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Squamous cell carcinoma antigen serum levels as prognostic parameter in patients with early stage vulvar cancer

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Abstract

Objective. To determine whether SCC-Ag serum levels can be used as a prognostic parameter in surgically treated early stage vulvar cancer.

Methods. SCC-Ag serum levels were measured preoperatively in 61 surgically staged patients with squamous cell vulvar cancer (UICC pT1 and pT2). Results were correlated to clinical data.

Results. Mean (standard deviation) SCC-Ag serum levels in patients with vulvar cancer were 1.5 (1.99) ng/mL. SCC-Ag serum levels were significantly higher in patients with pT2 vulvar cancer (2.2 [2.6] ng/mL) compared with patients with pT1 vulvar cancer (1.0 [1.2] ng/mL, $P = 0.034$). SCC-Ag serum levels were not associated with lymph node involvement ($P = 0.1$), tumor grade ($P = 0.6$), and patients' age ($P = 0.5$). Multivariate Cox regression models considering tumor stage, lymph node involvement, patients' age, and SCC-Ag serum levels as covariates showed that lymph node involvement ($P = 0.04$ and $P = 0.01$) and tumor stage ($P = 0.006$ and $P = 0.009$), but not SCC-Ag serum levels ($P = 0.8$ and $P = 0.6$), and patients' age ($P = 0.08$ and $P = 0.22$) are prognostic factors for disease-free and overall survival, respectively.

Conclusion. SCC-Ag serum levels cannot be used as an additional prognostic parameter in patients with surgically treated early stage vulvar cancer.

Keywords: Vulvar cancer; SCC-Ag; Prognosis; Serum; Tumor marker

Introduction

The Squamous Cell Carcinoma Antigen (SCC-Ag), a subfraction of the tumor associated antigen TA-4, is a glycoprotein, with a molecular weight between 42 to 48 kDa. SCC-Ag consists of 14 acidic and neutral subfractions and has been shown to be a member of the serine protease inhibitor family [1]. Whereas the neutral subfraction of the SCC-Ag may be expressed by malignant and non-malignant cells and usually remains in the cells, expression and secretion of the acidic subfraction are restricted to malignant cells [2].

The SCC-Ag has been widely investigated as a serum tumor marker for various human squamous cell carcinomas, e.g., lung, anal, esophageal, bladder, and cervical cancer [3–7]. In vulvar cancer, SCC-Ag serum levels have been proposed as a tumor marker indicating efficacy of therapy in primary and recurrent vulvar cancer [8]. SCC-Ag serum levels display good sensitivity/specificity characteristics in the follow-up of vulvar cancer patients, with lead-time effects seen in the majority of patients with regional and distant recurrent disease [9–11]. Furthermore, SCC-Ag serum levels have been shown to provide independent prognostic information with respect to disease-free and overall survival [12]. Of note, lymph node status was not considered as covariate in these analyses.

The aim of the present study was to evaluate the clinical value of SCC-Ag serum levels as prognostic parameter in

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patients with surgically treated early stage vulvar cancer also considering the influence of lymph node status.

Materials and methods

Patients

Clinical data were obtained retrospectively from files at the Medical University of Vienna, Department of Obstetrics and Gynecology. Sixty-one consecutive patients with invasive squamous cell vulvar cancer treated between August 1995 and March 2004 were included in our study. Approval for this study was obtained by the Institutional Review Board (IRB) at the Medical University of Vienna, Vienna, Austria. Patients with vulvar melanoma, adenocarcinoma, basal cell cancer, and verrucous carcinoma were excluded from our study.

Clinical management

Diagnosis of vulvar cancer was established preoperatively by punch biopsy. In patients with lesions with a depth of no more than 1 mm, no surgical staging of vulvar cancer was performed. All other patients but two (both patients were not subjected to a groin lymph node dissection due to medical reasons) underwent radical vulvectomy or radical tumor excision and bilateral groin lymph node dissection. In cases with a strictly lateral location of the tumor, only the unilateral groin was dissected. In cases of lymph node metastases, postoperative radiotherapy was applied according to standardized treatment protocols. Histologic staging and grading was performed according to the current International Union Against Cancer (UICC) classification.

All patients were followed up in 3 month intervals, including inspection, vagino-rectal and groin palpation, and serum tumor marker evaluation. The first follow-up visit was scheduled 3 months after the completion of primary therapy. In cases of clinically suspicious findings and/or tumor marker elevation, computed tomography was performed.

Serum assay

Patients' blood was obtained before surgery and during follow-up by peripheral venous puncture. Serum SCC-Ag levels were routinely analyzed using a commercially available microparticle enzyme immunoassay (IMx SCC MEIA, Abott Laboratories, Chicago, IL). The sensitivity of this SCC-Ag test was 0.3 ng/mL, intra- and inter-assay variability were less than 11%.

Statistical analysis

Values are given as means (standard deviation [SD]). Comparisons between unpaired groups were made using *t* tests. Pearson's correlation coefficient was calculated where appropriate. Survival probabilities were calculated by the product limit method of Kaplan and Meier. Differences between groups were tested using the log-rank test. The results were analyzed for the endpoint of disease-free and overall survival. Survival times of patients disease-free or still alive were censored with the last follow-up date. P values of <0.05 were considered statistically significant. We used the statistical software SPSS 11.0 for Windows (SPSS 11.0, SPSS Inc., Chicago, IL) for statistical analysis.

Results and discussion

Vulvar cancer UICC stages pT1a, pT1b, and pT2 were seen in 14, 25, and 22 cases, respectively. Histologically, all tumors were squamous cell vulvar cancers. Twenty tumors were graded as well, 35 tumors as moderately, and 6 tumors as poorly differentiated. Mean age of patients was 68.3 (16.7) years. Mean duration of follow-up was 38.5 (124.4) months. Twenty-three patients developed recurrent disease after primary therapy. Eighteen patients died of cancer-related death or had signs of progressive disease at the time of last observation. One patient died of myocardial infarction, and 42 patients had no evidence of disease at the time of last observation.

Preoperative mean SCC-Ag serum levels in patients with vulvar cancer were 1.5 (1.99) ng/mL. SCC-Ag serum levels broken down by tumor stage are given in Table 1. SCC-Ag serum levels were not associated with lymph node involvement ($P = 0.1$), tumor grade ($P = 0.6$), and patients' age ($P = 0.5$).

Tumor stage, lymph node involvement, tumor grade, patients' age, and SCC-Ag serum levels were analyzed as a prognostic parameter for disease-free and overall survival. For the univariate Kaplan–Meier analysis, we chose a cut-off level of 1.5 ng/mL, as the mean of SCC-Ag serum levels in our series, and 70 years for patients' age. The results of the univariate Kaplan–Meier analysis and the multivariate Cox regression model with respect to disease-free and

Table 1
Mean SCC-Ag serum levels broken down by tumor stage and lymph node involvement

UICC tumor stage	*n*	SCC-Ag serum levels (ng/mL)	*P*
pT1	29	1.0 (1.2)	0.034
pT2	22	2.2 (2.6)	
pT1, pN0	21	0.8 (1.2)	
pT1, pN1	5	1.5 (1.3)	
pT2, pN0	8	2.2 (1.8)	
pT2, pN1	12	2.5 (3.5)	

SCC-Ag serum levels are given as means (standard deviation). Some patients with pT1a and two patients with pT2 tumors did not undergo groin lymph node dissection.