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Case Report

Primary Leiomyosarcoma of the Mandibular Gingiva

Summary

Primary oral leiomyosarcomas are exceptionally rare lesions often associated with poor prognosis. We report a case of leiomyosarcoma arising in the anterior mandibular gingiva, which is a non-prevalent site of occurrence. Clinically, the tumor was far from being firm and solid as it is usually described in the literature. Light microscopy failed to confirm the true nature of the lesion on the biopsy specimen.

were free but the under surface of the lesion was infiltrating the bone. A complete workup followed, consisting of CT scans (face, neck, chest), upper and lower abdomen ultra sound and a skeletal scanning. The investigation proved negative for lesions elsewhere in the body. Consequently, the patient underwent a wider excision and a peripheral mandibulectomy, preserving the continuity of the mandible, since a partial mandibulectomy was denied by the patient. A split thickness skin graft was used to cover the inner surface of the lower lip and the anterior floor of the mouth. The post-operative period was uneventful. The histopathology report indicated both free soft (confirming the previous report) and hard tissue margins. The surgical ablation was followed by radiotherapy in another institution and according to their files the patient received 66 gray (Gy) locally in 33 fragments and 52 Gy in the neck in 26 fragments. Six months postoperatively the patient presented with osteoradionecrosis of the jaw, a pathologic fracture of the mandibular symphysis and edema of the lower lip. At that time, biopsies were taken, with negative results. The patient refused admission as well as the scheduled hyperbaric oxygen therapy; simultaneously, underwent a complete CT workout (brain, face, neck, chest, upper and lower abdomen), that was negative for pathology (LMS or colon adenocarcinoma). Two months later the

Introduction

Benign smooth muscle tumors, or leiomyomas, are common, well-circumscribed neoplasms that can arise from smooth muscle cells anywhere in the body, but are encountered most commonly in the uterus [1]. Leiomyosarcomas (LMS), their malignant counterpart, comprise 7% of head and neck sarcomas [2]. Primary LMSs rarely occur in the oral and maxillofacial region, probably due to paucity of smooth muscle tissue in the area [1,3]. Source of smooth muscle in the oral cavity may be the arterial tunica media, lingual duct, circumvallate papillae and pluripotential mesenchymal cells [1]. We present a case of oral LMS which exhibits an uncommon clinical appearance in a non-prevalent site and which also presents difficulties in the histopathologic diagnosis of the incisional biopsy.

Case Report

An 81-year-old Caucasian female attended the outpatient department, complaining of a painless mass in the region of her anterior mandibular ridge, causing difficulty in mastication. On examination the mass measured 4x3x3cm, was bluish-red in color, soft and friable in consistency and boss elated in appearance. The lesion was broad-based and firmly attached to the underlying tissues. The patient was partially edentulous and the only teeth remaining in the arch, were the 31,32,33. The three teeth were embedded in the mass with a grade 4 mobility. Extra orally, there were no clinical signs of cervical lymphadenopathy. The orthopantomogram was negative for bone lesion. Past medical history included a partial colectomy for an adenocarcinoma 10 months earlier. The clinical impression was that of an exophytic squamous cell carcinoma arising from the dentoalveolar mucous membrane. An incisional biopsy was carried out and the histopathology report indicated a pseudosarcomatous lesion. The lesion was excised along with the teeth and the basal bone of the mandible was curetted (Figure 1). The histopathology report was a surprise, as indicated a leiomyosarcoma. The margins

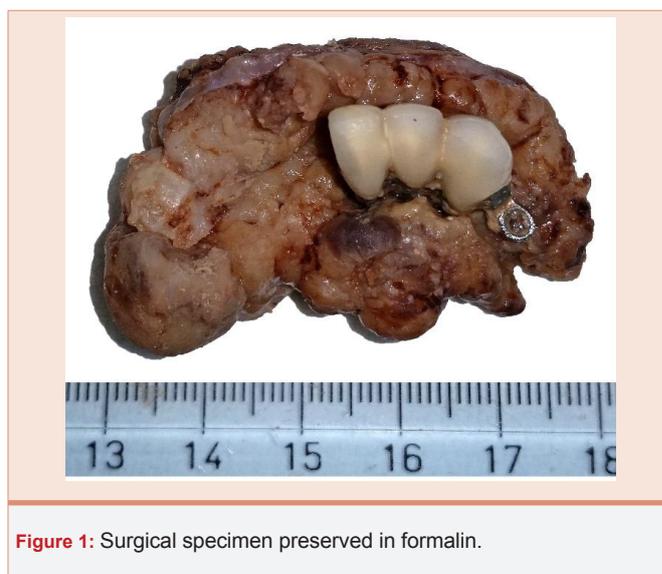


Figure 1: Surgical specimen preserved in formalin.



Figure 2: Soft tissue necrosis.

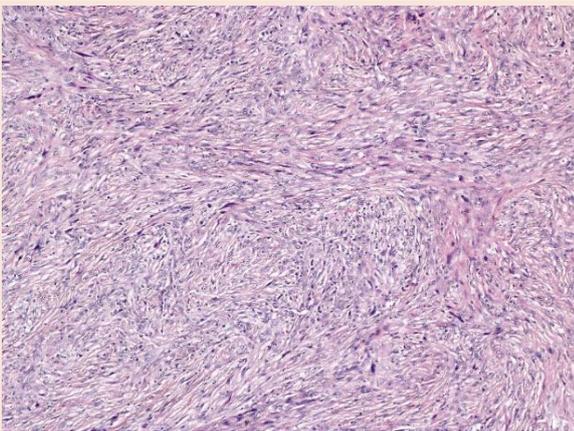


Figure 3: Spindle cell neoplasm arranged in a fasciculated pattern (100x).

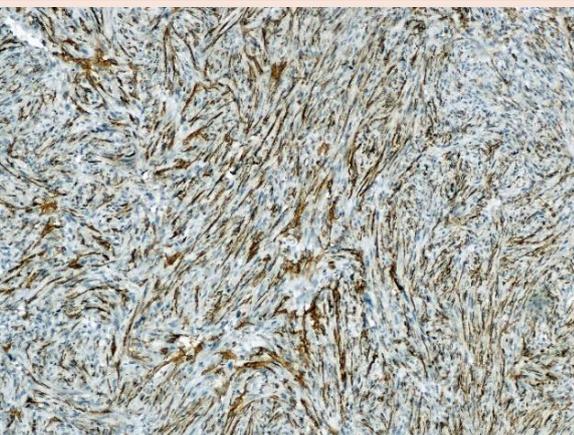


Figure 4: Strong and extensive positivity for SMA (200x).

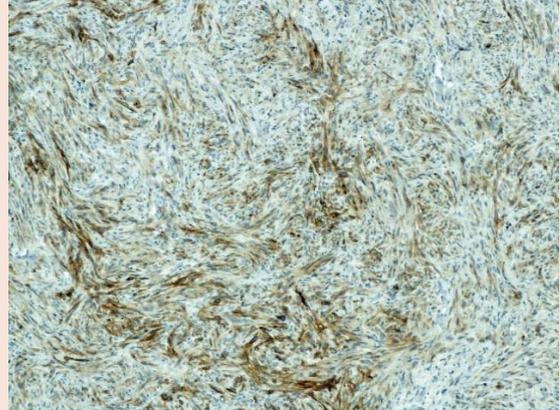


Figure 5: Strong and extensive positivity for h-caldesmon (200x).

patient admitted urgently in the hospital for an ischaemic necrosis in the lower face and upper neck region present for 15 days (**Figure 2**). On admission some basic laboratory parameters were as follows: White blood count 43.758, neutrophils 96,6%, urea 129 mg/dl, creatinine 1,9 mg/dl, C Reactive Protein 195,6 mg/dl). The patient's health deteriorated rapidly by developing renal and respiratory insufficiency, and died 5 days after admission.

Histopathology

According to the pathology report the neoplasm was composed of spindle cells arranged in a fasciculated pattern (**Figure 3**). It exhibited severe nuclear atypia and mitotic rate over 10 mitoses per 10 hpf. There were also extensive necrotic areas. Immunohistochemical studies revealed strong positivity for smooth muscle actin (SMA) and h-caldesmon (**Figures 4,5**). Epithelial Membrane Antigen (EMA) showed focal positivity. Desmin, CK, CD34, p63, CK14, S100, MART-1, ALK, LCA, CD21, CD23 were negative. These findings are in consistence with a grade 2 leiomyosarcoma.

Discussion

A leiomyosarcoma in the oral cavity may be primary or secondary. Metastatic tumors that affect the oral and perioral tissues are not common, yet they are still more frequent than primary leiomyosarcomas of this region [4,5]. In 1975, Farman published an extensive review including 7748 smooth muscle tumors of the whole body. According to this review, 7377 cases were located in the female genital tract (95%). Of the remaining 371 cases, 75% were located in the skin, 13% in the stomach, 5% in the intestines and 23% in the region of esophagus. Only 0.064% of smooth muscle tumors had an intraoral location [1,5]. There is a disproportionately high percentage of malignancies among smooth muscle tumors of the oral cavity compared with the same lesions in the female genital tract. The leiomyosarcoma / leiomyoma ratio is less than 1:200 for the female genital tract [6], whereas according to Farman's review, 20% of smooth muscle tumors in the oral cavity were malignant. Until 1980 only 23 cases have been presented in the English literature [7], while another 50 cases have been presented from 1980 to 2005 [5].

The clinical manifestation of oral LMS is usually that of a distinct, painless, circumscribed mass, which is firmly adhered to deeper planes, lacking specific symptoms that allow for its differentiation from other similar lesions [8,9]. There is no clear sex predilection, but it is noticeable that in the third and seventh decade, there were 50% more female than male patients. There were two peaks of occurrence, the first at the third decade and the second one at the sixth and seventh [5]. The ages of the patients ranged from 7 to 91 with a mean age of 44 [5]. According to a 2007 study, the sites affected in the oral cavity, in decreasing frequency, are the maxilla and mandible, tongue, buccal mucosa, soft palate, upper lip, and floor of the mouth [10]. Jaw bones have been the most prevalent location for this tumor, accounting for 45% to 68% of the reported cases [3,5,11,12], with the second more frequent site being the tongue [9,11]. The least affected sites were the gingiva and upper lip [5]. The majority of patients present without nodal and/or distant metastases [13].

The prognosis of LMS in the oral and maxillofacial region is usually poor with a high percentage of recurrence and metastasis [3,14]. The reported 5 year survival rate for the primary disease ranges from 50 to 60% [9,10,13]. A feature that seems to be related to decreased survival is bony involvement. In Kaplan-Meier survival estimate, the mean survival time of the group without bony involvement was approximately 14 months longer than the group with bony involvement [15].

Histologic grade has been considered as prognostic factor. There are two parameters that seem to be the most important, the mitotic index and the extent of tumor necrosis. Histologic grading is particularly useful as an indication of the probability of distant metastasis and overall survival, but is of poor value for predicting local recurrence which is mainly related to the quality of surgical margins [10]. The two most widely used classification systems are the NCI (United States National Cancer Institute) and the FNCLCC (French Fédération Nationale des Centres de Lutte Contre le Cancer). According to the methodology defined in 1984 and refined in 1999, the NCI system uses a combination of histologic type, cellularity, pleomorphism and mitotic rate for attributing a grade from 1 to 3. The FNCLCC system is based on a score obtained by evaluating three parameters selected after multivariate analysis of several histological features: tumor differentiation, mitotic rate and amount of tumor necrosis. The score is attributed independently to each parameter and the grade is obtained by adding the three attributed scores [16]. Lungs are the most common site of metastasis, while hepatic metastases are rather frequent. Regional lymph node metastasis of oral LMS is considered relatively rare; nevertheless, an increased incidence is linked to delayed diagnosis [7,17,18].

Histopathologically, this neoplasm is characterized by sheets of sweeping, alternating bundles and fascicles of densely packed spindle cells with abundant fibrillar eosinophilic cytoplasm and indistinct cytoplasmic borders. The nucleus is usually centrally located and blunt-ended, squared-off or cigar-shaped [1,6,10,18]. Histologic and ultra-structural features of oral LMSs are similar to those of soft tissue and bone LMSs. However, diagnostic challenges arise in the histopathologic examination, when sarcoma cells are poorly differentiated and develop at uncommon sites [3,18-20]. Masson's

trichrome staining and immunohistochemical evaluation for muscle antigens are helpful in diagnosis separating leiomyosarcoma from other sarcomas [1,5,18]. Positive reactions for desmin, vimentin, smooth-muscle actin and h-caldesmon have been demonstrated in this neoplasm [5].

The diagnosis is most often made on light microscopy and confirmed by immunohistochemistry [3,5,11,12]. Management protocols are lacking due to the rarity of oral lesions. The treatment of choice, is complete surgical resection with or without neck dissection depending on the status of the cervical lymph nodes. Tumor free margins are a prerequisite in order to control local recurrences [10,15]. The benefit from chemotherapy or/and adjuvant radiotherapy is that of reducing the recurrence or increasing the survival is considered minor. As a result of this ambiguousness, these modalities are most often considered a palliative measures for inoperable cases [11,15,21], even though some authors' reports beneficial effects [10,13,15].

Conclusion

Primary oral LMSs are rare tumors with a relatively small number of cases reported in the literature. They are often mistaken for other, more common lesions. Immunohistochemical methods are usually necessary to confirm diagnosis. Given the small number of cases presented, it is impracticable to draw conclusions with regards to the biologic behavior and management protocols yet. However, based on the available data, it is clear that LMS is an aggressive neoplasm with a high incidence of recurrence, metastasis and mortality.

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