Short Communication

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Correlation of Tissue Eosinophils with Prognosis in Head and Neck Cutaneous Squamous Cell Carcinomas

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ABSTRACT

BACKGROUND AND OBJECTIVE: The skin squamous cell carcinoma (CSCC) is the second most common skin cancer. The correlation between severe tissue eosinophilia with optimal and undesirable prognosis, or even an ineffectiveness effect was related. The aim of the present study was to investigate the correlation between tissue eosinophilia and prognosis in patients with head and neck squamous cell carcinoma.

METHODS: In this cross-sectional study, 33 patients with squamous cell carcinoma of the pathology department of Shahid Beheshti hospital of University of Babol University of Medical Sciences (age, sex, tumor site) were collected and histopathologic in the vascular and nervous invasions was studied. Numbers of eosinophils (eos.) were counted in 15 successive fields at invasive fronts of HNCSCCs (area of 15 fields=1.2mm^2) at×400 magnification with optical microscope. The correlation between the mean number of eosinophils per Mm² and the severity of eosinophilia (mild and severe) and clinical-histopathologic factors was analyzed.

FINDINGS: Mean eos/mm^2 was 99.1913±104.39897. Overall survival rate, disease-specific survival rate and disease-free survival rate were %72.72, %61.53% and %84.84, respectively. There was inverse significant correlation between disease-free survival with eos/mm^2 (p=0.043). There were no significant correlation between other clinical-histopathologic factors with mean eos/ mm^2.There were inverse significant correlations between 5-year overall survival rate and 5-year disease-free survival rate with severity of tissue eosinophilia (p=0.02 and 0.013 respectively).There were not significant correlations between 5-year disease-specific survival and other factors with severity of tissue eosinophilia.

CONCLUSION: There was inverse correlation between severity of tissue eosinophilia with survival.

KEY WORDS: *Head And Neck Squamous Cell Carcinoma, Eosinophil, Prognosis*.

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Introduction

The cutaneous squamous cell carcinoma (CSCC) is the second most common skin cancer (1-4). The eosinophilic correlation with prognosis has shown different results in squamous cell carcinoma. In some studies, tissue eosinophilia has no effect on patient prognosis (5), in some studies severe tissue eosinophilia, was an optimal prognostic factor for SCC (6-8), and in other studies, severe tissue eosinophilia was an undesirable prognostic factor for SCC (9-11). Regarding the existing contradictions, the aim of this study was to examine the correlation between tissue eosinophilia and clinical-histopathologic factors in head and neck CSCC.

Methods

This cross-sectional study was performed on 33 cases of head and neck squamous cell carcinoma after the adoption in Ethics Committee of Babol University of Medical Sciences with code of 155.1395MUBABOL.REC code. Patients 'demographic and clinical data were extracted from patients' files in the pathology department of Shahid Beheshti Hospital of Babol University of Medical Sciences and also by contact with patients. Histopathological slides were retrieved from the pathology archives. In case of information deficiency, the patient was excluded from the study. The samples were included in the study, which at least 5 years have passed since their cancer was diagnosed. Histopathologic slides were examined under an optical microscope (Olympus CH30, Tokyo, Japan, at a magnification of 400 ×) and numbers of eosinophils were counted in 15 successive fields at invasive fronts of invasive carcinoma (Fig. 1).

The total number of eosinophils divided by the total area of 15 fields (1.2 mm2) for each tumor was calculated and expressed as the mean number of eosinophils per Mm ² (Eos / mm2). Two degrees of eosinophilic tissue were considered 1. mild (0-67eosinophils / mm2) and severe (68 ≥) (5). Clinical data included age, sex, lesion site, history of smoking and alcohol consumption, tumor size, lymph node metastasis, distant metastasis, stage, overall survival, tumor survival and tumor-free survival, as well as histopathological data including nerve and vascular invasion. The data were entered into SPSS 20 software and analyzed by Mann-Whitney, Correlation, Kruskal-Wallis and Chi-Square tests. The correlation between the mean number of eosinophils and tissue eosinophilia severity with clinical-histopathologic factors in patients with head and neck CSCC were analyzes and p <0.05 was considered significant.

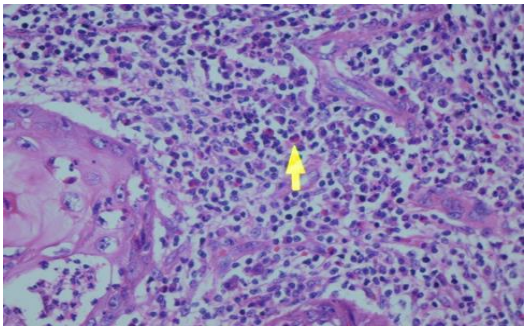

Figure1. Eosinophils in the invasive front of head and neck squamous cell carcinoma (400 x magnifications)

Results

The mean number of eosinophils varied between 83.8 ± 0.39 and 720.83 ± 124.31 in mm2. Eosinophilia was mild in 18 cases (54.5%) and was severe in 15 cases (15.5%). The total mean number of eosinophils was 99.19 ± 104.39. The mean follow up time for patients was 6.8 ± 2.2 years. The overall survival rate of 5 years, disease-specific survival rate of 5 years and the survival rate without disease of 5 years were 72.72%, 61.53% and 84.84% respectively (Table 1). Clinical-histopathological factors differentiated by eosinophilic severity are presented in Table 2. Statistical analysis showed no significant correlation between age, sex, lesion site, tumor size, history of smoking, history of alcohol consumption, vascular and nerves invasion, overall survival, metastasis to lymph node and stage with the mean number of eosinophils. (P-value was 0.634, 0.982, 0.33, 0.179, 21.556, 0.0, 0.829, 0.869, 053.134, 0.0, 0.093 respectively). There was a significant correlation between tumor-free survival with the mean number of eosinophils (p=0.043), that by increasing the mean number of eosinophils, tumor survival was reduced. There was no significant correlation between age, sex, lesion site, history of

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smoking, alcohol consumption, vascular and nerves invasion, clinical stage, tumor size and lymph node metastases with eosinophilia severity (P-value of 0.0612, 0.249, 0.586, 0.202, 0.296, 0.849, 0.607, 062.212, 0.0, 0.061). There was a significant correlation between the overall survival rate of 5 years and the survival rate of 5 years without tumor with eosinophilia severity (P-value of 0.02 and 0.013, respectively). Patients with severe eosinophilia had lower a 5-year overall survival rate and tumor-free survival rate of 5 years. There was no significant correlation between tumor specific survival rates of 5 years with eosinophilia severity.

Table1. Demographic, clinical and histopathological data of patients

Variable		Mean±SD
Mean age (years)		72.73±20.39
Overall survival (Years)		4.88±2.39 yeas
Tumor-free survival		3.94±1.49 years
		N(%)
Eosinophilia severity	Mild	18(54.5)
	Sever	15(45.5)
Sex	Male	27(81.8)
	Female	6(18.2)
Site	Scalp	21(63.6)
	Forehead	4(12.1)
	Face	4(12.1)
	Lips	4(12.1)
Smoking	Yes	15(45.5)
	No	18(54.5)
Alcohol consumption	Yes	2(6.1)
	No	31(93.9)
Tumor size	63.3 centimeters (average)	
Vascular invasion	Yes	16 (48.5)
	No	17 (51.5)
Nerves invasion	Yes	4 (12.1)
	No	29 (87.9)
Metastasis to lymph nodes	Yes	11 (33.3)
	No	22 (66.7)
Distant metastasis	Yes	0 (0)
	No	33 (100)
Clinical Stage	1	8 (24.2)
	2	5 (15.2)
	3	20 (60.6)

Table2. Clinical-histopathological factors differentiated by eosinophilia severity

Eosinophilia severity of the clinical-histopathologic factor		Mild (%)	Sever (%)
Tumor size		2.98cm	4.39cm
Vascular invasion		50	46.66
Invasion into nerves		16.66	6.66
Metastasis to lymph nodes		16.66	53.33
stage	stage I	38.88	6.66
	Stage II	11.11	20
	Stage III	50	73.33
Overall survival rate is 5 years		100	53.33
Disease-specific survival rate of 5 years		100	86.66
Disease-free survival rate of 5 years		100	66.66

Discussion

In this study, there was a significant reverse correlation between the disease-free survival and the mean number of eosinophils, which confirms the role of eosinophils in the development of SCC. From the result obtained, this hypothesis is proposed that eosinophils are likely to act in the development of head and neck squamous cell carcinoma, resulting in poor tumor-free survival. In our study, there was a significant reverse correlation between the overall survival rates of 5 years and the disease-free survival rate of 5 years with eosinophilia severity, suggesting that severe tissue eosinophilia in SCC patients' stroma was associated with undesirable clinical outcome.

The severity of severe tissue eosinophilia as an optimal prognostic factor in Dorta et al. (6) contrasts with our study. The cause of this contradiction can be related to the dual role of eosinophils. The anti-tumor role of eosinophils can be explained by direct and indirect action of tumorocidal activity of eosinophils through releasing of cytotoxic proteins and enhancement of permeability of tumor cells.

The role of eosinophils in tumor progression can be explained by stimulating angiogenesis by producing multiple angiogenic factors and producing matrix metalloproteinase (MMP), including MMP-9. In the study of Alrawi et al. (9), the invasive SCC had a higher eosinophilia index than non-invasive SCC and patients

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with lower eosinophilia index survived well. Their results were in agreement with our study results. The results of the study by Quaedvlieg et al. (10) on the correlation between the mean numbers of eosinophils with metastasis to the lymph node were inconsistent with our study, and Etit et al. (12).

The reason for this conflict may be the lack of patients with distant metastases in two last studies. The result of the study by Oliveira et al. (5) about the correlation between eosinophilia severity and clinical stage was contradictory with the results of our study, which can lead to a change in the distribution of patients from different stages in two studies. In the study of Oliveira et al. (13), severe tissue eosinophilia is a predictive factor for secret metastasis to lymph nodes and severe tissue eosinophilia is a useful histopathologic factor to enhance selective neck dissection in patients with primary OSCC. The result of the study by Jain et al. (7), OSCC, in the context of a significant reversal correlation between the numbers of eosinophils with metastasis was in contrasts with our result, which may reflect the dual role eosinophils in subsequent research. The results of our study showed that there is an inverse correlation between survival and tissue eosinophilia severity.

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