

A solitary, red, papillary–verrucous lesion on the mandibular alveolar mucosa

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CLINICAL PRESENTATION

A 60-year-old Caucasian male was referred by his dentist for diagnosis and management of an asymptomatic lesion, incidentally discovered during a routine dental examination. According to the patient, this was his first dental visit after more than 5 years. His medical history was significant for iron deficiency anemia; he had been smoking 10 cigarettes per day for about 42 years.

Clinical examination revealed a round, well-circumscribed, red, plaque-like lesion with a papillary–verrucous surface on the alveolar ridge distally to the decayed root of the mandibular right first premolar, measuring 0.8 × 0.5 cm (Figure 1). It was nontender on palpation, and the patient did not report pain or other neurologic symptoms in the area. There were numerous dental and periodontal problems, but the rest of the oral mucosa was normal. Cone beam computed tomography (CBCT), requested by his dentist for the preoperative planning of oral implant rehabilitation, did not reveal any bone abnormality in the area of concern (Figure 2, arrow).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of a solitary, red, papillary–verrucous lesion on the mandibular gingiva/alveolar ridge may include hamartomatous, reactive, and neoplastic lesions.

Linear epidermal nevus (verrucous epidermal nevus or linear verrucous epidermal nevus [LEN]) is an epithelial hamartomatous lesion, characterized by a papillomatous configuration and distribution along the skin tension lines of Blaschko.^{1,2} In most cases, LENs represent a manifestation of one of several syndromes, in particular

epidermal nevus syndromes; they do not show gender predilection and are congenital. Extremely rare cases of LENs on the lips, tongue, buccal mucosa, hard and soft palate, and gingiva have been described as solitary, plaque-like lesions of variable color with a papillary–verrucous surface. Microscopic examination shows a nondescript benign papillomatous lesion. Oral LENs do not recur after excision and do not pose a risk for malignant transformation. The lesion in this case could have been clinically consistent with an oral LEN, but it was not congenital because it first appeared in an adult patient; occupied an edentulous area, indicating late development; occurred after teeth became loose; and had an exclusively oral involvement, rendering such a diagnosis unlikely.

*A superficial lymphangioma*³ may manifest as a red, granular enlargement on the gingiva. It is a rare lesion that may be present at birth, but may remain unnoticed until adolescence.⁴ Most cases are multifocal, but solitary lesions on the mandibular gingiva have also been described.⁴ The characteristic vesicular configuration of the surface, corresponding to the numerous thin-walled lymph vessels occupying the papillary lamina propria is usually evident,⁴ and microscopic examination after surgical excision confirms the diagnosis. Rare occurrence of this lesion on the gingiva, late onset, and lack of a vesicular or “frog spawn” configuration on clinical examination do not favor this diagnosis.

Oral verruciform xanthoma (OVX) is an uncommon benign lesion of purportedly reactive or immunologic origin.^{5,6} Most patients are males in the 40–69-year age group. OVX manifests as a small, asymptomatic, solitary plaque on the gingiva/alveolar mucosa; its surface is described as papillary, granular, or verrucous, and its color ranges from white to red or pink. Diagnosis is made through microscopic recognition of the characteristic lipid-laden histiocytes, known as “foamy” or “xanthoma” cells. There are some cases of recurrence after surgical excision, but no case of malignant transformation. The clinical features of our case were consistent with the diagnosis of OVX.

Although *inflammatory papillary hyperplasia (IPH)* is identified with the presence of maxillary removable dentures, there are some reports in non–denture-wearing patients.^{7,8} It is an asymptomatic, multinodular, or

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Fig. 1. Clinical examination. A round, well-circumscribed, red, plaque-like lesion with a papillary–verrucous surface on the alveolar ridge is seen distally to the decayed root of the mandibular right first premolar.

papillary lesion that may have normal to red color but is almost exclusively located on the middle of the hard palate. Microscopic examination is not diagnostic. Possible etiologic factors in non–denture-wearing patients are a deep palatal vault and mouth breathing. Management of IPH includes identification and removal of the etiologic factors, while surgical excision depends on the functional needs of the patients. Although our patient had poor oral hygiene and was a smoker, the nonpalatal location of the present lesion ruled out this diagnosis.

Erythroplakia is a rare potentially malignant condition defined by the (unavoidable) rule of “diagnosis by exclusion” as a fiery red patch that “cannot be characterized clinically or pathologically as any other definable lesion.”^{9,10} It is a disease of middle-aged persons or older adults and does not show a specific site preference. It manifests as a mucosal depression rather than plaque, is sharply defined, and has a smooth, velvety, or granular surface. Microscopic examination reveals epithelial dysplasia, carcinoma *in situ*, or squamous cell carcinoma in almost 90% of case. Because it has the highest risk for malignant transformation among all potentially malignant lesions and this risk cannot be predicted by clinical examination alone, biopsy followed by complete excision of the whole lesion and

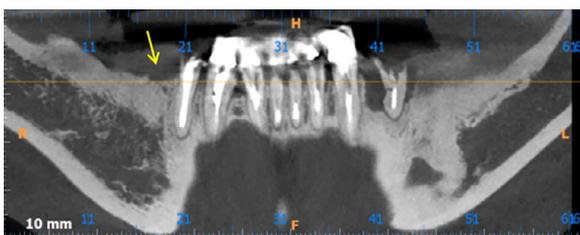


Fig. 2. Cone beam computed tomography scan. There is no bone abnormality in the area of concern (arrow).

close follow-up are mandatory. Erythroplakia would be an unusual diagnosis in the present case because this lesion was a plaque with a papillary–verrucous surface, not a depression.

The mandibular gingivae and the alveolar ridge are commonly involved by *squamous cell carcinoma* (SCC),¹¹ and 2 rare, low-grade variants of SCC, namely, *carcinoma cuniculatum* (CC) and *papillary squamous cell carcinoma* (PSCC), have a predilection for this site.^{11,12} SCC, CC, and PSCC are more common in older patients, and although their clinical appearance may be diverse, they may manifest as erythematous, papillary–verrucous lesions. An early gingival/alveolar ridge carcinoma may not invade the underlying bone,¹³ although SCC, CC, and PSCC are infiltrative tumors that cause bone destruction, with consequent tooth mobility, pain, or other neurologic symptoms.^{11,12} *Verrucous carcinoma* (VC), another low-grade variant of oral SCC, may be included in the differential diagnosis.¹⁴ However, it is more common on the tongue and usually presents as a longstanding, extensive, well-demarcated, papillary–verrucous plaque with surface projections and white color resulting from hyperkeratosis.¹⁴ SCC or one of its subtypes was strongly suspected in the present case, although there was no evidence of bone destruction on radiographic examination.

DIAGNOSIS AND MANAGEMENT

With the provisional diagnosis of gingival SCC, incisional biopsy was performed under local infiltration anesthesia. Microscopic examination of 5- μ m thick, formalin-fixed and paraffin-embedded tissue sections stained with hematoxylin and eosin showed a mucosal fragment superficially infiltrated by small epithelial nests (Figure 3A). The nests were composed of squamous epithelial cells centrally, with an occasional stellate, reticulum-like appearance, and palisading columnar basal cells with reverse nuclear polarization and subnuclear vacuolization peripherally (Figure 3B). In some nests, keratin pearls were seen. The overlying epithelium was spongiotic with interlacing areas of thinning and fine papillomatosis, and the rete pegs focally merged with the neoplastic nests. There was no evidence of dysplasia or ameloblastic differentiation. The stroma was fibrous, and a retraction effect was not found. The epithelial cells were negative for the epithelial-specific antigen Ber-EP4 (mouse monoclonal antibody, dilution 1:100; Dako, Glostrup, Denmark) (Figure 4). The final diagnosis was peripheral ameloblastoma (PA), follicular acanthomatous type.

The patient was referred to the oral and maxillofacial surgery clinic for total excision of the lesion, and the diagnosis was confirmed. The postoperative course was uneventful, and no recurrence has been observed during the 18-months follow-up period.

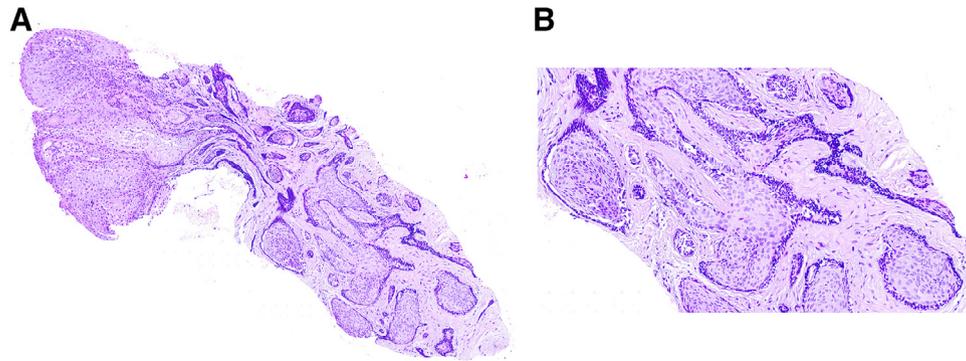


Fig. 3. Photomicrograph of the incisional biopsy specimen. (A) Mucosal fragment covered by spongiotic epithelium with interlacing areas of thinning and fine papillomatosis, superficially infiltrated by small epithelial nests. (B) The nests are composed centrally of squamous epithelial cells, occasionally having a stellate, reticulum-like appearance, and peripherally of palisading columnar basal cells with reverse nuclear polarization and subnuclear vacuolization (hematoxylin-eosin [H&E] stain, original magnification (A) $\times 40$, (B) $\times 200$). A high-resolution version of the image is available as eSlide: [VM05697](#).

DISCUSSION

PA accounts for 1%–10% of all ameloblastomas,¹⁵ and approximately 210 documented cases can be found in the English literature until 2018.¹⁶ It affects mostly male patients, in the 40–60-year age group.¹⁵ The posterior mandibular gingivae are the most commonly involved site, followed by the anterior mandibular and the maxillary gingivae.^{16,17} Although, by definition, PA arises on the tooth-bearing jaw,¹⁵ rare cases in extragingival sites (e.g., buccal mucosa) have been published.^{18,19}

PA manifests as an asymptomatic gingival swelling with normal to red color and a smooth, granular or papillary surface.¹⁷ Therefore, the clinical differential diagnosis is broad and ranges from reactive lesions, such as a fibrous epulis, peripheral ossifying fibroma, pyogenic granuloma, peripheral giant cell granuloma and papilloma, to neoplasms, such as squamous cell carcinoma or lymphoma.^{16,17,19–21} On radiographic examination, the underlying bone is found to be intact, although superficial bone depression, described as “cupping” or “saucerization” may be seen.^{16,17,22} Microscopically, most PAs are of the acanthomatous type.^{19,22} The clinical, radiographic, and histologic features of the present case were typical of PA.

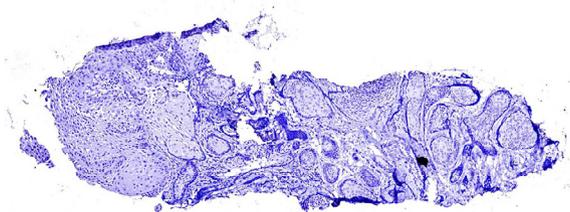


Fig. 4. Immunohistochemical stain shows lack of expression of anti-epithelial antibody Ber-EP4 (original magnification $\times 40$). A high-resolution version of the image is available as eSlide: [VM05698](#).

Considering the origin of PA, extrasosseous cellular remnants of dental lamina within the gingiva (“Serre’s pearls”) are implicated if the epithelial nests are not connected with the surface squamous epithelium or are separated from it with fibrous connective tissue,^{17,22} while the basal layer of the gingival epithelium is thought to be involved, when there is continuity of the nests with the epithelium,^{19,22–24} as in the present case. The latter, however, is rather arbitrary because ameloblastoma developing in the lamina propria could extend upward and come in contact with the overlying epithelium.²³ Signs of activity (e.g., elongated rete ridges and basal layer cells with basophilic cytoplasm and large hyperchromatic nuclei) in the epithelium adjacent to the area of continuity between PA and surface epithelium have also been associated with a possible origin of PA from the basal layer.^{19,22}

The main consideration in the microscopic differential diagnosis of PA is intraoral basal cell carcinoma. This is an extremely rare, infiltrative tumor, with approximately 6 documented cases reported to date. It may also show palisaded arrangement of the peripheral cells.²⁵ However, those cells lack reverse polarization and apical vacuolization, and mitoses, apoptotic cells, and a prominent retraction artifact are present.²⁵ Strong immunoreactivity for the anti-epithelial antibody Ber-EP4 may also facilitate diagnosis because this is not expressed in PA,²⁵ as was seen in the present case. Other lesions that should be included in the differential diagnosis are peripheral odontogenic fibroma, odontogenic gingival epithelial hamartoma, and peripheral squamous odontogenic tumor.^{20,22}

The innocuous clinical behavior of PA dictates conservative management,¹⁵ usually suprapariosteal surgical excision with 1–2-mm healthy margins.²⁰ The intact cortical jaw represents an efficient barrier to the intraosseous invasion of PA and, thus, has a good prognostic effect.¹⁷

Recurrence has been reported in up to 20% of cases,¹⁷ attributed to inadequate initial management, rather than to the tumor's biologic behavior.¹⁶

CONCLUSIONS

PA should be included in the differential diagnosis of a papillary–verrucous lesion on the gingiva/alveolar ridge.

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