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Low Grade Myofibroblastic Sarcoma of the Oral Cavity: A Case Report and Review of the Literature

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Abstract: Low-grade myofibroblastic sarcoma (LGMS) is a rare malignant neoplasm of the soft tissue with a predilection for the head and neck. To date, there are no optimal treatment strategies. This report describes a case of LGMS of the left side retromolar pad region in a 26-year-old otherwise healthy woman with initial presentation of a two-month history of a painless and progressively growing soft tissue mass. Incisional biopsy was completed revealing "fragments of granulation tissue with marked acute and chronic inflammation, and fibrosis". Based on history and physical examination, the decision was made to complete an excisional biopsy in the operating room due to the location of the lesion and the proximity of the lingual nerve. Pathology report then revealed "cellular myofibroblastic neoplasm, favor low grade myofibroblastic sarcoma". TNM staging was completed based on NCCN guidelines with subsequent imaging. The treatment plan included marginal resection of the left posterior mandible via trans-oral incisions with oncological margins, resection of lingual nerve with subsequent allogenic nerve grafting, extraction of left mandibular first and second molar, and complex primary closure. The patient is planned to have a secondary reconstruction via anterior iliac crest bone graft completed with simultaneous implant placement. We discuss the differential diagnosis, clinical, histological and therapeutic features of LGMS as it is understood in the literature.

Keywords: Low Grade Myofibroblastic Sarcoma, Oral Cavity, Head and Neck

1. Introduction

Low-grade myofibroblastic sarcoma (LGMS) is a rare atypical tumor composed of myofibroblasts with a predilection for the head and neck, especially in the tongue and oral cavity, although it has been reported to originate in other anatomical sites [1, 2, 10, 13]. Myofibroblasts, first described in granulation tissue by *Gabbiani* et al. (1971), are considered a distinct cell type and share similar morphological and functional features with fibroblasts and smooth muscle cells. [2, 8, 12, 13, 14] Histologically, they are bipolar spindle or stellate cells with ill-defined cytoplasmic membranes, eosinophilic fibrillar cytoplasm, and ovoid pale nuclei with small central nucleoli. [2, 10, 15] Immunohistochemically, myofibroblasts often express vimentin, muscle-specific actin (MSA), smooth muscle actin (SMA), calponin, and fibronectin, less frequently desmin and keratin, and they usually do not stain with antibodies to high-molecular-weight caldesmon (h-caldesmon), S-100 protein, and anaplastic lymphoma kinase (ALK). [1-3, 15] LGMS usually occurs in adulthood, often sparring children, with a slight male predominance. [1].

Clinically, the neoplasm will present as an indolent, painless mass that will have the tendency for local recurrence. Furthermore, metastasis is rare, only after prolonged periods of time. [1, 2, 4] The differential diagnosis includes benign reactive lesions such as nodular fasciitis, benign indolent and locally aggressive neoplasms such as dermatofibroma and fibromatosis, respectively, other low-grade myofibroblastic sarcomas such as infantile fibrosarcoma and inflammatory fibrosarcoma, and high-grade pleomorphic sarcomas that have prominent myofibroblastic differentiation. [1-3].

We report a case of LGMS that originated in the region of the retromolar pad soft tissues along with its clinical, histological, immunohistochemical and therapeutic features.

2. Case Report

In May 2020, a 25-year-old, gravida 1, para 1, female presented to the Department of Oral and Maxillofacial Surgery at St. Joseph's University Medical Center (SJUMC), New Jersey, U.S.A with a two-month history of a painless, progressively growing soft tissue lesion along the left retromolar pad region. She reported bleeding when brushing her teeth and pain when chewing food on the left side. She denied constitutional symptoms and tolerated a vegan diet and adequate fluid intake. Her medical history was significant for bicuspid aortic valve and mild asthma for which she was never hospitalized. Furthermore, she could not recall the last time she used her albuterol rescue inhaler. She denied any known food or drug allergies. Her surgical history was significant for third molar extractions more than five years. She denied smoking cigarettes and drinking alcohol but admitted to recreational marijuana use. A pregnancy UHCG test was given and the results were negative. Family history revealed a living grandfather who was treated for oral squamous cell carcinoma (OSCC) with resection and neck dissection and subsequent reconstruction with a pectoralis major flap. Her grandfather exhibited the cardinal risk factors associated with OSCC, including smoking cigarettes and alcohol use.

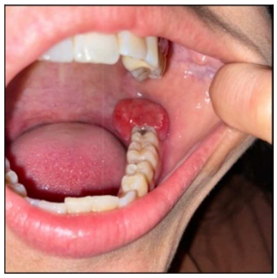

Figure 1. *Preoperative photograph showing a 2.7cm x 2.5cm x 2.0cm non-mobile, smooth, sessile, erythematous mass located along the left retromolar pad region.*

Examination revealed a 2.7cm x 2.5cm x 2.0cm non-mobile, sessile, smooth, erythematous, fibrous mass located along the left retromolar pad region (Figure 1). The lesion was non-friable, non-tender to light touch and extended above the mandibular occlusal plane. There were no signs of lymphadenopathy, the floor of mouth was soft, non-tender and non-elevated. The maximum incisal opening was approximately 40mm with full range of motion of the mandible. After a thorough history and physical examination was completed, a panoramic radiograph was taken (Figure 2). The panoramic radiograph revealed no signs of bony or dental pathology. Based on history and clinical presentation, our differential diagnosis included pyogenic granuloma, peripheral ossifying fibroma and peripheral giant cell granuloma.

Next, an incisional biopsy was completed under local anesthesia in the Oral and Maxillofacial Surgery Clinic revealing "fragments of granulation tissue with marked acute and chronic inflammation, and fibrosis". Based on our differential diagnosis, size and location of the lesion, the patient was optimized for general anesthesia to allow adequate excision of the lesion with non-oncologic margins (Figure 3). The surgical specimen was sent to SJUMC Pathology Department and the report unexpectedly indicated that the lesion was a low-grade sarcoma, with tumor present at resection margins. Immunohistochemical slides are presented in Figure 5. The patient was immediately informed of her results and the case was subsequently presented to the SJUMC Multidisciplinary Cancer Conference.

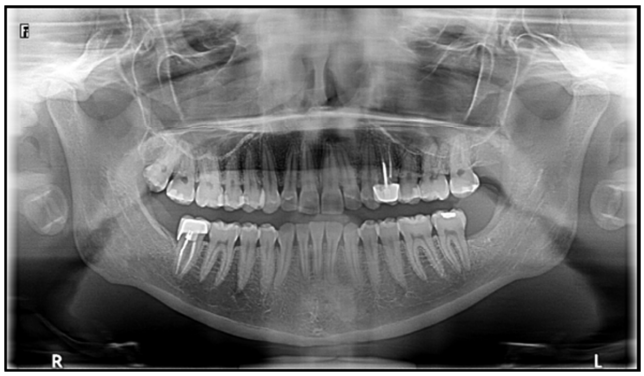

Figure 2. *Pre-operative Orthopantomogram. Note the soft tissue growth along the left retromolar pad region adjacent to left mandibular second molar.*

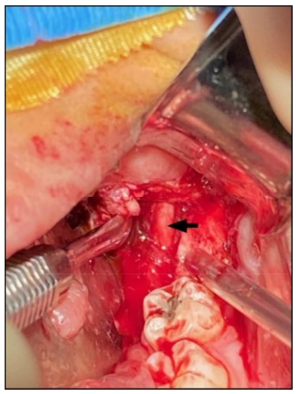

Figure 3. *Intraoperative photo during initial excision of lesion that was thought to be benign. Note the proximity of the lingual nerve (black arrow). The specimen was sent to pathology where the pathologist favored low grade sarcoma.*

In July 2020, the final pathology report, provided by the Department of Pathology, Immunology and Laboratory Medicine at Rutgers New Jersey Medical School revealed "cellular myofibroblastic neoplasm, favor low grade myofibroblastic sarcoma".

Clinical staging was determined to be stage 1B (T2N0Mx). Following NCCN guidelines, the case work up included: history and physical, multidisciplinary cancer conference, MRI with and without contrast, and chest imaging (CXR or CT without contrast as needed). [9] A CT thorax with and without contrast revealed no abnormalities. MRI of the face, neck and orbit with and without contrast revealed a 1.2 x 1.4 cm rim-enhancing nodule, either arising from or impinging, on the left lobe of the thyroid. Laboratory tests included a comprehensive metabolic panel and complete blood count with values within normal range.

On July 20, 2020, the patient underwent a marginal resection of the left posterior mandible via trans-oral incisions with oncological margins, resection of lingual nerve with subsequent allogenic nerve grafting, extraction of left mandibular first and second molar, and complex primary closure. The surgery was completed without complication and a Orthopantomogram was taken (Figure 4). At 4-hour post-operative check, the patient met criteria for discharge and went home that evening. Medications prescribed included amoxicillin, ibuprofen and a Medrol dose pack with recommendations for salt water mouth rinses twice daily and full liquid diet. All frozen sections and permanent specimens from July 20, 2020 revealed tumor-free margins.

On July 25, 2020 the patient visited the SJUMC Emergency Department due to surgical site dehiscence. She was afebrile, had no signs or symptoms of infection and was tolerating a full liquid diet. She reported following our recommendations and was consistently reliable with appointments and follow up visits. Recommendations were given to gently irrigate the wound with normal saline using a Monoject syringe and allow the surgical site to granulate by secondary intention. At that visit, a culture was taken at the surgical site revealing growth of *Streptococcus mitis* and *Streptococcus oralis*. Sensitivity tests showed resistance to Ampicillin, Penicillin, Clindamycin, Cefotaxime, Ceftriaxone, Erythromycin and Tetracycline with sensitivity to Levofloxacin, Linezolid, Moxifloxacin and Vancomycin. Levofloxacin was prescribed and the surgical site showed eventual improvement and granulation with no further signs of dehiscence.

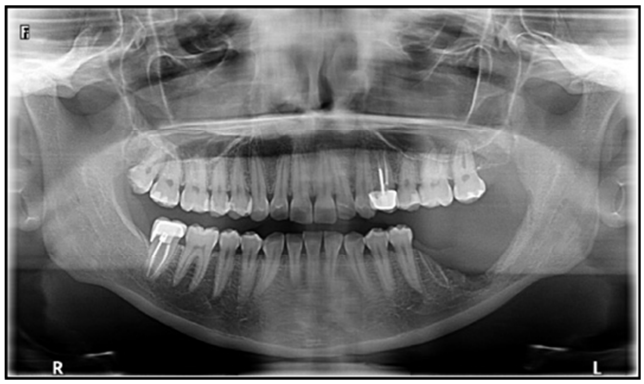

Figure 4. *Post-operative Orthopantomogram status post excision of lesion with oncological margins.*

The patient is currently being managed by SJUMC Department of Oral and Maxillofacial Surgery and SJUMC Department of Oncology. Following the recommendations offered at the SJUMC Multidisciplinary Cancer Conference, surgery was the primary treatment modality and chemotherapy and radiation were not utilized as additional treatments. Regarding the 1.2 x 1.4cm rim-enhancing thyroid nodule, a thyroid panel and consultation with endocrinologist was recommended. Generally, most thyroid nodules are benign and can be classified as adenomas, colloid nodules, congenital abnormalities, cysts, infectious nodules, lymphocytic or granulomatous nodules, or hyperplasia. We believe this lesion to be an incidental finding and unrelated to LGMS.

3. Discussion

Sarcomas are rarely seen in the head and neck region and make up less than 1% of all malignant head and neck tumors. [5] Our patient presented with a benign appearing growth emanating from the gingiva and as such was thought to be a pyogenic granuloma, peripheral ossifying fibroma or peripheral giant cell granuloma. This was also consistent with our first incisional biopsy and as such our original differential diagnosis did not include sarcoma. In establishing treatment options, location, size, systemic manifestation and histological differentiation are thoroughly evaluated. [5] Additionally, LGMS should be distinguished from fibromatosis, myofibromatosis, infantile fibrosarcoma, inflammatory fibrosarcoma, adult-type fibrosarcoma, and leiomyosarcoma.

Before therapy, the local extent of the neoplasm and the presence or absence of local and distant metastases must be determined. [5] Contrast-enhanced head and neck MRI with or without CT has proved to be a valuable tool for delineating the size of the tumor and the infiltration of neighboring tissue. [5, 9] A review from Massachusetts General Hospital found as tumor size increases, the risk of developing local recurrence and distant metastasis increases. The largest tumor diameter for our patient was 2.7cm, indicating a risk of 23% of recurrence and distant metastasis. [7] Metastatic surveys should include chest radiography, scintigraphic bone scanning and abdominal ultrasound and/or computed tomography. [5] In addition, we found it important to obtain a comprehensive metabolic panel and complete blood count to rule of distant metastasis and hematological cancers, respectively.

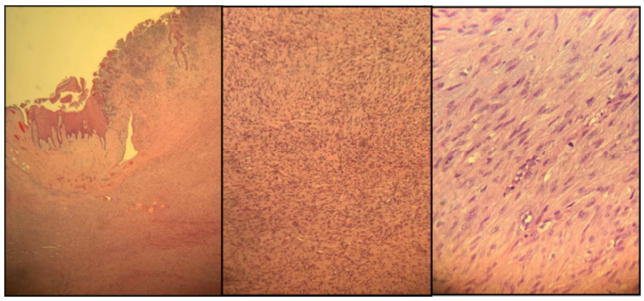

Figure 5. *Low-, medium- and high-power views (from left to right) The submitted hematoxylin and eosin stained sections demonstrate a spindle cell neoplasm. The cells are set in a fascicular pattern of varying length The spindle cells are mildly atypical and elongated with pointed ends in most areas. The chromatin is finely distributed The cytoplasm is ill defined and eosinophilic. The mitotic rate is 6 10 HPF.*

Histologically, LGMS is characterized by diffuse, infiltrative growth of spindle cells in a fascicular pattern exhibiting cellular atypia. These findings should easily rule out cases of fibromatosis. [3] Furthermore, myofibromatosis does not show nuclear atypia. [3] Infantile fibrosarcomas occur mainly in children and adolescents and inflammatory fibrosarcomas consist of an inflammatory component not typically seen in LGMS. [3] Adult-type fibrosarcomas have less eosinophilic cytoplasm compared to LGMS and leiomyosarcoma lacks a diffuse infiltrative

pattern. [3] LGMS demonstrates immunoreactivity for at least one myogenic marker [1, 3] and according to our final pathology report the tumor cells were diffusely immunoreactive to SMA with weak, focal immunoreactivity to caldesmon. The tumor cells were negative for beta-catenin, desmin, and myo-D1, S-100, CD34, and MUC4. Other authors have described different types of myogenic marker positivity and even noticed different markers in a single tumor emphasizing the myriad immunophenotype of myofibroblastic tumors. [1, 3].

Wide local excision remains the treatment of choice for LGMS. Radiation therapy is mandatory when adequate safety margins cannot be obtained and a re-operation is not possible. [5] Furthermore, it has been suggested that radiotherapy be avoided following resection as it may induce LGMS recurrence. [4] There is currently no guideline regarding the use of chemotherapy for patients with LGMS. [6] Adjuvant chemotherapy remains controversial in terms of prolonging survival and consensus in the literature has not been achieved. Some authors advocate adjuvant chemotherapy in cases where complete excision of tumor is difficult or if the tumor shows evidence of infiltration into adjacent tissue or if there is evidence of lymphatic and/or hematological spread. [6, 11] However, *Xu* et al. (2020) have come to the conclusion in their study that chemotherapy and radiation therapy showed limited effects on patient survival and that they should not be routinely performed to treat LGMS patients with negative margins. Furthermore, they found that nodal status was an independent prognostic factor for overall survival and age greater than 60 years and no surgical treatment were poor independent prognostic factors for overall survival. [6, 11].

4. Conclusion

LGMS is an extremely rare sarcoma and its indolent growth contributes to delay in diagnosis. [4, 11] The lesion in this case may have been mistaken for a typical benign growth, however, following relevant diagnostic and treatment algorithms led to a satisfactory outcome. Furthermore, there is no consensus recommending adjuvant therapies such as radiation and chemotherapy. Local recurrence even after many years of initial presentation is noticed rather than distant metastasis. [1] Our patient continues to be tumor-free at 9-month follow up and will be followed closely and offered reconstruction when appropriate.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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