Primary Malignant Melanoma of Maxillary Gingiva — A Case Report and Review of the Literature

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ABSTRACT

Dentists may encounter pigmented lesions in routine clinical practice. In most cases, the lesions are asymptomatic and benign in nature; however, rarely, a pigmented lesion can be a sign of malignancy. We report a case of malignant melanoma of the maxillary gingiva to highlight the importance of biopsy and periodic follow-up of patients with unusual focal pigmented lesions in the oral cavity.

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The oral cavity is a common site for various pigmented lesions: amalgam tattoo, melanotic macule, smoker's melanosis, racial pigmentation, nevus, drug-induced pigmentation, systemic diseases and, of course, melanoma. Although most pigmented lesions are benign and of no clinical consequence, clinicians must differentiate between the large number of benign lesions and the rare serious diseases, most notably melanoma. We report a case of misdiagnosed malignant melanoma and briefly review the differential diagnosis of oral pigmented lesions.

Case Report

A 32-year-old Asian woman reported for consultation regarding a rapidly growing pigmented mass in the maxillary anterior region. Three months earlier, she had developed an asymptomatic bluish-black patch on her anterior maxillary gingiva. Esthetic concerns prompted her to visit her dentist, who ruled out any pathology and suggested that this pigmentation was a normal variant for her ethnic group. The patient remained asymptomatic until 2 weeks before her visit to the clinic when she noticed "swelling" of her gums and some discomfort in chewing.

The patient was moderately built and nourished, and her vital signs were within normal limits. Intraoral examination showed a diffuse lesion extending from the right maxillary canine to the left maxillary canine region. On the labial side, the lesion was slightly elevated and displayed red-black discoloration (**Fig. 1**); on the palatal side, although the lesion was only slightly elevated between teeth 13 and 12, it was markedly exophytic between teeth 11 and 23 (about 1.5 cm in diameter) and the mass had an irregular border and a rough surface (**Fig. 2**). The central incisors within the lesion were mobile (grade 2). On palpation, there was no tenderness, bleeding or regional lymphadenopathy.

An intraoral radiograph could not be obtained because of difficulty in film placement.

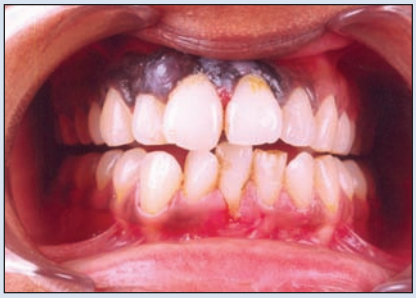

Figure 1: Intraoral photograph showing bluish-black pigmentation on the labial attached gingiva extending from the right maxillary canine region to the central incisor, crossing the midline and extending to the left lateral incisor.

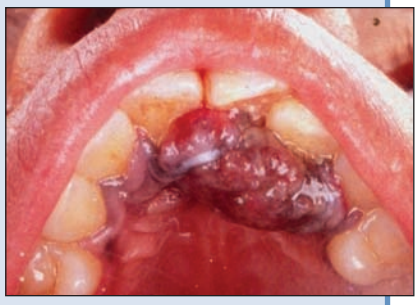

Figure 2: Intraoral photograph showing a black proliferative growth on the palatal aspect of the anterior teeth.

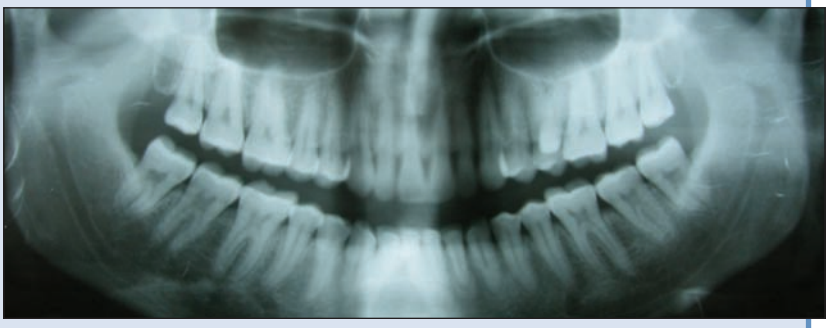

Figure 3: The panoramic radiograph did not reveal any abnormality.

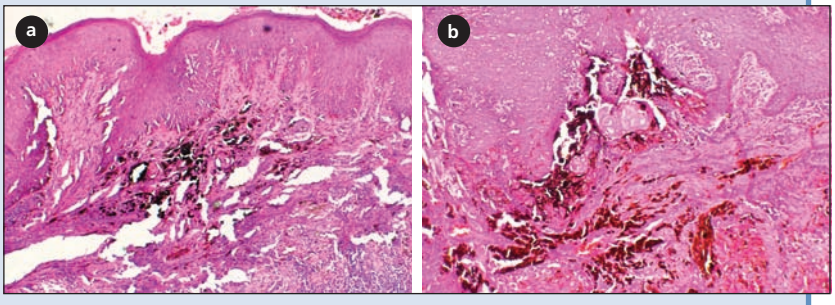

Figure 4: Photomicrographs showing infiltration of malignant melanocytes into the connective tissue (hematoxylin and eosin stain). Original magnification: **a.** ×10; **b.** ×40.

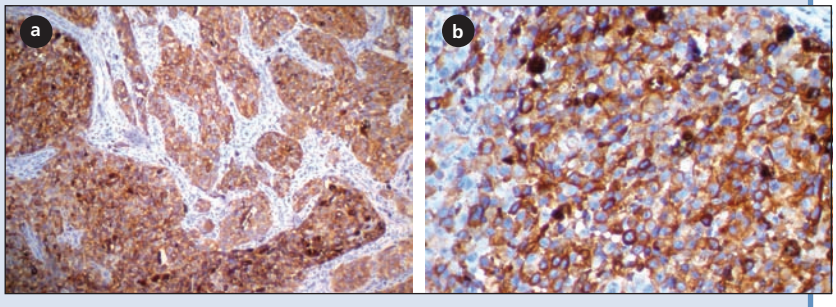

Figure 5: Photomicrographs showing HMB-45 positive malignant melanocytes (immunoperoxidase stain). Original magnification: **a.** ×10; **b.** ×40.

Although panorex has limited value in determining bone changes in anterior teeth, a panoramic radiograph was taken to evaluate possible marked bone destruction. No apparent abnormality was seen (**Fig. 3**). An incisional biopsy was performed under local anesthesia.

Hematoxylin- and eosin-stained sections of the biopsy specimen showed numerous atypical melanocytes at the epithelial connective tissue junction, proliferating laterally along the basal cell layer and infiltrating vertically into the deeper connective tissue (**Fig. 4**). The malignant melanocytes were pleomorphic and hyperchromatic and contained brownish-black granular pigment in the cytoplasm. The tumour cells stained intensely with HMB-45, an antibody to melanoma antigen, confirming the melanocytic nature of the lesion (**Fig. 5**). The lesion was diagnosed pathologically as malignant melanoma.

Discussion

Melanoma is a malignant neoplasm arising from the neural crest cells. During embryologic development, melanocytes migrate from the neural crest into the epithelial lining of the skin and, in the developed skin, they reside primarily in the basal epithelial layer.[1] Because the oral cavity develops from an ectodermal depression or invagination, the epithelial lining of the oral mucosa, similar to skin, normally contains melanocytes in its basal layer,[1–3] which can evolve into melanoma as in the skin.

Malignant melanoma is a deadly disease. Although it constitutes only 3%–5% of all cutaneous malignancies, it accounts for most skin cancer-related deaths (77%).[4] Oral melanoma is extremely rare and accounts for less than 1% of all melanomas[1,5,6] and 1.6% of all head and neck malignancies.

Despite the rarity of the disease, melanoma is the most important pigmented lesion in the oral cavity because of its deadly nature and most, if not all, oral biopsies of pigmented lesions are aimed at excluding malignant melanoma. It is well known that early diagnosis and treatment of melanoma can reduce mortality rate. If diagnosed early, when the

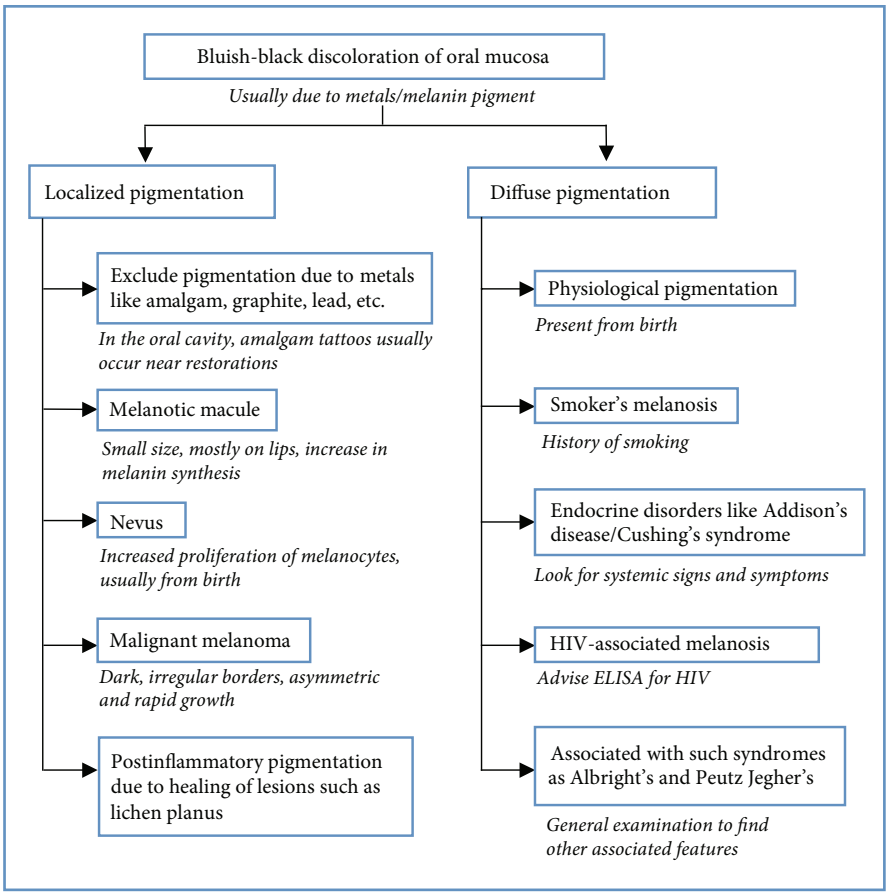

Figure 6: Differential diagnosis of pigmented lesions in the mouth, including characteristic features that help in diagnosis. ELISA = enzyme-linked immunosorbent assay. Note: Biopsy must be advised if there is an increase in size, a change in colour or any proliferative changes associated with a pigmented lesion.

malignant cells are limited to the epidermis or invasion is minimal, melanoma is either 100% curable by excision (for in situ lesion) or is associated with a 5-year survival rate of 95% (for lesions < 1 mm in thickness without ulceration).[7] In contrast, the 5-year survival rate for cutaneous melanomas > 4 mm thick with ulceration is only 45%.

For melanoma in the oral cavity, the prognosis is much worse: the 5-year survival rate is generally in the range of 10% to 25%, partly because detection is more difficult as pigmented lesions in the oral cavity are less visible than on the skin. For this reason, the dental profession plays an important role in the early diagnosis of oral melanoma. In our case, if the patient had been diagnosed immediately, when the lesion was flat and probably limited to the epithelium, the prognosis would have been much better; the 3-month delay resulted in > 4-mm thickness of the lesion and ulceration.

Differentiation of melanoma from various oral pigmented lesions can be a daunting task (**Fig. 6**) There are no striking features to distinguish oral melanoma from many other oral pigmented lesions. It is generally a disease of adults (usually > 40 years of age) and rare in people < 20 years; the female-to-male ratio is 3:1.[8] It can afflict any ethnic group, although the Japanese population appears to be more susceptible.[9,10] However, melanoma does have a predilection for certain oral sites — the hard palate and maxillary gingiva,[4,11–13] as in this case. Therefore, dentists should pay particular attention to pigmented lesions in these regions.

Clinical presentations of melanoma vary tremendously. It appears most commonly as a pigmented lesion varying from dark brown to blue-black, although some can be amelanotic.[14] In the latter case, it is not possible to make a clinical diagnosis of melanoma; only a biopsy can reveal the true nature of the lesion. A melanoma lesion can be flat (macule) or elevated (nodule or tumour), with or without ulceration or an erythematous border, and it can be small or large. However, dentists should be highly suspicious of malignant melanoma in the following situations (**Box 1**): variegation in colour (red to black-brown) within a pigmented lesion, particularly when it has an asymmetrical or irregular outline; sudden appearance of a large pigmented lesion, particularly when it has an exophytic component, as in this case, or has erythematous or ulcerated areas. It should be noted that even when melanoma becomes exophytic or ulcerated, it generally lacks the induration and rolled ulcerated border frequently seen in oral squamous cell carcinoma, the most common oral cancer. These features should not be used to judge whether a pigmented lesion is malignant, as the radial growth phase of melanoma could be prolonged with minimal or no invasion and, during this phase, atypical melanocytes exhibit a pagetoid (upward migration) mode of spread resulting in uniform epithelial thickening[1] and a lack of focal indurations.

Differential Diagnosis of Large Pigmented Lesions

Many melanomas grow rapidly; dentists should be particularly cautious when confronted with a large pigmented lesion, as in this case. Racial pigmentation, drug-induced pigmentation, smoker's melanosis and some syndromes can all present as a large area of pigmentation in the oral region.

Box 1 ABCDE warning signs suggestive of early melanoma

Asymmetry: The shape of the lesion is not the same on both sides.

Border irregularity: The edges are ragged, notched or blurred.

Colour variation: Pigmentation is not uniform and may display shades of tan, brown or black. White, reddish or blue discoloration is of particular concern.

Diameter: A diameter greater than 6 mm is characteristic of melanoma, although some may have smaller diameters. Any growth in a nevus warrants an evaluation.

Evolving: Changes in the lesion over time are characteristic. This factor is critical for nodular or amelanotic (nonpigmented) melanoma, which may not exhibit the classic criteria listed above.

This case should not have been confused with racial pigmentation, which is a physiological condition, for a number of reasons. First, racial pigmentation is more diffuse and, on gingiva, it will be generalized rather than confined to one quadrant as in this case. Second, racial pigmentation will be present from an early age; the sudden appearance of a pigmented lesion, as in this case, should immediately preclude the diagnosis of racial pigmentation. Duration of pigmentation is always critical in the differential diagnosis of oral melanoma. The rule of thumb is that if a pigmented area has not changed in 5 years, it cannot be melanoma and no biopsy is required. Third, racial pigmentation will always be flat and asymptomatic; the rapid development of elevated areas and symptoms in this case, again, strongly point to a diagnosis of melanoma. Unfortunately, many melanomas frequently remain asymptomatic and are not diagnosed until there is a breakdown of the epithelium or hemorrhage.[15]

Drug-induced pigmentation tends to be extensive and has a predilection for the hard palate. However, the appearance of such a pigmented area should be associated with the intake of a medication, particularly medications known to cause pigmentation. In the absence of any medication, melanoma should be suspected when a large pigmented area is present on the hard palate. Even in the case of a history of medication, if there is any doubt, a biopsy should be performed.

Smoker's melanosis or postinflammatory pigmentation may present as large pigmented areas, but this pigmentation tends to be brownish in colour and generally not as dark as melanoma. Smoker's melanosis is seen in people with a long habit of smoking and is frequently located on the mandibular anterior gingiva (in cigarette smokers) or the buccal mucosa (in pipe smokers). Postinflammatory pigmentation should be related to a previous condition, such as long-standing erosive lichen planus at the site.[16] Rarely, systemic diseases, such as Addison's disease, can present diffuse pigmentation, but a careful medical history should help to establish these conditions.

All of these conditions warrant a biopsy if a diagnosis of melanoma cannot be firmly excluded.

Differential Diagnosis of Small Pigmented Lesions

The most common oral pigmentations are a result of amalgam tattoo, melanotic macules and graphic tattoo (from pencil lead). These lesions are generally small (< 1 cm, although, in rare situations, amalgam tattoo can be large) and flat, grey-black to blue-black in colour (amalgam and graphic tattoos) or light to dark brown (melanotic macule). Occasionally, nevi also occur in the oral cavity as pigmented lesions and tend to be < 1 cm in diameter, although they can be either flat or elevated. Nevi vary in colour from amelanotic, to brown to blue-black.

For small pigmented macules, the most likely diagnosis is one of the above entities, particularly amalgam tattoo. Unfortunately, in rare cases, a small flat pigmented macule can represent an early stage of a malignant melanoma. Cases of melanoma have been reported to be preceded by an asymptomatic flat pigmented macule for periods of several months to 5 years[17] before they start to show the symptoms and signs of malignant melanoma, such as sudden growth, a change in colour or becoming exophytic and hemorrhagic. In this case, the elevated lesion was preceded 3 months earlier by a pigmented macule. In fact, approximately a third of melanomas are preceded by asymptomatic pigmented macules.[1] Thus, a biopsy of a benign-looking small pigmented lesion is warranted to rule out early melanoma, unless lesions have been present for a long time without change or the diagnosis of amalgam tattoo can be established firmly by radiographic demonstration of amalgam speckles or reliable history.

Surgery is believed to be the most effective treatment for melanoma. For cutaneous melanoma, wide resection with surgical margins of 2.5 cm is necessary.[18] Immunotherapy with interferon may also be beneficial.[18] If there is disseminated metastatic disease, chemotherapy and radiation therapy should be advised.[19] Dentists must coordinate with oral and maxillofacial surgeons, medical oncologists and radiation therapists to ensure proper management of cases of malignant melanoma.

Conclusions

The oral cavity is a common site for pigmented lesions, most of them benign. Dentists should keep the possibility of malignant melanoma in mind during any differential diagnosis of a pigmented lesion. When in doubt, the dentist should refer the patient to a specialist or perform a biopsy.

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