Type of manuscript: Case report

Synovial Sarcoma; A Rare Entity In Submandibular Gland

ABSTRACT:

INTRODUCTION: Salivary gland synovial sarcomas, constituting <1% of oral tumors, occurring mostly in young and adolescents age group, present diagnostic challenges. It is characterized by the presence of spindle cells and CKAE1/AE3, TLE-1, and CD99 positivity.

CASE SUMMARY: We present a 48-year-old male with a swelling in the left submandibular area with no other associated symptoms. Excisional histopathology was done and diagnosis of unifocal synovial sarcoma was made with positivity for CKAE1/AE3, TLE-1, and CD99 and negativity for S100 in tumor cells.

CONCLUSION: This report contributes to limited literature regarding this rare malignancy, shedding light on their clinical and diagnostic characteristics.

KEY-WORDS: Synovial sarcomas, submandibular gland, spindle cells, immunohistochemical markers.

INTRODUCTION:

Synovial sarcoma (SS) is a comparatively rare soft tissue sarcoma (STS) with indeterminate differentiation. Occurring mostly in young and adolescents age group, it represents 5–10% of all STS (1), with an incidence rate of 1.42/1,000,000 in young adults and 0.81/1,000,000 in children (2). It is usually localized in the deep soft tissue of lower limbs, particularly in the knee area (1).

Of all SSs, merely 10% happens in the head and neck region, generally in cervical and pharyngeal zones (1). It is largely taken as a high-grade tumor having poor prognosis, diagnosed by assessing morphology characterized by spindle cells and a mitotic rate of 23/10 per high power field and presence of immunohistochemical markers like CKAE1/AE3, TLE1 and CD99. (1) Early identification, coupled with comprehensive surgical excision and adjuvant radiotherapy, plays a pivotal role in the effective management of submandibular synovial sarcomas. (2,3)

Due to scarcity of cases, very limited studies have been reported in this field. Here, we will be presenting a case of 48-year-old adult male with rare submandibular synovial sarcoma, which constitutes 1% of head and neck cancers. (4) This case will help to enhance our understanding on diagnostic and management approaches of SSs.

CASE DESCRIPTION:

A 48-year-old male patient, tobacco addict, presented to otorhinolaryngology department at tertiary care hospital with chief complaint of a lump in the left submandibular area persisting for one year with intermittent pain radiating towards the ipsilateral ear, not associated with fever or any other symptoms.

On examination, a 5 cm lump on the left side of the lower aspect of the mandible was noted. The lump was non-tender, hard, non-reducible, adherent to underlying muscle layer with regular margins, and euthermic (figure.1). CT neck without contrast was advised which revealed enlarged left submandibular gland with approximately 3.9x2.5cm well–defined solid cum cystic lesion in it, having specks of calcification within. Posterolaterally and medially, it is indenting the sternocleidomastoid muscle and carotid space with intact intervening fat planes respectively (figure.2). Histopathological assessment of samples obtained by fine needle aspiration (FNA) demonstrated nuclear pleomorphism and high mitotic activity.

Patient was planned for surgical intervention in which submandibular gland, approximately 3 x 2.5 cm in size, was excised with close margins. Histopathological analysis revealed a unifocal synovial sarcoma characterized by spindle cells, with a mitotic rate of 23 per 10 high-power fields. There was no identified necrosis nor lymphovascular infiltration. The specimen showed positivity for CKAE1/AE3, TLE-1, and CD99 and negativity for S100 in tumor cells. CD34 and Caldesmon were negative in tumor cells but positive in endothelial cells and vessel wall, respectively (figure.3).

Staging according to the pTNM system revealed a primary tumor (pT2), no metastasis to regional lymph nodes (PN0), and no distant metastasis (pMX). The patient was subsequently referred for radiotherapy, and further follow-up will be essential for comprehensive management.

DISCUSSION:

Sarcomas, constituting a mere 1% of primary head and neck cancers, pose a diagnostic challenge due to their rarity and diverse histologic spectrum. (4) Imaging, particularly high-resolution CT scans and MRI, is pivotal in assessing size and location. (6) Surgical excision with adjuvant radiotherapy recommended for high-grade tumors, large lesions, and specific histological variants.

Synovial sarcomas (SS), a distinctive subset accounting for 5-10% of soft tissue sarcomas, primarily affect young adults. (5) The nomenclature 'synovial' is misleading, as the tumor's development is not confined to the synovium, and it can arise in various anatomical locations. (6) While 10% of SS involve the head and neck, the submandibular gland serves as an unusual primary site. (5) Therein, it clinically presents as a painless mass, often growing silently for months or even years.

While up to 20% of cases may exhibit associated calcifications visible on X-ray or CTS, MRI remains the primary diagnostic modality, revealing a nonspecific, heterogeneous deep soft tissue mass. Tissue biopsy obtained using a 14-gauge needle core is crucial for a conclusive diagnosis. (8) Grossly, synovial sarcoma presents as a tan or grey mass with multi-nodular or multi-cystic formations. Morphologically, it comprises dense cellular sheets of uniform, plump spindle cells growing in various patterns. Characterized by the t(X;18) chromosomal translocation, forming the SS18:SSX fusion oncogenes, synovial sarcomas are diagnosed through cytogenetics, FISH, PCR, or immunohistochemistry. (9) However, TLE1's (Transducin-like enhancer of split-1) diagnostic utility has gained prominence as an alternative to gold standard methods. Several studies and a meta-analysis identify TLE1 as a robust immunohistochemical marker, instrumental in discriminating synovial sarcoma from other sarcomas. Incorporating TLE1 identification with histological and morphological assessments enhances diagnostic efficiency, especially in resource-constrained settings. (8)

The standard treatment involves extensive surgical excision, often coupled with adjuvant radiation for larger and deeper lesions. Ongoing debate surrounds the role of chemotherapy in the therapeutic approach to synovial sarcoma. Prognosis is influenced by patient demographics, tumor characteristics, and treatment modalities. Factors such as age over 35 at diagnosis, epithelioid type, and localization outside the head and neck region are associated with worse prognoses. (1)

We identified three distinct case reports of synovial sarcomas in the submandibular region and one in the oral cavity. Most cases of synovial sarcomas are diagnosed around the age of 30, yet all instances affecting the oral cavity and submandibular salivary gland, including the case presented, were observed between ages 40 and 50 with one exception presenting at the age of eighteen. All five cases, including the current one, featured male patients (1). A similarity in ethnic background was noted, with the current case being Pakistani and two involving Indian individuals. Additionally, our patient had a consistent habit of betel nut consumption, while another individual had an extensive history of smoking. Both practices are established risk factors for various oral neoplasms. Disparities in the duration of symptoms preceding medical attention were observed, emphasizing the need for varied approaches to symptom recognition and healthcare seeking behavior. Immunohistochemistry (IHC) results exhibited variability, indicative of diverse molecular characteristics. Consistent positivity of TLE1, CKAE1 and CD99 markers, and negativity for CD34, Caldesmon, and S100 underscore the significance of these markers in accurate diagnosis. Imaging showed a well-circumscribed nodular hypoechoic mass, throughout. However, variations in tumor size, necrosis, and calcification were observed.

The presented case of synovial sarcoma in the submandibular gland is unique due to its rare occurrence in this anatomical site. (5) The case contributes valuable insights to the limited literature on these rare tumors, emphasizing the need for heightened awareness during diagnosis. Identification of specific immunohistochemical markers such as CKAE1/AE3, TLE-1, and CD99 add to the understanding of its molecular characteristics. (1) Despite these insights, study limitations include the use of CT instead of MRI and the absence of FISH/PCR to identify the fusion gene and inability to assess recurrence due to the patient being lost to follow-up.

We conclude that utilizing an optimal immunohistochemical panel, including TLE1, CKAE1/AE3, CD99, CD34, and S100, enhances the diagnostic accuracy of synovial sarcomas, especially in resource-constrained settings. (9) The case contributes to our understanding of synovial sarcomas, shedding light on their clinical characteristics and emphasizing the need for further research in this domain.

FIGURE LEGENDS:

Figure.1: 5 cm lump, palpated on the left side of the lower aspect of the mandible that was non-tender, hard, non-reducible, adherent to the muscle layer with regular margins.

Figure.2: CT head and neck without contrast showing left submandibular gland enlargement with approximately 3.9x2.5cm well–defined solid cum cystic lesion in it (indicated by green arrows), indenting the sternocleidomastoid muscle Posterolaterally and carotid space medially with intact intervening fat planes.

Figure.3: Histopathological slides revealing a unifocal synovial sarcoma characterized by spindle cells, positive for CKAE1/AE3, TLE-1, and CD99 and negative for S100 and CD34 in tumor cells.

STATEMENTS AND DECLARATIONS

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- Ethics approval: Approval was obtained from the ethics committee of Dr. Ziauddin Hospital for this specific case report.

- Informed consent for participation: Written informed consent was obtained from the patient.

- Informed consent for using picture: written informed consent was taken from patient to use the picture.

- Informed consent for publication: The patient consented to the submission of the case report to the journal for publication.

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