Comparison of serum CA 72-4, CA 19-9, CEA, and combined tumor markers levels in patients with laryngeal carcinoma and theirs prognostic value

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Abstract

Although tumor markers are valuable in evaluating the progression of disease in the monitoring of subsequent treatment modalities, one of the problems encountered in the diagnosis and postoperative follow up of patients with laryngeal carcinoma involves tumor markers. Because, the conventional tumor markers, such as CA 19-9 (Carbohydrate antigen) and CEA (Carcinoembryonic antigen) are all unreliable in the detection and clinical management of laryngeal carcinoma. In recent studies, a new tumor-associated glycoprotein antigen, TAG 72, has been identified. We aimed multivariate analysis of serum CA 72-4 (tumor-associated glycoprotein 72), CA 19-9, CEA and combined tumor markers (the combination of CA 72-4, CA 19-9, and CEA) levels in the clinical monitoring patients with laryngeal carcinoma (n=39) and healthy volunteers (n=39). In the preoperative period, sensitivities of CA 72-4, CA 19-9, CEA, and combined tumor markers were detected as 53.8 %, 30.7 %, 30.7 %, and 69.2 %, respectively. In the follow up period, sensitivities of CA 72-4, CA 19-9, CEA, and combined markers were detected as 77.7 %, 44.4 %, 55.5 %, and 100.0 %, respectively. Specificity of each studied tumor markers was detected as 94.8 %.

These findings indicate that serum combined tumor markers and CA 72-4 might be the more useful in the clinical monitoring of patients with laryngeal spino cell carcinoma than CA 19-9 and CEA.

Key words: *Laryngeal carcinoma, Tumor markers.*

Larinks kanserli hastalarda serum CA 72-4, CA 19-9, CEA ve kombine tümör marker seviyelerinin karşılaştırılması ve prognostik değerleri

Özet

Larinks kanserli hastaların tedavi etkinliklerinin takibinde çeşitli klinik ve laboratuvar tetkikleri kullanılmaktadır. Tümör markerleri de bu tetkiklerden birisidir. Ancak, CA 19-9 (Carbohydrate antigen) ve CEA (Carcinoembryonic antigen) gibi konvansiyonel tümör markerlerinin larinks kanserlerinin teşhisi ve takibinde tam güvenilir olmadıkları literatür taramasında görülmüştür. Son zamanlarda yeni bir tümör ilişkili glikoprotein antijen (CA 72-4) bulunmuştur. Bu prospektif çalışmamızda, yassı hücreli larinks kanserli hastaların (n=39) klinik takibinde ve sağlıklı gönüllüler üzerinde (n=39) serum CA 72-4, CA 19-9, CEA ve kombine tümör marker (CA 72-4, CA 19-9 ve CEA'in kombinasyonu) seviyelerinin çeşitli analizlerini yaparak etkinliklerini birbirleriyle karşılaştırmayı ve prognostik değerlerini saptamayı amaçladık. Çalışmamızda; CA 72-4, CA 19-9, CEA ve kombine tümör markerlerinin sensitiviteleri preoperatif dönemde sırasıyla %53.8, %30.7, %30.7 ve % 69.2 olarak ve postoperatif takip döneminde rekürrens gösteren olgular arasında %77.7, %44.4, %55.5 ve %100 olarak bulundu. Çalışılan tümör markerlerinin spesifiteleri de %94.8 olarak saptandı.

Çalışmamızda, larinksin yassı hücreli kanserlerinin postoperatif takibinde kombine tümör markerleri ve serum CA 72-4'ün CA 19-9 ve CEA'dan daha üstün olabileceği sonucuna varıldı.

Anahtar Kelimeler: *Laringeal karsinom, Tümör markerleri.*

Introduction

The various tumor markers are useful in evaluating the progression of disease status. In recent years, a new tumor-associated glycoprotein antigen known as CA 72-4 has been identified (1,2). In the present study, we aimed multivariate analysis of serum CA 72-4, CA 19-9, and CEA levels in the clinical monitoring patients with laryngeal spino cell carcinoma in the preoperative and follow up periods.

Material And Methods

Serum levels of CA 72-4, CA 19-9, and CEA were measured in 39 laryngeal carcinomas patients (39 males, 56±6.8 years) who underwent curative surgery with or without radiotherapy and carried out a median follow up period. All resected lesions were assessed and the results were organized according to the TNM classification. The resultant clinical stages are almost identical to the stages in the TNM classification (3). Patients in stages I and II had early laryngeal carcinoma, and those in stages III and IV had advanced laryngeal carcinoma. In addition, histopathological types were divided to 4 cathegories, as well-differentiated, moderate-differentiated, poorly-differentiated, and undifferentiated (4). All of these patients had the primary squamous cell carcinoma histopathologically.

The patients were followed for a median postoperative period of 14 months (range 6 to 25). Outpatient's visits were scheduled every 3 months for the first year and every 6 months thereafter. Also, 39 healthy volunteers (39males; 48±5.8 years and all of them were smoking)) were taken as the control group.

Blood samples were drawn preoperatively, in the postoperative 3rd day and at each visit. All samples were aliquated and stored at -70°C until assays were performed. CA 72-4, CA 19-9 and CEA assays were determined by commercially available kits: CA 72-4 (Boehringer Mannheim Immunodiagnostics, Germany), CA 19-9 (GI-MA assay: Chemiluminescent enzyme immunoassay, USA), and CEA (AxSYM System^R Tumor Markers CEA, Japan), respectively. The recommended cut-off points (95 % confidence limits as confirmed by our own healthy control subjets values) for normal CA 72-4, CA 19-9, and CEA assay results are 6.9 U/mL, 24.6 U/mL, and 5.2 ng/mL, respectively. Sensitivity, specifity and positivity rates were calculated for alone and combined tumor markers.

Results

Table I: The positivity rates of tumor markers in the preoperative and follow up period.

Sensitivity and specificity rates for tumor markers: In the preoperative period, sensitivities of tumor markers: CA 72-4, 53.8 %; CA 19-9, 30.7 %; CEA, 30.7 %; and combined tumor markers, 69.2 % have been found. In the follow up period, sensitivities of tumor markers: CA 72-4, 77.7 %; CA 19-9, 44.4 %; CEA, 55.5 %; and combined tumor markers, 100.0 % have been found (Table I). Also, specificities for each tumor markers in the healthy volunteers, 94.8 % have been found.

Table II: The positivity rates of early and advanced laryngeal carcinoma for CA 72-4, CA 19-9, and CEA levels of the serum, in the preoperative period.

Table I:

Period of Laryngeal Carcinoma	*Number of Patients*	*CA 72-4 >6.9 U/mL*	*CA 19-9 >24.6 U/mL*	*CEA >5.2 U/mL*	*Combined Markers*
Preoperative (total)	39	21 (53.8 %)	12 (30.7 %)	12 (30.7 %)	27 (69.2 %)
Follow up(recurrence)	9	7 (77.7 %)	4 (44.4 %)	5 (55.5 %)	9 (100 %)

Values in parenthesis show percentage of patients with elevated levels of the tumor markers.

Table II:

Stage of laryngeal carcinoma	*Number of Patients*	*CA 72-4 >6.9 U/mL*	*CA 19-9 >24.6 U/mL*	*CEA >5.2 U/mL*	*Combined Markers*
Early	22	9 (40.9 %)	2 (9.1 %)	4 (18.2 %)	10 (45.4 %)
Advanced	17	12 (70.5 %)	10 (58.8 %)	8 (47.0 %)	17 (100 %)
Total	*39*	*21 (53.8 %)*	*12 (30.7 %)*	*12 (30.7 %)*	*27 (69.2 %)*

Values in parenthesis show percentage of patients with elevated levels of the tumor markers.

Positivity rates for tumor markers: Positivity rates of early carcinoma with positive serum levels in the preoperative period had 40.9 % for CA 72-4, 9.1 % for CA 19-9, 18.2 % for CEA, and 45.4 % for combined tumor markers (Table II). Additionally, advanced carcinoma had 70.5 % for CA 72-4, 58.8 % for CA 19-9, 47.0 % for CEA, and 100 % for combined tumor markers.

The correlation among the degree of histopathologically differentiation and positivity rates of tumor markers were investigated. The positivity rates of well-differentiated type were 50.0 % for CA 72-4, 25.0 % for CA 19-9, 12.5 % for CEA, and 50 % for combined markers. Moderate-differentiated type were 42.8 % for CA 72-4, 14.2 % for CA 19-9, 21.4 % for CEA, and 64.2 % for combined markers. Poorly-differentiated type were 66.6 % for CA 72-4, 50 % for CA 19-9, 50 % for CEA, and 83.3 % for combined markers. Undifferentiated type were 63.6 % for CA 72-4, 45.4 % for CA 19-9, 45.4 % for CEA, and 81.8 % for combined markers (Table III).

Table III: The positivity rates of alone and combined markers in the different degree of differentiation types of patients with laryngeal carcinoma in the preoperative period.

Table III:

The Degree of Differentiation	*Number of Patients*	*CA 72-4*	*CA 19-9*	*CEA*	*Combined Markers*
Well-differentiated	8	4 (50.0 %)	2 (25.0 %)	1 (12.5 %)	4 (50.0 %)
Moderate differentiated	14	6 (42.8 %)	2 (14.2 %)	3 (21.4 %)	9 (64.2 %)
Poorly-differentiated	6	4 (66.6 %)	3 (50.0 %)	3 (50.0 %)	5 (83.3 %)
Undifferentiated	11	7 (63.6 %)	5 (45.4 %)	5 (45.4 %)	9 (81.8 %)
Total	*39*	*21 (53.8)*	*12 (30.7)*	*12 (30.7)*	*27 (69.2)*

Values in parenthesis show percentage of patients with elevated levels of the tumor markers.

Discussion

More recent studies have shown that measurements of the new serum marker CA 72-4 may be useful and correlate well with disease stage and activity (1,2). The prognosis of patients testing positive for the tumor markers in the preoperative period was worse than in patients testing negative. Because, the patients testing negative in preoperative period had not any false positivity value for recurrence in the follow up period. This might be depend to the predominance of advanced laryngeal carcinoma among patients with elevated levels of tumor markers. Additionally, 7 cases for serum CA 72-4, 5 cases for CEA, and 4 cases for CA 19-9 during follow up period had higher values than alone cut off points, respectively. However, 9 cases for combined markers were higher value than cut off points. This condition showed that combined markers and CA 72-4 are the most effective of the markers in the follow up laryngeal carcinoma, respectively.

The positivity rates of alone and combined tumor markers in the early and advanced laryngeal carcinoma was investigated. The present study suggests that positivity rates of serum combined markers and CA 72-4 in the patients with early and advanced laryngeal carcinoma are a most reliable marker.

The correlation among levels of alone and combined markers in the different degree of differentiation of patients with laryngeal carcinoma was assessed. It showed that combined tumor markers and CA 72-4 are the most effective of the tumor markers studied in the preoperative period.

The literature reviewed for evaluation of tumor markers of patients with laryngeal carcinoma was encountered only in Mevio et al.'s study (5), and additionally, any report for CA 72-4 in patients with laryngeal carcinoma was not encountered in the literature review (to our knowledge). Also, the evaluation of tumor markers for oral cavity and nasopharyngeal cancers as cases with squamous cell carcinoma were encountered in the literature review (6,7). In Mevio et al.'s study , sensitivities of tumor markers: CA 19-9, 30 %; CEA, 10 % and specificities of tumor markers : CA 19-9, 94.4 %; CEA, 85 % were found. Also, the results of our study suggest that the sensitivity of the CA 19-9 assay for laryngeal carcinoma is 30.7 % and its specificity is 94.8 %. Our data, agree with the findings of Mevio et al.'s. In contrast, the sensitivity of the CEA assay is 30.7 % and specificity is 94.8 % and our data do not agree

with the findings of Mevio et al. (5). This result might be arises from different localisation of the tumor and different population of patients.

Also, in Kurokawa et al.'s study, the sensitivities were 34.5% for CEA and 6.9% for CA 19-9 in patients with oral squamous cell carcinoma (6). Therefore, CEA levels in our study was not different from CEA levels in Kurokawa et al.'s study. In contrast, sensitivity of CA 19-9 in our study were not in accordance with Kurokawa et al.'s study. This state might be depends on different population of patients, different localisation of the tumor, and elevation in the rate of patients with early laryngeal carcinoma. Also, in Kuo et al.'s study, patients with nasopharyngeal squamous cell carcinoma were selected for a study to measure tissue polypeptide antigen (TPA), CA 125, CA 19-9, CEA, and AFP. CA 19-9 and CEA in our study were similar to CA 19-9 and CEA in Kuo et al.'s study (7).

According to our study, combined tumor markers and CA 72-4 may be the more useful in the clinical monitoring of patient with laryngeal carcinoma than CA 19-9 and CEA. Larger prospective studies are needed to confirm the reliability of these marker for laryngeal carcinoma.

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