Non-pigmented intramucosal nevi in a young female patient: A rare case report
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Abstract
Oral melanotic nevi can be categorized as hamartomas, developmental malformations or melanocytic tumors, which are benign in nature originating from proliferating defective melanoblasts of the neural crest cells either in the epithelium or in connective tissue. It is an uncommon oral lesion causing focal pigmentation. Clinically, it presents as an asymptomatic, smooth flat or slightly elevated lesion, which may or may not exhibit brown or brown-black coloration. Predominately it is located on the palate and rarely involving the gingiva and lips. Using histological criteria, four types of nevi have been described intra-orally. This paper presents a case report of a 23-year-old female having pain and swelling in maxillary anterior tooth region since 5-6 years. Excisional biopsy of the lesion was performed and was sent for microscopic examination. Histopathologic examination showed fibrocellular connective tissue stroma having nests or theques of nevus cells underlying surface epithelium. Diagnosis of oral non-pigmented lesions should be confirmed after careful clinical and histopathological examination as the differential diagnosis consists of a range of reactive, benign or malignant lesions.

Keywords
Intra-mucosal nevi, melanoblasts, melanoma

Introduction
The oral cavity has various forms of pigmented lesions and having multiple etiologies. Such lesions represent a variety of clinical features, varies from physiologic changes (e.g., racial pigmentation) to systemic illnesses (e.g., Addison’s disease) to malignant neoplasms (e.g., Melanoma and Kaposi’s sarcoma). Pigmented nevus is a tissue malformation resulting from the excessive proliferation of nevus cells. Nevi in cutaneous layers are classified into three groups on the basis of histological locations of the nevus cells. Junctional nevi are located in the basal epithelial layers, intradermal nevi are located within the connective tissue, compound nevi are located in both the basal epithelial layers and connective tissue. Oral pigmented nevi follow the same classification of dermis however the term intramucosal is replaced by intradermal. Melanocytic tumors of the oral mucosa which are benign in nature originate from melanoblasts cell of the neural crest which are defective and causes focal oral pigmentation. Although intradermal nevi are common lesions seen in the large majority of the population, whereas they are rare intraorally found only in 0.1% population.

This paper presents a case of intra-mucosal oral melanotic nevus on gingiva in a young female presenting with a history of occasional pain.

Case Report
A 23-year-old female presented with swelling and pain in anterior tooth region from last 5 to 6 years. Patient was relatively asymptomatic 6 years back when she noticed a very small nodule in the anterior tooth region. The swelling progressed slowly to the present size associated with occasional pain. On inspection, a solitary swelling was present between right upper lateral incisor and canine which was round in shape and approximately 2 mm × 2 mm in size. Mucosa over the swelling appeared white with pink margins, which were smooth and not associated with any discharge.

On palpation, swelling was smooth with well-defined edges, firm in consistency and non-tender. Differential diagnosis of
fibroma, peripheral ossifying fibroma, peripheral giant cell granuloma, and peripheral odontogenic fibroma was given. Under local anesthesia excisional biopsy was performed and mass was sent for histopathological examination [Figure 1].

Microscopic examination
Hematoxylin and eosin stained section showed parakeratinized stratified squamous epithelium with thin, elongated rete ridges and fibrocellular connective tissue stroma having nests or theques of nevus cells [Figure 2].

The nevus cells were larger round to ovoid epithelioid with abundant cytoplasm and some with intracellular pigmentation. Basal cells of overlying epithelium shows proliferating melanocytes containing intracellular melanin pigmentation (showed in arrows) [Figure 3]. Based on histopathological features, final diagnosis of intramucosal nevus was given.

Treatment
Lesion was removed surgically by taking surrounding normal mucosa along with the biopsy of the lesion.

Follow up the case had been done for 6 months which do not show any recurrences.

Discussion
Oral melanocytic nevi (OMNs) are benign tumors of melanocytes. Becker in 1927 first identified melanocytes in the oral epithelium; a few years later Laidlaw and Cahn isolated melanocytes from samples of gingival tissue. During early intrauterine life, precursors of melanocytes, melanoblasts become differentiated dendritic cells and migrate to the epidermis from the neural crest. After approximately 10 weeks of gestation the head and neck region represents the first part of the body where melanocytes appear. The basal layer of epithelium has the melanocytes, which do not contact each other and present between the basal keratinocytes of oral mucous membranes. Dendrites of melanocytes reach a number of keratinocytes in the close vicinity, and melanin is transported and transmitted to these keratinocytes through these dendrites. Most widely accepted the theory of abtropfung states that nevus cells migrate from the epidermis to the dermis and proliferate during the development of melanocytic tumors. Another widespread belief is that nevus cells have dual origin either from melanocytes or from neural structures. More specifically nevus cells located in the epidermis either in the basal cell layer or in the upper part of dermis is derived from melanocytes while which are located in the lower part of dermis are derived from neural structures specifically Schwann cells. Furthermore, the theory of Hochstringerung which is more congruous with current research than theories involving epidermal origin states that melanocytes derived from the neural crest migrate up from the dermis to the epidermis.

Morphologically, the melanocytic proliferation can be divided into three phases:

1. Junctional nevus (proliferation of benign neoplastic melanocytes along the epithelial-mesenchymal junction);
2. Compound nevi (migration of these cells into the mesenchymal compartment); and
3. Subepithelial naevi (melanocytes are located within the sub epithelial compartment).

These steps correspond to the histologic variants of OMNs. Zone of differentiation often are seen throughout the lesion. The

![Figure 1](image1.png)

**Figure 1:** Excisional biopsy of the growth

![Figure 2](image2.png)

**Figure 2:** (a and b) Photomicrograph showing nests/theques of nevus cells within the connective tissue (H and E stain, ×10)

![Figure 3](image3.png)

**Figure 3:** Photomicrograph of round to ovoid shaped nevus cells (H and E stain, ×40)
superficial cells present in theques and typically appear larger and epithelioid, with abundant cytoplasm, frequent intracellular melanin. These variations are classified as Type A nevus cells (epithelioid). Nevus cells of the middle portion of the lesion have less cytoplasm, are rarely pigmented and appear much like lymphocytes. This variation is classified as Type B nevus cells (lymphocyte-like). Deeper nevus cells appear spindle-shaped, much like Schwann cells or fibroblasts. Authorities classify this variation as Type C nevus cells (spindle-shaped).[9]

Different types of melanocytic nevi are congenital and acquired. Congenital melanocytic nevi are present at birth while those developing after birth are referred to as acquired nevi. Less common nevus subtypes include blue nevus, combined nevus, and Spitz nevus. Probably, most melanocytic nevi of the oral mucosa are acquired, even though some cases of congenital nevi have been reported. Sizes range from 0.1 to rarely, 3.0 cm. OMNs typically are well-circumscribed round or oval macules or papules, but polyloid larger lesions have been reported as well. OMNs have been reported to occur in a multiple fashion may be elevated or flatter. Elevated acquired nevi are usually lightly pigmented while flatter lesions tend to be more darkly pigmented.[10] Variation in colors is also specific for the identification of OMN’s. Colors vary from brown to blue, bluish-gray, or black; generally an individual lesion has a similar color throughout. Rare non-pigmented nevi are on record. The hard palate, buccal mucosa and gingiva are most commonly affected.[11]

King et al. in 1967 reported 0.1% of the pigmented oral nevi in Negro patients examined at his medical center. According to their study oral pigmented nevus was relatively a common lesion, which because of its small size and innocuous behavior was usually overlooked. Buccal mucosa is the most common intraoral location and intramucosal nevi the most common type.[12]

According to the clinicopathologic study of 32 new cases done by Buchner and Hansen found that intraoral nevi were much less common than intradermal nevi. They also supported the earlier reports that the intramucosal nevi were the most common type of nevus followed in decreasing order by the common blue nevus, compound nevus, and junctional nevus.[13]

Further Buchner and Hansen in 1980 analyzed data of 77 cases, along with 32 new cases and revealed that oral mucosal nevi were not rare and often misdiagnosed (especially those that were clinically non-pigmented) indicating that they were far more common. Buchner and Hansen in their another review stated that blue nevus is most frequently located on the hard palate, whereas, for intramucosal nevus, buccal mucosa was the most frequent site.[14]

Although rare, clonal expansion of cells is responsible for malignant transformation of nevi to melanoma therefore transformation of melanocytes, in existing nevi must occur before the clonal expansion. Melanomas of the oral cavity have OMNs as their precursor in only a small number of cases because of the rarity of oral nevi and their uncertain biologic behavior.[11]

The present was a rare case of intramucosal nevus occurring over the gingiva and was free of pigmentation clinically.

Conclusion

A careful diagnostic approach should be used when confronting non-pigmented lesions in the oral cavity, because non-pigmented OMNs clinically can mimic an early amelanotic melanoma or any other benign or malignant neoplasms. Surgical removal of suspected nevi is recommended because overall, the risk of transformation of particular acquired melanocytic nevi to melanoma is approximately 1 in 1 million. However, it is generally advised that biopsy be performed for all unexplained oral lesions, especially because of the extremely poor prognosis for oral melanomas. In contrast, no treatment is usually recommended for vascular and exogenous pigmentation. Similarly, a conservative approach is used for melanocytic macules, smoker’s melanosis, pigmements associated with drug therapy and systemic diseases.

References
