Clinical significance of salivary CD44sol levels in laryngeal carcinomas.

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ABSTRACT

Objectives: to describe our results about the clinical significance of CD44s salivary levels in laryngeal carcinomas and analyze its emerging role as a diagnostic and prognostic factor.

The study design was prospective. Patients with laryngeal cancer who underwent surgery at the Division of Otolaryngology, University of Catanzaro, were selected and recruited from January to December 2012. In the study, 12 patients with benign head and neck disease were also included as a control group.

In the last 30 years, progress in the treatment of head and neck cancer has improved the quality of life of patients through the use of more innovative surgical techniques and multimodal treatments aimed at organ preservation. However, the survival of patients with advanced disease stage has not improved. The main causes of death are represented by the recurrence of loco-regional disease and the appearance of distant metastases not responding to conventional treatments.

Recently, more convincing studies have emerged that attach to a specific tumoral subpopulation of cells, called “cancer stem cells” (CSCs), metastatic ability and chemoresistance and radioresistance. This cell subpopulation has been identified in various solid tumors. Clinical studies about CSC characterization in head and neck tumors confirm the important role of CD44 as a biomarker of these cells.

The CD44 molecule is a type I transmembrane glycoprotein with the functions of adhesion molecule and intracellular mediator for the internalization of hyaluronic acid (HA); the interactions between HA and CD44 influence its adhesion to the extracellular matrix and are involved in aggregation, proliferation, and cell migration and angiogenesis. All these biological properties are increased in tumor cells. In pathological conditions such as cancer, the extracellular domain of the CD44 receptor detaches and is released into biological fluids as a soluble fraction of the receptor CD44s.

In our previous study, we have investigated the expression of CD44-soluble fraction (CD44s) in patients with laryngeal cancers, with very encouraging results: CD44s levels in patients with laryngeal cancer were significantly higher than those in the control group, supporting the use of salivary CD44s test for screening and early diagnosis of laryngeal carcinoma, with high sensitivity and specificity, in agreement with other published studies.

The purpose of this study was to validate the usefulness of salivary CD44s detection in patients during the follow-up after surgical treatment for laryngeal cancer, to compare them with those of the same patients registered at the time of diagnosis (preintervention), and to assess the reliability of the test as a prognostic indicator.

METHODS AND MATERIALS

The study design was prospective. Twenty-one patients with laryngeal cancer who underwent surgery at the Division of Otolaryngology, University of Catanzaro, were selected and recruited from January to December 2012. In the study, 12 patients with benign head and neck disease were also included as a control group.

For each patient, clinical-anamnestic data were collected in a database, with regard to the location of the primary tumor, the clinical staging by the AJCC tumor staging system, type of performed surgical treatment, pathology, and pso-pathological staging. Finally, the data were recorded relating to any disease recurrence and loco-regional or distant metastases detected during the follow-up period.

Sample collection was conducted on the day before surgery and 3 months during the follow-up, with suitable sterile containers, without any means of dilution or preservation.

RESULTS

Twenty-one of the 33 total patients enrolled in the study were affected by squamous cell carcinoma of the larynx. The control group consisted of 12 patients with benign disease of the head and neck region. In patients with laryngeal carcinoma, CD44s levels were significantly higher than those in the control group: 7.07 ± 33.8 and 12.4 ± 8.7 ng/mL, respectively (p < 0.001), as previously observed (Figure 1).

By analysis of the clinical data in relation to the concentrations of salivary CD44s, we found that statistically significant differences between the study groups according to tumor site, histological grading, and clinical staging of T and N.

Sensitivity and specificity derived from various predicted probability cut points based on the ROC curve are the following: at cutoff points greater than 18.5 ng/mL, sensitivity and specificity of the test are 100% and 83.3%, respectively, with 2 false-positives and 0 false-negatives. Best accuracy was obtained using a predictive probability cutoff point of 25 ng/mL, with corresponding estimates of both sensitivity and specificity of 100%.

CONCLUSIONS

The obtained results from this study are encouraging: in fact, it validates the use of ELISA determination of salivary CD44s for diagnosis of head and neck tumors, and it is one of the first applications of a clinical tumor marker, with easily identifiable and highly specific and uninvasive method, as a prognostic factor in the follow-up of patients with laryngeal cancer.

REFERENCES


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Figure 1. Mean levels of salivary CD44s according to presurgical time and successive visits of follow-up (3 and 6 months).

Figure 2. Mean levels of salivary CD44s according to presurgical time and successive visits of follow-up (3 and 6 months).

Figure 3. Mean levels of salivary CD44s levels in control and cancer groups with graphic statistical difference.

ROC Curve. Receiver – Operator Characteristic curve