Oral Oncology (2007) 43, 911–919

available at www.sciencedirect.com

ScienceDirect

journal homepage: http://intl.elsevierhealth.com/journals/oron/

ORAL ONCOLOGY

Squamous cell carcinomas arising from different types of oral epithelia differ in their tumor and patient characteristics and survival

Jaana Rautava [a,*], Marjaana Luukkaa [b], Kristiina Heikinheimo [a], Jouni Alin [c,f], Reidar Grenman [d], Risto-Pekka Happonen [a,e]

[a] Department of Oral and Maxillofacial Surgery, Institute of Dentistry, University of Turku, Lemminkäisenkatu 2, FIN-20520 Turku, Finland
[b] Department of Oncology and Radiotherapy, Turku University Central Hospital, FIN-20520 Turku, Finland
[c] Department of Biostatistics, University of Turku, FIN-20014 Turku, Finland
[d] Department of Otorhinolaryngology — Head and Neck Surgery, Turku University Central Hospital, FIN-20520 Turku, Finland
[e] Department of Oral Diseases, Turku University Central Hospital, FIN-20520, Turku, Finland

Received 27 July 2006; accepted 1 November 2006
Available online 25 January 2007

KEYWORDS
Epithelium;
Mouth;
Oral cavity cancer;
Squamous cell carcinoma;
Presentation;
Survival;
Young adults

Summary A hypothesis that OSCCs originating from different types of oral epithelia may have different patient and tumor characteristics was evaluated in this retrospective analysis of 188 patients with primary OSCC treated at Turku University Central Hospital, Turku, Finland in 1988–1997. The tumors were categorized according to the type of oral epithelium from which they have originated: (1) specialized epithelium (dorsal tongue) (2) keratinized (masticatory) epithelium, (3) non-keratinized (lining) epithelium, and (4) tongue epithelium (epithelium on the lateral border of the tongue). The relevant clinical data, including age, sex, social status, and risk behavior of the patients and clinical presentation, histopathological grading, and treatment of the tumors, as well as the follow-up information, were collected from the patient charts of the hospital. In general, tumor and patient characteristics of OSCCs and survival rates were found to be in line with those of recent analyses reported from other industrialized countries. However, OSCCs in young patients (4.8%) seemed to be clinically at a lower stage and histologically more highly differentiated than those of the other patients. Eight out of 9 (89%) OSCCs in the young patients were located on the lateral tongue. The 5-year recurrence-free rates of the patients according to the epithelial origin of the tumors were as follows: masticatory epithelium 42%, lining epithelium 57%, and epithelium of the lateral border of the tongue 61%. In

* Corresponding author. Tel.: +358 2 333 81; fax: +358 2 333 8356.
E-mail address: jaana.rautava@utu.fi (J. Rautava).
[f] Present address: Numos Ltd., Vasamatie 6 B, FIN-02630 Espoo, Finland.

1368-8375/$ - see front matter
doi:10.1016/j.oraloncology.2006.11.012

conclusion, the tumors originating from different types of oral epithelia may have distinct properties with regard to their clinical behavior and responsiveness to the different treatment modalities. It would seem to be meaningful to investigate the molecular characteristics of the different types of oral epithelium in order to elucidate possible differences in their susceptibility to malignant transformation.

Introduction

In the past, squamous cell carcinoma of the oral cavity (OSCC; ICD-10 C00.2—6) was primarily found in elderly men (in their 60s and 70s) with the risk factors being tobacco and excessive alcohol use.[1,2] However, some studies have shown an increased incidence of OSCC among young adults, i.e. patients under 40 years of age.[3—5] Especially the number of carcinomas of the tongue seems to be increasing.[5] An analysis based on 5042 tongue carcinomas filed in the Scandinavian tumor registries found a five-fold increase among young men and a six-fold increase among young women between the years 1960 and 1994, compared with a two-fold increase in older age groups.[3] Young patients have been reported to have 5.5—6.6% of all OSCCs.[3,6,7] In Finland, the proportion of young adults among all the patients with tongue carcinoma has varied between 4.3% and 8.6% during the years 1953—1992.[8]

The overall 5-year survival rate of patients with OSCC is less than 50%.[9,10] According to a comprehensive literature review by Llewellyn et al.,[11] there are controversial results concerning the possible differences in the etiology and biological nature of OSSC between young and elderly patient groups. However, two recent case-control studies have indicated that OSCC in the age groups under and over 40 years is a similar disease with comparable survival figures.[7,12—15]

OSCCs are often diagnosed at an advanced stage.[16] At the time of detection, OSCC is clinically most often a solitary lesion. However, a number of molecular biological studies have corroborated the field cancerization concept, according to which oral mucosa at the same site is affected more widely than can be clinically and microscopically detected.[17—19] The tongue and the floor of the mouth are risk sites for the development of OSCC.[4] Nonetheless, OSCC in the retromolar trigone region has been found to have the lowest survival figures compared to other intraoral subsites.[20]

We hypothesize that the varying data regarding the clinical presentation and behavior of OSCCs may at least in part be explained by the type of epithelia they have originated from. There are three different types of epithelia in the oral cavity: keratinized masticatory mucosa, non-keratinized lining mucosa and specialized mucosa of the tongue (Fig. 1).[21] These three epithelia have significant differences in their development, structure and function.[22] The turnover time (the transition of a cell from the cell basal layer to the outermost layer and desquamation) of the keratinized epithelium is about 50 days, and that of the non-keratinized epithelium 25 days.[22] The keratin layer on the surface of the keratinized epithelium acts as a barrier against the outer environment.[23] The non-keratinized epithelium lacks the specific proteins required for this barrier function. Indeed, there are differences in the cellular protein content and molecular characteristics between keratinized and non-keratinized epithelia. For example, cytokeratins (Ck), i.e. cytoskeletal proteins maintaining cell and tissue integrity, are expressed in oral epithelial cells in a differentiation-specific manner. Ck5 and Ck14 are found in the basal cells of all oral mucosal epithelia, while suprabasal cells of the keratinized oral mucosal epithelium express Ck1 and Ck10 and those of the non-keratinized epithelium Ck4 and Ck13.[24] Moreover, we have shown that expression of the adhesion protein

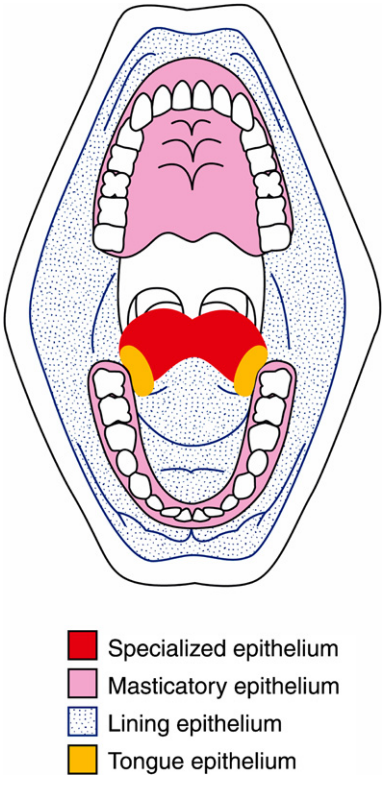

Figure 1 Areas of oral cavity lined by keratinized, non-keratinized and specialized epithelia. Yellow area in the lateral border of the tongue represents the transition area of specialized epithelium to lining epithelium, referred to as tongue epithelium in the study.