Low-grade Gingival Leiomyosarcoma in a Child

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ABSTRACT

Leiomyosarcoma (LMS) of the oral cavity, a rare mesenchymal tumor exhibiting smooth-muscle differentiation, is extremely uncommon in childhood. The most frequent location of childhood LMS is the gastrointestinal tract, particularly the stomach. The purpose of this paper is to report a case of leiomyosarcoma affecting the gingival tissues and mandible of a 9-year-old girl with peculiar clinical, microscopic, and radiographic features. Clinical and radiographical examinations revealed a gingival growth affecting the primary mandibular right first molar with inflammatory features. The lesion was initially suspected to be pyogenic granuloma and was removed by excisional biopsy. Microscopic findings showed a hypercellular proliferation of mesenchymal spindle cells, suggesting malignant spindle cell neoplasm. Immunohistochemical, histochemical, and radiographic studies were undertaken, and the final diagnosis established was a low-grade leiomyosarcoma in the gingiva. **(J Dent Child 2008;75:301-5)**

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Leiomyosarcoma (**LMS**) is a malignant neoplasm of smooth muscle origin uncommon in the oral cavity and extremely rare in childhood.[1-6] Primary lesions are usually found in the soft tissue or in a visceral location, including the gastrointestinal, urinary, and female genital tracts.[3,4,7,8] Occurrence in the head and neck regions is considered rare. It most commonly affects the nose and paranasal sinuses, skin and subcutaneous tissue, and the cervical esophagus.[8,9] In the oral cavity, the maxillary sinus, mandible, and maxilla appear to be the predilection sites for LMS,[5,6,9-11] but other reported intraoral locations have included the cheek, tongue, hard and soft palates, lips, floor of the mouth, and gingiva.[1,5,8-13]

Oral LMSs do not present any significant gender predilection and have been reported to occur over a wide age range (mean age=44.3 years; range=1-88), peaking in the sixth and seventh decades of life.[5,8,9] Female patients presented the highest incidence in their 30s, however, whereas males had a more even age distribution.[5] Oral LMS in childhood is exceedingly rare, and only 11 previous cases have been reported in the dental literature.[1,2,13-20] The purpose of this is to report a case of primary leiomyosarcoma located in the gingival tissue of a 9-year-old girl.

CASE REPORT

In May, 2005, a 9-year-old female with proliferative lesions in the gingival mucosa of the alveolar bone in the primary mandibular right first molar was referred to the Goiás Oral Medicine Center at the Federal University of Goiás Dental School, Goiânia, Brazil. Twenty-five days earlier, the patient

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had seen her general dental surgeon in an upstate town complaining of localized pain and spontaneous bleeding. The dental surgeon extracted her primary mandibular right first molar, which did not show any alteration when submitted for a periapical examination. As the problem of the lesion was not solved with the extraction of the primary molar and the gingival tissue continued to grow, it was recommended that the patient undergo treatment at our clinic. An interview with her did not reveal any familiar or systemic disorder or jaw lesion.

A clinical examination showed normal facies, and there was no regional lymphadenopathy. An intraoral examination revealed a proliferated gingival lesion with a polypoid blue-red nodule with a maximum diameter was 4 cm in the primary right vestibular and lingual molar regions. It was slightly tender on palpation and was not attached to the surrounding tissues. Using these features as a basis, a benign lesion of an inflammatory nature, such as a pyogenic granuloma, was our first diagnostic hypothesis.

An intraoral radiograph showed superficial bone destruction and resorption of the distal root of the primary mandibular right second molar (Figure 1). After a complete radiographical investigation, however, we considered other more aggressive lesions, such as the giant cell peripherical lesion or even malignant neoplasms—since the lesion had a clinical history of rapid growth. An extensive excisional biopsy was performed and the first primary molar was extracted. The surgical samples were promptly immersed in 10% neutral buffered formalin for 24 hours and embedded in paraffin. Sections of 5-µm thickness were cut and stained with hematoxilin and eosin.

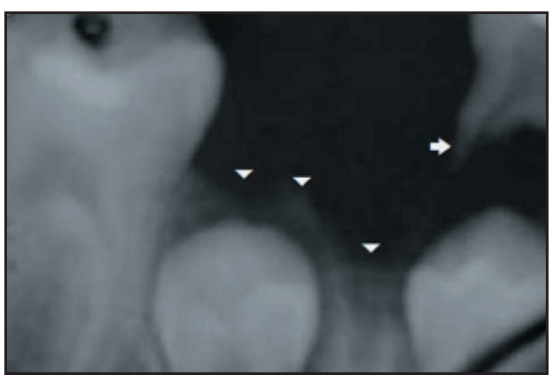

Figure 1. Periapical radiograph demonstrating resorption of the distal root of the first right primary molar (arrow) and superficial bone destruction (arrowhead).

A microscopic examination of the specimen demonstrated an irregularly distributed malignant spindle cell neoplasm with sarcomatous features. The neoplasm consisted of intersecting bundles of spindle-shaped cells. The bundles of neoplastic cells contained blunt-ended or "cigar-shaped," elongated nuclei, arranged in dense interlacing fascicles. Typical and atypical mitoses were readily detected in varying degrees (5 to 10 mitosis per 10 high-power fields; Figure 2). On the superficial plane, hyperplasic gingival epithelium was noticed, and in the subepithelial core the presence of granulomatous tissue was noted. The tumor cells also showed prominent eosinophilic cytoplasm with occasional paranuclear vacuolization and contained occasional PAS-positive granules. Neither coagulative tumor necrosis nor hemorrhage was observed. In the postoperative follow-up of the patient, continuous proliferations of the lesion were seen. When a sarcomatous neoplasm was diagnosed, the patient was asked to undergo further tests to identify possible metastatic lesions and to obtain a better definition of the tumor. A panoramic radiography examination, magnetic resonance image study, immunohistochemical study, abdominal ultrasound scanning, blood tests, myelogram, and conventional chest X ray examinations were carried out.

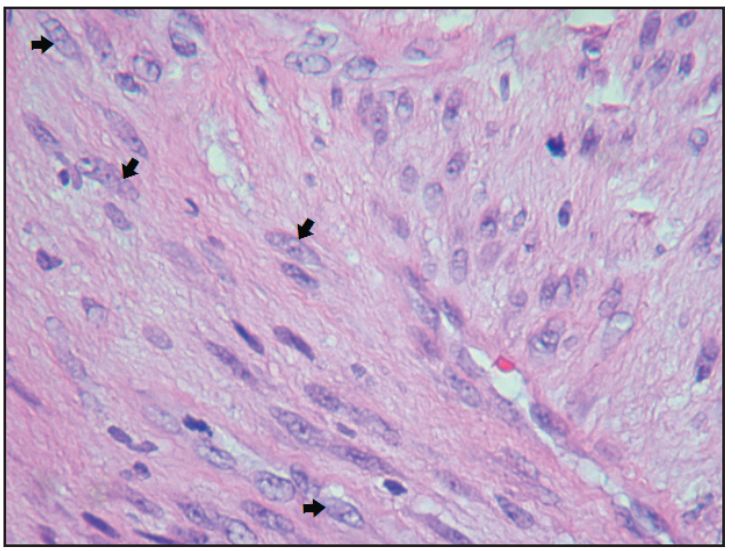

Figure 2. Photomicrograph showing spindle-shaped cells with cigar-shaped nuclei (arrow) arranged in interlacing bundles (Hematoxylin-Eosin, original magnification X100).

The panoramic image showed superficial bone resorption and indicated that the cortex around the tooth crown of the first and second mandibular premolars were intact (Figure 3). A magnetic resonance image (MRI) showed

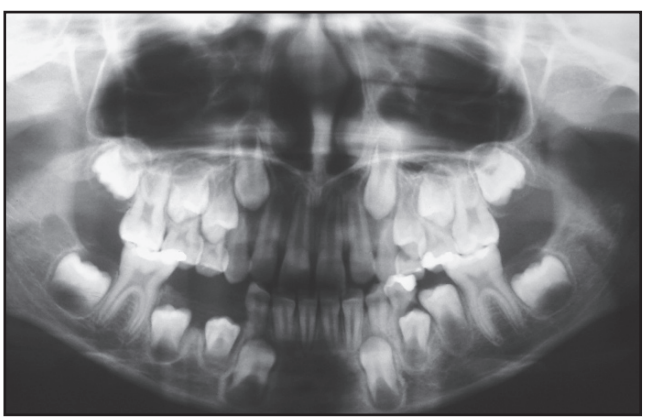

Figure 3. Panoramic radiograph demonstrating absence of primary tooth molars and superficial bone destruction.

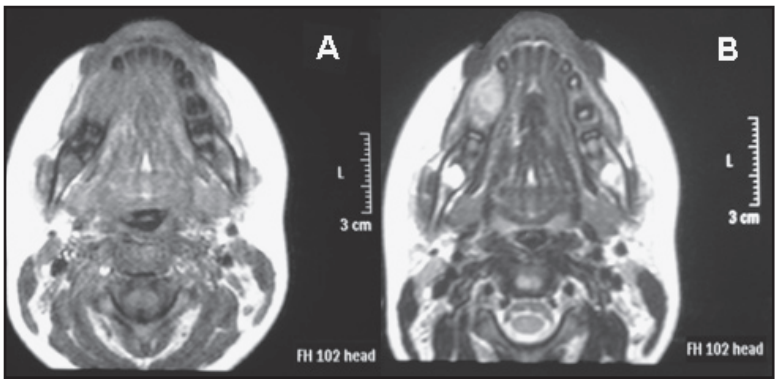

Figure 4. Magnetic resonance images, in T–1 (a) and T with contrast (b), showing hyposignal of the lesion and delimitation of the lesion on the external surface.

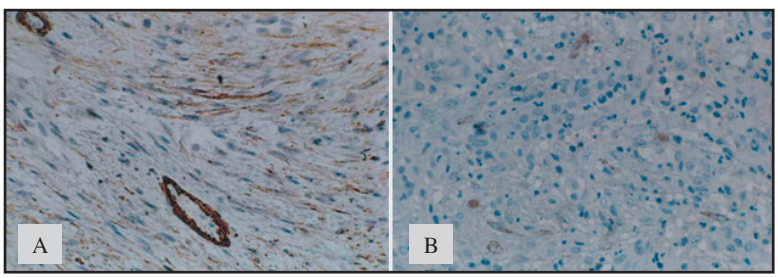

Figure 5. Photomicrograph A displays a strongly positive immunohistochemical reaction with antibodies against actin (muscle specific), and photomicrograph B shows a focal expression of desmin in the tumor cells (a and b: Immunohistochemical staining, original magnification X100).

that the neoplasm was superficial and had not infiltrated the surrounding tissues (Figures 4a and 4b). The abdominal ultrasound, blood tests, bone scan, myeogram, and conventional chest X ray did not show any abnormalities.

The immunohistochemical study (streptavidin-biotin method) showed strong immunoreactivity for actin (muscle-specific and α-smooth-muscle-actin) antibodies (clones HFF35 and 1A4, Dako, Carpinteria, Calif), and focal immunoreactivity for the desmin antibodies (clone D-33, Dako; Figures 5a and 5b), whereas all the other antigens (S-100, CD117, CD34, pan-cytokeratins and CD57) tested did not show any immunoreactivity. In addition, approximately 20% to 30% of tumoral cells were positive for Ki-67 protein (clone MM1, Novocastra, Newcastle, UK).

After carrying out the various studies and using these features as a basis, a diagnosis of low-grade gingival leiomyosarcoma was established and a segmental mandible resection was performed, while preserving the basilar cortex. A histopathological study of the surgical specimen showed free margins. The postoperative follow-up was uneventful, and the patient is currently being monitored at 3-monthly intervals. Eleven months after the tumor excision, the patient is progressing and the tumor shows no signs of recurrence.

DISCUSSION

Oral LMS is extremely rare in children and, to our knowledge, only 11 cases have been previously described in the dental literature.[1,2,13-20] In these pediatric patients with intraoral LMS, 3 were located in the tongue, 1 in the floor of the mouth, 2 in the soft palate, 1 in the lip, 2 in the mandible, 1 in the maxilla, and 1 in the gingiva (mandibular). The mean age of these 11 children was 11.3 years (range=1-15 years), and there was no gender predilection.[1,2,13-20] Signs and symptoms of oral LMS depend on the site of the tumor, however, pain was common to all cases.[1,2,9,14-17] In the tumors with infiltrative growths and whose primary origin was in the maxilla and mandible, it has been noted that the surrounding teeth became loose at an early stage.[1,9] This paper presents the additional case of oral LMS in a pediatric patient (9-year-old girl) located in the gingival mucosa of the mandibular right alveolar bone with painless symptomatology and spontaneous bleeding.

In general, LSMs are aggressive and tend to recur and metastasize.[6,21] In the pediatric cases of oral LMS reported in the English literature, metastasis and deaths occurred in 3 patients with lesions in the soft palate, floor of the mouth, and gingiva.[2,15,16] LMSs in soft tissue, however, appear to have a better prognosis, in large part due to the fact that most cases are morphologically low grade.[3] In our case, neither local recurrence nor metastasis were observed after almost 1 year of follow-up.

LMSs occurring in the maxilla, mandible, and oral tissue regions with scanty or absent smooth muscle structures occur possibly because of the tunica media of blood vessels, major neurovascular structures, and myoepithelial cells or from pluripontential, undifferentiated, mesenchymal cells.[9,22-24]

In our case, the neoplasm showed right-angle cells intersecting with bundles of spindle cells with elongated, vesicular to hypercromatic, lobulated or indented nuclei, and blunt ends (cigar-shaped), suggesting a diagnosis of malignant spindle cell neoplasm. Other authors concur with these microscopic findings.[3,4,7] Another relevant fact was the intracytoplasmatic glycogen positivity demonstrated by PAS and Masson trichrome stains, which showed longitudinally oriented parallel red fibrils within the cytoplasm. This, too, has been recorded in the literature.[4] In fact, many different types of tumor of prominent spindle cell components may be difficult to differentiate from LMS if morphology alone is used as a basis for diagnosis. Because mesenchymal neoplasm of spindle cells had been previously diagnosed, an immunohistochemical study was conducted to confirm the true nature of these spindle cells, since, in this specific case, the histopathology suggested LMS.[5,10,19,21] In the case of the lesions shown in Table 1, a differential diagnosis must be made as well as an immunohistochemical study.[3,4-10]

Table 1. Tumors of spindle cells with differential antigenic reactivity

Tumors	Immunoreactivity
Spindle cell carcinoma	Cytokeratin +
Malignant myoepithelioma	Cytokeratin and Actin +
Melanoma	S-100 protein and HMB 45 +
Anaplastic lymphoma	CD 45 and CD 30 +
Solitary fibrous tumor	CD 34 and Vimentin +
Fibrosarcoma	Diagnosis by exclusion – S-100 protein +
Rabidomyosarcoma	Desmin and Actin +

The results of our immunohistochemical study were actin (α–smooth muscle and muscle specific) strongly positive and desmin focally positive. All cytokeratins tested were negative, as was S-100 protein. The Ki-67 index was greater than 20% cell positive, and CD-117 was negative. Desmin is a useful marker of the smooth-muscle derivation of sarcomatous tumors.[3,4,7,10] According to Fletcher,[3] no more than 70% to 80% of leiomyosarcomas are desmin positive and often only focally. In our case, the desmin was focally positive. This immunoreactivity was also observed in one of the cases reported by Nikitakis et al.[5] This focally positive desmin may reflect not only loss of differentiation, but also the varied phenotype of normal smooth muscle. Regarding both the Ki-67 index and CD-117, our data were consistent with Thompson and Fanburg-Smith's[7] results. In soft tissue LMS in general, the CD-117 is normally negative, compared to the gastrointestinal tract, where it is positive.[4]

In summary, since oral leiomyosarcomas are very rare and aggressive tumors with a high incidence of recurrence and metastasis and a low survival rate, an early and accurate diagnosis followed by radical treatment is important to improve the prognosis of these tumors. A diagnosis of oral LMS, however, should not be made solely on the basis of immunoassays when appropriate morphologic features are absent.

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