68.05	28.153
intraoral	M.C.C 1	22	136	63.37	28.994
	M.C.C 2	25	139	60.07	26.572
	Margin 1	15	145	48.13	30.877
	Margin 2	16	131	46.00	27.317

***M.C.C refers to central area of tumor, Margin refers to marginal area of tumor. 1 & 2 refer to first and second observer respectively.**

Table2: Comparison of mast cell densities in intraoral and lower lip SCCs and comparison between central and marginal areas for both observers

mast cell densities in intraoral and lower lip SCC	P value
M.C.C 1*	0/014
M.C.C2	0/013
Margin 1	0/015
Margin 2	0/008

***M.C.C refers to central area of tumor, Margin refers to marginal area of tumor. 1 & 2 refer to first and second observer respectively**

Table3: correlation between mast cell densities in intraoral and lower lip SCCs and between central and marginal areas for both observers

Location of tumor		number	Correlation factor	P value
Lower lip	M.C.C 1 & Margin 1	20	.950	.000
	M.C.C2 & Margin 2	20	.969	.000
Intraoral	M.C.C 1 & Margin 1	30	.926	.000
	M.C.C2 & Margin 2	30	.940	.000

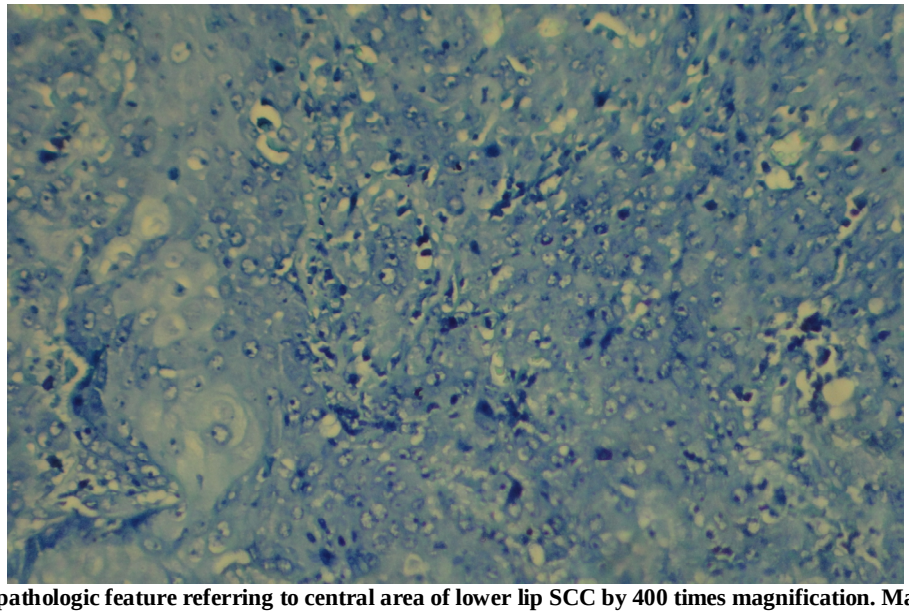

Fig1: Histopathologic feature referring to central area of lower lip SCC by 400 times magnification. Mast cells were marked through Toluidine-blue staining

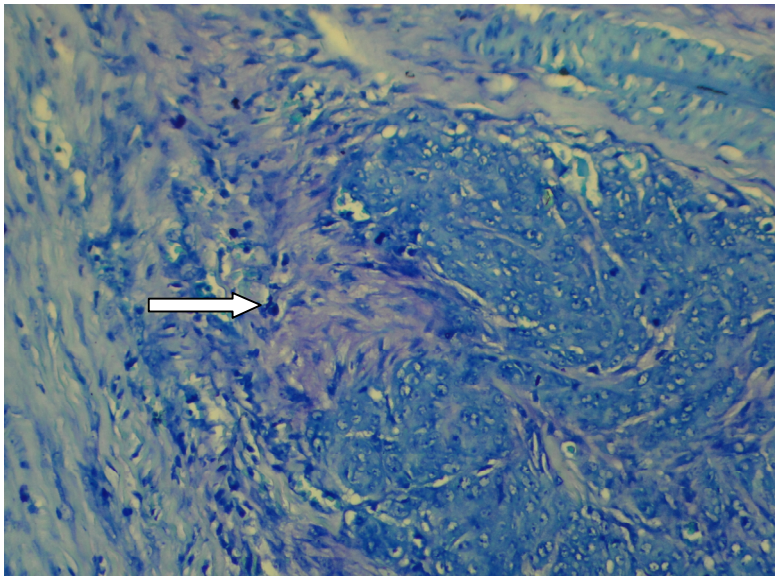

Fig2: Histopathologic feature referring to marginal area of intraoral SCC by 400 times magnification. Mast cells were marked through Toluidine-blue staining.

DISCUSSION:

The importance of mast cells in pathogenesis of SCC in many studies has been proved [4,5,7,9,12]. So far, many studies have been conducted about the correlation of mast cells and different types of malignant and benign tumors and also, a considerable increasing of mast cell densities in marginal area of malignant tumors in contrast with benign cases and normal tissue [10-12,15]. In respect of such investigated studies in this research, mast cells are known important in angiogenesis, pathologic conditions and also tumorogenesis of SCC [16-21]. However, another factors except mast cell were reported in study of Jahanshahi et al [16] contributing in angiogenesis of intraoral SCC. In the best of our knowledge, there was no study in regard to compare mast cell density in lower lip and intraoral SCC. Parizi et al [17] concluded that mast cell densities were lower in oral SCCs compare to these cutaneous tumors except lower lip samples. In the present study, mast cell densities were found higher in lower lip SCC; surprisingly in close amounts to Parizi et al [17] count of these cells in cutaneous SCCs.

Regarding to more precise evaluation through pattern of mast cell densities, it was studied in both marginal and central area of tumor in the present study and found it significantly higher in central area similar to Parizi et al reports [17].

Mast cells carried some adherent molecules and also different types of immunologic responding receptors which react through several specific and non-specific stimulators. These wide spread biologic efficacies and also presence of them close to inflamed and neoplastic tissue enable these cells to play important role during pathologic, immunologic and physiologic procedures.[19,22]

Recent findings demonstrate that aggregated mast cells around tumoral cells have biphasic effect. It means, sometimes they lead to tumor progression but may show inhibitory effect through development of tumorogenesis in other situations.[12,22]

This paradoxical efficacy could be explained by two following points: first, mast cells release widespread mediators with different efficacy including inductive and inhibitory actions [23]. Second, phenotypic expression of these cells is variable and secretory pattern of them differs through their microenvironment. By then, mast cells enable release mediators through selective pattern. [24]

So, in respect to better prognosis of lower lip SCCs vs intraoral ones [3], increased density of mast cells in lower lip SCCs in the present

findings reflects inhibitory effect of these cells through tumorogenesis process. It means microenvironment in lower lip and cutaneous SCCs make changes through induction of inhibitory effect of mast cells resulted in reduction of their effects in progression of tumorogenesis. However more widespread studies are recommended in future for definite evaluation.

CONCLUSION:

It seems, corresponding to better prognosis of lower lip SCCs vs intraoral ones, increased density of mast cells in lower lip SCCs in the present findings reflects inhibitory effect of these cells through tumorogenesis process.

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CONFLICT OF INTEREST:

We have no conflict of interest in this study.

AUTHOR'S CONTRIBUTION:

Sareh Farhadi designed the study, reported the results and prepared the manuscript, Ferial Taleghani and Zhaleh Mohsenifar revised the manuscript, Fatemeh Shahsavari support the thecnical procedures and revised the manuscript, Mohammad Javad Kharazifard prepared the statistical analyses.

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