RESEARCH COMMUNICATION

Squamous Cell Carcinoma Antigen and Cancer Antigen 125 in Southern Indian Cervical Cancer Patients

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Abstract

Our objective was to evaluate the diagnostic value of squamous cell carcinoma antigen (SCC-ag) and cancer antigen (CA) 125 serum tumor markers for the detection of cervical cancer. Abnormal SCC-ag(>1.5 ng/mL) and CA125 (>35 U/mL) levels were found in 64.2% and 18.9% of a series of SCC patients and in 25.0% and 42.6% of adenocarcinoma (AC) patients. The SCC-ag and CA 125 markers appeared rather specific for cervical SCCs and ACs, respectively, also correlating with clinical stage and lymph node metastasis, but not tumor size or patient age. In conclusion, SCC-ag and CA 125 are useful and reproducible markers for advanced stage disease and thus prognosis of cervical cancer.

Keywords: Cervical cancer - squamous cell carcinoma antigen- CA-125 - adenocarcinoma/SCC

Asian Pacific J Cancer Prev, **11**, 1745-1747

Introduction

Cancer of the cervix is a major burden on women's health worldwide. It is the second most common cause of cancer-related death among women globally (Jamal et al., 2006). The women of poorer communities are mostly affected with this disease. It is evidenced that approximately 83% of the world's new cases and 85% of all cervical cancer deaths reported are from developing countries where screening programs are not well established or minimally effective (Cherenji et al., 2001; Moodley et al., 2006). This condition affects not only the health and lives of the women, but also their children, families and their communities at large.

Tumor markers, which are proteins or enzymes produced by tumor cells or generated by host cells in response to tumorigenesis, are frequently used for screening and monitoring in oncology. The expression of tumor-specific antigens varies, however in general tumor cells express several different unique antigens. During the past decade a number of potential useful serum tumor markers have been developed. Squamous cell carcinoma antigen (SCC-ag) is a sub fraction of the tumor antigen TA-4 and was isolated from a squamous cell carcinoma (SCC) of the uterine cervix (Kato et al., 1987). Cancer antigen (CA) 125 is a tumor marker mainly used for monitoring of impact of treatment in patients with adenocarcinoma of cervix. In previous studies, tumor markers SCC-ag and CA 125 for SCC and adenocarcinoma (AC), respectively are used clinically in the treatment of cervical cancer, but the sensitivity of these markers is low (Tsai et al., 2006; Harris et al., 2007). It was observed that the percentage of elevated levels of these markers vary from one study to another, fundamentally depending on cut-off value, tumor stage and clinical situation of the patient. In the present study we evaluated serum tumor markers in cervical cancer patients.

Materials and Methods

A total of 163 patients with a histologic diagnosis of cervical cancer and attending at Rohini hospital over the period 2006 through 2009. The ages of the 163 patients ranged from 24-82 years. Patients were clinically staged according to international FIGO (International Federation of Gynecology and Obstetrics) guidelines. The clinical stage of disease was FIGO stage I in 35, II in 30 and III in 30 squamous cell carcinoma (SCC) patients and stage I in 30, II in 18 and III in 20 adenocarcinoma (AC) patients.

Preoperative blood samples were drawn from patients and stored at -80ºC until assayed. All the serum samples were assayed for SCC-ag and CA 125. The SCC-ag was measured using a SCC EIA kit (Fujirebio Diagnostics, Inc. Sweden). A value of 1.5 ng/ml was chosen as the upper limit of normal. This cut off value represents the 99th percentile in a group of 38 healthy subjects. The CA 125 was measured by enzyme immunoassay method (BioCheck, Inc Diagnostic Kit; ELISA, Antuos 2010 Germany). For this assay the cut off level of 35U/ml was chosen, representing the 99 th percentile in a normal population. Preoperative serum levels for SCC antigen and CA 125 were compared with clinical and histopathological parameters.

Statistical analyses were performed with the statistical

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Table 1. General Characteristics of Cervical Cancer Patients

Characteristics	SCC (%)	AC (%)
Age(Mean ± SEM)	49.4±1.5	50.7±1.6
Clinical stage of disease		
I	35(36.8)	30(44.1)
II	30(31.6)	18(26.5)
III	30(31.6)	20(29.4)
Tumor size		
<4cm	65(68.4)	48(70.6)
>4cm	30(31.6)	20(29.4)
Lymph node		
Negative	64(67.4)	49(72.1)
Positive	31(32.6)	19(27.9)
SCC-ag		
Abnormal	61(64.2)	17(25.0)
Normal	34(35.8)	51(75.0)
CA 125		
Abnormal	18(18.9)	29(42.6)
Normal	77(81.1)	39(57.4)

SCC, squamous cell carcinoma; AC, adenocarcinoma; SCC-ag, squamous cell carcinoma antigen; CA, cancer antigen

package, Graph-Pad Prism for Windows software (version 4; San Diego, CA, USA). Statistical significance was defined as a probability value (p-value) <0.05. The correlation between markers expression and the other variables was assessed with the ANOVA followed by Newman keuls test.

Results

A total of 163 patients were recruited for this study. In this patient population the mean age was 50.1 years . The patient's characteristics are described in Table 1. SCC-ag was elevated in 64.2% of SCC patients at diagnosis and its levels were significantly higher in stage III ($p<0.01$) as shown in Figures 1 and 2. Levels of CA125 in SCC patients were elevated in 18.9. Mean preoperative levels of CA125 antigen were not increased significantly and no significant difference was observed from healthy individuals to SCC patient clinical stages.

CA 125 was elevated in 42.6% of AC patients at diagnosis and its levels were significantly higher in stage III ($p<0.01$). Levels of SCC-ag in AC patients were elevated in 25% but did not significantly differ between healthy individuals and AC patient's clinical stages.

Elevated serum SCC-ag levels were found in SCC, stage I-37.1%, stage II- 70.0%, stage III-90.0% and CA 125 levels were found in AC, stage I-26.7%, stage II-44.4%, stage III-65.0%, respectively. The sensitivity and specificity of markers are represented in Figure 3.

Preoperative serum SCC-ag levels in SCC were correlated with clinical stage, lymph node metastasis, but no association was observed between marker levels and tumor size and patient age. Preoperative serum CA 125 levels in AC was correlated with clinical stage and lymph node metastasis, but no association was observed between

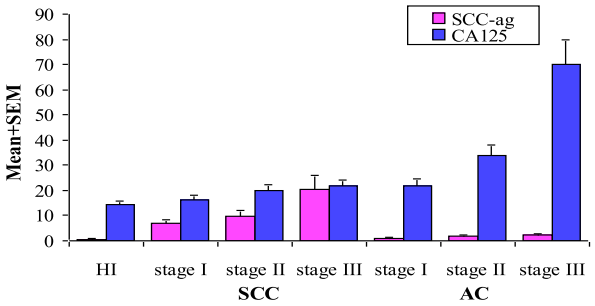

Figure 1. Preoperative Mean ± SEM SCC-ag and CA 125 Values in HI (Healthy Individuals) and Cervical Cancer Patients. SCC, squamous cell carcinoma; AC, adenocarcinoma; SCC-ag, squamous cell carcinoma antigen; CA, cancer antigen; SCC stage III-SCC-ag**p<0.01; AC stage III -CA125**p<0.01

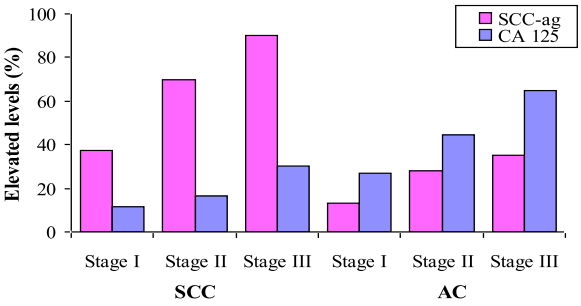

Figure 2. Percentage of Elevated Levels of SCC-ag and CA 125 in Cervical Cancer Patients. SCC, squamous cell carcinoma; AC, adenocarcinoma; SCC-ag,squamous cell carcinoma antigen; CA, cancer antigen

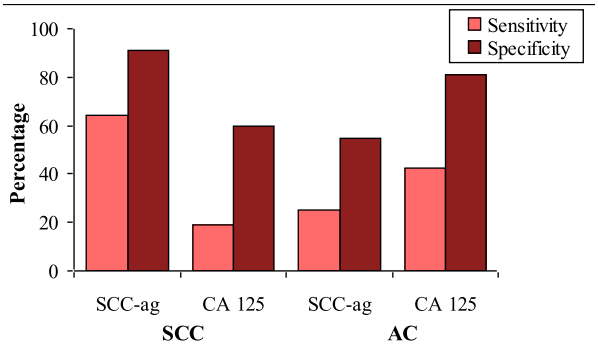

Figure 3. Sensitivity and Specificity of SCC-ag and CA 125 in Cervical Cancer Diagnosis. SCC, squamous cell carcinoma; AC, adenocarcinoma; SCC-ag, squamous cell carcinoma antigen; CA, cancer antigen

marker levels and tumor size, or patient age.

Mean ± SEM values for tumor markers for different stages of the disease and categorization of patients according to cutoff values are shown in Figure 1 and Table 1, respectively.

Discussion

Tumor markers have widespread uses in oncology. Potential clinical applications of tumor markers are to facilitate the early diagnosis, offer a guide for the evaluation of prognosis, to help in selecting patients for adjuvant chemotherapy, and to help in assessing the response to therapy. Moreover the serum level of an ideal

marker should increase pathologically in the presence of a neoplasm (high sensitivity), but should not increase in the absence of neoplasm (high specificity), relate to tumor burden and metastatic spread, reflecting the current status of disease (Hasan et al., 2005). Routinely used markers for cervical cancer are squamous cell carcinoma antigen(SCC-ag) and cancer antigen (CA) 125. In our study we found that the SCC-ag and CA125 are relatively specific for squamous carcinoma of cervix and adenocarcinoma of cervix, respectively. The SCC-ag had elevated levels in SCC and AC 64.2% and 25.0%, respectively and CA 125 had elevated levels in SCC and AC 18.9% and 42.6%, respectively.

Elevated serum SCC-ag levels were found to be 37.1 in stage I SCC, and CA 125 levels were found to be 26.7 in stage I AC. These results confirm that both SCC-ag and CA 125 are not suitable for early detection of disease (Leon et al., 1997; Misuhashi et al., 2009). No significant increase was observed in mean serum levels of SCC-ag in SCC, stage I and stage II patients. However, as found by others (Nagan et al., 1994), significant higher SCC-ag levels were found for stage III lesions. In the case of CA125 significant increase was observed in mean serum levels in AC, stage III patients (Misuhashi et al., 2009). We did not find a correlation between tumor marker levels and tumor size, age in SCC and AC patients, respectively. Our results strongly correlate with the results of Leon et al., 1997.

In conclusion, serum SCC-ag and CA 125 markers are not useful for early detection for cervical cancer but useful indicators for advanced stage and prognosis of the disease.

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