Intraoral Cellular Blue Nevus: Report of a Unique Histopathologic Entity and Review of the Literature

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GOAL

To understand intraoral cellular blue nevus to better manage patients with the condition

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Describe the clinical presentation of blue nevi.
2. Identify the 3 types of blue nevi.
3. Distinguish intraoral blue nevi from malignant blue nevus or melanoma.

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The blue nevus is found most frequently on the skin; however, in rare instances, it has been reported on oral mucous membranes. Intramucosal nevi make up more than one half of all reported intraoral melanocytic nevi. The common blue nevus is the second most common variant. Among the 3 variants of blue nevi, the cellular variant occurs less frequently than the common and combined variants. We present a rare case of intraoral cellular blue nevus that occurred on the oral mucosa of the hard palate. Because of the clinical and microscopic resemblance of the cellular blue nevus to melanoma and the rarity of this lesion in the

oral cavity, recognition and accurate diagnosis are critical.

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Nevi are malformations of the skin and mucosa that are either congenital or developmental. Nevi may originate from the surface epithelium or the underlying connective tissue.[1] Cutaneous melanocytic nevi are the most common human tumors worldwide, with an average of 10 to 40 nevi found in every white adult.[2] Intraoral melanocytic nevi are uncommon and mostly arise on the palate or gingiva, though any mucosal site may be involved.[3-5] The most common melanocytic nevi encountered in the oral cavity are the intramucosal type (63%), followed by blue nevi (19%), compound nevi (9%), junction nevi (5%), and combined nevi (4%).[4] The intraoral blue nevus is similar in appearance to its cutaneous counterpart; however, there is a greater tendency for nonpigmentation, and the papillary surface changes typically present on skin lesions usually are lacking.[5,6] The greatest diameter of the lesion usually is 4 to 6 mm.[4] Three variants of blue nevus are recognized: common, combined, and cellular.[6] Intraoral blue nevi present as asymptomatic, slightly raised, blue-black, well-circumscribed lesions.[4,5] Most blue nevi are present at an early age. The most common location of the intraoral blue nevus is the hard palate.[4,5] A limited number of intraoral blue nevi have been reported; however, no cases of intraoral cellular blue nevus have been reported.[6] In a review of 130 cases of melanocytic nevi by Buchner et al,[6] the authors refuted that one report of cellular blue nevus by Miller et al[7] actually was more compatible with the common blue nevus. Therefore, our case of intraoral cellular blue nevus is the first report of this entity in the oral mucosa.

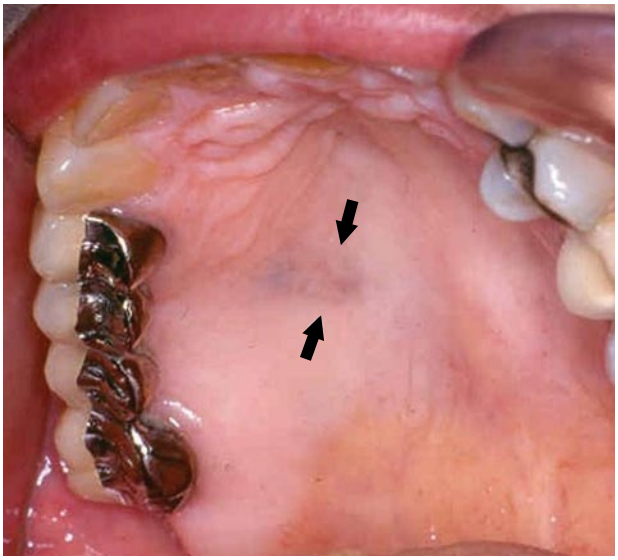

Figure 1. A discrete, bluish grey, flat, 15×10-mm lesion on the hard palate. The arrows point to the lesion.

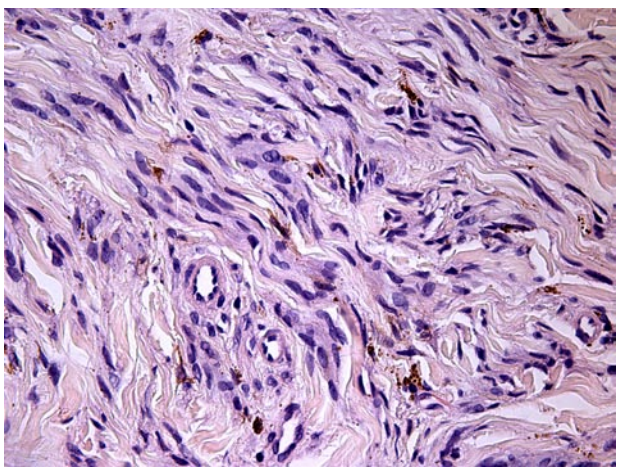

Figure 2. A benign proliferation of elongated oval-shaped and spindle-shaped dendritic melanocytes with prominent melanin pigmentation (H&E, original magnification ×40).

Case Report

A 66-year-old white woman presented with an asymptomatic pigmented lesion on the right side of the hard palate (Figure 1). Results of a clinical examination revealed a discrete bluish grey 15×10-mm lesion with pinkish white indistinct borders. The lesion had been present for approximately one month. The patient's past medical history included a cardiac murmur and allergy to penicillin. She smoked approximately 10 cigarettes a week. A 4-unit porcelain-fused-to-metal bridge was present on the maxillary right premolar to molar area; several amalgam restorations were present on the opposing side. The clinical differential diagnosis included exogenous or endogenous pigmentation, intraoral melanocytic nevus, melanotic macule, and malignant melanoma. An excisional biopsy was performed and the specimen was submitted for histopathologic examination.

Microscopic examination revealed a benign proliferation of elongated oval-shaped and spindle-shaped dendritic melanocytes with prominent melanin pigmentation (Figure 2). These cells were grouped in a fascicular pattern in irregular nests within the lamina propria (Figure 3). The surrounding stroma appeared sclerotic. Focal cytologic atypia, including nuclear pleomorphism, hyperchromasia, and focal nuclear inclusions, also were noted (Figure 4). No mitoses or necroses were noted. The entire specimen was surfaced by orthokeratinized epithelium. These microscopic findings were consistent with the

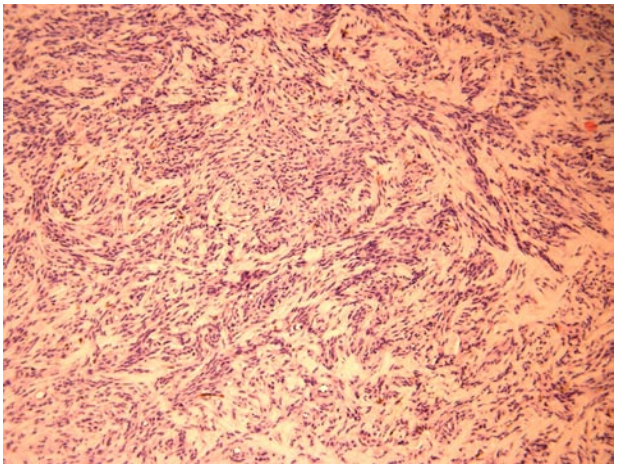

Figure 3. Spindled nevus cells grouped in a fascicular pattern in irregular nests within the lamina propria (H&E, original magnification ×10).

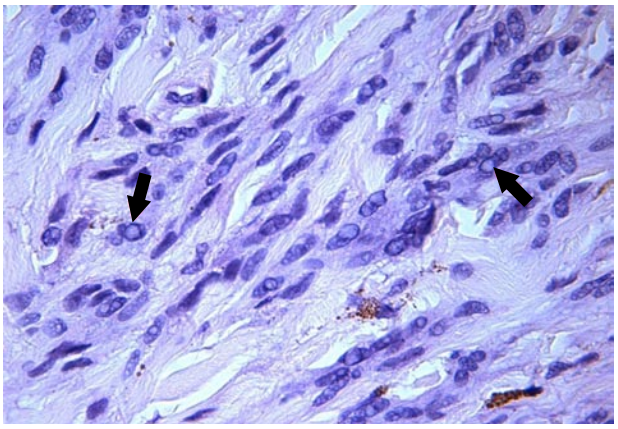

Figure 4. Nuclear pleomorphism with hyperchromasia and scattered aggregates of melanin were noted as well as focal cytologic atypia and focal nuclear inclusions (arrows)(H&E, original magnification ×63).

diagnosis of intraoral cellular blue nevus with focal cytologic atypia. Several dermatopathologists were consulted and concurred with the diagnosis.

Comment

Blue nevus was first described by Tièche[8] in 1906 as small, sharply defined, blue to blue-black spots mostly seen on the face and extremities.[9] The blue color of the nevus is due to the presence of melanin deep within the dermal melanocytes and the Tyndall effect.[2,9] The variation in color is related to the depth of the melanocytic cells in the dermis, the amount of melanin present, and the presence or absence of melanin in the cells of the overlying epidermis. These lesions usually are solitary, though multiple blue nevi in the same patient have been reported.[9]

Blue nevi generally occur on the skin of the hands, feet, and buttocks; however, in rare instances, they have been observed in mucous membranes, including the oral mucosa.[2,4,5] The first case of intraoral blue nevi was reported by Scofield[9] in 1959. Three types of blue nevi are recognized: common, combined, and cellular.[4] The common blue nevus appears as a small, well-circumscribed, dome-shaped, slate blue or blue-black nodule. The lesion rarely exceeds 1 cm in diameter. The combined blue nevus is a variant that contains both a blue nevus and an overlying melanocytic nevus.[10]

The cellular blue nevus often is clinically similar to the common blue nevus but is a rarer form. The cellular variant typically measures 1 to 3 cm in diameter and usually is larger than the common variant.[11,12] These lesions are elevated, smooth-surfaced, gray-blue to bluish black papules or plaques.[2,11,12] The lesions are most often solitary and found on the buttocks and sacral region and occasionally on the dorsal hands and feet.[2,10]

A histologic continuum exists from the common to the cellular blue nevus.[10] The cellular blue nevus is a compact lesion in the dermis and hypodermis and assumes an hourglasslike shape.[11,12] Microscopically, the cellular blue nevus is highly cellular and is composed of aggregates of oval-shaped, spindle-shaped, or polyhedron-shaped melanocytes arranged in a multitude of patterns, including biphasic, alveolar, neuroid, or fascicular. Melanophages are found between the cellular islands.[9,11,12]

The most important cytologic features differentiating the cellular variant of blue nevi from the atypical variant include the absence of mitoses, substantial nuclear pleomorphism, foci of necrosis, and admixtures of clear cells with hyperpigmented spindle cells.[13,14] The term *atypical blue nevus* has been reserved for lesions that exhibit the typical features of blue nevus, as well as cellular atypia, prominent nucleoli, and an elevated mitotic index of less than 2 mitotic figures per millimeter.[10,13,14]

Intraoral blue nevi, both common and cellular, are rare lesions.[5,6] It is important to distinguish these lesions from malignant blue nevus or melanoma.[12-14] Malignant blue nevus is identified by the presence of aggregates of cytologically abnormal dermal melanocytes, which usually form nodules in a preexisting blue nevus, or the occurrence of melanoma at the site of an excised blue nevus.[12,15,16] Many findings suggest a diagnosis of malignant blue nevus, including lesions larger than 3 cm, presence of nuclear pleomorphism, atypical mitotic figures, necrosis, expansile and destructive growth pattern, and a lack of biphasic appearance.[15-17] However, the most important criterion distinguishing

malignant blue nevus from cellular blue nevus is the presence of atypical mitoses.[16-18] Our case displayed focal cytologic atypia but failed to display any mitotic figures.

Because blue nevi usually are large, surgical excision with a wide border is recommended. All intraoral pigmented lesions should be excised with a wide border and examined microscopically.[4,5] An incisional biopsy of modestly sized pigmented lesions is contraindicated to avoid inducing metastasis if the lesion is a malignant melanoma.[7]

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