Abstract. This study was performed to investigate the serum levels of vascular endothelial growth factor (VEGF) in patients with oral and oropharyngeal cancer. The study population included 86 patients with untreated cancer of this region. VEGF serum levels varied considerably and showed no correlation to tumour size or locoregional spread. The wide variety of VEGF serum levels make this marker difficult to handle for initial diagnostics or monitoring of therapy.

Angiogenesis is a crucial step in the processes of tumour growth, progression, and metastasis. Angiogenic factors are being investigated for their involvement in the mechanisms that pave the way to invasive growth and distant spread of oral and oropharyngeal malignancies. Vascular endothelial growth factor (VEGF) is thought to be an important angiogenic factor. Recent studies showed that oral squamous cell carcinoma (OSCC) is associated with an elevated VEGF concentration in serum (1, 2). Higher levels of VEGF correlated with lymph node metastasis and clinical stage of OSCC (1, 2). This association was also discussed for lung cancer and other malignancies of the upper aerodigestive tract (3). The aim of this study was to determine VEGF in oral and oropharyngeal squamous cell carcinoma.

Patients and Methods

A commercially available sandwich enzyme-linked immunosorbent assay (ELISA) kit for human VEGF (Quantikine® human VEGF kit cat. No. DVE00; R & D Inc., Minneapolis, MN, USA) was used to determine VEGF in the sera of 86 patients with squamous cell carcinoma of oral and oropharyngeal carcinoma. Peripheral venous blood was obtained from pretreatment patients. After 12 hours of fasting, 5 ml of venous blood samples were drawn into a tube and centrifuged at 3,000 rpm for 10 minutes. Serum samples were stored at –80°C until the date of analysis. All patients were histologically diagnosed and staged according to the tumour, node and metastasis system (TNM system, UICC 2002; T4: 46, T3: 8, T2: 26, T1: 2, T0: 2 and Tx: 2 patients; N3: 0, N2: 45, N1: 25, N0: 13 and Nx: 3 patients; M0: 75, M1: 5 and Mx: 6 patients). Anatomical regions, such as the floor of the mouth or the cheek, were identified as primary site of lesions. Tumours with the same primaries were classified as separate groups in order to identify possible selectivity of the assay for tumour localisation. Correlative statistics (Pearson) were performed to identify correlations between VEGF serum values and T, N and M stages.

Results

The sera were obtained from 24 females and 62 males (age range: 20 to 75 years). The VEGF values varied considerably (range: 10 to 2322 pg/ml, mean: 505.3 pg/ml, median: 388 pg/ml). VEGF serum levels showed no correlation to T, N or M stage (p > 0.5) and only a slight correlation to tumour localisation (Pearson’s correlation: 0.257, p < 0.019).

Discussion

The results did not support the current hypothesis that serum VEGF values correlate to TNM staging of oral cancer. First reports on VEGF values in OSCC patients showed a correlation to clinical stage and nodal metastasis (1, 2). Indeed, several investigations have revealed an increased vascularity during the transition from normal oral and oropharyngeal mucosa to invasive carcinoma. Furthermore, the association of tumour angiogenesis and tumour progression to oral and oropharyngeal cancer is well characterized (4). Increased expression of VEGF in tissues was demonstrated to be an indicator of poor prognosis in
OSCC but was not able to distinguish between lymph node-positive and node-negative cases (5). On the other hand, any correlation of VEGF serum values to clinical parameters (staging, prognosis) in oral and oropharyngeal cancer was ruled out (6). Therefore, the contribution of VEGF to the development of oral malignancies is currently disputed due to conflicting results in recent reports (7). One reason for the wide range of serum VEGF values are possibly the different cellular sources of the protein, including inflammatory cells (8). Recently, Shang et al. re-evaluated OSCC patients for their VEGF findings (9). These authors found a close correlation of clinical stage and regional lymph node status to the immunohistochemically calculated VEGF-stained microvessel density and VEGF serum levels (9). However, the range of VEGF serum levels was wide both in OSCC patients and healthy controls (9). Further studies need to define cut-off levels to provide a basis for disease-dependent and therapy-related alterations of VEGF levels in vivo.

References