

Correlation of proliferating cell nuclear antigen and bcl-2 expression with tumor front grading and metastasis in laryngeal squamous cell carcinoma

C. BORAN¹, L. YILDIZ², B. KANDEMİR², F. KARAGOZ², S. BARIS², O. AYDIN²

¹Department of Pathology, Abant Izzet Baysal University, Izzet Baysal Medical Faculty, Bolu, Turkey, e-mail: cetinboran@yahoo.com;

²Department of Pathology, Ondokuz Mayıs University School of Medicine, Samsun, Turkey

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This study was designed to examine the immunohistochemical expression of proliferating cell nuclear antigen (PCNA) and bcl-2 protein in 45 cases with advanced laryngeal squamous cell carcinoma who had undergone total laryngectomy with unilateral modified radical neck dissection, and the relation of this expression to some prognostic factors such as tumor front grading and neck lymph node metastases. Sections were reevaluated for routine histologic grade, tumor front grading and neck lymph node metastases, and were stained with monoclonal antibodies against PCNA and bcl-2. Significant correlation was present between the severity of PCNA expression and incidence of lymph node metastasis ($p < 0.05$). No correlation was found between the severity of PCNA expression and tumor front grading. Bcl-2 expression did not associate with either parameters.

In conclusion, PCNA is important in predicting prognosis and no association is present between the bcl-2 protein expression and prognostic factors.

Key words: Laryngeal carcinoma, prognosis, tumor front grading, neck lymph node metastases, bcl-2 protein, PCNA.

Carcinoma of the larynx is the most common head and neck neoplasm in adult patients; it represents about 0.7% of the total cancer mortality [21]. Histopathologic grade has consistently proven unsatisfactory in predicting survival and prognosis [4, 5]. After treatment based on clinical parameters, many patients still are not cured and some patients that are cured may have been treated successfully with less extensive therapy [24]. For predicting the outcome of laryngeal cancer treatment modality decision is of paramount importance for the physician. Thus, the specific biology of the tumor is probably of critical importance in predicting prognosis. In this study, we made a comparison between expression of bcl-2 protein and proliferating cell nuclear antigen (PCNA) with some parameters which had been shown to correlate with tumor progression formerly, and we tried to obtain an idea about specific biology of the tumor.

PCNA, originally known as a cyclin, is a 36-kD nuclear protein that acts as a co-factor for DNA polymerase- δ . PCNA is synthesized in the late G1 and S phase of the cell cycle. It has been suggested that the presence of an in-

creased number of PCNA-positive cancer cells is associated with aggressive malignant behavior [3, 13].

The bcl-2 proto-oncogene has been considered to be a cell death suppressor gene that regulates the programmed cell death – apoptosis. The growth rate of neoplasms depends on the proliferation and death rates of cancer cells. Apoptosis may be related in part to the death rates of cancer cells as a negative regulating system in the growth of neoplasms. Mutations in the bcl-2 gene inhibit apoptosis, which may contribute to the development of tumors and modify their clinical behavior [11, 17, 23].

Regional lymph node metastases at the time of diagnosis were found to carry a poor prognosis in laryngeal carcinoma. Patients who presented with no regional lymph node metastases had significantly better disease-free and overall survival rates than those with involved lymph nodes [5, 8]. Tumor front grading (TFG) was proven to be associated with prognosis in squamous cell carcinomas in larynx and other locations [4, 12, 26].

The purpose of this study was to analyze the expression of PCNA and bcl-2 protein in squamous cell carcinoma of the