The Prognostic Significance Of Histopathologic Parameters In Squamous Cell Carcinoma Of The Larynx

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In this report correlations between prognosis and some histopathologic parameters were evaluated in a series of 100 laryngeal squamous cell carcinoma cases. The histopathologic parameters were keratinization, mitotic activity, nuclear atypia, tumor infiltration into the thyroid cartilage, vascular invasion, perineural invasion, tumor associated tissue eosinophilia, stromal lymphoplasmocytic infiltration and stromal desmoplasia. When the results were assessed by statisticial methods, it was observed that prognosis was significantly poor in patients having nuclear atypia and stromal desmoplasia. Significant correlation was not observed between other histopathologic parameters 'and prognosis; but it was noted that having recurrences had a negative impact on survival. [Turk J Med Res 1993, 11 (4):199-201]

Key Words: Laryngeal carcinoma, Histopathology, Prognosis

Squamous cell carcinoma of the larynx (SCCL) is not an uncommon disease and it is one of the more curable head and neck cancers. It is known that comparably staged and treated patients with SCCL may have a diverse clinical outcome. There are some reports concerning the effects of various parameters, like tumor localization, stage, different therapeutic approaches, DNA content and histologic characteristics on biologic behaviour of SCCL (1-7). In this study, we evaluated a series of 100 cases of SCCL with a follow up period between 36 months and 7 years and we investigated the effects of keratinization, mitotic activity, nuclear atypia, thyroid cartilage invasion, vascular invasion, perineural invasion, tumor associated tissue eosinophilia (TATE), stromal lymphoplasmocytic infiltration and desmoplasia on prognosis.

MATERIALS AND METHODS

In this study 113 patients operated between 1985 and 1989 having a follow up period between 36 months and 7 years were selected from the archives of Ear Nose and Throat Department of Ankara University Medical Faculty. These cases had been classified according to the TNM staging system using the criteria of American Joint Committee on Cancer (8), and total or supraglottic laryngectomy had been performed (supraglottic horizantal laryngectomy in Ti, T_2, and some T_3 cases; total laryngectomy in some T_3 and all of the T_4 cases). In all of the 113 cases unilateral or bilateral cervical lymph node dissection had also been performed. The glass slides of these patients were examined. Twelve cases were excluded due to insufficient material or due to tumor invasion in surgical resection margins and one other case was excluded because it was an in situ carcinoma. The Hematoxylin-Eosin stained sections of the remaining 100 cases were examined by two pathologists (SDS, SE), who were blinded to the clinical outcome.

Tumors were designated as well, moderately or poorly keratinizing according to the extent of keratinization. Mitosis was evaluated by counting mitoses on 10 High Power Fields (HPF) on the section which showed the highest mitotic activity. Scores 1,2 and 3 corresponded to 0-5 mitosis/10 HPF, 6-15 mitosis/10 HPF and more than 15 mitosis/10 HPF respectively. Nuclear atypia and pleomorphism was designated as mild, moderate or severe. Infiltration of tumor cells in thyroid cartilage, vascular invasion and perineural invasion were evaluated either as present or absent. TATE was assessed 0 to 4 by counting 10 HPF's by the following criteria: 0:0-2 eosinophils per HPF, 1:3-10 eosinophils per HPF, 2: 11-20 eosinophils per HPF, 3: 21-30 eosinophils per HPF, 4:31 or more eosinophils per HPF Lymphoplasmocytic host inflammatory response was subjectively graded 1+ to 3+.

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Table 1. Histopathologic characteristics of 100 cases of SCCL

Characteristics of tumor		%	Characteristics of stroma		%
Keratinization	Poor	22	Tate	0	60
	Moderate	52		1	33
	Well	26		2	6
Mitosis	0-5/10HPF	53		3	1
	6-15/10HPF	37	LP	mild	33
	over15/10HPF	10	infiltration	Moderate	57
Nuclear Atypia	mild	15		severe	10
	modérete	74		peresent	17
	severe	11	Desmoplasia	absent	83

Finally desmoplasia in the tumor stroma was evaluated as present or absent.

Results were assessed by chi square, Kaplan-Meier life analysis and Mantel Haentsel chi square methods to find histological and prognostic correlations. P values below 0.05 were considered statistically significant.

RESULTS

The results of the analysis of the histopathologic variables are presented in Table 1. According to the table majority of the cases (52%) was moderately keratinizing, mitotic activity was usually low (53% between 0-5/10 HPF), 74% of the cases had moderate nuclear atypia and 97% of the cases did not invade cartilage tissue. When host responses were evaluated, it was understood that most of the cases were concentrated in low TATE groups (93% had score 0 or 1). Lymphoplasmocytic infiltration was modereta in more than half of the cases (57%) and desmoplasia was absent in 83% of the cases. During the histological examination the assesment of vascular invasion was usually very difficult due to artificial separation around some tumor islands and only in two cases tumor plugs within vascular lumina, covered by endothelial cells were noted. Perineural invasion was observed in one tumor.

When these results were assessed by statistical methods, there was a statistically significant correlation between nuclear atypia and recurrence (recurrences being higher in severe atypia group). Having desmoplasia in the stroma correlated with a poor cilinical outcome (more recurrences, lower survival). Correlation between keratinization-recurrence, keratinization-survival and nuclear atypia-survival was not statistically significant but the results were promising to achieve significant results in a larger group. No correlation were observed between other histopathological parameters and prognosis. The effects of cartilage, vascular and perineural invasion on prognosis were not statistically evaluated because number of positive cases was small for these parameters.

DISCUSSION

A set of seven histologic parameters were evaluated to assess their prognostic significance in 100 cases of SCCL. After an analysis using Kaplan-Meier life analysis and Mantel-Haensel chi square methods, two variables affecting prognosis were identified: Nuclear atypia and stromal desmoplasia.

Keratinization is the major criterium in determining the tumor differentiation. When the distribution of cases according to the degree of keratinization was examined, it was observed that more than half of the cases were concentrated in moderately keratinizing group. This finding is consistent with the series of Pera et all (6), but in the series of Eiband (5) the well differentiated tumors are dominating. In this study, correlation between keratinization-recurrence or keratinization-survival was not statistically significant correlation between poor prognosis and poor keratinization in a larger study group. In the literature there are some studies correlating differentiation with prognosis (6) but some authors think that differentiation has no effect on either disease-free or overall survival rates (5).

Mitotic index was low in most of the cases and our results were similar to that Pera et all (6) but contrasted with the findings of Crissman et all (4): Mitotic activity had no impact on prognosis.

In this study, we observed that 89% of cases showed mild or moderate degree of nuclear atypia and we noted a singnificant correlation between severe nuclear atypia and recurrences; but the correlation between atypia and survival was not significant in this series. However, Goldsmith et al and Crissman et al found no significant correlation between nuclear atypia and prognosis in their series (1,4).

Some eosinophilotactic factors have been isolated from human tumors. The impact of TATE in different tumors are studied and controversial results are reported (2,3,9-11). We observed high TATE scores (2 or 3) in 7% of our cases. In spite of the fact that there are some studies showing that tumor-associated tissue eosinophilia is a favorable prognostic indicator for

SCCL (2,3), no such correlation was observed in this study.

Infiltration of the tumor periphery by lymphoreticulary cells is a common feature of many malignant neoplasms and usually an association of this infiltrate with improved prognosis is reported (7). We observed moderate to severe lymphoplasmocytic stromal infiltration in 67% of our cases but stromal lymphoplasmoctyic infiltration had no impact on prognosis.

Tumor desmoplasia is a common feature in several malignant tumors and there are different opinions about the effect of desmoplasia in human tumors. Martin et al reported a positive effect of desmoplasia in rat colonic cancer and suggested that fibrous encapsulation could have a role in tumor regression. Others have argued that scuh an encapsulation might reduce the access of host immune cells to the tumor and hence it might help tumor growth (12). Goldsmith et al could not find any prognostic influence of desmoplasis in SCCL (2). By contrast, our results suggest that presence of desmoplasia effects prognosis negatively.

In this study we concluded that the presence of desmoplasia and nuclear pleomorphism are negative prognostic indicators. Furthermore, poor keratinization may have a negative impact on prognosis. However, the histological characteristics are not the sole prognostic parameters; stage, localization, therapy and DNA content of the tumor may have great effects on prognosis.

Larinks kanserlerinde histopatolojik kriterlerin prognoza etkisi

Bu çalışmada Ankara Üniversitesi Tıp Fakültesi Kulak Burun Boğaz Kliniğinde larenjektomiile tedavi edilen 100 yassı hücreli larinks karsinomu olgusunun histolojik bazı özellikleri ile nüks ve sağkalım arasındaki ilişkiler araştırılmıştır. Prognostik değerleri araştırılan keratinizasyon, hücresel atipi, mitotik aktivite, tiroid kıkırdağına infiltrasyon, vasküler invazyon, perinöral invazyon, stromal desmoplazi, lenfoplazmositer iltihabı infiltrasyon ve tümör ile ilişkili doku eozinofilisi parametreleri arasında, atipinin şiddetli olması ve stromal desmoplazi varlığının prognozu kötü yönde etkilediği anlaşılmış, diğer parametrelerin prognozu istatistiksel düzeyde anlamlı olarak etkilemediği saptanmıştır. Ayrıca lokal nükslerin meydana gelmesinin prognozu beklenebileceği şekilde kötü etkilediği tesbit edilmiştir.

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REFERENCES

1. Goldsmith MM, Pillsburg HC. Pathologic and cytometric indicators of biologic behaviour in laryngeal cancer. Newyork: Laryngeal Canser at. Silver KE, 1991; 27-32
2. Goldsmith MM, Cresson DH, Askin FB. The prognostic significance of stromal eosinophilia in head and neck cancer. Otolaryngol Head Neck Surg 1987; 96:319-24.
3. Goldsmith MM, Belchis DA, Gresson DH, Merritt WD, Askin FB. The importance of the eosinophil in head and neck cancer. Otolaryngol Head Neck Surg 1992; 106:27-33.
4. Crissman JD, Liu WY, Gluckman JL, Cummings G. Prognostic value of histopathologic parameters in squamous cell carcinoma of the oropharynx. Cancer 1984; 54:2995-3001.
5. Eiband JD, Elias EG, Suter CM, Gray WC, Didolkar MS. Prognostic factors in squamous cell carcinoma of the larynx Am J Surg 1989; 158:314-17.
6. Pera E, Moreno A, Galindo L. Prognostic factors in laryngeal carcinoma: A multifactorial study of 416 cases, Cancer 1986; 58:928-34.
7. Underwood JCE. Lymphoreticular infiltration in human tumors: Prognostic and biological implications: A review Br J Cancer 30:538-547.
8. Beahrs OH, Myers MH. Manual for staging of cancer. American Joint Committee On Cancer, ed. 2. Philadelphia: JB LippicottC., 1983:38-9.
9. Lowe D, Fletcher CDM, Gower RL. Tumor associated eosinophilic in the bladder. J Clin Pathol 1984; 37:500-502.
10. Iwasaki K, Torisu M, Fujimura T. Malignant tumor and eosinophils: Prognostic significance in gastric cancer. Cancer 1986; 58:1321-27.
11. PretlowTB, Keith EF, Cryar AK, et al. Eosinofil infiltration of colonic carcinomas as a prognostic indicator. Cancer Research 1983; 43:2997-3000.
12. Halvorsen TB, Seim E. Association between invasiveness, inflammatory reaction, desmoplasia and survival in colorectal cancer. J Clin Pathol 1989; 42:162-66.