

Papillary and verrucous lesions of the oral mucosa

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Abstract

A wide variety of papillary and verrucous lesions can affect the oral mucosa. Benign and reactive lesions (e.g. squamous papilloma, verruciform xanthoma) usually present little diagnostic difficulty. However, premalignant and malignant verrucous and papillary lesions pose a much greater diagnostic challenge, not helped by often confusing terminology. For example, papillary hyperplasia is a reactive inflammatory condition, whereas the term “verrucous hyperplasia” is often used to describe a potentially malignant lesion, which is probably part of the spectrum of verrucous carcinoma. A classical verrucous carcinoma, with an exo-/endophytic growth pattern and a “pushing” invasive front is easily identified, but many exophytic verrucous proliferations can also show endophytic growth. These can reasonably also be considered as verrucous carcinoma and managed accordingly. The distinction becomes academic in the face of conventional invasion, when squamous cell carcinoma is the appropriate diagnosis. This review aims to summarise and highlight the key features seen in these lesions, and to provide a practical approach for tackling these entities in routine diagnostic practice.

Keywords papillary carcinoma; precancerous conditions; verrucous carcinoma

Introduction

There are few more diagnostically challenging areas of oral pathology than papillary and verrucous lesions. Not only is the terminology confusing (Table 1), but some normal oral mucosal structures, inflammatory polyps and viral papillomas as well as dysplastic and malignant lesions may share microscopic appearances. Clinical information and an adequate biopsy are essential for accurate diagnosis. The purpose of this review is to highlight the histological features which provide guidance in the assessment of this difficult group of lesions, paying particular attention to verrucous ‘hyperplasia’ and verrucous carcinoma.

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Benign

- Viral papillomas
 - Squamous papilloma
 - Verruca vulgaris
 - Condyloma acuminatum
 - Multifocal epithelial hyperplasia (Heck’s disease)

- Fibro-epithelial polyps
- Verruciform xanthoma
- Papillary hyperplasia
- Pyostomatitis vegetans
- Sialadenoma papilliferum
- Acanthosis nigricans
- Darier’s disease
- Cowden syndrome

Potentially malignant

- Verrucous hyperplasia
- Proliferative (verrucous) leukoplakia

Malignant

- Verrucous carcinoma
- Papillary carcinoma
- Carcinoma cuniculatum

Table 1

Normal papillary structures of the lingual mucosa

Covering the entire anterior two-thirds of the dorsum of the tongue are filiform papillae with parakeratinised surface projections and a prominent granular layer. The latter in particular can be reminiscent of that seen in viral papillomas. Filiform papillae are characteristically lost in disease processes such as geographic tongue (erythema migrans), lichenoid reactions, chronic candidal infection or chronic anaemia. Fungiform papillae, which are mushroom-shaped structures bearing scattered, paler staining taste buds within the surface stratified squamous epithelium, are located along the lateral aspects of the tongue dorsum. These may persist in conditions where the filiform papillae are lost, and thus appear more prominent. The circumvallate papillae are located at the junction of the anterior two-thirds with the posterior one-third of the tongue and number approximately twelve in number. They are surrounded by a “ditch” lined by stratified squamous epithelium containing many taste buds, which leads to the serous minor salivary glands (of von Ebner) embedded within the lingual musculature.

Viral papillomatous lesions

The vast majority of these are squamous papillomas, but verruca vulgaris and condyloma acuminatum also occur. Diagnosis is usually straightforward; most are less than 10 mm in maximum dimension and the histopathological features are more or less similar to those of lesions occurring on the skin. HPV association has been demonstrated in these lesions, none of which carry any premalignant connotation.

Squamous papillomas are hyperplastic lesions that may affect any intraoral site. Association with low-risk HPV (types 6 and 11) is recognised.¹ On microscopy, finger-like projections of

hyperplastic, keratinising stratified squamous epithelium with underlying fibro-vascular cores are seen. The length and number of fronds is variable, with some papillomas showing a broad, papillo-nodular surface morphology. Should the dorsum of the tongue be affected, the fronds are usually longer than adjacent filiform papillae. Viral cytological changes are minimal. Squamous papillomas are frequently inflamed, and in about 10% of them candidal hyphae can be demonstrated with PAS stains.²

Verruca vulgaris most commonly affects the lips and the palate.³ Association with low-risk HPV (2, 4, 40, 57) has been reported.¹ These lesions may appear histologically similar to squamous papilloma, but coarse keratohyalin granules and koilocytic changes are also typically seen.

Condyloma acuminatum are HPV-associated (6 and 11),¹ and tend to affect the lips more often than intra-oral sites. These are often sexually transmitted, and may be associated with immunosuppression when multiple. They may demonstrate pronounced papillary epithelial hyperplasia, in addition to the cytological features of viral infection listed above. When rete ridge hyperplasia is prominent, confusion with verrucous hyperplasia in misorientated biopsies may be encountered by the unwary. Close clinico-pathological correlation and HPV *in situ* hybridisation would be prudent in such situations.

Multifocal epithelial hyperplasia is rare in the UK, but typically affects younger patients living in crowded accommodation, particularly in South America. It is associated with HPV types 13 and 32, presenting as multiple mucosal nodules which may clinically resemble fibro-epithelial polyps. Histologically, acanthosis and parakeratosis are seen, together with characteristic “mitosoid” bodies (keratinocytes with coarse, clumped chromatin with a pattern resembling a mitotic spindle) that provide a useful diagnostic hint.

Reactive papillary and nodular lesions

Fibro-epithelial polyps

These rarely cause any diagnostic difficulty, but lesions affecting the tip of the tongue in particular may have a striking papillo-nodular

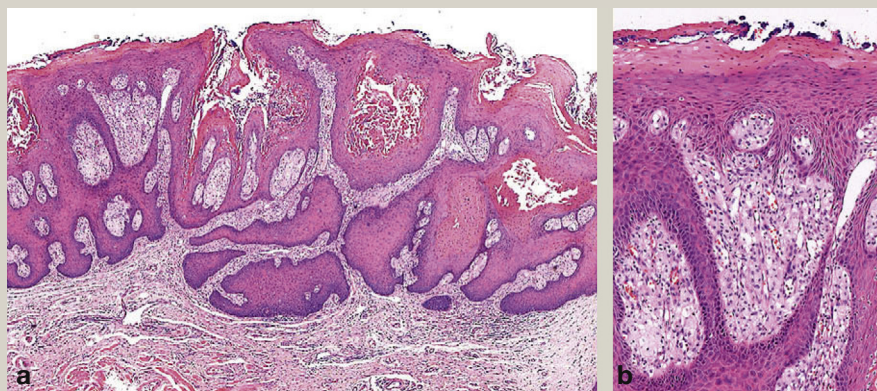
morphology. The florid, multiple lesions seen in the context of Cowden syndrome (PTEN hamartoma syndrome) have identical histological features.

Verruciform xanthoma

This reactive proliferation often presents as a solitary, painless nodule in the oral cavity, most commonly affecting the gingiva, alveolar ridge and the palate. Any age, but particularly the fifth to seventh decades, may be affected, and there is a more-or-less equal sex incidence. HPV infection is not implicated in the aetiology, which remains unknown. Histologically, verruciform xanthomas have sharply defined peripheral and deep borders, and exhibit an exophytic growth pattern. The surface stratified squamous epithelium is often verrucous but can occasionally be composed of flat-topped papillae (Figure 1a) covered by a thickened layer of parakeratin which has a tendency to stain orange with H&E. There are also broad, hyperplastic rete ridges between which are keratin plugs. Superficial microabscesses may be associated with candidal infection (Figure 1b). Characteristically, the connective tissue papillae are filled with foamy histiocytes which express macrophage markers (Figure 1b). Occasional xanthoma cells may appear within the epithelium or deeper connective tissue. Touton giant cells are absent and there are no systemic implications.

Papillary hyperplasia

This is another reactive lesion which most commonly, though by no means invariably, affects the palatal mucosa supporting a denture (Figure 2). However, the lesion does not necessarily resolve following correction of any prosthetic problem, and some patients affected by papillary hyperplasia do not wear dentures (e.g. mouth breathers). Histologically, there are multiple papillary projections of hyperplastic epithelium, each with a vascular connective tissue core. Diagnostic difficulty is usually the result of an inadequate or poorly orientated biopsy, which may give rise to a pseudo-epitheliomatous appearance. Candidal infection is typical, but again not inevitable, and the lesion may persist after anti-fungal therapy. The lamina propria is often chronically



a Verruciform xanthoma showing spikes of parakeratin and flat-topped papillae, with deep clefts filled with keratin. **b** At higher power, there is hyperparakeratinization and connective tissue papillae which are filled with xanthoma cells. Superficial abscesses suggest the presence of candidal infection.

Figure 1

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