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ORIGINAL ARTICLE

Langerhans cell counts in oral epithelial dysplasia and their correlation to clinicopathological parameters

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Background/Purpose: Langerhans cells (LCs) are antigen presenting cells. This study assessed the LC counts in oral epithelial dysplasia (OED) and their correlation to clinicopathological parameters.
Methods: This study examined the LC counts in the epithelia and subepithelial connective tissues of 58 patients with OED (21 mild, 18 moderate, and 19 severe OED lesions) and 10 specimens of normal oral mucosa (NOM) by anti-S-100 protein immunostaining.
Results: We found that the mean LC counts in the epithelia or subepithelial connective tissues increased significantly from NOM samples through mild and moderate OED to severe OED samples. In addition, a significant correlation was found between higher mean LC counts in the dysplastic epithelia of OED samples and OED lesions with thicker epithelial layers ($p < 0.001$) or wider inflammatory zones ($p < 0.001$), and between higher mean LC counts in the subepithelial connective tissues of OED samples and OED lesions with wider inflammatory zones ($p < 0.001$). Moreover, the nine OED lesions with malignant transformation had a significantly lower mean LC count than the 49 OED lesions without malignant transformation.
Conclusion: The significant and gradual elevation in LC count from NOM through mild and moderate OED to severe OED lesions suggests an upregulation of immunosurveillance ability in OED patients during the early oral carcinogenesis process. A low LC count in OED lesions

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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may suggest the partial loss of immunosurveillance ability against dysplastic cells; this in turn favors the malignant transformation of an OED lesion into oral cancer.

Introduction

Oral cancers represent a major health problem. Oral squamous cell carcinoma (OSCC) is the most frequent malignant tumor of the oral cavity and the sixth most common cancer in the world, representing 2—4% of annually diagnosed malignancies in the United States.[1] In Taiwan, oral cancer ranks as the fifth most prevalent type of cancer in both sexes and was the fourth most common cancer in males in 2013.[2] The main etiologies of OSCC and oral potentially malignant disorders (OPMD) in Taiwan are areca quid chewing, cigarette smoking, and alcohol consumption.[3,4] Oral epithelial dysplasia (OED) is a kind of OPMD lesion that may develop into OSCC. The malignant transformation rate is 4—11% for moderate OED lesions and 20—35% for severe OED lesions.[5] The high malignant transformation rate for OED lesions suggests that we need a biomarker to predict which OED lesions will transform into a malignancy.

Langerhans cells (LCs) are bone marrow-derived dendritic cells that reside within the suprabasal and spinous cell layers of oral stratified squamous epithelium. LCs work as antigen-presenting cells that phagocytose antigens in the oral epithelium, migrate from the oral epithelium to the lamina propria and further to the paracortical area of the draining lymph node, where they process the antigen proteins into antigenic peptides and present the antigenic peptides to T cells. Consequently, T cell-mediated effector mechanisms against specific antigens, including dysplastic and cancer cell antigens, are activated.[6]

Previous studies have shown the presence of LCs in normal, dysplastic, and cancerous oral epithelia, as well as in stromal connective tissues. However, the LC counts in normal, dysplastic, and cancerous oral epithelia are controversial. Some investigators have shown a gradual increase in LC number from normal oral mucosa (NOM) to OED and further to OSCC.[7—11] However, others demonstrated a gradual decline in LC number during the progression of oral carcinogenesis.[12—14] These conflicting results suggest the urgent need for further study to clarify the role of LCs in the entire oral carcinogenesis process, especially in areca quid chewing and cigarette smoking-associated oral carcinogenesis.

Recently, head and neck SCC patients with a high LC count in the intratumoral and stromal compartments were found to have a longer recurrence-free survival, and those with a high LC count in the stromal compartment were also observed to have a longer overall survival.[7] High LC count in head and neck SCC suggests augmented immunosurveillance against SCC cells in head and neck SCC patients. However, it is still not clear whether LC count increases in areca nut chewing and cigarette smoking-associated OED lesions during their development into OSCC lesions.

In this study, we used an immunohistochemical technique to determine the LC count in the tissue sections of 58 patients with OED and 10 NOM samples. The LC counts in NOM and OED samples were calculated and compared between groups to see whether LC number increased from NOM to mild and moderate OED and further in severe OED lesions. The correlations between the LC counts in OED samples and clinicopathological parameters of OED patients were analyzed statistically to evaluate whether LC count in the epithelia or subepithelial connective tissues was related to epithelial thickness, inflammatory zone width, and the malignant transformation potential of OED lesions.

Methods

Patients and specimens

Formalin-fixed, paraffin-embedded specimens from 58 patients with OED (56 men and 2 women; mean age, 49 years and range, 19—82 years) including 21 patients (21 men; mean age, 43 years and range, 19—71 years) with mild OED, 18 patients (17 men and 1 woman; mean age, 52 years and range, 40—82 years) with moderate OED, and 19 patients (18 men and 1 woman; mean age, 53 years and range, 36—71 years) with severe OED were included in this study. Diagnosis of OED was based on histological examination of hematoxylin and eosin-stained tissue sections. All patients received total surgical excision of their OED lesions at the Department of Oral and Maxillofacial Surgery, National Taiwan University Hospital, Taipei, Taiwan, during the period from 2000 to 2007. Specimens were obtained from total surgical excision of the lesions. Of the 58 OED lesions, 37 (64%) were located in the buccal mucosa, 15 (26%) in the tongue, three (5%) in the labial mucosa, one (2%) in the gingiva, one (2%) in the retromolar area, and one (2%) in the hard palate. OED lesions were further classified into mild, moderate, and severe OED, when enough dysplastic cells were present in the basal one third, the basal two thirds, or more than the basal two thirds but not the complete layer of the oral epithelium, respectively. According to these definitions, there were 21 (36%) mild, 18 (31%) moderate, and 19 (33%) severe OED lesions included in this study.

Ten biopsy specimens of NOM were obtained from 10 healthy individuals (9 men and 1 woman; mean age, 35 years and range, 20—53 years) without any oral habits during extraction of impacted permanent mandibular third molars after obtaining informed consent, and used as controls.