Oral Nevi

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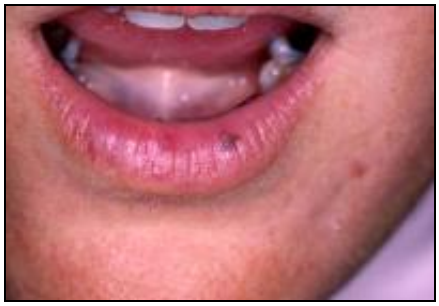
Background

Nevi are benign proliferations of nevus cells located either entirely within the epithelium, in both the epithelium and underlying stroma, or in the subepithelial stroma alone. They are best categorized as hamartomas rather than true neoplasms. Nevi of the oral cavity are usually called mucosal melanocytic nevi or intramucosal nevi. In 1943, Field and Ackermann may have reported the first documented case of an intraoral nevus.[1] Comerford and his coworkers were the first to propose the term intralamina propria nevus.[2] King et al adopted the less anatomically specific term, intramucosal nevus, which clinicians more easily understand.[3]

White adults have 10-40 cutaneous nevi on average, but intraoral lesions are rare.

On the basis of the histologic location of the nevus cells, cutaneous nevi can be classified into 3 categories. The first category, junctional nevus, is when nevus cells are limited to the basal cell layer of the epithelium. The second category, compound nevus, is used if the cells are in the epidermis and dermis. The third category, intradermal nevus, is when nests of nevus cells are entirely in the dermis. Oral nevi follow the same classification; however, the term intradermal is replaced by intramucosal.

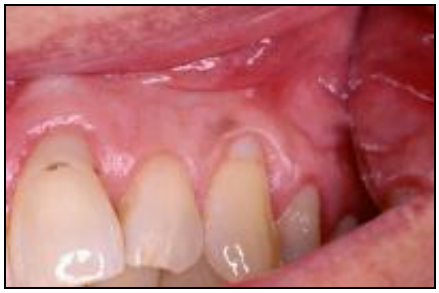
Nevi may also be classified as congenital or acquired (see Histologic Findings). Oral acquired melanocytic nevi evolve through stages similar to those of nevi on the skin. Junctional nevi that are first noted in infants, children, and young adults typically mature into compound nevi. Then, during later adulthood, the lesions mature into intramucosal nevi. By far, the most common mucosal type is the intramucosal nevus, which accounts for more than one half of all reported oral nevi. Note the image below.



Intramucosal nevus on the lower lip. This brown papule measured 0.6 cm in diameter and was only slightly raised. Melanotic macules are invariably flat.

The common blue nevus is the second most common type found in the oral cavity. The proportion of total nevi that are blue nevi is greater in the mouth than in the skin; blue nevi account for 25-36% of all oral nevi, according to

different studies. Junctional and compound nevi account for only 3-6% of all oral nevi, and only a few cases of congenital nevi, cellular blue nevi, Spitz nevi, balloon cell nevi,[4] and combined nevi have been reported. With the probable exception of halo and dysplastic nevi, all of the cutaneous subtypes of nevi have been found in the oral mucosa. Note the image below.



Blue nevus on the gingiva. This 1-cm saucer-shaped tan macule on the gingiva has histologic features consistent with those of a blue nevus, which is the second most common type of oral nevus. This location is atypical because most blue nevi occur on the palate.

The term nevus is used in reference to many other hamartomatous or neoplastic entities that are not composed of nevus cells or melanocytes. These entities include white sponge nevus, epidermal nevus syndrome (nevus unius lateris), nevus sebaceous, blue rubber-bleb nevus syndrome,[5, 6, 7, 8] nevoid basal cell carcinoma syndrome, and widespread intramucosal nevus associated with hypertrophy of the oral mucosa and alveolar bone. This article reviews only true melanocytic nevi.

Pathophysiology

Although little doubt exists that nevus cells arise from the neural crest, whether the cells represent true melanocytes or a closely related but distinct cell type is debatable. Melanocytes of the oral epithelium are localized to primarily the tips of the rete ridges. They have a small, regular nucleus along the basal cell layer and a dendritic cytoplasm that contains melanosomes. Melanocytes transfer melanosomes to neighboring keratinocytes.

Supporting their distinction from melanocytes, nevus cells have rounded cytoplasms and lack the dendritic processes typical of melanocytes. Nevus cells have similar nuclear morphologic features, but their cytoplasm is ovoid, rounded, or spindle shaped. In addition, nevus cells have no contact inhibition and are able to form nests and clusters of cells. Normally, melanosomes are retained by nevus cells and not transferred to adjacent keratinocytes. Nevus cells also have the ability to migrate from the basal cell layer into the underlying submucosa.

Melanocytic cells derived from the neural crest migrate to the skin and oral mucous membranes during embryogenesis, and both locations are characterized by melanin production in the epithelial component. Nevus cell formation probably begins with the proliferation of melanocytes along the basal cell layer, and it is possibly associated with elongation of the rete ridges. Nevus cells either lack contact inhibition or lose it shortly after the proliferation process begins. They retain melanin pigment and form a nest or thèque. On the skin, this process usually results in the formation of a flat tan-to-brown junctional nevus measuring less than 0.5 mm in diameter.

Nevus cells probably continue to proliferate in the basal cell layer and then protrude into the submucosa. Eventually, they separate from the epidermis. Junctional nests are lost later, and nevus cells become confined to the submucosa. As the nevus cells penetrate into the submucosa, their pigmentation diminishes; approximately 15% of intramucosal nevi are nonpigmented. Melanocytic nevi can be present at birth, they may appear shortly after birth, or they may develop during childhood and early adulthood. Most cutaneous nevi develop in patients younger than 35 years. In studies of oral nevi, 85% of lesions are found in patients younger than 40 years.

Epidemiology

Frequency

United States

Literature from the early 1950s suggested that primary melanoma of the oral mucosa was more common than intramucosal nevi.[9] At that time, oral melanomas were reported far more commonly than oral nevi. King and associates investigated this observation by performing a prospective study to determine the incidence of oral nevi.[3] In 4191 patients examined, 3 nevi were found. None of the nevi was found in white patients. The study population had a black-to-white ratio of 2.3:1, indicating that both races were well represented. One white patient

had what clinically appeared to be an oral nevus, but biopsy was deferred because of the patient's comorbidities.

According to the data of King et al, the estimated incidence of oral nevi in black patients in the United States is 3 cases per 2912 patients (rate, 0.1%). This incidence is probably similar in the white population, because 1279 white patients were examined, and one probable nevus was found.

In 1979, Buchner and Hansen determined the incidence of oral nevi by reviewing accession diagnoses from a large oral pathology service.[10] They found 32 cases among 20,731 surgical specimens (rate, 0.15%); this finding again suggested that nevi are rare in the oral cavity relative to those in the skin.

One potential reason for the relative scarcity of oral nevi may be that they are too small to be easily detected (see Physical).

International

Racial differences are found in the incidences of cutaneous nevi, with whites having more lesions than Asians or blacks. No such racial differences have been found with oral nevi.

Mortality/Morbidity

Numerous references support the association between melanocytic nevi of the skin and malignant melanoma. However, no case of melanoma arising in or around an oral melanocytic nevus has been described.

- Residual nevus components are contiguous with cutaneous malignant melanoma in 18-72% of cases, depending on the study. Similarly, 18-85% of patients with melanoma have a history of a nevus at the site of a primary melanoma. In contrast, the literature on oral conditions is devoid of references that document an oral nevus in association with a mucosal melanoma. In a study of 119 oral melanocytic nevi by Meleti et al, no association with melanoma was found despite the preponderance of both these lesions in the palate.[11]
- Although approximately one third of mucosal melanomas are associated with a preceding mucosal melanosis, in patients in whom biopsy was performed, the melanoma was thought to arise from atypical melanocytic hyperplasia, not a benign melanocytic nevus.
- In a few documented cases, he associated pigmentation consisted of completely benign mucosal melanosis.

Race

Oral nevi are found in persons of all races.

- Oral nevi are reported more frequently in whites, in whom 55% of reported oral nevi occurred. Approximately 23% of oral nevi reported in the literature occurred in black patients.
- In the largest study of race and mucosal nevi, Asians represented 14% of the patients with oral nevi and 7% of patients were Hispanic. This study was conducted in an area with a large population of Asians, blacks, and Hispanics. The apparent predominance of oral nevi in whites is likely due to the over-representation of this group among patients who underwent biopsies.
- No objective evidence confirms that oral nevi are more common in whites than in others, and the data from King et al suggest that the incidences are similar among black patients and white patients.[3]

Sex

- Most studies have revealed that oral mucosal nevi are slightly predominant in women rather than men.
- One large study had a female-to-male ratio of 1.5:1. The intramucosal type of nevus was especially common; 64% of these lesions occurred in females. Blue nevi occurred almost equally among male patients and female patients.

Age

In one large study of patients with oral nevi, the patients were aged 3-85 years. The mean age of all patients was 35 years, but male patients tended to be a few years older than the female patients.

- Patients with junctional or compound nevi were relatively young; they were aged 22 and 24 years,

respectively, whereas the mean age of patients with intramucosal nevi was 35 years.
- The average age of patients with blue nevi was 38 years.
- The incidence of oral nevi was highest in patients aged 20-40 years, who accounted for almost one half of the patients.

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