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Case Report

Orofacial Rhabdomyosarcoma of a Young Girl: Report of a Case and Review of the Literature

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Abstract

Rhabdomyosarcoma (RMS), a tumor of skeletal muscle origin, is the most common soft tissue sarcoma encountered in childhood and adolescence. These tumours are derived from mesenchymal tissue with a tendency toward myogenic differentiation that probably originates from immature and highly invasive satellite cells associated with the embryogenesis of skeletal muscle. Some of these tumours are associated with high rates of recurrence and metastasis. The diagnosis is made by microscopic analysis and auxiliary techniques such as Immunohistochemistry, electron microscopy, cytogenetic analysis, and molecular biology. We report here a case of orofacial RMS in a 16-years-old girl and provide an updated review of the literature, focusing mainly on the clinicopathological aspects, diagnosis and treatment of RMS of the head and neck.

Keywords: *Rhabdomyosarcoma; Head & Neck; Children & Adolescents; Immunohistochemistry*

Introduction

Rhabdomyosarcoma (RMS) is a malignant soft tissue neoplasm of skeletal muscle origin which was first described by Weber in 1854 [1] but the published documentation was done by Stout in 1946 [2,3]. RMS accounts for 6% of all malignancies in children under 15 years of age. The common sites of occurrence are the head and neck region, genitourinary tract, retroperitonium, and, to a lesser extent, the extremities [1,4]. In the head and neck region, the most commonly affected sites are the orbit, paranasal sinuses, soft tissues of the cheek [5,6]. RMS is relatively uncommon in the oral cavity, and the involvement of the jaws is extremely rare. Intraoral RMS corresponds to 10 to 12% of all head and neck Rhabdomyosarcoma [1,7]. Clinically manifestations 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 [1,8,9].

The use of contemporary, multi-agent chemotherapy, radiotherapy, and surgery has made treatment of the disseminated disease possible, and has significantly improved overall survival from 25% in 1970 to 70% in 1991. About 35% of RMS arises in the head and neck. According to their anatomical location and propensity for invasion of the central nervous system, these RMSs are divided in orbital, parameningeal and non-orbital non-parameningeal forms. Parameningeal tumours carry the worst prognosis [10,11].

The histopathological and molecular spectrum manifested by RMS has led to many classification systems. These differing morphological features were recognized in the mid-1900s by Horn and Enter line who divided rhabdomyosarcomas into embryonal (ERMS), alveolar, botryoid, and pleomorphic subtypes. Thus, a proliferation of subtle differences in diagnostic criteria had developed [10,12,13]. Histologically, embryonic RMS is characterized by a mixture of Pleomorphic and skeletal immature muscle cells, the so-called rhabdomyoblasts

which have a distinctive eosinphilic-rich cytoplasm representing poorly formed myofilaments and proliferate in a myxoid loose stroma [14,15]. RMS has been associated with familial syndrome such as neurofibromatosis, the li-fraumen, Beckwith - wiedemann, and Costello syndrome, many of these families have germ line inactivating mutations of the p53 tumor suppressor gene, whose normal function involves cell cycle regulation and in the maintenance of genomic integrity [14,16]. Hypoploidy may lead to inactivation of tumor suppressor genes which might lead to disturb cell cycle [14,17].

Within the microscopic patterns, the embryonal type is the most frequent in oral cavity. Undifferentiated/pleomorphic is very rare in children. Rhabdomyosarcomas are associated with high rates of recurrence and generalized metastases manifestations through haematogenous and/or lymphatic routes [5].

Rhabdomyosarcoma is treated by a combination of surgery, chemotherapy (vincristine, cyclophosphamide, dactinomycin, adriamycin, ifosfamide, VP-16) and radiation. In some cases stem cell transplant (Allogenic/Autologous) may also be applied.

The objective of this article is to describe a case of an oral embryonic RMS in a very young patient with diagnosis being achieved through clinical, histopathological and immunohistochemical investigation.

Case Report

A 16-year old girl was referred to the department of Oral & Maxillofacial Surgery of Dhaka Dental College & Hospital in August 2011 for the investigation of painful swelling in her mouth. On history taking, her parents reported that the disease had started as a painless swelling in May 2011, and that she had received oral and parenteral antibiotics for the past 4 months; however, the treatments were ineffective, and she was therefore referred to us. Written informed consent was obtained from her parent for further investigations.

Clinical examination showed severe facial asymmetry. A large, firm, and non-tender growth was noted on the left cheek which later on caused pain was found pushing the tongue backward causing respiratory distress. The skin had appeared stretched and inflamed. The opening of the mouth was partly restricted. Intraoral examination revealed an extensive mass involving the buccal mucosa. Extra oral examination showed extensive left sided swelling of face with ill-defined limits and smooth surface. Left submandibular and upper jugular lymph nodes were palpable and occupied all buccal vestibule. During intra-oral examination, a normal-colored mass was verified, with smooth surface and fibrous consistency involving the left buccal mucosa. At the time of admission, the patient exhibited an extensive swelling in the oral cavity with imminent airway obstruction. An intra-oral exam could not be performed properly owing to the extent of the tumor. This red, large, firm and tender mass extended from left upper buccal vestibule to lower buccal vestibule measuring approx. 5 cm x 4 cm with grayish area of central necrosis. It was fixed and bled on probing.

The orthopantomogram revealed irregular bony destruction and resorption of the anterior border of the ramus and partly maxillary tuberosity. The area was devoid of sclerotic border but the lower border was intact. Computerized tomography revealed a soft tissues mass isodense to the muscles (3.5 x 1.8) overlying the left maxillary bone with sign of bony erosion and the lesion showed heterogeneous enhancement and displacement of the adjacent structures. An incisional biopsy was performed, and the specimens disclosed rhabdomyosarcoma. Patient was operated under general anaesthesia, local excision of the lesion was done with lower lip splitting sub-mandibular incision and four pieces for free margin was performed along with resection of part of the bone involved. Histopathological section showed mixture of four cell types. Eosinophilic spindle cell, arranged in fascicles. Round eosinophilic cells, large and intermediate in size, with small nucleus and granular eosinophilic cytoplasm, interspersed among other cell type, Broad elongated eosinophilic cells, with cross striations. Small round and spindle cells with dark staining nuclei and little cytoplasm and report came as embryonal rhabdomyosarcoma. The immunohistochemical tests were positive for desmin, vimentin and muscle actin, and negative for cytokeratins and S100 protein. Myogenin showed a cytoplasmic and nonspecific background staining. Subsequently the patient was treated employing adjuvant chemotherapy under VAC protocol (vincristine, actinomycin-D, and cyclophosphamide) alternated with ifosfamide/vepeside, and complementary radiotherapy. Post-surgery follow up was performed for six months. But the patient was lost then for further follow up.

Discussion

Rhabdomyosarcoma is the most common soft–tissue sarcoma of childhood and adolescence. Of all soft tissue sarcomas, Rhabdomyosarcoma accounts for only 2-5% tumours in adults but approximately 60% tumours in children [5,18]. Our patient was 16 years old and did not fall in the very high-risk category. Head and neck Rhabdomyosarcoma is anatomically divided in two categories: parameningeal (including nose, nasopharynx, paranasal sinuses, mastoid region, infra- temporal and pterygopalatine fossae and middle ear) and non-parameningeal (which include scalp, orbit, parotid gland, oral cavity, oropharynx and larynx). Most common site of involvement in oral cavity is the tongue followed by the soft palate, hard palate, and buccal mucosa [5,19,20].

Rhabdomyosarcoma arises from the immature mesenchymal precursor cells committed to skeletal muscle lineage or embryonal muscular tissue origin displaced during early development. WHO defined Rhabdomyosarcoma as a highly malignant tumor of rhabdomyoblasts in varying stages of differentiation with or without cross striation.

RMS commonly affects children below 7 years of age. Some authors find bi-modal age distribution the first peak in children aged 2-6 years and the second peak in adolescents. The predominant sites include pharynx, orbit, oral cavity (soft palate, posterior mandibular region, cheeks, lips, tongue) followed by paranasal sinuses, neck and ear.

In the case we presented here, the lesion was involving partially the maxillary tuberosity along with left buccal mucosa and was extensive in size measuring 5 x 4 cm in dimensions. Geeta., *et al*. found this tumor to be fast growing and infiltrative and appearing as an enlarging, painless or slightly painful mass which supported our findings. Initial symptoms were vague, and mimicked other benign neoplastic, inflammatory, or infectious processes. Diagnosis of this tumor is based on histological findings. A careful histological examination is required to differentiate Rhabdomyosarcoma from other more frequent and aggressive lesions affecting the concerned site. Features favouring Rhabdomyosarcoma over soft-tissue sarcomas such as fibro sarcoma, Discussion leiomyosarcoma and neurofibrosarcoma was the presence of Rhabdoid cells but definitive confirmation requires Immunohistochemistry.

Rhabdomyosarcoma is rarely seen in adults but the embryonal variant occurs more common and later proceeded by Pleomorphic variant [11].

The histopathological and immunohistochemical report of our case confirms Embryonal Rhabdomyosarcoma. Although myogenin is considered a sensitive and specific marker for RMS, more specific than desmin and muscle-specific actin and more sensitive than myoglobin [10], in our cases, clinicopathological data, morphology and the immunohistochemical panel were more useful in the RMS diagnosis than myogenin alone.

BARNES noted that the tongue and palate are the most commonly affected intra-oral sites of RMS which differs from our cases whereas the clinico-epidemiological analysis on Nigerian population by OA FATUSI, identified the palate and cheek as the most common intra-oral sites and no tongue lesion was recorded resembling our finding [5].

To evaluate imaging findings of Rhabdomyosarcoma of the head and neck in adults, CT findings of head and neck Rhabdomyosarcoma have been described as showing poorly defined, inhomogeneous soft-tissue masses destroying adjacent bone.

F. GHAVIMl has proposed the multi-disciplinary protocol for the treatment of Embryonal Rhabdomyosarcoma for children under 15 years with surgical removal of the tumor followed by chemotherapy, and also with radiation therapy in patients with gross or microscopic residual disease which we also followed while performing the treatment protocol for our patient though our patient was found a bit older [14].

Prognosis of RMS is relatively poor compared to that of other oral soft tissue malignant lesions [10,11] and depends on the clinical staging and the anatomic site of the tumor [10]. An early and accurate diagnosis of the tumor and a combined therapeutic approach involving surgery, chemotherapy, and radiation therapy are known to dramatically improve the survival rates, as seen in cases recorded

over the past 20 years [8]. Effective surgical excision is challenging in cases of RMS of the head or neck region owing to the involvement of other crucial structures in these locations.

Although a marked improvement in the survival rates has been reported in patients with RMS in recent years, a poor prognosis in patients > 10 years old, delay diagnosis, and lack of cooperation from the patient and the family are reported to have a negative impact on the prognosis, as in our case.

In spite of advances in the field of surgery, chemotherapy and radiotherapy the recurrence of 30 percent Rhabdomyosarcoma has been observed. ALBERTO S. PAPPO analysis proposes a probability of five year survival of such patients. The prognosis depends on several factors including initial diagnosis, histological subtype, disease group, and stage [6]. But in our case we could only be able to follow up only 6 months after surgery.

Conclusion

Despite marked improvement in RMS survival over the past decades, it is known that, in addition to a poor prognosis for patients over ten-years old, delays in diagnosis have a profoundly unfavourable impact on prognosis. When a non-resolving nodule arouses suspicion, before the clinician begins antibiotic/anti-inflammatory therapy, support for the hypothesis of infection or inflammatory disease must be obtained from anamnesis and physical examination. Otherwise, a biopsy should be performed and the patient immediately referred to a recognized diagnostic center. Therefore High degree of suspicion, early diagnosis, and a multidisciplinary treatment approach would be of great importance in such cases. Because the initial management of any tumor is critical to a satisfactory outcome of the disease.

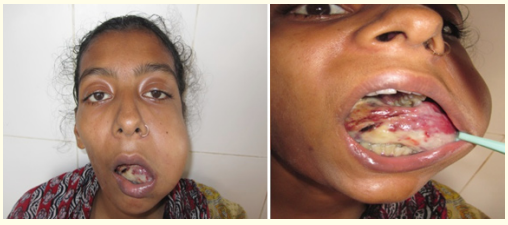

Figure 1: *Pre-operative view.*

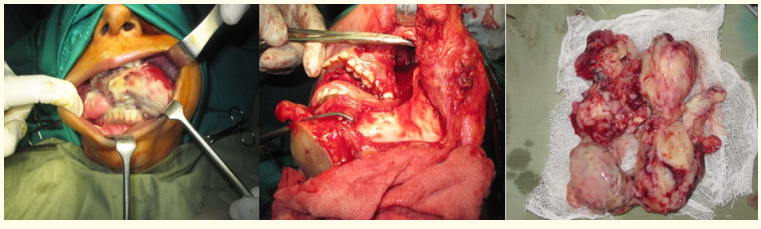

Figure 2: *Per-operative view.*

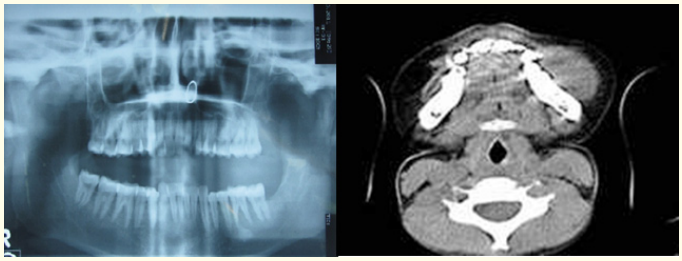

Figure 3: *Radiographic and CT scan view.*

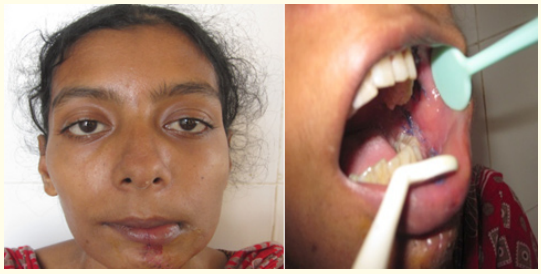

Figure 4: *Post-operative view.*

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