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ORAL SQUAMOUS PAPILLOMA ASSOCIATED WITH HPV: DIFFERENTIAL DIAGNOSIS WITH OTHER VERRUCOUS LESIONS

PAPILOMA ESCAMOSO ORAL ASSOCIADO AO HPV: DIAGNÓSTICO DIFERENCIAL COM OUTRAS LESÕES VERRUCOSAS

PAPILOMA ESCAMOSO ORAL ASOCIADO AL VPH: DIAGNÓSTICO DIFERENCIAL CON OTRAS LESIONES VERRUGOSAS

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ABSTRACT

Oral squamous papilloma is a benign epithelial lesion primarily associated with human papillomavirus (HPV) infection, clinically characterized by verrucous or papillomatous projections affecting the tongue, palate, and buccal mucosa. Despite its non-neoplastic nature, it presents clinical similarities with other verrucous lesions of the oral cavity, such as verruca vulgaris, condyloma acuminata, focal epithelial hyperplasia, and verrucous carcinoma, making differential diagnosis a clinical and histopathological challenge. Recent studies indicate a higher prevalence of low-risk genotypes, such as HPV 6 and 11, in oral squamous papilloma, although high-risk types, such as HPV 16 and 18, may be associated with the potential for malignant transformation. The literature highlights the importance of detailed histopathological analysis, complemented by immunohistochemical tests and polymerase chain reaction (PCR), as fundamental tools for accurate diagnostic differentiation. Correct differentiation of oral squamous papilloma from other verrucous lesions enables appropriate therapeutic approaches, prevents erroneous approaches, and contributes to targeted clinical monitoring, with a direct impact on dental practice and the prevention of complications.

Keywords: Oral Papilloma. Human Papillomavirus. Differential Diagnosis. Oral Lesions. Oral Pathology.

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RESUMO
O papiloma escamoso oral é uma lesão epitelial benigna associada principalmente à infecção pelo papilomavírus humano (HPV), sendo caracterizado clinicamente por projeções verrucosas ou papilomatosas que acometem língua, palato e mucosa jugal. Apesar de sua natureza não neoplásica, apresenta semelhanças clínicas com outras lesões verrucosas da cavidade oral, como verruga vulgar, condiloma acuminado, hiperplasia epitelial focal e carcinoma verrucoso, o que torna o diagnóstico diferencial um desafio clínico e histopatológico. Estudos recentes apontam maior prevalência de genótipos de baixo risco, como HPV 6 e 11, no papiloma escamoso oral, embora os tipos de alto risco, como HPV 16 e 18, possam estar associados ao potencial de transformação maligna. A literatura destaca a importância da análise histopatológica detalhada, complementada por exames imuno-histoquímicos e pela reação em cadeia da polimerase (PCR), como ferramentas fundamentais para uma distinção diagnóstica precisa. A correta diferenciação do papiloma escamoso oral frente a outras lesões verrucosas possibilita condutas terapêuticas adequadas, previne abordagens equivocadas e contribui para o acompanhamento clínico direcionado, com impacto direto na prática odontológica e na prevenção de complicações.

Palavras-chave: Papiloma Oral. Papilomavírus Humano. Diagnóstico Diferencial. Lesões Bucais. Patologia Bucal.

RESUMEN
El papiloma escamoso oral es una lesión epitelial benigna asociada principalmente a la infección por el virus del papiloma humano (VPH), caracterizada clínicamente por proyecciones verrugosas o papilomatosas que afectan la lengua, el paladar y la mucosa bucal. A pesar de su naturaleza no neoplásica, presenta similitudes clínicas con otras lesiones verrugosas de la cavidad oral, como la verruga vulgar, el condiloma acuminado, la hiperplasia epitelial focal y el carcinoma verrugoso, lo que convierte el diagnóstico diferencial en un desafío clínico e histopatológico. Estudios recientes indican una mayor prevalencia de genotipos de bajo riesgo, como los VPH 6 y 11, en el papiloma escamoso oral, aunque los tipos de alto riesgo, como los VPH 16 y 18, pueden estar asociados con el potencial de transformación maligna. La literatura destaca la importancia del análisis histopatológico detallado, complementado con pruebas inmunohistoquímicas y reacción en cadena de la polimerasa (PCR), como herramientas fundamentales para una diferenciación diagnóstica precisa. La correcta diferenciación del papiloma escamoso oral de otras lesiones verrugosas permite abordajes terapéuticos adecuados, previene abordajes erróneos y contribuye a un seguimiento clínico específico, con un impacto directo en la práctica odontológica y en la prevención de complicaciones.

Palabras clave: Papiloma Oral. Virus del Papiloma Humano. Diagnóstico Diferencial. Lesiones Orales. Patología Oral.

1 INTRODUCTION

Oral squamous papilloma (OEP) is a benign epithelial lesion characterized by exophytic mucosal growth, often assuming a warty or papillomatous appearance. These clinical changes occur, in large part, as a result of infection by the human papillomavirus (HPV), an etiological agent widely studied in the oral cavity due to its potential to associate with benign and malignant disorders (Ribeiro et al., 2017). The literature shows that, although PEO is mostly linked to low-risk genotypes, such as HPV 6 and 11, there are reports of association with high-risk subtypes, especially HPV 16 and 18, which reinforces the need to pay attention to its potential for transformation (Mashhad Dental School Authors, 2015).

The differential diagnosis of PEO is a clinical challenge, since other verrucous lesions of the oral cavity share similar aspects. Among them, verruca vulgaris, condyloma acuminata, focal epithelial hyperplasia, and verrucous carcinoma stand out. All these conditions have clinical characteristics that may overlap, requiring a careful and multidimensional analysis (the histologic differentiation..., 2003). From this perspective, histopathology continues to be the main diagnostic tool, although complementary methods, such as immunohistochemistry and polymerase chain reaction (PCR), have been gaining ground because they enable viral detection and identification of HPV subtypes, increasing diagnostic accuracy (study, 2011; study, 2014).

The prevalence of HPV in oral lesions has been the subject of several investigations in recent years. Systematic reviews indicate that viral infection is present not only in benign lesions, but also in potentially malignant lesions and carcinomas, evidencing the complexity of the interaction between viruses and epithelial tissue (systematic review, 2020; systematic review, 2021). In the Brazilian context, epidemiological studies have shown considerable prevalence of HPV in different types of oral mucosal lesions, reinforcing the importance of early clinical and laboratory recognition (systematic review, 2015).

In addition to the epidemiological aspects, the literature shows that the correct differentiation of PEO from other verrucous lesions has relevant clinical implications. In the cases described, papilloma can appear in less common locations, such as the hard palate, where it can be confused with potentially malignant lesions, leading to mistaken therapeutic conducts (study, 2023). In addition, the identification of high-risk genotypes in certain papillomatous lesions reinforces the need for clinical surveillance, especially in

immunosuppressed patients, in whom the risk of progression is higher (study, 2011; study, 2014).

Thus, understanding the clinical, histopathological, and virological criteria that underlie the differential diagnosis of PEO is essential for contemporary dental practice. Deepening this topic allows not only to avoid diagnostic mistakes, but also to support prevention strategies, appropriate treatment, and targeted follow-up of patients (Ribeiro et al., 2017; Systematic Review, 2020).

Thus, this study aims to review the literature on oral squamous papilloma associated with HPV, highlighting the main criteria that enable its differentiation from other verrucous lesions of the oral cavity, emphasizing the importance of accurate diagnostic methods for clinical safety and for the prevention of complications.

2 METHODOLOGY

This study is characterized as a narrative review of the literature, focusing on oral squamous papilloma associated with HPV and its differential diagnosis in relation to other verrucous lesions of the oral cavity. To this end, the PubMed, Scopus, SciELO and LILACS databases were searched, recognized for their comprehensiveness and reliability in the area of oral health. The search included publications between 2003 and 2025, ensuring the inclusion of classic and recent studies on the subject.

The search strategies used DeCS/MeSH descriptors, including "oral papilloma", "human papillomavirus", "differential diagnosis", "oral lesions" and "oral pathology", combined by Boolean operators "AND" and "OR" to optimize the retrieval of pertinent articles. Original studies, systematic reviews, case reports, and literature reviews that addressed clinical, histopathological, or virological aspects relevant to the differential diagnosis of oral squamous papilloma were selected. Publications without access to the full text, duplicates, or with an exclusive focus on non-verrucous lesions or those unrelated to HPV were excluded.

The selection of studies occurred in two stages: initially, the analysis of titles and abstracts to assess relevance in relation to the theme; then, the full text was read in full to extract detailed information on the location of the lesions, clinical characteristics, histopathological findings, association with HPV, viral types detected, diagnostic methods, and strategies for differentiation from other verrucous lesions.

The information extracted was organized in a systematic manner, allowing the comparison of clinical aspects, histological patterns, associated HPV types, and diagnostic tools used, such as histology, PCR, and immunohistochemistry. This approach made it possible to synthesize the available evidence, providing a broad and critical view of oral squamous papilloma and its differential diagnosis, offering subsidies for clinical practice and future research.

3 FINDINGS

The literature review revealed that oral squamous papilloma (OEP) has a predilection for regions such as the tongue, palate, and jugal mucosa, occurring in patients of different age groups, although it is more frequent in young and middle-aged adults. Clinically, PEO manifests as exophytic, papillomatous, or warty lesions, usually slow-growing, painless, and asymptomatic, which can lead to delays in clinical diagnosis (Ribeiro et al., 2017; Mashhad Dental School Authors, 2015). Studies indicate that most lesions are associated with low-risk HPV, especially types 6 and 11, while high-risk genotypes, such as HPV 16 and 18, are less frequent, but represent a relevant factor in the evaluation of the potential for malignant transformation, especially in immunosuppressed patients or those with long-term lesions (study, 2011; Study, 2014).

The differential diagnosis of PEO includes several verrucous lesions of the oral cavity, including verruca vulgaris, condyloma acuminata, focal epithelial hyperplasia, and verrucous carcinoma. Each of these conditions has specific histological characteristics that allow them to be distinguished: condyloma acuminata, for example, has koilocytosis and marked epithelial hyperplasia; Verruca vulgaris is characterized by digitiform papillae and hyperkeratosis; Verrucous carcinoma, on the other hand, demonstrates acanthotic epithelial growth with irregular borders and limited invasive pattern, and is often associated with high-risk HPV (the histologic differentiation..., 2003; study, 2014).

In addition to histopathological analysis, complementary methods have been shown to be essential for the identification of HPV and differentiation of lesions. Techniques such as immunohistochemistry allow the visualization of specific viral proteins, while polymerase chain reaction (PCR) enables the detection and typing of the virus, contributing to the clarification of ambiguous cases and supporting therapeutic decisions (systematic review, 2020; systematic review, 2021). The literature also highlights that the correct interpretation of these tests is essential to differentiate benign

papillomas from lesions with malignant potential, minimizing unnecessary interventions and ensuring adequate clinical follow-up.

The reviewed studies also show that PEO can appear in atypical clinical presentations, such as single lesions on the hard palate, gingival mucosa, or unusual areas, increasing the complexity of the differential diagnosis and requiring detailed clinical attention (study, 2023). The distribution of lesions in the oral cavity and the association with risk factors, such as smoking, immunosuppression, and previous exposure to HPV, have been consistently reported, indicating the need for individualized evaluation of patients.

The comparative analysis of the data allowed the organization of the main verrucous lesions in terms of clinical and histological characteristics and viral association, facilitating the understanding of recurrent patterns and specificities that distinguish each entity. Table 1 summarizes this information, providing a practical guide for dentists and researchers when performing differential diagnosis and therapeutic planning.

Table 1

Clinical and histological characteristics and association with HPV of the main verrucous lesions of the oral cavity

Warty Injury	Frequent Location	Clinical Features	Histological Aspects	HPV Associated
Oral Squamous Papilloma	Tongue, palate, jugal mucosa	Exophytic, papillomatous, asymptomatic lesion	Epithelial papillae with regular nucleus, parakeratosis	HPV 6, 11 (low risk)
Condyloma Acuminatum	Jugal mucosa, lip	Multiple lesion, verrucous surface	Koilocytosis, epithelial hyperplasia	HPV 6, 11 (low risk)
Verruca Vulgaris	Tongue, palate, gums	Lesion rounded, rough surface	Hyperkeratosis, digitiform papillae	HPV 2, 4, 40 (low risk)
Focal Epithelial Hyperplasia	Jugal mucosa, tongue	Single, elevated, mucosal-like lesion	Circumscribed epithelial hyperplasia	No clear association
Verrucous Carcinoma	Tongue, palate	Slow growth, warty appearance, invasive potential	Acanthotic epithelium, irregular borders, limited invasion	HPV 16, 18 (high risk)

4 DISCUSSION

The analysis of the results reveals that oral squamous papilloma (OEP) is a benign lesion of high clinical relevance, mainly due to its association with the human papillomavirus (HPV) and the overlapping of characteristics with other verrucous lesions of the oral cavity. Studies indicate that PEO has a predilection for areas such as the

tongue, palate, and jugal mucosa, corroborating previous findings that indicate these regions as the sites most frequently affected by papillomatous lesions (Ribeiro et al., 2017; Mashhad Dental School Authors, 2015). Clinical recognition of these lesions is essential, considering that their exophytic and papillomatous appearance can be confused with other conditions of diagnostic importance, such as verruca vulgaris, condyloma acuminata, focal epithelial hyperplasia, and verrucous carcinoma (the histologic differentiation..., 2003).

The predominant association of PEO with low-risk HPV, especially types 6 and 11, reinforces its benign character; However, the eventual presence of high-risk genotypes, such as 16 and 18, requires clinical attention, because although rare, it may represent a risk factor for malignant transformation (Study, 2011; Study, 2014). This finding highlights the importance of detailed histopathological evaluation and the use of complementary techniques, such as immunohistochemistry and PCR, which allow viral typing and increase the accuracy of differential diagnosis (systematic review, 2020; systematic review, 2021).

The data obtained also show that, although generally asymptomatic, some lesions may appear in atypical places or show prolonged growth, complicating clinical identification and increasing the risk of mistaken conduct (study, 2023). In this context, the integration of clinical, histological, and virological information is essential for adequate management, avoiding unnecessary treatments and allowing targeted clinical follow-up.

In addition, the literature suggests that individual factors, such as immunosuppression, smoking habits, and previous exposure to HPV, can influence both the occurrence and evolution of lesions, reinforcing the need for a personalized approach for each patient (systematic review, 2015). The correct differential diagnosis not only ensures the appropriate therapeutic choice, but also contributes to the prevention of complications and to the education of the patient about risk factors and preventive measures.

Table 1, present in the results, summarizes the clinical and histological characteristics and the association with HPV of the main verrucous lesions of the oral cavity, offering a practical resource for professionals and researchers. The comparison of these lesions shows recurrent patterns, but also important particularities that help in early recognition and diagnostic differentiation. For example, the koilocytosis seen in condyloma acuminatum or the acanthotic pattern of verrucous carcinoma are critical

histological features that should be carefully evaluated (the histologic differentiation..., 2003; study, 2014).

Therefore, PEO should be approached in a multidimensional manner, considering clinical, histological, and virological aspects, with special attention to the presence of high-risk HPV, lesion location, and morphological characteristics. The discussion of the findings suggests that the integration of these factors is decisive for contemporary dental practice, promoting more accurate diagnoses, appropriate treatments, and efficient preventive follow-up, contributing to clinical safety and oral health of the population (Ribeiro et al., 2017; Systematic Review, 2020)

5 CONCLUSION

HPV-associated oral squamous papilloma is a benign lesion of significant clinical relevance, whose exophytic and papillomatous presentation may mimic other verrucous lesions of the oral cavity, such as verruca vulgaris, condyloma acuminata, focal epithelial hyperplasia, and verrucous carcinoma. The literature review shows that accurate diagnosis depends on the integration of clinical, histopathological, and virological information, including the use of complementary techniques such as immunohistochemistry and PCR for HPV identification and typing.

Low-risk HPV, especially types 6 and 11, is predominantly associated with oral squamous papilloma, giving it a benign character; however, the eventual presence of high-risk genotypes, such as HPV 16 and 18, reinforces the need for careful clinical follow-up, especially in immunosuppressed patients or those with long-term lesions. The correct differentiation of oral squamous papilloma from other verrucous lesions is essential to avoid inappropriate conducts, enabling appropriate therapeutic interventions and preventive follow-up, in addition to contributing to the early detection of alterations with malignant potential.

In addition, the comparative analysis of the clinical and histological characteristics and the viral association of verrucous lesions, as summarized in Table 1, provides a practical and guiding resource for dentists and researchers, facilitating informed diagnostic and therapeutic decisions. Thus, detailed knowledge about oral squamous papilloma and its relationship with HPV is essential for contemporary dental practice, promoting clinical safety, prevention of complications, and improvement in the quality of patient care.

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