Gingival Leiomyosarcoma in a Young Woman
Case report and literature review

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Abstract: Leiomyosarcoma (LMS) is a rare mesenchymal malignancy, of which 3–10% of cases occur in the head and neck region. We report a 22-year-old woman who was referred to the University Hospital of Siena, Italy, in 2016 with an ostensibly benign asymptomatic lump on the mandibular gingiva. The lesion grew rapidly, causing otalgia in the right ear. An excisional biopsy was performed and primary LMS was diagnosed histologically. Subsequently, the patient underwent radical re-excision of the perilesional mucosa, a partial bone resection and the extraction of four teeth. No recurrences or metastases were detectable at a 20-month follow-up. This report discusses the differential diagnosis of LMS with regards to other benign and malignant lesions and reviews the recent literature on primary and secondary oral LMS. Due to its innocuous clinical features—including its asymptomatic nature and presentation at a young age—this aggressive malignancy can go undetected; therefore, an early histopathological diagnosis is crucial.

Keywords: Leiomyosarcoma; Soft Tissue Neoplasms; Gingival Neoplasms; Smooth Muscle Tumors; Otalgia; Immunohistochemistry; Case Report; Italy.

Case Report

A 22-year-old Caucasian woman was referred to the Department of Dentistry at the University Hospital of Siena, Italy, in 2016 with otalgia in the right ear and asymptomatic swelling on the lower right lingual gingiva and an asymptomatic swelling on the lower right lingual gingiva. She had initially noticed the swelling approximately two years prior, which she had initially noticed approximately two years prior.

A 22-year-old woman was referred to the University Hospital of Siena, Italy, in 2016 with otalgia in the right ear and an asymptomatic swelling on the lower right lingual gingiva, which she had initially noticed approximately one month beforehand. The patient’s medical history indicated that she was in good health and was not currently taking any medication. An examination of the oral cavity revealed a slightly tender, non-tender, non-mobile mass measuring 2.5 cm in diameter. The mass was firm to palpation and fixed to the underlying bone. The patient reported no history of trauma, radiation, or chemotherapy.

Histopathologically, the lesion was characterized by a tumor composed of interlacing bundles of spindle-shaped cells with abundant eosinophilic cytoplasm and indistinct cell borders. The tumor cells were positive for smooth muscle actin and negative for desmin and S100 protein. Immunohistochemical staining revealed positivity for muscle-specific actin and negativity for smooth muscle actin. The lesion was diagnosed as a primary leiomyosarcoma of the gingiva.

The patient underwent a radical re-excision of the perilesional mucosa, a partial bone resection, and the extraction of four teeth. No recurrences or metastases were detectable at a 20-month follow-up.

This report presents a case of oral LMS in a young patient which was rapidly diagnosed and resulted in a positive outcome. As the patient was disease-free following radical surgical excision, further surgery, chemotherapy or radiation therapy was avoided.

Immunohistochemistry: Case Report; Italy.

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oral cavity revealed a hard, non-painful, reddish-pink, non-haemorrhagic gingival swelling around the first lower right molar (i.e. tooth number 46) [Figure 1A]. The rest of the ear, nose and throat examination was normal. An orthopantomogram and periapical X-ray of tooth number 46 appeared normal [Figures 1B and C]. An excisional biopsy was subsequently performed under local anaesthesia, with the excised lesion measuring 1.5 x 1.2 cm [Figure 2]. Following the surgery, the patient was prescribed a six-day course of antibiotics consisting of 1g of amoxicillin and clavulanic acid twice daily.

The excised mass was fixed in buffered formalin. A histopathological examination showed an unencapsulated tumour with pushing margins and an absence of infiltrative growth patterns. The lesion consisted of bundles of spindle cells intersecting at right angles, with well-defined brightly eosinophilic cytoplasm, cigar-shaped pleomorphic nuclei and occasional paranuclear vacuoles [Figure 3A]. There were a few microfoci of coagulative necrosis and 13–15/10^5 mitoses in a high-power field at x400 magnification (corresponding to about 1 mm^2) [Figure 3B]. Immunohistochemistry was performed on 3-μm-thick sections using the BenchMark ULTRA® automated staining system (Ventana Medical Systems Inc., Roche Diagnostics, Monza, Italy). The ultraView Universal DAB Detection Kit® (Ventana Medical Systems Inc.) was used with horseradish peroxidase multimer chromogen diaminobenzidine in order to stain positive structures brown. The neoplastic cells were positive for smooth muscle markers, including h-caldesmon (clone e89), HHF35, myosin, smooth muscle actin (clone 1A4) and smooth muscle myosin monoclonal antibody-1 [Figures 3C and D]. The Ki-67 labelling index (clone MIB-1) was approximately 30–40%. All other tested antibodies were negative, including activin receptor-like kinase, cluster of differentiation (CD)34, e-Kit, desmin, DOG1, oestrogen receptors, pankeratin, progesterone receptors, skeletal muscle actin and S100.
Smooth muscle tumours rarely develop in the head and neck region; however, if present, they occur mainly in the walls of blood vessels, the erector pili musculature of the skin, the circumvallate papillae of the tongue and in the myoepithelial cells of the salivary glands. Soft tissue LMS can be divided into retroperitoneal/ intra-abdominal, cutaneous/subcutaneous and vascular subgroups, with distinct clinical and biological differences despite their similar histology. The most common intraoral site for LMS appears to be the tongue, usually as a result of metastasis from a primary tumour in the uterus, gastrointestinal tract or retroperitoneum. Oral LMS may also involve the jaw bones, cheek, gingiva, floor of the mouth, mandible, soft or hard palate and lips. These tumours present with a wide range of clinical features, including painless or painful smooth rubbery firm masses with or without ulceration, tooth mobility, epistaxis, nasal obstruction, otalgia and a variety of other symptoms depending on the site of the lesion.

As a result of this diagnosis, further surgery was deemed necessary. Preoperatively, a contrast computed tomography (CT) scan showed thickening of the soft tissue adjacent to the inferior right hemimandibular surface, without bone or neck lymph node involvement. A metastatic work-up was negative, including CT imaging of the chest, abdomen and pelvis and a bone scan. A gynaecological examination and transvaginal ultrasound was also normal. However, an magnetic resonance imaging (MRI) scan showed increased mucosal impregnation near teeth number 46 and 47. Subsequently, under general anaesthesia an excision of the perilesional mucosa, a partial bone resection sparing the lingual and mandibular nerves and the extraction of teeth number 45–48 was performed. Postoperatively, the patient was prescribed antibiotics (1 g of ceftriaxone per day) along with an anti-discolouration mouthwash containing 0.2% chlorhexidine and hyaluronic acid.

The patient was discharged two days later with no complications. Every three months, she attended follow-up appointments wherein MRI and chest and abdominal ultrasounds were performed. A whole-body CT scan was also undertaken six months after the surgery, with positron-emission tomography/CT performed at 12 months. At the time of writing, 20 months after the radical surgery, there were no signs of local recurrence or metastasis and the patient appeared healthy.
Squamous cell carcinomas and their rarer spindle cell variants, sarcomatoid carcinomas, are the most frequent overall and spindle cell malignancies in the oral cavity, respectively.10,11,17 As such, all other malignant lesions with a spindle cell morphology were excluded in the present case due to their rare occurrence at this site. Moreover, the morphological features of the lesion—including the fascicles of spindle-shaped cells with abundant eosinophilic cytoplasm, blunt-ended cigar-shaped nuclei, high mitotic rate and pleomorphism—were consistent with a diagnosis of LMS; this was also supported by the immunohistochemical results of an extensive panel of antibodies.8,18 While metastasis from primary LMS arising in another site could not be excluded histologically, a high percentage of uterine LMS express oestrogen and/or progesterone receptors, which were negative in this case.19 Table 1 summarises the main differential diagnoses of LMS and their various histopathological features.1–17

Besides early diagnosis, the prognosis of oral LMS patients depends on the tumour grade, size, site and treatment.20–22 Currently, there are no standard criteria for therapy, although the complete excision of the tumour with wide surgical margins is recommended.7,23,24 The five-year survival rate among patients with primary oral LMS is 55%, with bone involvement and metastasis significantly associated with poorer prognosis.24 Lung and cervical lymph node metastases frequently occur, with the regional lymph nodes affected in >15% of oral LMS cases.4 Distant metastases, mostly in the lungs, occur in approximately 39% of patients with oral LMS; in addition, LMS lesions arising in the uterus, gastrointestinal tract and retroperitoneum sometimes metastasise to the lungs, brain, bone and oral cavity.4,25 As such, preoperative staging of the whole body is mandatory. In the present case, the regional lymph nodes were free and systemic tests did not reveal any metastasis; hence, no adjuvant therapy was given. However, regular follow-up is essential to rapidly detect recurrence.

**Conclusion**

Smooth muscle tumours of the oral cavity are exceedingly rare. A diagnosis of oral LMS should be established histologically and supported by immunohistochemical analysis using specific markers. In certain cases, such as the one presented here, early
radical excision constitutes the treatment of choice. Critically, LMS should be considered in the differential diagnosis of oral masses as early diagnosis and aggressive treatment are essential to ensure a good prognosis and patient survival. Lifelong periodical follow-up is also recommended.

References