A well-circumscribed lobulated tumor on the hard palatal mucosa in a child

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CLINICAL PRESENTATION

A 9-year-old Caucasian female presented with a nontender, slow-growing mass on the right hard and soft palate, measuring 2.0 × 1.5 cm. On examination, the lesion presented as a well-circumscribed, soft tissue tumor with a lobulated appearance covered by normal-appearing oral mucosa (Figure 1). There was no ulceration and no induration. Adjacent teeth were vital, and a source of infection was not identified. There was no palpable lymphadenopathy. Computed tomography images indicated that there was no bone erosion or tooth resorption. The patient was healthy without any medical conditions and was not taking any medications.

An incisional biopsy was performed and the specimen was evaluated histopathologically. Three years after the incisional biopsy, the patient returned because the mass continued to expand. The patient did not report any pain or paresthesia. Medical history was unremarkable and she was not taking any medications. On examination, the lesion exhibited a lobulated appearance and was covered by normal-appearing mucosa without evidence of pigmentation or ulceration. The lesion appeared to have an increased size and measured 2.5 × 1.5 cm. The lesion was excised, and there was no involvement of the underlying bone.

DIFFERENTIAL DIAGNOSIS

A slow-growing, lobulated, and firm palatal soft tissue mass in a child elicits an extensive differential diagnosis. The lack of symptoms and multilobulated appearance of the lesion without significant radiographic findings ruled out an infectious etiology. The mass was confined mostly to the hard palatal mucosa and did not invade the underlying bone, and as such, central odontogenic tumors and primary osseous pathologic conditions were excluded. Peripheral odontogenic tumors were unlikely because the location of the tumor was centered around the midpalatal mucosa rather than the gingival margin. Our differential diagnosis was focused on salivary gland and soft tissue tumors.

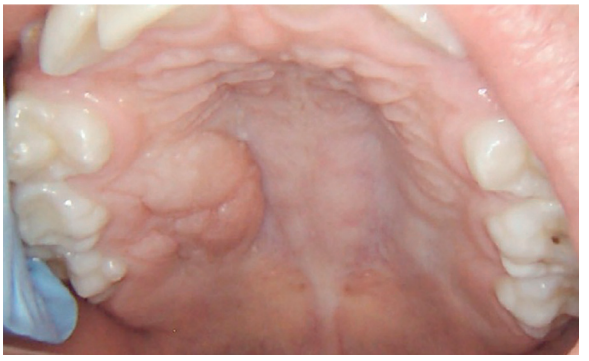

Fig. 1. A well-circumscribed, firm tumor with a lobulated appearance covered by normal oral mucosa, measuring 2.0 × 1.5 cm, was present on the hard palatal mucosa without evidence of pigmentation.

The palatal mucosa is the most common location for minor salivary gland neoplasms.[1] Salivary gland neoplasms are rare in the pediatric population, and the mean age of occurrence is 15.1 years.[2] The most common benign salivary gland neoplasm in pediatric patients is pleomorphic adenoma (70.6% of all salivary gland neoplasms), appearing as a slow-growing, painless, and firm mass.[1,2] Mucoepidermoid carcinoma, the most common salivary gland malignancy in children (13.4% of all salivary gland neoplasms), was also a consideration.[1,2] Low-grade salivary gland malignancies are slow growing and may appear innocuous or present with surface epithelial papillary hyperplasia.[3]

Due to the indolent growth pattern over a few years, we focused on benign mesenchymal neoplasms. Benign peripheral nerve sheath tumors (e.g., neurofibroma, schwannoma, and solitary circumscribed neuroma) are the most common soft tissue tumors in the oral cavity, and the hard palatal mucosa is a common intraoral site.[4] These tumors typically present as a

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slow-growing, firm, smooth-surfaced, and painless nodule or diffuse mass covered by normal mucosa, whereas the tumor in our case was multilobulated.[4] Benign peripheral nerve sheath tumors may arise at any age and are usually solitary lesions. When multiple, syndromes such as neurofibromatosis or multiple endocrine neoplasia should be considered.[4]

Other benign mesenchymal neoplasms, such as those of myofibroblastic, muscular, and adipocytic origin, were also considered. Myofibroblastic tumors, such as myofibroma and nodular fasciitis, are in the differential diagnosis. Myofibroma is a benign spindle cell tumor consisting of myofibroblasts with a predilection for the head and neck region, and 8% of myofibromas occur on the palatal mucosa.[5] Myofibroma commonly occurs in children or young adults (mean age 21.7 years), presenting as a firm, painless, rapidly enlarging mass, and it sometimes can be mistaken for a malignant tumor because of rapid enlargement.[5] Recurrence is noted in 10% of cases.[5] Nodular fasciitis, a clonal proliferation of myofibroblasts associated with *USP6* gene rearrangement, also typically exhibits a clinical history of rapid growth and presents as a nodule or mass.[6,7] Although nodular fasciitis mainly arises in young adults, more than half of the intraoral counterparts (58%) develop between the fourth to fifth decade of life.[6]

Congenital hamartomatous lesions (i.e., leiomyomatous hamartoma) and benign myocytic neoplasms (e.g., leiomyoma and rhabdomyoma) are also included in our differential diagnosis. Leiomyomatous hamartoma is a benign, self-limiting proliferation of smooth muscle cells that typically occurs in the first year of life.[8] It is a rare entity in the oral cavity; hard palatal mucosa and tongue are the most common intraoral locations.[8] Leiomyomatous hamartoma typically presents as a pedunculated or polypoid mass with an indolent nature, similar to our present case.[8] Leiomyoma is a benign tumor of mature smooth muscle cells, predominantly occurring in the uterus, gastrointestinal tract, and skin.[9] Intraoral counterparts are uncommon, typically occurring on the lips or palatal mucosa, with 75% representing angioleiomyoma (vascular leiomyoma).[9,10] Leiomyoma usually occurs in the fourth to fifth decade with a slight female predilection and presents as a firm, slow-growing, painless mass covered by normal oral mucosa.[9] Rhabdomyoma is a benign neoplasm of mature striated muscle cells with a predilection for the head and neck region.[11] Of the two subtypes of head and neck rhabdomyoma, adult rhabdomyoma is more prevalent in middle-aged male patients (4:1 male:female) in the seventh decade with a mean age 60 years (range 33-80), whereas fetal rhabdomyoma occurs in pediatric patients, with the oral cavity as one of the common sites.[12,13] Clinically, intraoral rhabdomyoma appears as an asymptomatic, solitary or multinodular mass and is commonly found in the floor of mouth, soft palate, and base of tongue.[12]

Lipoma, a benign tumor of mature adipose tissue, typically presents as a solitary, soft, asymptomatic nodule.[14] Intraoral lipomas tend to occur on the buccal mucosa and buccal vestibule, with the palatal mucosa being the least common site; children are rarely affected.[14] Other tumors such as solitary fibrous tumor are less common, and vascular tumors would tend to have a bluish hue. Finally, the palatal mucosa is a common site of occurrence for lymphoma, and some can be low grade and slow growing. However, this is uncommon in patients in the first decade of life.

DIAGNOSIS AND MANAGEMENT

An excision was performed and the histopathologic results were compared with the original biopsy specimen. Both specimens had benign epithelial hyperplasia with an undulated surface and elongated, interconnected rete ridges (Figure 2 A and B). The mass was composed of a dense diffuse infiltrate of small epithelioid melanocytes that filled and expanded the deep lamina propria; some of the melanocytes had hyperchromatic nuclei (Figure 2 B-D). These melanocytes were arranged in clusters, theques, or bands, streaming through collagen bundles with only focal melanin deposition (Figure 2 C-E). Focal junctional activity was noted (Figure 2 E). Melanocytes were present adjacent to the vessel walls or within the ductal epithelium (Figures 2 C and 3 C). There was mild variation in nuclear shape and size, but mitoses were not identified. The majority of the melanocytes had cytoplasmic positivity for MART-1 (Figure 3 A) and nuclear and cytoplasmic positivity for p16 (Figure 3 B and C), with a small population of cells in the junctional component and just beneath the epithelium having cytoplasmic positivity for HMB-45. MIB-1 labeling index was <5% (Figure 3 A). The palatal mass was diagnosed as intraoral congenital melanocytic nevus (CMN). No recurrence was reported at 1 year follow-up.

DISCUSSION

CMN consists of a benign proliferation of melanocytes at birth or shortly after birth.[15] Compared with acquired cutaneous melanocytic nevi, cutaneous CMNs are usually larger with variation in color, shape, and clinical morphologic characteristics.[15] CMN is not an uncommon entity on the skin with an estimated prevalence of 0.5%-31.7%.[15] The clinical appearance of cutaneous CMN may change with age; initially it commonly presents as a pigmented macule.[15] Cutaneous CMN can be further categorized

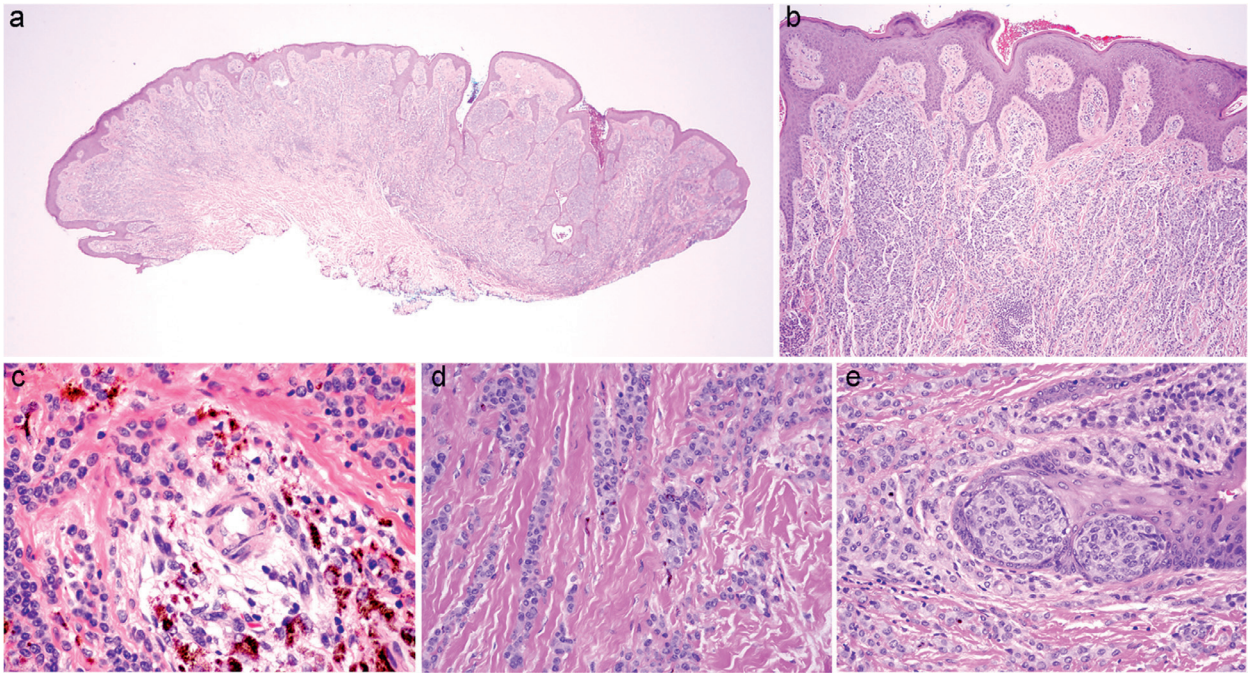

Fig. 2. (**A**) Undulated epithelial hyperplasia with many epithelioid melanocytes expanding and filling the lamina propria (hematoxylin-eosin [H&E], ×20). (**B**) Dense diffuse infiltration of melanocytes in the lamina propria. The majority of the melanocytes were epithelioid with some exhibiting hyperchromatic nuclei. The overlying mucosa exhibited a lobulated configuration with elongated, irregularly interconnected rete ridges (H&E, ×100). (**C**) The melanocytes with focal melanin deposition were present adjacent to the vessel wall (H&E, ×400). A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM04601. (**D**) Some epithelioid melanoctyes formed strands and bands, streaming between collagen bundles. There was minimial melanin deposition in the melanocytes (H&E, ×400). A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM04601. (**E**) Focal junctional activity with nested melanocytes (H&E, ×400). A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM04601.

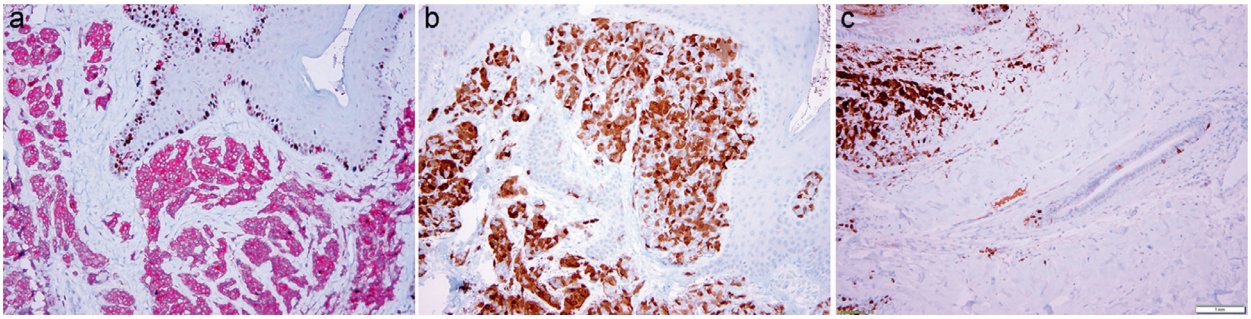

Fig. 3. (**A**) The majority of the melanocytes had cytoplasmic positivity for MART-1 (red), and MIB-1 labeling index was < 5% (brown) (×200). A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM04603. (**B**) The melanocytes exhibited nuclear and cytoplasmic positivity for p16 (×200). A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM04605. (**C**) The melanocytes were positive for p16, and some melanocytes were present in the ductal epithelium (×200). A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM04605.

based on size into small (<1.5 cm), medium (1.5-19.9 cm), and large/giant (>20.0 cm) lesions.[15] Most cutaneous CMN are medium in size, and giant CMN are far less common.[15] *N-Ras* mutations have been identified in many CMNs, whereas melanoma typically harbors *B-RAF* mutations.[15]

Intraoral CMN is extremely rare, with only six cases reported in the English literature.[16-21] Two of these six articles did not provide a complete clinical and histopathologic description of the intraoral CMN and were excluded from the following discussion.[17,19] Including our present case, all intraoral CMN occurred in female patients, with all cases noted within the first two decades of life (Table I).[16,18,20,21] One case occurred on the palatal mucosa as in this case.[20] Clinically, all the previous reports of intraoral CMN had either uniform or scattered

Table I. Clinical features of the intraoral CMN reported in the English literature

Authors	*Age*	*Gender*	*Location*	*Clinical features*	*Management*	*Follow-up*
Takeda[16]	7	F	Labial mucosa	Brownish-black, firm nodule present since birth and had not changed in size or color, 0.7 × 0.7 cm	Excision	No recurrence after 3 years
Allen and Pellegrini[18]	3	F	Posterior mandibular ginigva	Sharply demarcated, slightly elevated, dark brown plaque, 0.8 × 1.5 cm	Excision	No recurrence after 6 months
Gilbert et al.[20]	19	F	Hard palatal mucosa	Well-demarcated plaque with a slightly pebbled texture, 1.2 × 1.1 × 0.3 cm	Excision	Patient failed to return for follow-up
Marangon et al.[21]	16	F	Buccal mucosa	Diffuse swelling with papular surface, scattered pigmentation and ill-defined border, 5.0 × 4.0 cm	Incision	No recurrence after 11 years
Present case	9	F	Hard palatal mucosa	Well circumscribed, lobulated tumor covered by normal oral mucosa with no pigmentation, 2.5 × 1.5 cm	Partial excision, followed by excision	No recurrence after 1 year

CMN, congenital melanocytic nevus.

pigmentation, with a nodular, polypoid, or plaquelike appearance, and measured 0.7-5.0 cm.[16,18,20,21] However, in our present case, there was no clinical pigmentation and only minimal pigmentation on histopathologic examination. Including the present case, no recurrence has been reported after surgical removal.[16,18,20,21]

Histopathologically, intraoral CMN is a well-circumscribed nodule with a papillomatous or polypoid configuration, consisting of a proliferation of melanocytes with a nested and diffuse pattern exhibiting downward maturation.[21] There is variable melanin deposition and a lack of mitotic figures in melanocytes, and up to 30% of cutaneous CMNs have been reported with cytologic atypia in melanocytes.[15,21] Junctional activity or involvement of vessel walls or salivary ducts can be present, as in the present case. In addition to histopathologic evaluation, immunohistochemical studies can distinguish congenital nevus from melanoma. Melanocytes in CMN are positive for MART-1 and p16 but negative or minimally positive for HMB-45. MIB-1 positivity is present in less than 5% of the melanocytes in the superficial lamina propria, in keeping with its benign nature.[21,22]

On the skin, CMN may be associated with the development of melanoma, although the relative risk of developing a melanoma from an existing CMN varies from study to study.[23] Larger size and the presence of satellite CMN are correlated with malignant transformation.[15] Neuromelanosis (cerebral melanosis) is a congenital abnormality with melanocytic proliferation in the leptomeninges and brain parenchyma. It is termed neurocutaneous melanosis (NCM) when neuromelanosis is associated with a CMN.[24] NCM may lead to various clinical symptoms, such as headache, vomiting, photophobia, and seizures.[24] There is a well-established association between NCM and giant CMN, with NCM occurring in 2.5%-45% of patients with cutaneous giant CMN.[15] However, this association has not been noted in intraoral CMN. In addition, mucosal nevi are associated with 31% of large cutaneous CMNs.[15]

Excision is the first-line treatment for CMN; however, the efficacy of reducing malignant transformation is still not proven.[25] Lifelong surveillance for recurrence or development of malignant melanoma is recommended.[25]

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