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Expression of CD83 in Gingival Lesions: Diagnostic Potential in Oral Lichen Planus and Oral Lichenoid Reactions

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ABSTRACT

Oral lichen planus (OLP) and oral lichenoid reactions (OLR) are chronic immune-mediated conditions affecting the oral mucosa, often involving the gingiva. Their overlapping clinical and histopathological features make accurate diagnosis challenging. CD83, a transmembrane glycoprotein expressed on mature dendritic cells, is a key regulator of immune responses through its role in antigen presentation and T-cell activation. This study evaluates the expression of CD83 in gingival tissues affected by OLP and OLR, aiming to establish its diagnostic potential. Seventy-two gingival tissue samples, including 31 OLP, 30 OLR, and 11 normal gingiva, were analyzed using immunohistochemistry. CD83-positive cells were quantified in the basal, suprabasal, and connective tissue regions. The results demonstrated significantly elevated CD83 expression in OLP and OLR compared to normal gingiva, with OLP exhibiting the highest levels. Reticular and erosive subtypes of OLP displayed distinct expression patterns, reflecting variations in immune activity and disease progression. These findings underscore the importance of CD83 as a biomarker for distinguishing OLP from OLR and normal gingiva. Elevated CD83 expression correlates with heightened immune activity, suggesting its relevance in pathogenesis and diagnostic differentiation. The study advocates for further research to validate CD83's clinical utility in managing gingival lesions and improving diagnostic precision in immune-mediated oral conditions.

Keywords: CD83, Dendritic Cells, Gingival Lesions, Oral Lichen Planus, Oral Lichenoid Reactions

1 Introduction

ORAL lichen planus (OLP) and oral lichenoid reactions (OLR) are chronic inflammatory conditions that predominantly affect the oral mucosa, including the gingiva. Both disorders are characterized by immune-mediated pathogenesis involving T-cell activation and chronic inflammation. OLP is widely regarded as an autoimmune disease, while OLR is typically associated with external triggers such as dental materials, medications, or allergens [1-5]. Despite their distinct etiologies, the clinical and histopathological similarities between OLP and OLR complicate their differentiation, posing challenges for accurate diagnosis and appropriate treatment planning [6-8].

The clinical manifestations of OLP and OLR include white striations, erythema, and ulcerations, often localized to the gingiva. Histologically, both conditions exhibit basal cell degeneration, subepithelial lymphocytic infiltration, and hyperkeratosis [9]. However, differentiating OLP from OLR is critical, as OLP has a recognized potential for malignant transformation, whereas OLR is generally considered benign [10-13]. Current diagnostic approaches rely on a combination of clinical evaluation and histopathological findings, which may not always provide definitive differentiation.

Dendritic cells play a central role in the immune pathogenesis of OLP and OLR. These antigen-presenting cells are essential for initiating and regulating T-cell responses. Among dendritic cell markers, CD83 has

emerged as a significant molecule. CD83 is a transmembrane glycoprotein expressed during dendritic cell maturation and is involved in antigen presentation and the modulation of immune responses [14]. Its expression has been implicated in various autoimmune and inflammatory diseases, making it a promising biomarker for immune-mediated conditions [15-17].

This study focuses on evaluating CD83 expression in gingival tissues affected by OLP and OLR, aiming to establish its diagnostic relevance. By comparing CD83 expression across basal, suprabasal, and connective tissue regions, this research seeks to elucidate its role in distinguishing OLP from OLR. Furthermore, the study investigates variations in CD83 expression between reticular and erosive subtypes of OLP, providing insights into the immunological differences underlying these clinical subtypes.

The findings of this research have significant implications for clinical practice. Accurate differentiation of OLP from OLR is crucial for guiding treatment decisions and monitoring disease progression, particularly given the malignant potential of OLP. By highlighting CD83 as a diagnostic biomarker, this study contributes to improving diagnostic precision and advancing the understanding of immune-mediated gingival conditions.

2 Materials and Methods

2.1 Study Design

This cross-sectional analytical study was conducted to evaluate the expression of CD83 in gingival lesions of oral lichen planus (OLP) and oral lichenoid reactions (OLR). The study adhered to ethical guidelines and was approved by the institutional ethics committee (Ethics Code: IR.MUBABOL.REC.1397.010).

2.2 Sample Collection

A total of 72 gingival tissue samples were analyzed:

- 31 OLP samples: Subdivided into 16 reticular and 15 erosive subtypes.
- 30 OLR samples: Diagnosed based on clinical and histopathological criteria.
- 11 Normal Gingival Tissues (Control): Obtained from patients undergoing minor oral surgeries, such as impacted tooth extractions, with minimal inflammation.

Inclusion criteria included confirmed histopathological diagnosis of OLP or OLR based on World Health Organization (WHO) criteria. Exclusion criteria included samples with inadequate epithelium or evidence of secondary infection.

3 Immunohistochemical Analysis

3.1 Tissue Preparation

Formalin-fixed, paraffin-embedded tissue blocks were sectioned at 4 µm thickness. Sections were deparaffinized, rehydrated, and subjected to antigen retrieval using citrate buffer (pH 6.0) in a microwave for 20 minutes

3.2 Primary and Secondary Antibodies

Sections were incubated with a primary anti-CD83 monoclonal antibody (clone HB15e, 1:100 dilution; Dako, Glostrup, Denmark) for 1 hour at room temperature. Secondary antibody conjugated with horseradish peroxidase (HRP) was applied for 30 minutes at 37°C. Diaminobenzidine (DAB) was used as a chromogen, and hematoxylin was applied for counterstaining.

3.3 Positive and Negative Controls

- Positive control: Human lymph node tissue known to express CD83.
- Negative control: Sections processed without the primary antibody.

3.4 Cell Counting

CD83-positive cells were identified by their brown-stained cytoplasm and counted manually in six randomly selected high-power fields (HPFs) under a light microscope (Olympus BX41, Tokyo, Japan). Cell counts were recorded in basal, suprabasal, and connective tissue regions.

3.5 Statistical Analysis

Data were analyzed using SPSS software version 24.0 (SPSS Inc., Chicago, IL). Mean and standard deviation (SD) were calculated for CD83-positive cell counts. Statistical comparisons between groups were performed using ANOVA and post-hoc Games-Howell tests. A p-value < 0.05 was considered statistically significant.

4 Results

4.1 CD83 Expression Across Groups

CD83 expression was significantly higher in OLP and OLR tissues compared to normal gingiva ($p < 0.001$). Among OLP subtypes, reticular lesions exhibited the highest mean expression, followed by erosive subtypes. OLR tissues displayed intermediate levels of CD83 expression, which were lower than OLP but higher than normal gingiva.

Table 1 summarizes the mean CD83-positive cell counts in basal, suprabasal, and connective tissue regions for all groups.

Table 1. Mean CD83-positive cell counts across groups.

Group	Basal region (mean±SD)	suprabasal region (mean±SD)	Connective tissue (mean±SD)
OLP (reticular)	10.45±1.23	12.78±1.54	8.34±1.12
OLP (erosive)	8.76±1.12	10.45±1.36	6.78±1.01
OLR	6.89±1.04	8.34±1.27	4.56±0.98
Normal gingiva	2.45±0.87	3.67±0.91	1.78±0.56

4.2 *Regional Differences in CD83 Expression*

CD83-positive cells were most abundant in the suprabasal region across all groups, followed by the basal and connective tissue regions. The suprabasal region in OLP (reticular subtype) exhibited the highest mean cell count (12.78 ± 1.54).

Figure 1 illustrates the regional distribution of CD83-positive cells in OLP, OLR, and normal gingiva.

4.3 *Statistical Comparisons*

Post-hoc analysis revealed significant differences in CD83 expression between:

- OLP and OLR ($p = 0.008$).
- OLP and normal gingiva ($p < 0.001$).
- OLR and normal gingiva ($p = 0.015$).

4.4 *Subtype-Specific Findings*

Reticular OLP showed significantly higher CD83 expression than erosive OLP in all regions ($p < 0.05$).

Figure 2 highlights the differences in CD83 expression between reticular and erosive subtypes of OLP.

4.5 *Correlation with Clinical Features*

Elevated CD83 expression correlated with lesion severity and extent of inflammation, particularly in reticular OLP. These findings emphasize the diagnostic relevance of CD83 in distinguishing OLP from OLR and normal gingiva.

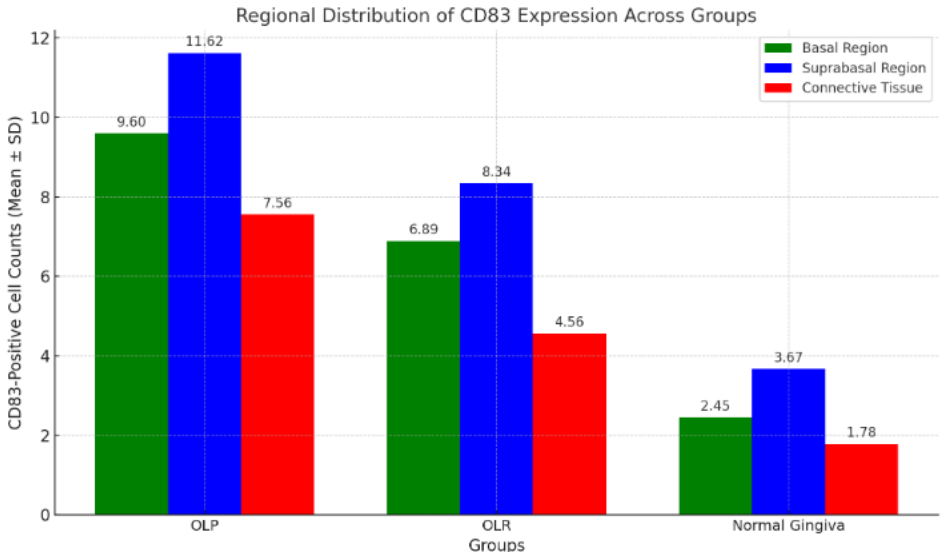

Fig. 1. CD83-positive cell counts in basal, suprabasal, and connective tissue regions across OLP, OLR, and normal gingiva. The suprabasal region consistently exhibited the highest expression levels.

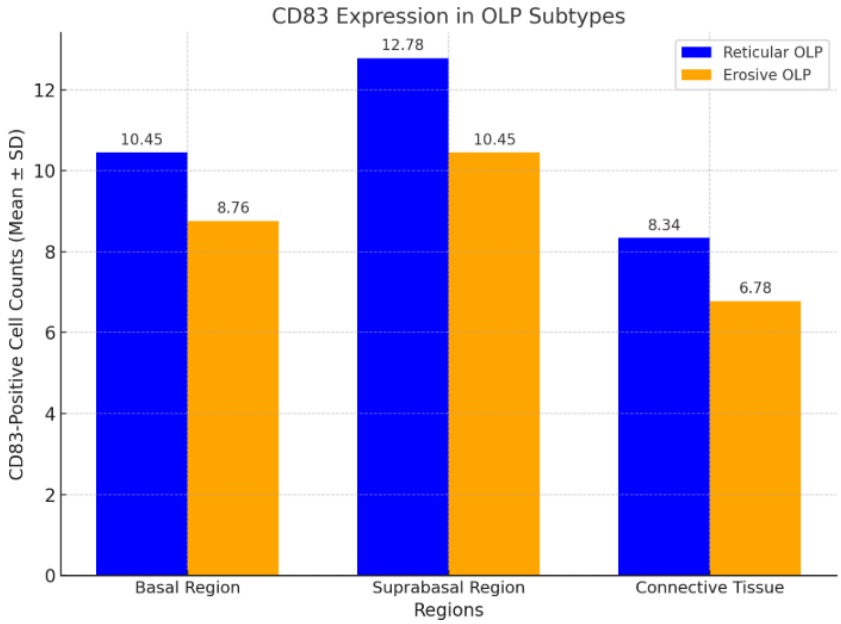

Fig. 2. Comparison of CD83-positive cell counts between reticular and erosive OLP subtypes. Reticular lesions exhibited higher expression in all tissue regions.

5 Discussion

The findings of this study highlight the diagnostic potential of CD83 in distinguishing oral lichen planus (OLP) from oral lichenoid reactions (OLR), aligning with previous research emphasizing the importance of immune markers in oral mucosal conditions. For instance, Tampa et al. demonstrated the relevance of immune biomarkers in identifying malignant transformation potential in OLP, a result that mirrors our findings, where CD83 expression was significantly elevated in OLP tissues, particularly in the reticular subtype [18]. This congruence suggests that CD83 plays a crucial role in the immune pathogenesis of these lesions, further supporting the work of Seyedmajidi et al., who also observed variations in immunological markers between OLP and OLR [19].

However, while our results are consistent with existing literature, they also offer novel insights. For example, while De Rossi and Ciarrocca emphasized histopathological overlaps between OLP and OLR, our data indicate distinct CD83 expression patterns that may enhance diagnostic precision. This divergence may be attributed to methodological differences, such as our focus on immunohistochemical quantification across specific tissue regions. These findings underscore the complexity of immune-mediated gingival conditions, where factors like lesion subtype and tissue microenvironment significantly influence biomarker expression, as also noted by E. Zinser et al. [20].

In comparison to Kulkarni et al., who found consistent expression of other dendritic cell markers in inflammatory oral lesions, our study reveals a more varied pattern of CD83 expression between OLP subtypes and OLR [21]. This discrepancy might be due to differences in sample populations or diagnostic criteria. These variations highlight the need for further investigation to elucidate the role of CD83 in the immunopathogenesis of gingival lesions.

The implications of these findings are significant for clinical practice. As H.-Z. Su et al. noted, the understanding of dendritic cell markers can inform targeted therapeutic strategies [22]. Our study builds on this by offering a nuanced perspective on CD83 expression, suggesting its potential as a biomarker for differentiating OLP from OLR and for monitoring disease progression. This is particularly relevant in the context of managing immune-mediated oral conditions, where precise diagnosis is essential to guide treatment decisions and mitigate risks of malignant transformation.

Despite these contributions, several limitations must be acknowledged. First, the relatively small sample size may limit the generalizability of our findings. Future research should aim to include larger, more diverse populations to validate these results. Additionally, as noted by Alrashdan et al., variability in diagnostic criteria across studies may influence findings [23]. Addressing these limitations through standardized methodologies could refine our understanding of CD83's role in gingival lesions.

6 Conclusion

This study provides compelling evidence for the diagnostic utility of CD83 in distinguishing OLP from OLR and normal gingiva. The findings confirm elevated CD83 expression as a hallmark of heightened immune activity in OLP, with subtype-specific variations offering deeper insights into disease progression. These results not only corroborate existing theories but also introduce new perspectives that warrant further exploration. Future studies should focus on larger cohorts and consider integrating molecular analyses to fully elucidate the mechanisms underlying CD83 expression. Such efforts could advance diagnostic precision and therapeutic approaches in immune-mediated oral conditions.

Conflict of Interest: The author declares no conflict of interest.
Financing: The study was performed without external funding.
Ethical consideration: The study was approved by King Khalid University, Abha, Saudi Arabia

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