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Embryonal rhabdomyosarcoma of oral cavity with extensive osteolysis of the mandible – A rare case report

Vidya Jayaram *, *S. Jayachandran*, *Y. Hemavathy Bhaskar*

Department of Oral Medicine and Radiology, Tamil Nadu Govt. Dental College and Hospital, Chennai 600003, Tamil Nadu, India

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ABSTRACT

Rhabdomyosarcoma is a malignant tumor of skeletal muscle. It is the most common soft tissue sarcoma in children and adolescents. It rarely occurs in oral cavity and accounts for 0.04% of all head and neck malignancies. The incidence is 4.5 per 1 million children and 50% of cases are seen in the first decade of life. In this paper, we report a rare case of oral rhabdomyosarcoma in a 3 year old boy with involvement of buccal mucosa and extensive destruction of the mandible.

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1. Introduction

Rhabdomyosarcoma was first described by Weber in 1854. Most common sites involved are head and neck (40%), genito-urinary tract (25%), and extremities (20%). [1]

Anatomically rhabdomyosarcoma is divided into 2 subtypes: Parameningeal (including rhabdomyosarcoma of nasopharynx, paranasal sinuses, nose, infratemporal fossa and pterygopalatine fossa) and non-parameningeal (including disease of the oral cavity, oropharynx, larynx).[2]

International classification of rhabdomyosarcoma comprises the following categories based on histologic features – embryonal, spindle cell, botyroid, alveolar, rhabdomyosarcoma not otherwise specified and sarcoma not otherwise specified.[3] The histologic subtypes of RMS, embryonal and alveolar, have been found to have distinct genetic alterations that may play a role in the pathogenesis of these tumors.[4]

Embryonal rhabdomyosarcoma is known to have loss of heterozygosity (LOH) at the 11p15 locus with loss of maternal genetic information and duplication of paternal genetic information.[5,6] This is the location of the insulin like growth factor-II (IGF-II) gene. It is now known that IGF-II is normally imprinted, with expression occurring exclusively from the paternal allele. Recently, RMS has been shown to have loss of imprinting (LOI), with re-expression of IGF-II from the normally silent maternal allele. Thus, LOH with paternal disomy or LOI with bi-allelic expression could both lead to a 2x-gene dosage effect with overexpression of IGF-II. Embryonal RMS appears to overproduce IGF-II which has been shown to stimulate RMS tumor cell growth.[7]

2. Case report

A 3 year old boy was referred to the Department of Oral Medicine and Radiology with chief complaint of swelling in the

* *Corresponding author.*
E-mail address: dr.vidyajayaram@gmail.com (V. Jayaram).

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Fig. 1 – (a) Frontal profile of patient and (b) intra-oral growth on right buccal mucosa.

right lower jaw region since 2 months. The swelling was initially small and progressively increased in size. There was an associated discomfort on mastication and deglutition.

Extra-oral examination revealed diffuse swelling present in right parotid region, measuring 6 × 5 cm. The swelling was tender and firm (Fig. 1a). A solitary right submandibular lymph node was palpable, non-tender and firm.

Intra-orally, a well-defined growth was present on right buccal mucosa extending from 84 region to right retromolar trigone region, measuring about 5 × 4 cm, obliterating the buccal vestibule. The growth interfered with occlusion. The surface of lesion was smooth except for superior surface which was ulcerated in relation to 55 due to trauma from the opposing tooth. The growth was non tender and firm (Fig. 1b).

Computed tomography scan revealed a heterogeneous mass lesion involving both superficial and deep lobes of parotid gland (Fig. 2) causing compression of oropharynx and extensive osteolytic destruction of adjacent mandible (Fig. 3a).

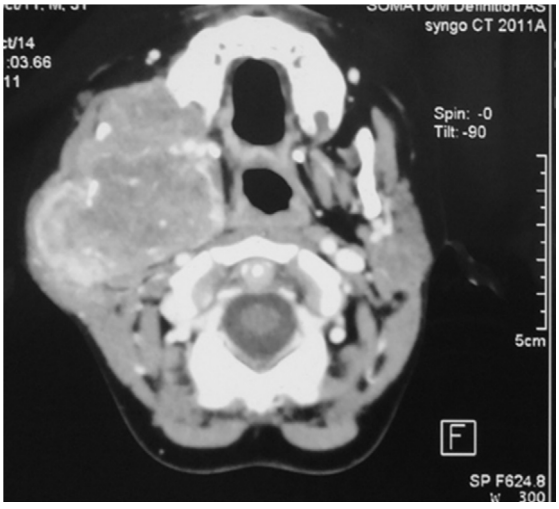


Fig. 2 – Axial section shows lesion involving both superficial and deep lobe of parotid.

CT contrast revealed intense vascularity in mass lesion (Fig. 3b). USG abdomen revealed normal study.

With the above clinical and radiological findings, a provisional diagnosis of soft tissue sarcoma of oral tissues on right side was given, with a differential diagnosis of mucoepidermoid carcinoma and osteosarcoma.

Histopathology examination revealed mucosal squamous epithelium with sub epithelial edema, vascular proliferation with detached fragments of fat and surrounding tissue showing infiltration of cells with prominent nucleoli and clear cytoplasm with occasional cells showing eosinophilic cytoplasm. Many mitoses were seen (Fig. 4). Histopathology report was suggestive of malignant small round cell tumor consistent with Embryonal rhabdomyosarcoma.

The proposed treatment plan was a combination of radiotherapy and chemotherapy. After 5 cycles of chemotherapy consisting of vincristine (1.5 mg/m^2), Adriamycin (60 mg/m^2), cyclophosphamide (100 mg/m^2), ifosfamide (1.6 mg/m^2), etoposide (100 mg/m^2), patient was subjected to radiotherapy. The tumor showed considerable reduction in size with complete resolution of intra oral growth after five months (Fig. 5). Patient is currently under follow up and is being monitored for treatment related complications (Fig. 6).

3. Discussion

Rhabdomyosarcoma is an aggressive malignant skeletal muscle neoplasm derived from primitive mesenchymal tissue. Approximately 60% of soft tissue sarcomas in children are rhabdomyosarcoma.[8]

Intraoral rhabdomyosarcoma corresponds to 10–12% of all head and neck rhabdomyosarcoma.[9] Incidence of rhabdomyosarcoma is highest in children aged 1–4 years.[10] There is a slight predilection for males.[11] Intraorally tongue and palate are the most common sites.[12] We present here, the case of a 3 year old boy with embryonal rhabdomyosarcoma involving right buccal mucosa.

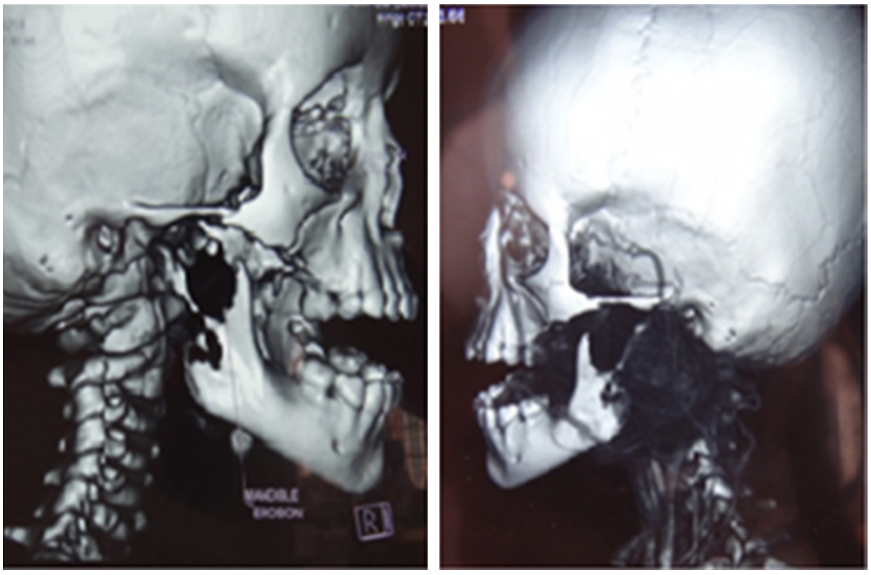


Fig. 3 – (a) Reformated CT shows osteolysis of right ramus of mandible. (b) CT contrast shows intense vascularity in mass lesion.

Clinically, the manifestation of rhabdomyosarcoma may vary from a small cutaneous nodule to an extensive fast growing facial swelling, which may be painless or occasionally associated with pain, trismus, paresthesia, facial palsy and nasal discharge. The time interval between onset of symptoms and correct diagnosis of head and neck rhabdomyosarcoma is estimated at 1–17 months.[13]

Among histological variants, Embryonal rhabdomyosarcoma is the most frequent in oral cavity which constitutes 70–80%.[14] Our patient presented with histologic variant, Embryonal rhabdomyosarcoma.

The histopathological differential diagnosis of Embryonal rhabdomyosarcoma includes other histological variants of rhabdomyosarcoma and other small round cell tumors like Ewing's sarcoma, Non-Hodgkin's lymphoma and neuroblastoma. Alveolar rhabdomyosarcoma exhibits small, round, densely appearing cells lined up along spaces reminiscent of pulmonary alveoli, giving rise to the term ''alveolar''. The botyroid variant of embryonal rhabdomyosarcoma, is defined by the presence of subepithelial aggregates of tumor cells known as cambium layer.[4] Spindle cell variant of rhabdomyosarcoma is composed mainly of elongated spindle cells arranged in a fasciculated or storiform pattern mimicking smooth muscle fibers.[15]

The presence of strap cells is deemed to be strongly associated with rhabdomyosarcoma. The finding of cells with more abundant cytoplasm eccentrically located nuclei, bi/multinucleated tumor cells in background of mucosubstance helps to distinguish RMS from other small round cell tumors.[16]



Fig. 5 – Shows resolved intra-oral growth.

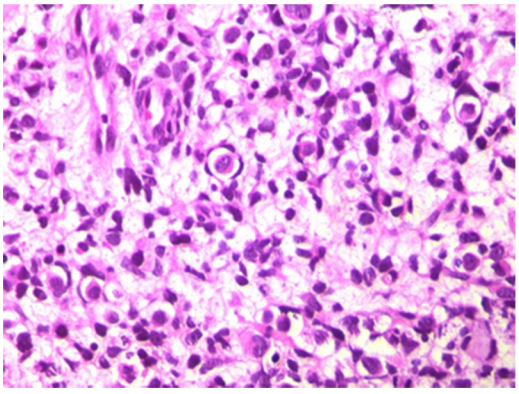


Fig. 4 – Low power resolution shows cells with clear to eosinophilic cytoplasm having prominent nucleoli and cells with nuclear pleomorphic and mitotic figures.

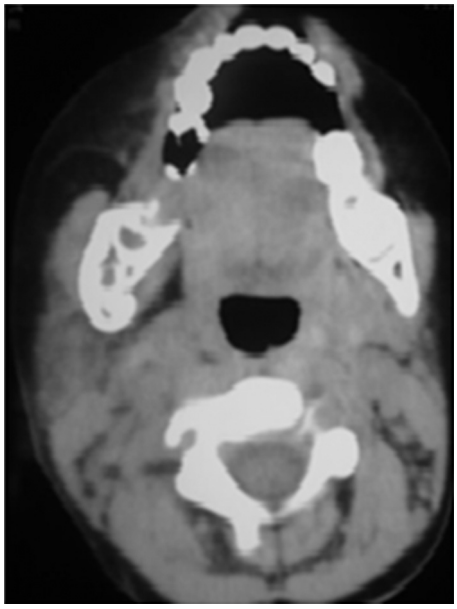


Fig. 6 – Axial section shows residual mass seen in parotid gland.

Our case presented with strap cells and the above mentioned features of RMS.

The role of immunohistochemistry (IHC) in rhabdomyosarcoma is to confirm their skeletal muscle lineage. The two overall most useful markers in rhabdomyosarcoma diagnosis are desmin and myogenin. Desmin is highly sensitive for all tumors with skeletal differentiation but somewhat nonspecific because it may also stain smooth muscle cells and occasionally even myo-fibroblasts. It is also positive in desmoplastic small round cell tumor and alveolar soft part sarcoma and should therefore never be used as the sole marker to diagnose RMS. MyoD1 and myogenin are very specific for skeletal muscle differentiation with only rare reports of nuclear staining in nonrhabdomyosarcomatous tumors.[17] IHC is also useful in identifying skeletal muscle proteins like alpha-actin, myosin, myoglobin and Z-band proteins. IHC staining pattern is not reliable in subtyping rhabdomyosarcomas.[4] Unfortunately in the present case, muscle markers were not done because of the need to initiate treatment at the earliest and the lack of affordability by the patient.

Treatment approaches to rhabdomyosarcoma includes surgery, radiation therapy and chemotherapy. Effective surgical excision is challenging in cases of rhabdomyosarcoma of the head and neck region owing to involvement of other crucial structures.[18] Formerly surgical excision was the only therapeutic modality available for rhabdomyosarcoma. However combination therapy (radiotherapy and chemotherapy) has replaced surgery as the standard of care with encouraging results.[6]

VAC (Vincristine + Actinomycin-D + Cyclophosphamide) has been the gold standard for combination chemotherapy in the treatment of most cases of rhabdomyosarcoma. Consecutive large randomized trials have allowed for modifications of this combination tailored to specific subgroups according to clinical group and site of disease.[4] In our patient chemotherapy followed by radiotherapy was given.

Post treatment complications include trismus, oral mucositis and bleeding, difficulty in mastication and deglutition, dental sensitivity, dental caries, arrested development of teeth and mandible. Parents must be counseled regarding such complications and the need for long term monitoring for the same.[19]

Prognosis of rhabdomyosarcoma is relatively poor compared to that of other oral malignant lesions and depends on clinical staging, anatomic site of the tumor and histologic subtype.[9] Embryonal type has a better prognosis, 83% survival rate.[20]

4. Conclusion

Rhabdomyosarcoma is a highly aggressive neoplasm capable of rapid local invasion and bony infiltration. Hence there is the need for early diagnosis and prompt treatment. We conclude that in children, any fast growing swelling should be carefully examined with a high degree of suspicion of this entity. We further emphasize review visits during and after the treatment period and reinforce the importance of continued oral hygiene maintenance.

Conflicts of interest

The authors have none to declare.

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