Verrucous Hyperplasia: A case report on a controversial entity

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Abstract
Oral verrucous hyperplasia is a verruco-papillary lesion of the oral mucosa which possesses enigmatic features which make the diagnosis very much challenging; especially owing to the fact that it can clinically resemble other verruco-papillary lesions of the oral mucosa. Therefore, a meticulous approach, by means of standardized clinical and histological criteria should be executed to differentiate oral verrucous hyperplasia from other verrucous and papillary lesions of the oral mucosa.

This case report depicts a rare presentation of oral verrucous hyperplasia, occurring on the gingiva in a 43-year-old female patient.

Key words: verrucous hyperplasia, verruco papillary lesion

Introduction
Oral verrucous hyperplasia (OVH) is a histopathological entity, which is included in verruco-papillary lesions (VPLs) of the oral mucosa which can transform into verrucous carcinoma, its malignant but clinically similar equivalent, as well as to squamous cell carcinoma. Verruco-papillary lesions (VPLs) of the oral mucosa consist of a wide spectrum of entities including benign, potentially malignant and malignant disorders which are challenging to be diagnosed both clinically and histopathologically. Particularly, OVH is more diagnostically challenging and is clinically indistinguishable from oral verrucous carcinoma, oral papillary squamous cell carcinoma (PSCC) and oral conventional squamous cell carcinoma with papillary features (CSCC). Therefore, the process of establishing and applying a well-defined set of clinical and histological diagnostic criteria in order to differentiate these indistinct group of lesions has been launched during the recent few years.

All through the course of evolution of VPLs of the oral mucosa, introducing the term ‘verruccous hyperplasia’ by Shear and Pindborg (1980) and differentiating it from other verruco-papillary lesions, has stamped a remarkable landmark in the process of nomenclating VPLs of the oral cavity.

However, this entity has been and is still being amended in terms of clinical, histological and terminological aspects, throughout the years, which makes itself an entity subjected to repeated reclassifications. A detailed account on different classifications of this entity will be presented later.
Also, OVH has been found to occur in the background of Oral Submucous Fibrosis (OSF). The lesion can appear as a large, exophytic growth, giving a clinical impression of a malignancy, but does not show any dysplastic changes histopathologically. Therefore, this deceptive nature of OVH (in the background of OSF) should be diagnosed accurately, in order to avoid overtreatment.7

Histopathology plays a crucial role in diagnosing this particular entity, thus, histopathological criteria, to favour the diagnosis of OVH, and to differentiate it from other verruco-papillary lesions have been established.

The prognosis and the natural history of OVH is evidenced by its malignant transformation into verrucous carcinoma or squamous cell carcinoma.5,6

**Case history**

A 43-year-old female was referred to the Dental Hospital Peradeniya, with regard to a whitish lesion on the gingiva, in relation to 44-48 region, which had been lasting for a period of one year, neither causing any symptoms such as pain, burning sensation or ulceration, nor, showing any increment in size with time.

The patient is devoid of any past medical history, but has a relevant habit history, which she reveals as a practice of chewing arecanut since a duration of 1 ½ years, with a gradual increment in the amount of consumption with time. She also is on the habit of smoking tobacco, 2-3 times per month, for a span of 15 years.

On examination, there were no aberrant extra oral findings. Intra orally, a whitish, non-scrapable plaque like exophytic growth was evident on the gingival margin, in relation to 44-48 region (Figure 1). The lesion did not show any signs of bleeding, erythematosous areas, induration or discharges.

An incisional biopsy was performed on 03rd of April 2017. The histopathological analysis carried out from the obtained specimen exhibited exophytic mucosa covered by hyperorthokeratinized stratified squamous epithelium without any evidence of cytological atypia accounting to epithelial dysplasia (Figure 2). Thus, the final diagnosis was confirmed as verrucous hyperplasia and slim rete projections (X10).

As the lesion did not show any evidence of dysplastic changes, surgical excision of the lesion was not performed, and the patient is currently on review appointments.
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Discussion

Verruco-papillary lesions (VPLs) of the oral mucosa inheritably possess a formidable image with regard to diagnosis, proven by exhibiting approximately similar clinical and histopathological images. Oral verrucous hyperplasia (OVH) is one of them which has been identified to be an entity with perplexing nature, drawing pathologists’ attention toward it, up to the recent past.

The clinical picture of OVH generally presents as a white or pink elevated oral mucosal plaque or mass with a verrucous or papillary surface, and has been found to occur more commonly in the buccal mucosa, with a possible correlation with certain habits such as quid placement in the buccal vestibule. The quid may be either tobacco-betel-lime quid or, areca nut quid. Smoking has been observed to be the second most common aetiological factor.

Relevant literature discloses a male predilection (2:1) with a mean age between 30-60 years. When considering the age and gender of occurrence, it is reasonable to mention that the mean age is the 4th decade of life with a male predominance.

In comparison, the present case agrees with the literature in terms of age, but apparent deviations are evident with regards to gender and the site. Also, the patient has a habit history, which agrees with relevant literature findings.

Time to time, OVH has been subdivided into different categories, by various eminent pathologists. Initially, Shear and Pindborg, the pioneers of coining the term ‘verrucous hyperplasia’, described two subdivisions according to their clinical and histopathological variations, namely the ‘sharp’ variant and the ‘blunt’ variant. Clinically, the ‘sharp’ variant comprises long, narrow, heavily keratinized verrucous processes where the lesions appear whiter, accounting to the heavy keratinization, while the ‘blunt’ variant consists of broader, flatter, less keratinized verrucous processes.

Later, in, 2009, a new classification, primarily based on the histological features, was introduced by Wang et al. There, this entity was subjected to renaming as ‘plaque-type’ and ‘mass-type’. Despite the histological features being the prime criteria for this differentiation, separate clinical features have been suggested for these two varieties. Thus, the ‘mass-type’ lesions manifest as solitary or multiple, protuberant, mass-like verrucous whitish pink lesions whereas the ‘plaque-type’ lesions portray as whitish verrucous plaques.

VPLs of the oral mucosa have been found to occur in the background of oral potentially malignant disorders such as Oral Submucous Fibrosis (OSF). OVH is one such entity which can concurrently exist with OSF. The importance of this phenomenon is that verrucous growths (including OVH) which co-exist with OSF can clinically mimic a malignancy, but the histopathological findings do not show any invasion. Therefore, verrucous growths in OSF can misguide the clinician by providing a clinical diagnosis of squamous cell carcinoma, which ultimately leads to needless overtreatment. Therefore, the diagnosis of these lesions should not be made purely clinically, thus should be confirmed histopathologically, to avoid unnecessary overtreatment.

A malignant transformation rate of 3.1% and mean malignant transformation duration of 54.6 months has been observed with regards to this entity.

Also, it is important to mention that OVH is an entity which had been considered as a morphological variant, or a precursor of verrucous carcinoma by some authors. Therefore, due emphasis has been given to differentiate oral verrucous hyperplasia from verrucous carcinoma.
In order to accomplish this goal, Shear and Pindborg performed a comprehensive histological analysis, considering the growth pattern, rete morphology and the degree of cytological atypia. The characteristic histological feature here is that, OVH shows an exophytic growth in relation to the adjacent normal epithelium whereas verrucous carcinoma shows an exo-endophytic growth pattern. Slim, pointed and anastomosing rete projections can be identified with respect to OVH, while, in contrast, verrucous carcinoma comprises broad and elongated rete processes. Cytological atypia, associated with epithelial dysplasia has been identified as a significant associated feature (66%) in OVH. Yet, acquiring good biopsy, with adequate margins and adjacent normal epithelium is mandatory to provide a confirmatory diagnosis of OVH, as the presence of pushing deep margins or the obvious invasion of the epithelium towards the underlying connective tissue, which is evident in verrucous carcinoma, should be excluded.

OVH and Proliferative Verrucous Leuko-plakia (PVL) are two clinically interrelated oral mucosal lesions where the former is a part of the development spectrum of the latter. PVL begins as a keratotic lesion and develops gradually into a multifocal, widespread keratotic lesion with a high frequency of malignant transformation and recurrences. Verrucous hyperplasia, verrucous carcinoma and squamous cell carcinoma can co-exist within PVL. Despite the interaction, several differences can be identified between these two entities. PVL is more commonly seen in elderly females where OVH is frequent in males. The age of occurrence of PVL is 70.2 years while OVH occurs at an age range of 30-60 years. OVH occurs as a solitary lesion and PVL manifests a multifocal lesion.

Histopathological analysis has been identified as the sole investigatory component in the diagnosis of OVH; therefore, the relevant criteria are worth mentioning.

The histological criteria for diagnosis of verrucous hyperplasia include:

- Epithelial hyperplasia with parakeratosis or hyperkeratosis and a verrucous surface
- Absence of invasion of the hyperplastic epithelium into the lamina propria as compared with the adjacent normal mucosal epithelium.

Histologically, the ‘sharp’ variant and the ‘blunt’ variant presumptively correspond with the clinical features mentioned above. With regard to differentiation of the newly introduced ‘plaque-type’ and ‘mass-type’ variants, a surface keratin layer of more than 40 microns was ascerted as a differentiator between them. Lesions portraying a verrucous surface with solitary or multiple protruding masses of epithelial growth showing minimal connective tissue cores and surface keratin thickness of less than 40 microns were named as the ‘mass-type’ while lesions exhibiting a verrucous surface, epithelial hyperplasia, and a surface keratin layer of more than 40 microns were named as ‘plaque-type’. Keratinization of the epithelium can be either parakeratinized or orthokeratinized.

However, despite the presence of various subcategories, oral verrucous hyperplasia has been identified to be a confusing entity, for the name conveys a histopathological image rather than a clinical picture. Therefore, previously described lesions, are now collectively called as ‘Exophytic verrucous hyperplasia’, the term which has now become the limelight of verrucopapillary lesions. The newly termed ‘Exophytic verrucous hyperplasia’ has been accepted to indicate the clinical entity that represents the microscopic diagnosis if verrucous hyperplasia. Thus, separate clinical and histological criteria for the diagnosis of ‘Exophytic verrucous hyperplasia’ have been forth put recently.

**Clinical criteria for diagnosing verrucous hyperplasia of the oral cavity**
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a) These lesions clinically present in two forms: i) as an exophytic, fleshy verruca-papillary outgrowth with a white and/or pink surface color and ii) as a white, plaque-like exophytic verruca lesion. The latter may mimic verrucous leukoplakia. In both instances the clinical term ‘exophytic verruca hyperplasia’ should be used.

b) Exophytic verruca hyperplasia may occur in any anatomical site in the oral cavity and in general would be more than 1 cm in size.

c) Unlike proliferative verruca leukoplakia (PVL) exophytic verruca hyperplasia is a discrete and solitary lesion.

d) Exophytic verruca hyperplasia may co-exist in a patient presenting with oral submucous fibrosis.

e) The clinical presentation of exophytic verruca hyperplasia could masquerade as a squamous cell carcinoma or verruca carcinoma. Absence of induration is a cardinal feature of exophytic verruca hyperplasia.

Histological criteria for diagnosing verruca hyperplasia of the oral cavity

a) Keratinized exophytic verruca-papillary processes seen. Keratin plugging may be present.

b) Epithelium is hyperplastic with both basal cell hyperplasia and acanthosis.

c) Absence of downward growth of the hyperplastic epithelium into the lamina propria when compared with the level of the basement membrane of the adjacent normal epithelium.

d) Epithelial dysplasia may or may not be present.

e) Subepithelial lymphocytic infiltration as a host response may or may not be present.

f) Verruca hyperplasia should be clearly differentiated from verruca carcinoma which exhibits frank downward growth of the epithelial processes below the level of the basement membrane of the adjacent normal epithelium.

g) Verruca hyperplasia should be differentiated from squamous cell papilloma by its size and by the presence of a prominent fibrovascular core in the latter.

h) In a small biopsy without adjacent normal mucosal epithelium particular attention should be paid to exclude other pathologies such as squamous cell papilloma and verruca carcinoma.

It has been proposed that of the above, criteria (a), (b) and (c) must be present to make a histopathological diagnosis of OVH.

The management of OVH focuses more towards wide surgical excision with a 5mm margin, which has been considered as the conventional mode of treatment. Nevertheless, new treatment modalities have been introduced to overcome the possible drawbacks of surgical intervention, mainly being the formation of large scars and higher degree of invasiveness. Topical 5-aminolevulinic acid-mediated photodynamic therapy (ALA-PDT) is one such modality which is advantageous over the surgical treatment. Cryotherapy also has been suggested as an alternative treatment modality with successful outcomes.

Conclusion
This case report presents a case of oral verruca hyperplasia with multiple deviations from the ideal clinical presentation, and discusses about its deceiving features in several aspects.
### Table 1. Comparison of the present case with literature

<table>
<thead>
<tr>
<th></th>
<th>Evidence from literature</th>
<th>Present case</th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td>30-60 years (4th decade)</td>
<td>43 years (5th decade)</td>
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<tr>
<td><strong>Gender</strong></td>
<td>Male predilection</td>
<td>Female</td>
</tr>
<tr>
<td><strong>Site</strong></td>
<td>Commonest– buccal mucosa</td>
<td>Gingiva</td>
</tr>
<tr>
<td><strong>Histopathological features</strong></td>
<td>Presence of keratinized exophytic verruco-papillary processes.</td>
<td>Exophytic mucosa covered by hyperorthokeratinized epithelium. No evidence of epithelial dysplasia.</td>
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<tr>
<td></td>
<td>Epithelial hyperplasia with both basal cell hyperplasia and acanthosis.</td>
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<td></td>
<td>Absence of downward growth of the hyperplastic epithelium into the lamina propria when compared with the level of the basement membrane of the adjacent normal epithelium.</td>
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<tr>
<td></td>
<td>Epithelial dysplasia may or may not be present.</td>
<td></td>
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<tr>
<td><strong>Management</strong></td>
<td>Wide surgical excision</td>
<td>No intervention; follow up is in progress.</td>
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<td></td>
<td>Cryotherapy</td>
<td></td>
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<td></td>
<td>5-ALA mediated photodynamic therapy</td>
<td></td>
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<tr>
<td><strong>Complications</strong></td>
<td>Malignant transformation into verrucous carcinoma or squamous cell carcinoma.</td>
<td>No observations until now.</td>
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### Table 2. Differential diagnoses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Clinical features</th>
<th>Histopathological features</th>
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<tbody>
<tr>
<td><strong>Verrucous hyperplasia</strong></td>
<td>Exophytic, verruco-papillary outgrowth with a white and/or pink surface, or, as a white, plaque-like exophytic verrucous lesion.</td>
<td>Keratinized exophytic verruco-papillary processes with or without keratin plugging. Hyperplastic epithelium with both basal cell hyperplasia and acanthosis. Absence of downward growth of the hyperplastic epithelium into the lamina propria when compared with the level of the basement membrane of the adjacent normal epithelium. Rete processes are pointed, ragged, slender and anastomosing. Prominent fibrovascular core.</td>
</tr>
<tr>
<td><strong>Verrucous carcinoma</strong></td>
<td>Exo-endophytic verruco-papillary growth</td>
<td>Presence of downward growth of the epithelial processes below the level of the basement membrane of the adjacent normal epithelium. Broad, elongated, rete ridges resembling elephant’s feet.</td>
</tr>
<tr>
<td><strong>Papillary squamous cell carcinoma</strong></td>
<td>Exophytic, verruco-papillary outgrowth</td>
<td>Minimally keratinized exophytic verruco-papillary processes. No frank downward growth of the epithelial processes below the level of basement membrane of the adjacent normal epithelium showing pushing border effect. No keratin plugging.</td>
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References


