

CASE REPORT

Alveolar rhabdomyosarcoma of maxilla

Anuradha Ananthaneni, Puneeth Horatti Kuberappa, G Vijay Srinivas, Mohammad Asif Kiresur

Department of Oral Pathology and Microbiology, Saint Joseph Dental College, Eluru, Andhra Pradesh, India

Address for correspondence:

Dr. Puneeth Horatti Kuberappa,
Department of Oral Pathology and Microbiology,
Saint Joseph Dental College, Eluru,
Andhra Pradesh, India.
E-mail: puneeth.hk19@gmail.com

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ABSTRACT

Rhabdomyosarcoma (RMS), a malignant neoplasm of skeletal muscle origin, is the most common soft tissue sarcoma seen in childhood and adolescence. The most frequent site is the head and neck accounting for 40% of all cases and other involved sites are genitourinary tract, retroperitoneum, and to a lesser extent, the extremities. RMS is relatively uncommon in the oral cavity and the involvement of the jaws is extremely rare. Here, we report a case of 50-year-old female with oral RMS involving maxillary alveolar region with clinical, radiological, histopathological and immunohistochemical findings.

Key words: Alveolar rhabdomyosarcoma, malignant tumor, rhabdomyoblasts

INTRODUCTION

Rhabdomyosarcoma (RMS) is a malignant mesenchymal neoplasm that exhibits skeletal muscle cells with varying degrees of differentiation. RMS was first described by Weber in 1854,^[1] and defined as a separate entity by Arthur Purdy Stout.^[2] About 35–40% of RMS occur in the head and neck region and the oral cavity accounts for 10–12% of these.^[3] The most commonly affected areas are head and neck, genitourinary tract, retroperitoneum and to a lesser extent the extremities. In the head and neck, frequently affected sites are orbit, paranasal sinuses, soft tissues of the cheek and the neck. Oral RMS is rare and when occurring, it is more frequent in the soft palate.^[1]

This article presents an unusual case of RMS arising in the left maxillary alveolar region in an adult patient.

CASE REPORT

A 50-year-old female patient presented with a complaint of painful swelling in the left upper jaw that was present since 8 months. History revealed that she had undergone extraction of her mobile and painful left maxillary third molar 2 months back. Later, she noticed a small painful swelling that gradually increased to reach the present size.

Intraoral examination revealed a diffuse ulceroproliferative growth on the left alveolar mucosa in the third molar region of size approximately 4 cm × 3 cm extending anteroposteriorly from distal aspect of the 25 to maxillary tuberosity and mediolaterally 4 mm away from the midline of the palate and laterally encroaching the vestibule [Figure 1]. Mucosa over the lesion appeared erythematous with yellowish slough. The swelling was associated with pain and discomfort on mastication and deglutition.

Intraoral periapical radiograph irt 25, 26, 27 shows well-defined radiolucency with irregular border and on the alveolar ridge irt 26, 27 shows diffuse rarefactions surrounding the bone [Figure 2a]. Maxillary occlusal radiograph shows a well-defined radiolucent bony defect in the left posterior region of palate in relation to 26 and 27 [Figure 2b]. Spiral computed tomography showed a soft density lesion measuring 5 cm × 3.5 cm involving alveolar process of the left maxilla and extending into the adjacent pharyngeal mucosal space [Figure 3].

An incisional biopsy was done. Microscopic examination showed round cells with large nucleus, a thin rim of eosinophilic cytoplasm with prominent nucleoli and few cells with clear cytoplasm arranged in pseudo alveolar pattern with central

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discohesive floating cells [Figure 4a and b]. The cytoplasm of tumor cells showed positive staining with phosphotungstic acid hematoxylin (PTAH) and Masson trichrome [Figure 5a and b]. Few strap cells showed PTAH positive staining with no evidence of cross striations [Figure 6a]. For confirmatory diagnosis panel of immunohistochemical markers was done and the tumor cells showed strong positivity for vimentin [Figure 6b] and Myo-D [Figure 7a] and were negative for epithelial membrane antigen [Figure 7b] and S-100, [Figure 7c]. Correlating the clinical, radiographical, histopathological and immunohistochemical findings the case was diagnosed as alveolar RMS (ARMS). After final diagnosis, the patient was referred to higher cancer center for further appropriate treatment.

DISCUSSION

WHO defined RMS as a highly malignant tumor of rhabdomyoblasts in varying stages of differentiation with or without cross-striation.^[4] It represents 5–15% of all malignant solid tumors and 4–8% of all malignant diseases in children

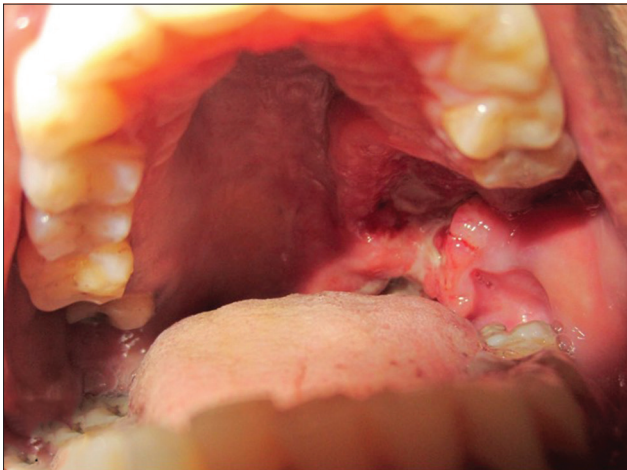


Figure 1: Intraoral photograph showing diffuse ulceroproliferative growth on the left alveolar mucosa in the third molar region

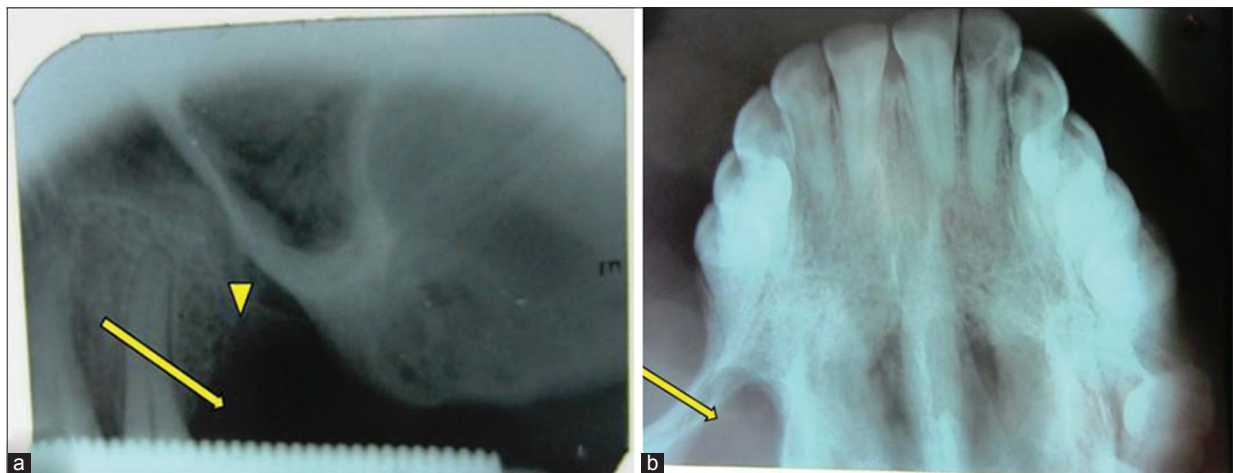


Figure 2: (a) Intraoral periapical radiograph shows well-defined radiolucency with irregular border (arrow) in relation to 25 and the alveolar ridge. (b) Occlusal radiograph showing well-defined radiolucency (arrow) in the left alveolar ridge in relation to 26 and 27

under 15 years of age. It is rare in individuals older than 45 years of age and it accounts for only 2–5% tumors in adults.^[2] Intraoral RMS corresponds to 10–12% of all head and neck RMSs.^[5]

The striated muscle origin of ARMS was first proposed by Riopelle and Theriault.^[6] RMS arises from immature mesenchymal cells that are committed to skeletal muscle lineage, but these tumors are also known to arise in tissues in which striated muscle is not normally found, such as urinary bladder.^[7] The exact histogenesis of RMS is unknown, but it is accepted that RMS results from malignant proliferation of embryonic mesenchymal tissue rather than degeneration from healthy striated muscles. This would allow RMS to develop in areas devoid of mature striated muscles.^[3] The possible origin of RMS in the present case could be from head of masseter which has its insertion at the maxillary tuberosity and was seen invading into the surrounding alveolus. Another possible source of origin could be from the embryonal mesenchymal elements that are housed in tuberosity region.

Genetic alterations may play a role in the pathogenesis of the RMSs. ARMS have a characteristic translocation between the long arm of chromosome 2 and the long arm of chromosome 13, referred to as $t(2;13)(q35;q14)$. This translocation fuses the *PAX3* gene (regulate transcription during early neuromuscular development) with the *FKHR* gene (a member of the forkhead family of transcription factors). It is hypothesized that this fusion transcription factor inappropriately activates transcription of genes that contribute to a transformed phenotype. The variant $t(1;13)(p36;q14)$ fuses with *PAX7* gene located on chromosome 1 with *FKHR*. Patients with tumors expressing the *PAX7-FKHR* fusion tend to be younger and are more likely to present with lesions of the extremities, suggesting a distinct clinical phenotype. DNA ploidy and RAS oncogene mutations have been described in RMS cell lines and tumor specimens. It is not known whether these alterations are involved in RMS tumor pathogenesis or reflect secondary abnormalities that occur during tumor progression.^[8]

In head and neck region the RMSs accounts for 36% of these tumors and are anatomically divided in two categories: Parameningeal (including nose, nasopharynx, paranasal sinuses, mastoid region, infra-temporal, pterygopalatine fossae and middle ear) and nonparameningeal (which include scalp, orbit, parotid gland, oral cavity, oropharynx and larynx). In the oral cavity, the most common sites are tongue, palate and buccal mucosa.^[1] In adolescents and adults, there is a greater

tendency for involvement of trunk and extremities, with a predilection for alveolar and pleomorphic subtypes.^[9] RMS shows twice more predilection for maxilla than mandible.^[3]

Oral RMS occurs more commonly in males and majority are seen in first two decades of life (mean age 19.6 years). Rarely like the present case who is a 50-year-old female, cases are reported in an older age group. Patients with RMS may present signs and symptoms such as pain, paresthesia, loss of teeth and trismus as a result of factors such as advanced tumor stage, infiltrative growth and tumor location.^[10] Pain, proptosis, diplopia, strabismus, decreased hearing, nasal obstruction, dysphagia, cervical lymphadenopathy are other signs and symptoms.^[11] In the present case pain, dysphagia and cervical lymphadenopathy are reported.

Along with computed tomography scanning, Magnetic resonance imaging also clues for the incidence of RMS in the head and neck. It presents as a homogeneous mass with intense or minimally hyperintense, relative to muscle on T1-weighted images and hyperintense, relative to both muscle and fat on T2-weighted images, with post-contrast images showing enhancement of the tumor.^[12]

Based on histopathologic features, RMSs can be divided into embryonal, alveolar and pleomorphic types. The embryonal

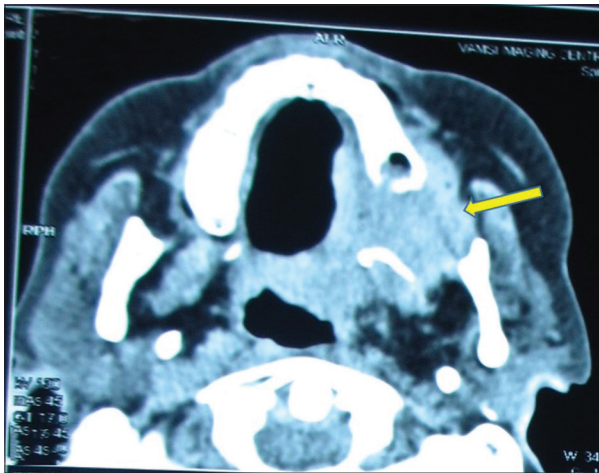


Figure 3: Spiral computed tomography showed a soft density lesion involving alveolar process of the left maxilla which is extending into the adjacent pharyngeal mucosal space

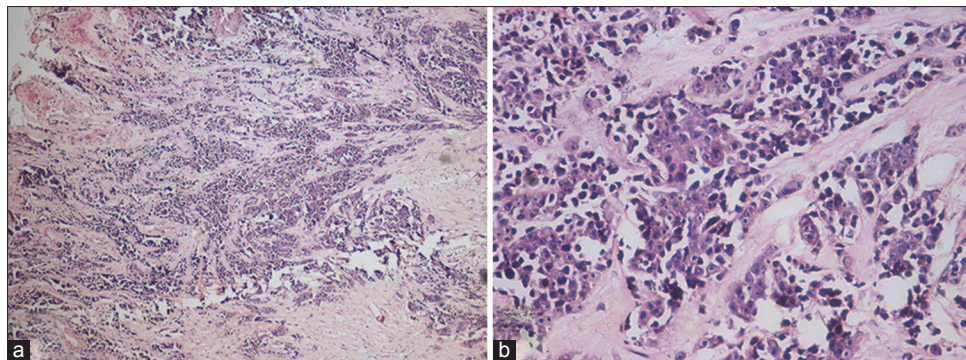


Figure 4: (a) Photomicrograph showing tumor cells with a thin rim of cytoplasm and few cells with clear cytoplasm arranged in pseudoalveolar pattern (H&E stain, ×40). (b) Photomicrograph showing large uninucleated cells with eosinophilic cytoplasm (H&E stain, ×200)

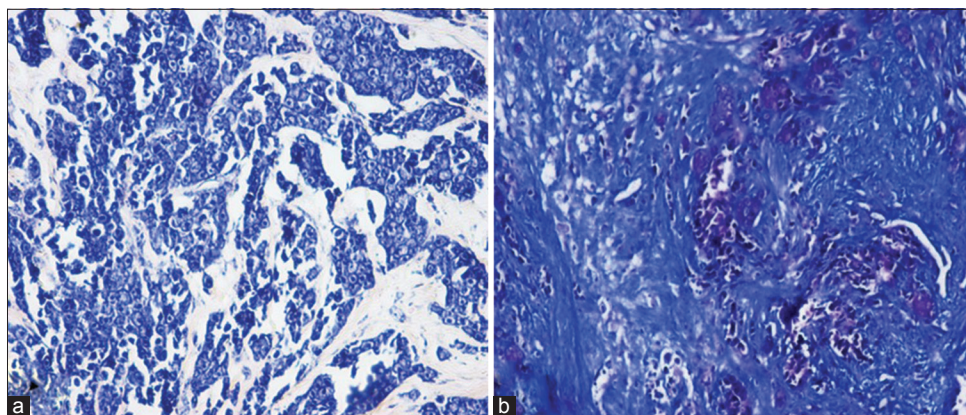


Figure 5: (a) Photomicrograph showing cytoplasm of tumor cells to be positive for positivity with phosphotungstic acid hematoxylin (PTAH stain, ×100). (b) High power view showing positivity for Masson trichrome with the cytoplasm of the cells taking up the red stain (Masson trichrome stain, ×100)

type presents the subtypes: Classic, spindle cell and botryoid.^[13] The most common histological type of RMS is embryonal, representing 50–70% of all cases. The alveolar subtype is the second most common, accounting for approximately 20–30% of the cases. The pleomorphic subtype is the rarest and comprises about 5% of the cases.

Microscopically, ARMS can show one of three patterns: A typical or classic pattern, a solid pattern and a mixed alveolar and embryonal pattern. In each of these patterns, the primary cell population is a primitive round cell, usually 10–15 μm in diameter. Nuclei are hyperchromatic, with inconspicuous nucleoli and range from round to oval to spindle shaped. Some tumors may contain scattered large multinucleated giant cells. In the typical or classical alveolar pattern, fibrovascular septae are seen separating the tumor cells into nests. Toward the center of these nests, the cells are discohesive and float freely. At the periphery, the cells are attached to the fibrous septae by cytoplasmic processes. This pattern, which gives this tumor its name, mimics the lung, where open alveolar spaces are linked together by a fibrovascular architecture. If this “alveolar” pattern is seen, even focally, in a malignant tumor that shows muscle differentiation, then the tumor is best diagnosed as an ARMS. The present case presented with classical finding of ARMS.

The solid pattern of ARMS is seen when the cells are closely packed, forming sheets without an alveolar pattern. Most tumors contain foci of more solid tumor growth. Solid areas

can range from focal to the predominant pattern. The solid variant of ARMS typically lacks the fibrovascular septae seen in the typical ARMS. Cytologically, solid variant of ARMS are similar to typical ARMS. Usually, if the tumor is well sampled, a more characteristic alveolar pattern with fibrous septa is focally observed.

A tumor can be classified as a mixed embryonal/alveolar pattern if both an embryonal morphology and alveolar patterns are present.^[14] Many special stains can be used to make an accurate and rapid diagnosis of RMS using light microscopy. Massons trichrome stains the cytoplasm of differentiated rhabdomyoblasts in deep red and also helps in identification of “ribbon” and “strap” cells, PTAH stains these myoblasts-deep blue and assists in studying myofibrils and cross-striations.^[2] RMSs are positive for muscle-specific actin, desmin, and nuclear skeletal muscle-specific myoregulatory proteins, including MyoD1 and myogenin (*myf4*).^[14] Intense staining for myoglobin, desmin and specific muscle actin is proportional to the rhabdomyoblast differentiation degree.^[1]

Age at presentation and the anatomic site of the presumed primary tumor are important factors which are considered in the formulation of a differential diagnosis when the biopsy is an undifferentiated or poorly differentiated neoplasm. The differential diagnosis for RMS is very long and includes the small round cell tumors, tumors with rhabdoid morphology, as well as miscellaneous soft tissue tumors. Small round

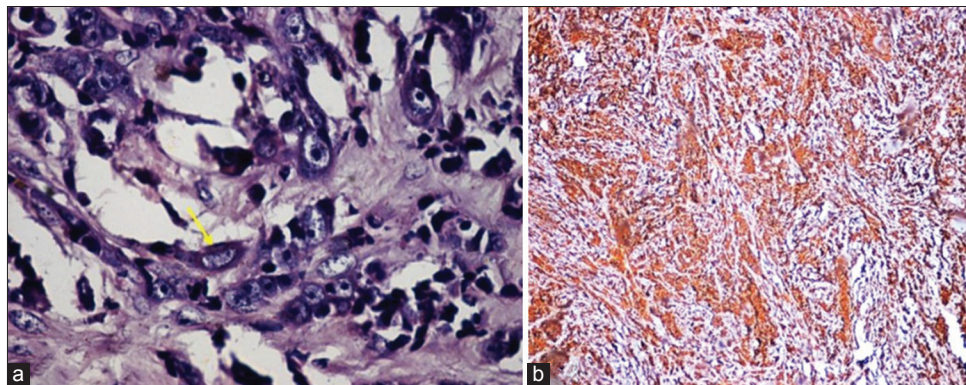


Figure 6: (a) Photomicrograph showing strap cells positive for phosphotungstic acid hematoxylin stain (PTAH stain, $\times 400$) (b) Photomicrograph showing tumor cells to be positive for vimentin (IHC stain, $\times 100$)

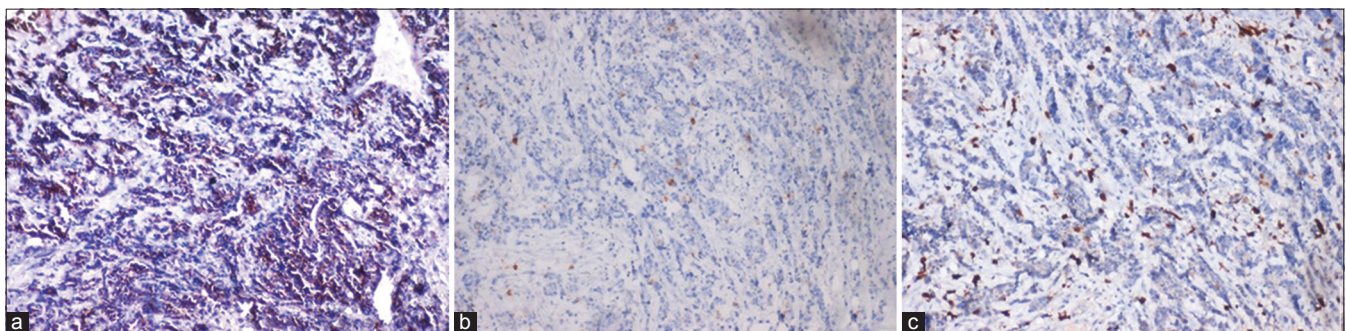


Figure 7: (a) Photomicrograph showing tumor cells to be positive for Myo-D (IHC stain, $\times 200$). (b) Photomicrograph showing tumor cells being negative for epithelial membrane antigen (IHC stain, $\times 100$). (c) Photomicrograph showing tumor cells to be negative for S-100 (IHC stain, $\times 200$)

cell tumors, namely, Ewing sarcoma (ES), neuroblastoma, lymphoma and desmoplastic small round cell tumor can mimic RMS. The cells of ES are usually round to oval with little cytoplasm and scant stroma with perivascular rosette-like growth pattern and geographic necrosis. RMS will express desmin and myoregulatory skeletal muscle specific markers that are absent in ES. When eosinophilic cytoplasm in RMS is not prominent, lymphoma is in the differential diagnosis. Immunohistochemistry helps to distinguish between the two. Immunohistochemistry helps to distinguish the two. Extrarenal rhabdoid tumor and rhabdomyoma, tumors with “rhabdoid features,” including carcinomas, sarcomas and melanomas are other differentials. Poorly differentiated malignant melanoma can be confused with RMS. Immunohistochemistry helps to distinguish the two, with antibodies such as HMB-45 and other melanocytic markers selectively expressed in melanoma and not RMS. The key feature in most of these tumors is abundant hard inclusion-like eosinophilic cytoplasm. Rhabdomyoma can also be in the differential diagnosis of an RMS. Both can be found in the head and neck and are skeletal muscle tumors. Particularly difficult is the distinction between fetal rhabdomyoma and RMS; mitotic activity and necrosis would favor the latter. Adult rhabdomyoma with “spider cells” may look similar to a spindle cell RMS. As compared with RMS, cross striations are actually more appreciable in fetal rhabdomyoma.^[14] Other differentials include alveolar soft part sarcoma that was the diagnosis in several instances. The uniform endocrine or organoid pattern of alveolar soft part sarcoma and its large cells, often containing diastase-resistant, periodic acid-Schiff-positive crystalline material, were readily distinguishable from the disorderly pattern and small, poorly differentiated cells of alveolar RMS.^[15]

ARMSs differs from embryonal RMS by virtue of its occurrence in older patients, distinctive pseudoalveolar pattern, usual absence of strap cells and strong myogenin rather than MyoD1 expression.^[16] In few cases, the presence of vacuolated tumor cells and the result of washed-out intracellular glycogen-raised the question of a liposarcoma.^[15]

The tumor spreads locally to invade adjacent structures and may also spread distantly through lymphatics and hematogenous routes. The most frequent sites of distant metastasis are regional lymph nodes, lungs, bone marrow, bones, central nervous system, heart, liver and the breast.^[7]

Local control is the main objective in the treatment of head and neck RMS. Multimodality treatment protocols; including surgery, radiotherapy and chemotherapy have improved the outcome in the past decades. In 1998, Schowenburg *et al.* described the AMORE protocol for patients with RMS of the head and neck which consisted of ablative surgery, moulage technique with after loading brachytherapy directed to the residual tumor after multiagent chemotherapy followed by reconstructive surgery.^[13]

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Conflicts of interest

There are no conflicts of interest.

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