An ulcerative nodule on the dorsal tongue in an 8-year-old boy

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CLINICAL PRESENTATION

An otherwise healthy 8-year-old boy was consulted in July 2020, presenting with a 20-day history of a painless tongue growth associated with trauma. According to his parents, the lesion initially appeared as a “blood-filled blister” and had evolved into an ulcerated swelling. Intraoral examination revealed a reddish, sessile nodule with an ulcerated surface in the tongue dorsum's midline (Figures 1A and 1B). Although the lesion was asymptomatic, the patient reported slight discomfort when swallowing. The patient's medical and family histories were unremarkable and non-contributory to systemic conditions or malignancy. Given the history of trauma, location, and clinical appearance, the primary differential diagnoses were reactive lesions or benign mesenchymal tumors. An incisional biopsy was performed under local anesthesia to elucidate the diagnosis, and 3 weeks after the procedure, the lesion presented an accelerated growth, doubling its initial size, now appearing as an aggressive dome-shaped nodule. (Figures 1C and 1D).

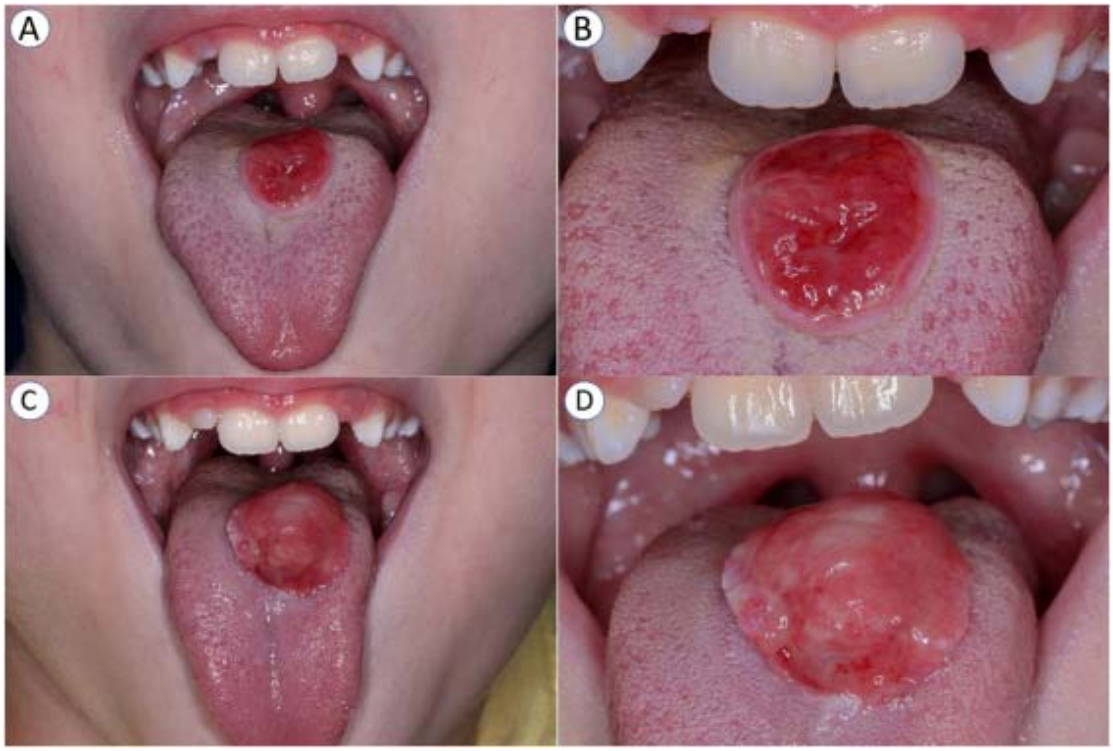

Fig. 1. Clinical features. **(A, B)** A firm and ulcerated broad-based nodule involving the dorsal tongue, 20 days after the initial trauma, at which time the incisional biopsy was performed. **(C, D)** Three weeks after the incisional biopsy, the tumor appeared aggressively as a large dome-shaped reddish nodule with superficial ulceration.

DIFFERENTIAL DIAGNOSES

Nodules affecting the tongue dorsum, particularly in pediatric patients, include various differential diagnoses. Due to the patient's history of trauma and the exuberant rapid growth after a surgical procedure, the clinical hypotheses were an inflammatory process, reactive lesions, and mesenchymal lesions.[1]

Inflammatory process

Lingual abscesses (LA) are uncommon conditions that mainly affect adults. Despite exposure to constant trauma, the tongue is resistant to inflammatory processes due to abundant blood and lymphatic flow, muscle anatomy, a thick mucosal surface, and saliva's cleansing action.2, 3, 4 When they occur, LA most commonly affects the anterior portions of the tongue, originating from direct trauma. Clinically, patients initially present slight tenderness and swelling of the tongue that gradually progresses, causing extreme pain and sensitivity, fever, odynophagia, dysphagia, and limitation of tongue movement. An LA in the posterior third of the tongue may cause dyspnea and respiratory obstruction.[2] Imaging exams tend to reveal hypodense images with irregular borders. Rare cases of LA have been reported in children with patients presenting with an acute inflammatory process that develops within days, associated with systemic symptoms (i.e., fever), different from what was observed in our patient.[3]

Reactive lesions

Pyogenic granuloma (PG) is a nonneoplastic vascular lesion representing a tissue response to local irritation or trauma. The PGs present as ulcerated reddish smooth or lobulated masses that predominantly involve the gingiva, although sites such as the tongue, lips, and buccal mucosa may be affected.[5] Although PGs can develop at any age, it is most common in children and young adults. Microscopically, PG shows a proliferation of endothelial cells and small, dilated capillaries resembling granulation tissue. The overlying epithelium is often ulcerated, and a mixed inflammatory cell infiltrate is typically seen in the underlying connective tissue. Treatment consists of conservative surgical excision followed by electrodesiccation to control bleeding.[6]

Mesenchymal lesions

Hamartomas and choristomas compose a group of lesions that consist of a tumor-like proliferation of normal mature tissues, the former being endogenous to the site of occurrence and the latter being exogenous.[7,8] In the oral cavity, both lesions present a striking predilection to the tongue dorsum, frequently affecting pediatric patients. In a recently published review, most cases seem to be congenital or affect children up to 5 years of age, contrasting with the evolution of the present case.[7,8] Tongue hamartomas and choristomas clinically present as firm, normal-colored, smooth-surfaced nodular or polypoid lesions usually in the tongue base, a location that may be predisposed to embryologic disturbances.[9] Microscopically, the most common tissue proliferations encountered are smooth muscle, adipose tissue, skeletal muscle, and osseous and cartilaginous elements.[7] Surgical excision is the treatment of choice.

Hemangiomas are benign vascular neoplasms and represent the most common tumors that develop during infancy and childhood.[10] According to the International Society for the Study of Vascular Anomalies, hemangiomas are classified as infantile or congenital; the former occurring days or weeks after birth and growing until 6 to 8 months of age before involuting, whereas the latter is fully developed at birth with minimal postpartum growth.[10] Although most hemangiomas present a predilection to the head and neck region, oral manifestations are uncommon and often involve the buccal mucosa, tongue, palate, and lips.[11] Clinically, lesions are usually asymptomatic and may vary from flat to nodular, smooth-surfaced lesions presenting a soft consistency. The color may range from red to purple according to the location, depth of tissue involvement, and degree of vascular congestion of the affected area.[11] Persistent lesions may be treated with several alternative methods, including sclerotherapy, cryotherapy, laser surgery, corticosteroids, and surgical excision.[11,12]

Nodular fasciitis (NF) is a benign myofibroblastic lesion in the young patients' upper extremities, head and neck, and trunk. The clinical appearance of NF in the oral and maxillofacial region is nonspecific. Its prevalence in children is low, with 10% of reported cases presenting in the pediatric population.[13] Interestingly, NF commonly presents spontaneous regression when not surgically resected; pathologists initially hypothesized NF to be a reactive process due to this peculiar biological behavior. However, based on molecular findings in the recurrent *MYH9-USP6* fusion, it is currently recognized as a “transient” neoplasm.[9] Microscopic features consist of spindle cells typically arranged in a tissue culture-

like architecture, sometimes resembling a sarcoma due to its high cellularity and mitotic activity. An accurate diagnosis can save the patient from inadequate treatment. Recurrence rates are low after treatment, and surgical excision is considered curative.[13]

Fetal rhabdomyoma (FRM) is a rare, benign soft tissue tumor demonstrating a spectrum of skeletal muscle differentiation.[14,15] An FRM showing immature cells within an abundant myxoid stroma is classified as myxoid FRM, whereas highly cellular and more differentiated tumors represent juvenile FRM. Both myxoid and juvenile FRMs may affect children and occur almost exclusively in the head and neck region, including the postauricular region, orbit, tongue, nasopharynx, and soft palate. In both subtypes, male patients are more commonly affected than female patients.[14,15] The recommended treatment is local surgical excision, and recurrence is often attributed to incomplete removal.[14,15]

Other uncommon benign mesenchymal neoplasms such as granular cell tumors, schwannoma, neurofibroma, ectomesenchymal chondromyxoid tumors, benign fibrous histiocytoma, angioleiomyoma, and solitary fibrous tumors may also present as soft tissue masses affecting the tongue.[16] Still, most of these tumors occur in middle-aged adults, rarely affecting pediatric patients.

Rhabdomyosarcoma (RMS) is a malignant neoplasm of skeletal muscle origin and represents childhood's most common soft tissue sarcoma.[17] Approximately 90% of all RMS are in patients younger than 25 years of age, and almost 70% are in children younger than 10 years of age. RMS has a distinct predilection to the head and neck region, with parameningeal and orbit being the most frequent sites.17, 18 Intraoral RMSs are uncommon; when they occur, the palate, tongue, and buccal mucosa are mainly involved.[19] Clinically, the tumor often presents as a painless, infiltrative mass that may grow rapidly and cause extensive facial swelling.[15] Microscopically, RMS presents a vast spectrum of histopathologic features composed of malignant neoplastic cells exhibiting various degrees of skeletal muscle differentiation, classified into 4 main subcategories: embryonal, alveolar, spindle cell/sclerosing, and pleomorphic. Most cases of RMS are treated with a combination of surgery, radiation therapy, and chemotherapy.[18,20] A multidisciplinary approach is essential for these patients.

DIAGNOSIS

Histologic examination of the incisional biopsy showed a benign mesenchymal neoplasm with exophytic growth, and an ulcerated surface of superficial granulation tissue with a prominent chronic inflammatory infiltrate. The underlying connective tissue consisted of a hypercellular proliferation of spindle cells arranged in intertwined fascicles and whorls with pushing borders. These cells ranged from large and elongated with eosinophilic cytoplasm and oval nuclei with tapered ends to small polygonal or spindle cells with scant eosinophilic cytoplasm and round basophilic nuclei arranged around irregular blood vessels, mimicking a hemangiopericytoid pattern. There were no signs of necrosis or atypical cells; however, some typical mitotic figures were identified (Figure 2).

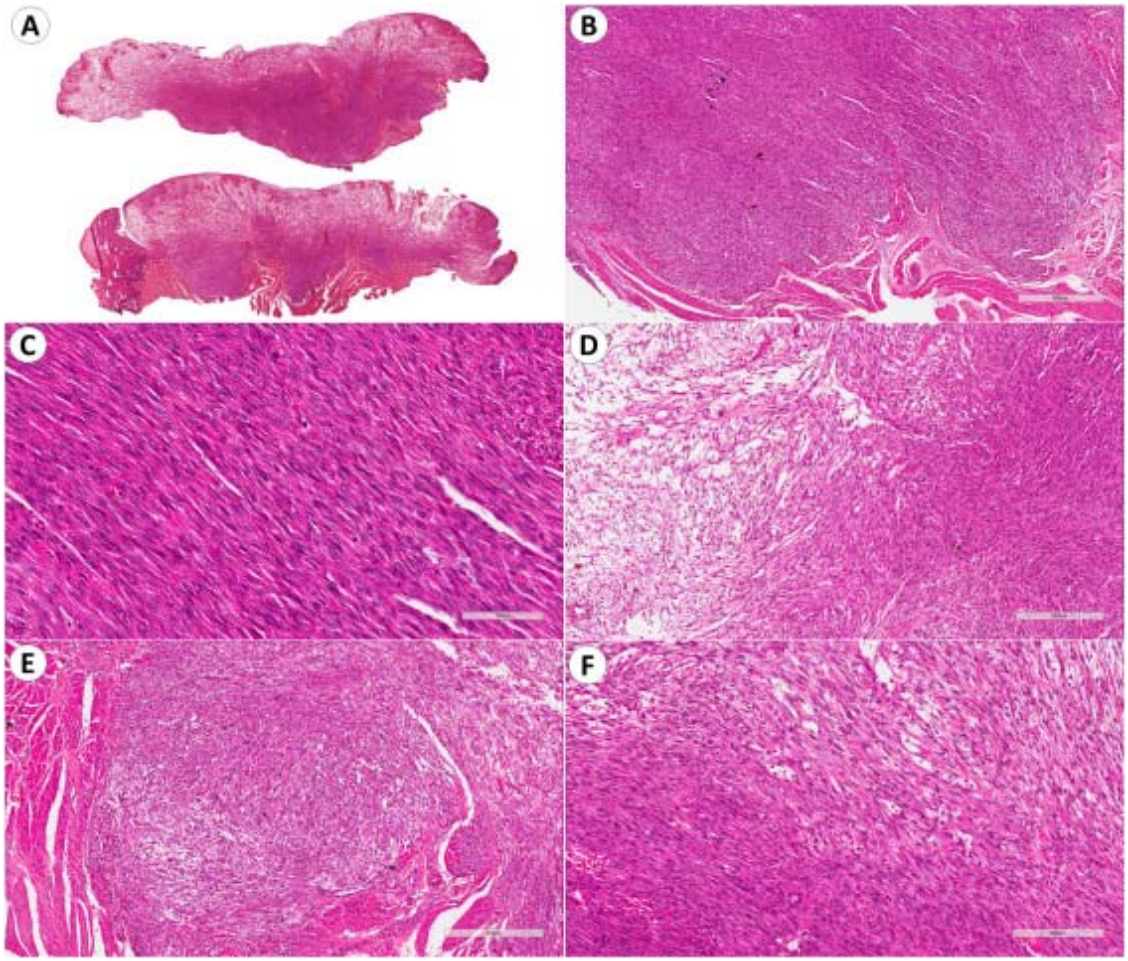

Fig. 2. Histopathologic features. **(A)** Panoramic of the incisional biopsy specimen. The tissue presented with an ulcerated surface with subjacent granulation tissue at low magnification. Note the presence of myoid nodules in the lower region of the upper fragment. **(B, C)** In the deeper aspect, the tumor appeared as a hypercellular spindle cell neoplasm with pushing borders proliferation of spindle-shaped cells (myofibroblasts) arranged in intersecting fascicles. The cells presented vesicular nuclei, eosinophilic cytoplasm, and occasional typical mitoses. **(D)** The biphasic pattern of the fascicles of spindled cells next to areas of round small cells. **(E, F)** A vague zoning phenomenon is noticed between hypercellular areas contrasting with hypocellular areas. A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM06776.

The immunohistochemical stains showed positivity for smooth muscle actin and HHF-35 and negativity for AE1/AE3, epithelial membrane antigen, S100 protein, CD34, CD68, CD99, desmin, MyoD1, myogenin, h-caldesmon, and Bcl-2. The proliferative cell index for Ki-67 was high (70%; Figure 3). Based on the clinical, histopathologic, and immunohistochemical findings, a final diagnosis of myofibroma of the tongue was established.

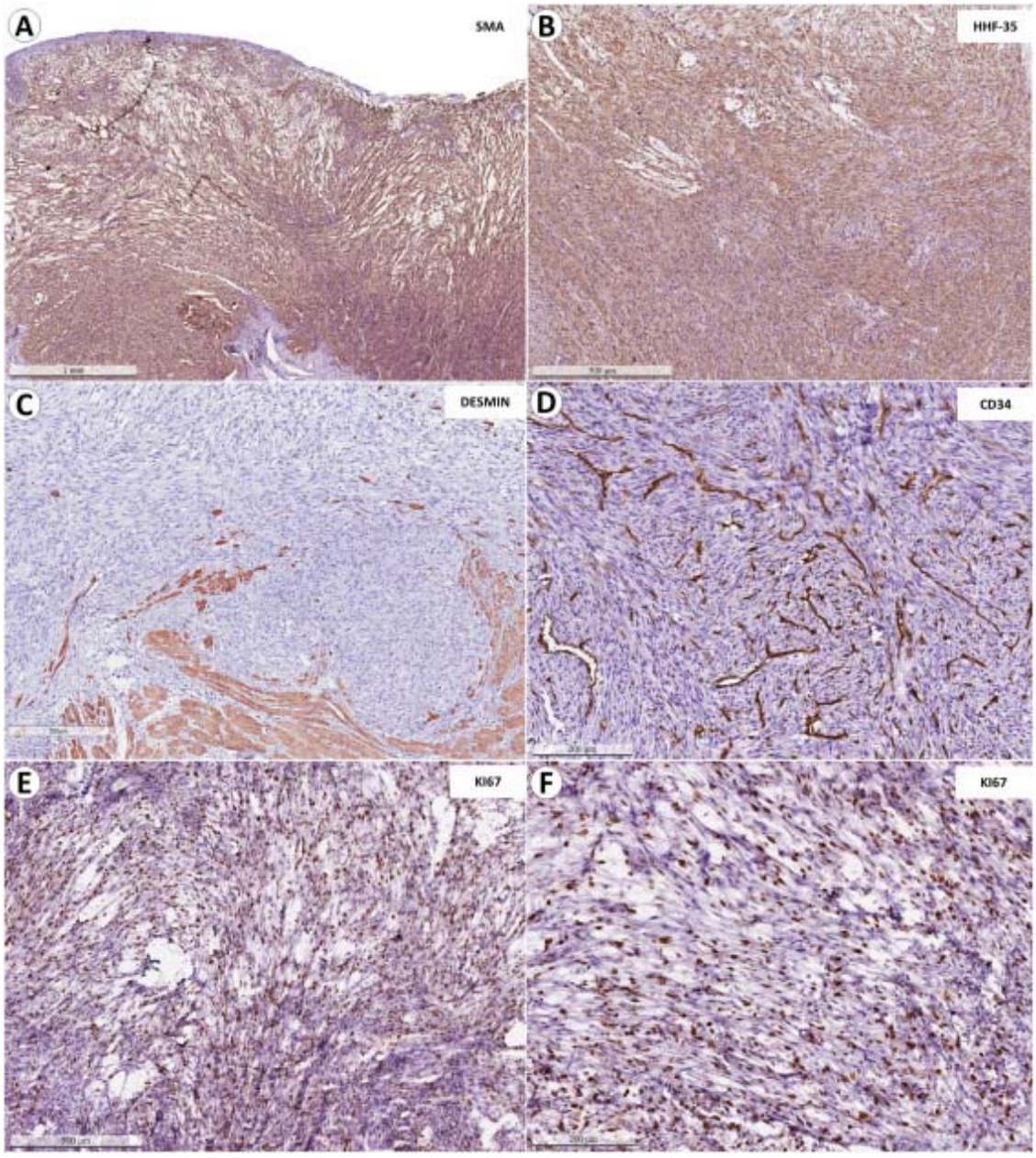

Fig. 3. Immunohistochemistry features. **(A, B)** Diffuse and strong positivity for smooth muscle actin and muscle-specific actin, confirming the smooth muscle profile of the neoplastic cells. **(C)** Desmin was negative in the tumor and showed positive internal control with the skeletal muscle of the tongue. **(D)** CD34 reactivity in normal blood vessels. **(E, F)** Ki67 high proliferation index showing increased cellularity and a high proliferation (around 70%).

MANAGEMENT

The patient underwent a complete surgical excision and has been in follow-up for 2 years without any signs of recurrence (Figure 4).

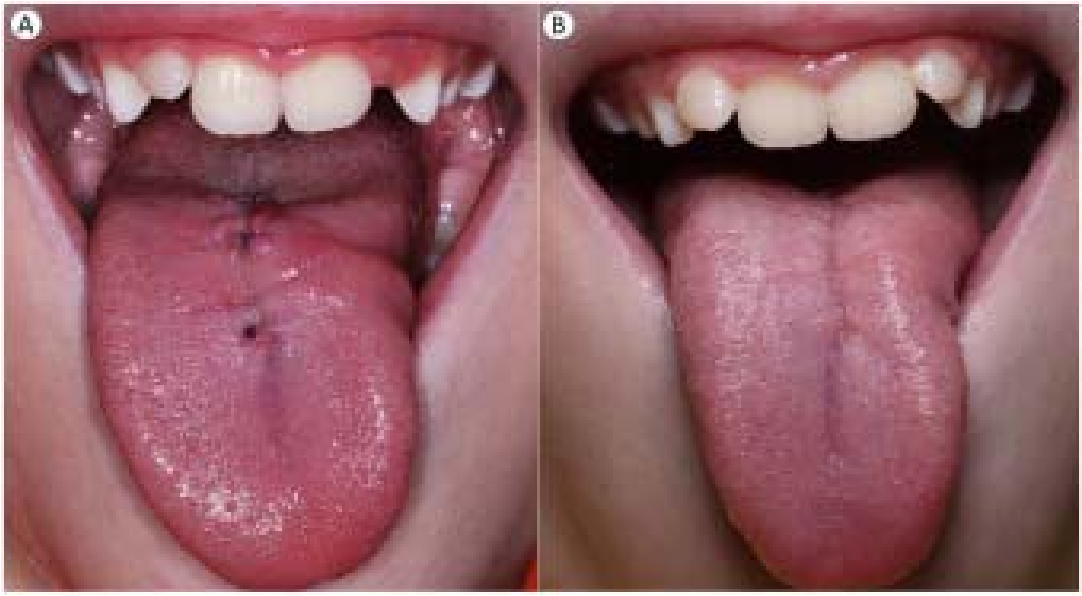

Fig. 4. Clinical aspect of the patient's tongue **(A)** 8 days post-excision and **(B)** 2-year follow-up with no signs of recurrence.

DISCUSSION

Myofibroma is a benign mesenchymal neoplasm with myofibroblastic differentiation, most commonly arising as a dermal or subcutaneous head and neck lesion, rarely manifesting in the oral cavity. [21,22] In the present case, a myofibroma was located at the dorsal tongue in an 8-year-old child with an unusual location and aggressive clinical appearance. It is important to share clinical cases with such features to consider myofibroma as a differential diagnosis in the oral cavity and exclude any mesenchymal malignancy.

The current largest case series of myofibroma of the oral cavity in the English-language literature was published by Smith et al.,[22] who assessed 24 cases. According to the literature, oral myofibroma may affect patients in a wide age range (from birth to 84 years) with an average age of 23.1 years and show a slight female preponderance (50.6%) over males (49.3%). The most frequent oral locations were associated with mobile mucous membranes (49.5%), followed by intraosseous lesions (42.5%) and lips (7.7%). Most intraosseous lesions occurred in patients under 20 years.22, 23

The first series of myofibroma in adults was described in 1989 by Daimaru et al.[22] Myofibroma of the oral cavity is an uncommon lesion, and the histopathologic diagnosis may be challenging. Most oral myofibromas were reported in the mandible or buccal mucosa, whereas tumors affecting the tongue are exceedingly rare.[24]

Solitary and multicentric forms of myofibroma show identical histologic features.22, 23, 24 Gross examination generally shows well-circumscribed and unencapsulated lesions; however, visceral and deep soft tissue lesions may be less demarcated. At low magnification, the lesions reveal a nodular growth pattern with characteristic "light" and "dark" biphasic areas, although any components may predominate.[22] Myofibromas are composed of

interlacing fascicles of spindle cells with tapered or blunt-ended nuclei and eosinophilic cytoplasm, as was seen in the present case. Nuclear atypia is, at most, mild, as seen in our case. The mitotic index is usually low; however, typical mitotic figures can be common in areas of more immature appearance. The current case showed appreciable mitotic activity and raised concerns about a higher-grade injury. These features can lead to a malignant entity suspicion. A subset of myofibromas may show atypical features such as hypercellularity, predominant fascicular growth, infiltration of surrounding tissue, perineural extension, and intravascular growth.[25] Correct classification requires the identification of typical areas within the lesion.[1] The diagnosis of myofibroma can be challenging when a limited amount of tissue is available, given the overlapping clinical and histologic features of entities characterized by spindle cell morphology.

According to the 5th Edition of the World Health Organization Classification of Head and Neck Tumors, myofibromas and myopericytomas represent lesions within the same morphologic spectrum and have been classified as pericytic tumors.[26] As previously known, immature pericytes can differentiate into various cell types, including glomus cells, myopericytes, vascular smooth muscle cells, and myofibroblasts.[27] Recently, advanced studies have shown that *PDGFRB* mutations are a key pathogenic driver for both familial and sporadic cases of myofibroma and myopericytoma, confirming the close relationship between both entities.[26] The shared myopericytic phenotype explains the histopathologic overlap between myofibromas and myopericytomas; however, some subtle features may aid in distinguishing both lesions. The intrinsic myofibroblastic presentation may result in the biphasic appearance classically seen in myofibromas. In contrast, delicate myoid spindle cells growing in a concentric pattern around numerous small blood vessels remain a feature typically associated with myopericytomas.[28]

A subset of cellular myofibromas and/or myopericytomas presenting atypical features, including diffuse hypercellularity, increased mitotic activity, and in some cases, a distinct immunoprofile, have been reported harboring recurrent *SRF-RELA* fusions. This constellation of histopathologic findings may represent a diagnostic pitfall specifically regarding pediatric patients, causing possible confusion with sarcomas with myogenic differentiation.[29] Given the rarity of these tumors, follow-up data suggest a benign clinical course with rare local recurrences despite the microscopic findings.[29]

In conclusion, myofibroma involving the dorsal tongue is exceedingly rare. Myofibromas may present clinical and histopathologic features that overlap with benign and malignant spindle cell tumors. Knowledge of this benign neoplasm and its inclusion in the differential diagnosis of oral cavity lesions can prevent misdiagnoses and unnecessary aggressive therapies. Although rare, clinicians should consider myofibroma in the differential diagnosis of aggressive-appearing nodular tongue lesions in pediatric patients.

ETHICAL APPROVAL

This study is in accordance with the ethical standards of the Research Ethics Committee of the Piracicaba Dental School and accepted with the following number: 72775717.8.3001.5418 and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Declarations of interest

None.

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