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Original Article

# Significant association of high-grade inflammation and thick lining epithelium with the increased number of Langerhans cells in dentigerous cysts

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Received 19 May 2017; received in revised form 17 June 2017; accepted 20 June 2017

## KEYWORDS

Langerhans cell;  
Dentigerous cyst;  
Inflammation;  
Lining epithelium;  
Immunosurveillance

**Background/purpose:** Langerhans cells (LCs) are antigen-presenting cells. This study assessed the LC counts in 80 dentigerous cysts (DCs).

**Methods:** The CD1a-positive LC numbers in the lining epithelia and subepithelial connective tissues were counted at 80 DC sites without inflammation, 33 DC sites with mild/moderate inflammation, and 9 DC sites with severe inflammation from 80 DC specimens.

**Results:** The mean LC counts in the lining epithelia and subepithelial connective tissues increased significantly from no inflammation ( $0.5 \pm 0.5$  and  $0.2 \pm 0.3$  cell/high-power field or HPF, respectively) through mild/moderate inflammation ( $6.8 \pm 1.8$  and  $2.4 \pm 2.0$  cells/HPF, respectively) to severe inflammation DC sites ( $18.9 \pm 7.0$  and  $6.7 \pm 5.8$  cells/HPF, respectively; all P-values < 0.001). DC sites with inflammation had thicker lining epithelia than those without inflammation. Moreover, the mean LC counts in the lining epithelia and subepithelial connective tissues of DCs were significantly higher in the thicker lining epithelium (>50  $\mu\text{m}$ ) group ( $7.4 \pm 6.5$  and  $2.6 \pm 3.4$  cells/HPF, respectively) than in the thinner lining epithelium ( $\leq 50$   $\mu\text{m}$ ) group ( $0.5 \pm 0.5$  and  $0.2 \pm 0.3$  cells/HPF, respectively; both P-values < 0.001).

**Conclusion:** A significant association of high-grade inflammation and thick lining epithelium with the increased LC number in DCs is found. The finding of few LCs in the lining epithelia

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<http://dx.doi.org/10.1016/j.jfma.2017.06.011>

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Please cite this article in press as: Chang C-H, et al., Significant association of high-grade inflammation and thick lining epithelium with the increased number of Langerhans cells in dentigerous cysts, Journal of the Formosan Medical Association (2017), <http://dx.doi.org/10.1016/j.jfma.2017.06.011>

of DCs without inflammation indicates the reduced immunosurveillance ability against DC lining epithelial cells in DC patients. It needs further studies to confirm the role of reduced immunosurveillance in the enlargement of the DC.

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## Introduction

Dentigerous cyst (DC) is the most common type of developmental odontogenic cyst, consisting of approximately 20% of all epithelium-lined cysts of the jaws.<sup>1</sup> Although the pathogenesis of the DC is still not clear, apparently it develops by accumulation of fluid between the reduced enamel epithelium and the tooth crown. Radiographically, three different types of the DC are found. The central-typed DC encloses the crown of an unerupted tooth and is attached to the tooth at the cemento-enamel junction. The lateral-typed DC grows laterally along the root surface and partially surrounds the crown. The circumferential-typed DC extends along the mesial and distal root surfaces of an unerupted tooth so that a significant portion of the root appears to be within the cyst. Histopathologically, the uninfamed DC is usually lined by thin nonkeratinized stratified squamous epithelium. Mucous cells may be found in the focal areas of the lining epithelium. The inflamed DC may be lined by thick nonkeratinized stratified squamous epithelium with hyperplastic rete ridges.<sup>1</sup>

Langerhans cells (LC) are dendritic cells that reside within the stratified squamous epithelium of skin and the mucosa of the upper gastrointestinal and female genital tracts. LCs are usually located at the suprabasal and spinous cell layers of the epithelium and constitute 2–8% of the intra-epithelial cell content.<sup>2</sup> LCs have Fc-IgG and C3 receptors, express immune response-associated (Ia) antigens, and function as antigen-presenting cells and allogeneic stimulatory cells to primed T lymphocytes.<sup>3</sup> Previous studies have shown that after 3 weeks, the majority of LCs in parental skin which has been transplanted on to F1 hybrids are of recipient origin, indicating that the LCs are derived from a mobile pool of cells. Moreover, in skin from radiation-induced bone marrow chimeric animals, up to 80% of the epidermal LCs are derived from the bone marrow of the donor animals; this further suggests the bone marrow origin of the epidermal LCs.<sup>3</sup>

There are few previous studies describing the presence of LCs in the lining epithelia and subepithelial connective tissues of DCs.<sup>4–6</sup> In addition, it was still not clear whether the LC counts in the lining epithelia and in the subepithelial connective tissues of DCs were associated with the grade of inflammation in the subepithelial connective tissue, the thickness of the lining epithelium, and clinical parameters of the DCs. In this study, we used the anti-CD1a immunostaining to study the LCs in a relatively large series of 80 DCs. The LC numbers in the lining epithelia and subepithelial connective tissues of DC samples were separately counted at many DC sites with or without inflammation. We tried to elucidate whether the LC counts in the lining epithelia and subepithelial connective tissues of DC

samples were associated with the grade of inflammation in the focal fibrous cystic wall, the thickness of the lining epithelium, and the clinical parameters including the patients' age and gender as well as the location and size of the DC.

## Materials and methods

### Patients and specimens

Formalin-fixed, paraffin-embedded specimens from 80 DC patients (57 men and 23 women, mean age  $34 \pm 18$  years, range 5–67 years) were included in this study. Diagnosis of the DC was based on histological examination of hematoxylin and eosin-stained tissue sections. The DC was characterized as having flattened nonkeratinized stratified squamous epithelium of 2–4 cells in thickness overlying a thin layer of fibrous connective tissue wall without inflammation or with a focal mild, moderate or severe chronic inflammatory cell infiltrate. All patients received total surgical enucleation of their DC lesions at the Department of Oral and Maxillofacial Surgery, National Taiwan University Hospital (NTUH), Taipei, Taiwan during the period from 2005 to 2009. Specimens were obtained from total surgical excision of the lesions. Of the 80 DC lesions, 30 (37.5%) were found in the maxilla (23 in the anterior and 7 in the posterior region) and 50 (62.5%) in the mandible (all in the posterior region). Moreover, the 80 DC-associated teeth contained 30 maxillary teeth (including 2 right upper central incisors, 1 right upper lateral incisor, 3 right upper canines, 1 right upper second premolar, 3 right upper third molars, 2 left upper central incisors, 1 left upper canine, 3 left upper third molars, and 14 mesiodentes) and 50 mandibular teeth (including 1 right lower first premolar, 1 right lower second premolar, 23 right lower third molars, 4 left lower second premolars, 1 left lower first molar, 1 left lower second molar, 18 left lower third molars, and 1 supernumerary left lower second premolar). The mean greatest dimension of the DC measured from the panoramic radiographs was  $2.7 \pm 1.0$  (range 0.9–5.6) cm. All the 80 DCs were primary DCs and no recurrent DC was included. This study has been reviewed and approved by the Institutional Review Board of NTUH.

### Immunohistochemical staining for Langerhans cells

The immunohistochemistry for identification of LCs in various lesional tissues has been described previously.<sup>6–21</sup> In brief, all the specimens for immunostaining were fixed in 10% neutral formalin, embedded in paraffin, and cut in serial sections of 4  $\mu$ m. Immunohistochemical staining was

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