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Rhabdomyosarcoma , Embryonal Rhabdomyosarcoma , Oral , Head and neck.

"PRIMARY EMBRYONAL MANDIBULAR RHABDOMYOSARCOMA WITH MULTIPLE METASTASIS IN A YOUNG GIRL" :A CASE REPORT

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ABSTRACT

An embryonal rhabdomyosarcoma (ERMS) is a most common , primitive, malignant, soft tissue sarcoma in children under 15 yrs of age. It is considered to result from malignant transformation of primitive mesenchymal cells. Although it has a predominance for head and neck region , it is found less often in oral cavity. Here we report a case of ERMS of mandible in a 13 year old young girl. Clinical and pathologic findings are described , which were confirmed by histochemical and immunohistochemical stains. Three cycles of chemotherapy resulted in over 50% reduction in size of the mass. However, increase in size was noted subsequent to completion of therapy . In nine months, the patient developed multiple metastases, radionuclide bone scan showed increased tracer uptake on left side of mandible in angle, ramus region, and right pubis region . Patient died despite chemotherapy .

Introduction:

Rhabdomyosarcoma (RMS) is the most common malignant soft tissue tumor. It was first described by Weber in 1854.This pathology was first delineated as a distinct entity by Arthur Purdy Stout. First case from india was reported by Mehra (1960) . RMS primarily involves the head and neck region and shows a characteristic age distribution , most of the patients being with in the second decade of life[1]. It was sub – classified by Horn and Eterline in to embryonal , alveolar , botryoid , and pleomorphic subtypes [2]. The embryonal and botryoid variants occur in children between birth and 15 years age group, while the alveolar type occurs in young adults between age group of 10 to 25 yrs and the pleomorphic variant occur in older people between the age group of 50 to 60 yrs [1]. ERMS is a primitive , malignant , soft tissue sarcoma that recapitulates the phenotypic and biological features of embryonal skeletal muscles [3]. 28% of RMS occur in head and neck , and amongst them , 0.04% occur as intra-oral tumours [5,6].Its occurrence in children is common , but in adults , it is extremely rare [4,6]. Rhabdomyosarcoma tends to present as an expanding mass, resulting in pain and symptoms related to the compression of nearby structures. Metastases can lead to pain in the bones, difficulty with respiration due to lung nodules or pleural effusion, anemia, thrombocytopenia, and neutropenia, with 5-yearsurvival rate less than 30% [7]. In contrast, confined disease treated with combined surgery, radiation and chemotherapy has a 5-year survival rate of over 80% [7].

Here we report a case which on incisional biopsy appeared to be soft tissue sarcoma and following immunohistochemical staining and radionuclide bone scan , a definitive diagnosis of ERMS was established.

Case report: A 13 year female patient reported to department of oral and maxillofacial surgery with a chief complaint of painful swelling over left side of face from past 9 months. History reveals spontaneous appearance of small swelling extraorally near left angle region of lower jaw 9 months back. There was also pain in the swelling for which patient used to take analgesic. The swelling gradually increased in size over the period of 2 months to involve whole of left side of face and also a small lump appear intraorally near left posterior tooth(Fig.1)

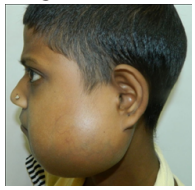

Fig.1 Swelling over left mandibular region

Then patient consulted to department of paediatric oncology where patient was diagnosed as a case of embryonal rhabdomyosarcoma and was given 3 cycles of chemotherapy over period of 3 months. During chemotherapy cycles swelling reduced to half in size and also Intraoral lump disappear. Then after 3 cycles of chemotherapy swelling again increased in size to involve whole of left side of face and also intraorally a larger size lump reappeared.

On extra oral examination swelling was seen measuring about 8 cm antero-posteriorly extending from 1 cm from left commissure of lip to angle of mandible and 6 cm superoinferiorly 4 cm from outer canthus of eye extending to lower border of mandible. Overlying skin was normal in color.On palpation swelling is firm and tender in nature. Overlying skin was warm.On Intraoral examination a pedunculated mass was seen attached over left retromolar triangle extending lingually and measuring about 4x3 cm. mouth opening reduced to 6 mm. On palpation mass was tender in nature and bleed on probing(Fig.2)

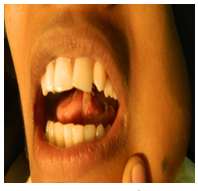

Fig.2 Ulceroproliferative growth in left mandibular region

Biopsy was done and sample was sent for histopathological examination. Histopathology findings revealed spindle ovoid cells disposed in sheets with variable cellularity in varing stage of myogenic differentiation. The tumour cells had hyperchromatic to vesicular nuclei. Rhabdomyoblast with eccentric nuclei, variable amount of eosinophilic cytoplasm in variable number and stage of differentiation was seen in a myxoid stroma. Mitosis and necrosis was also evident. Further special stains were performed for confirmation, classification and to determine prognostic information. In the present case, Desmin and vimentin stain were positive(Fig.3 , 4 and 5)

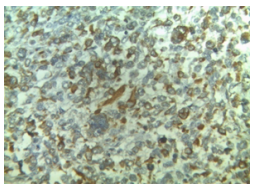

Fig.3 Tumor cells showing positive staining With Desmin

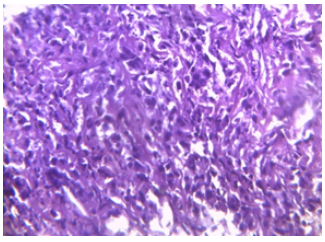

Fig.4 Tumor cells in the connective tissue stroma (H & E staining)

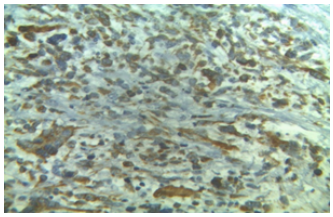

Fig.5 Tumor cells showing positive staining With Vimentin

Initially orthopantomogram was done which showed osteolytic lesion over left side of mandible(Fig.6).

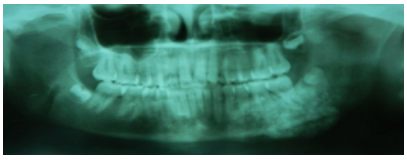

Fig.6 OPG showing destructive lesion

CT Scan of face was done which showed sclerotic lesion involving the angle and ramus of mandible on left side associated with a large heterogenous enhancing soft tissue with osteoblastic matrix in left buccal and masseter space(Fig.7 and 8). Also there is osteoblastic subperiosteal component in sublingual space of size 2.0x1.3 cm, displacing the adjacent structures. There was associated sunburst type periosteal reaction

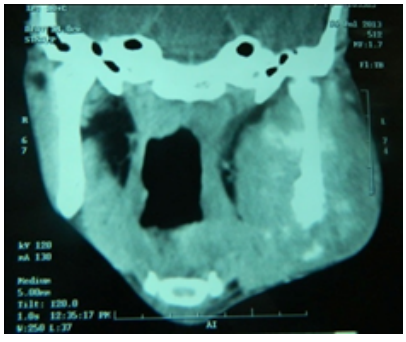

Fig.7 Coronal View

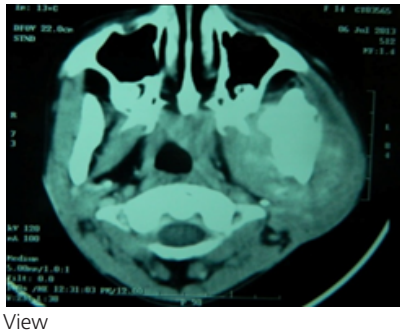

Fig.8 Axial View

Radionuclide Bone scan was done using 20 mCi of 99m-Tc MDP. Scintigraphic picture revealed increased tracer uptake in left half of mandible and superior ramus of right pubis.

After nine months, the patient developed multiple metastases and died despite having chemotherapy.

To present this case for academic pupose parental consent was taken on behalf of patient .

Discussion: RMS is a highly malignant tumor of mesenchymal origin. It represents 5 – 15 % of all malignant solid tumors and 4 – 8 % of all malignant diseases in children under 15 yrs of age [8]. It is rare in individuals older than 45 years of age [1].Horn and Enterline observed that embryonal and botryoid varieties are seen in paediatric age groups.Head and neck is the principal location of RMS and accounts for 36% of these tumors. Based upon the primary site of involvement of tumor, RMS of head and neck has been subdivided in to orbital and non orbital types. The non orbital RMSs are further subdivided in to the parameningeal and non para meningeal types [1,8]. The tumors of oral cavity are included under non- orbital and non – parameningeal group, which accounts for 28% of head and neck RMSs [9,10]. 60% of RMSs are of embryonal subtype[3,4,11]. Though they are most common in children, the average age of occurrence is 7.5 years, with a slightly male predilection [6]. Our patient was female and was older than this average age. A site predilection with in the oral region has not been well established [12]. The soft palate appears to be the most common site for oral RMS as stated by some authors .The present case involves the mandibular posterior region. The patients with oral RMSs often have a rapidly enlarging painless mass , usually larger than 1 cm in diameter at time of presentation [10,13,14], with local infilteration , pain , ankyloglossia, paresthesia , and trismus. Primary RMS of head and neck are rarely associated with lymphatic spread [8,9]. Pain and trismus was the main presenting symptom in the case reported in this paper.

Tsokos et al.,[15] developed a new classification scheme related to prognosis. They classified RMS in to two groups : those with favourable histological feature and prognosis and those with unfavourable histologic feature and prognosis. Prognostically, the embryonal type is more favourable followed by alveolar type .Histologically , the most common type of head and neck RMSs are of embryonal type , so was the present case [1,12]. Further more in the IRS I, II trials , 71% of tumors were of embryonal , and 13 % were of alveolar type[9]. There are 3 commonly used staging systems for rhabdomyosarcoma: clinical(surgicopathologic), TNM, and IRS (Intergroup Rhabdomyosarcoma Study) staging [16]. IRS clinical grouping is particularly useful because previous studies have indicated comparatively favourable and unfavourable prognostic groups. The IRS classification includes four groups, based on tumour respectability[17].

Group 1 includes localized disease, completely resected. Group 2 includes total gross resection with evidence of regional spread. Group 3 includes incomplete resection with gross residual disease. Finally, Group 4 includes distant metastatic disease present at onset. As per IRS staging our case was in stage IV at the time of diagnosis.

The cytogenetic abnormalities of embryonal and alveolar RMS are distinct .Embryonal rhabdomyosarcoma is characterized by a consistent loss of heterozygosity for multiple closely linked loci at chromosome 11p15.5. This loss of heterozygosity may result in activation of tumor suppressor gene or genes , including the human tyrosine hydroxylase gene. Others have reported trisomy 8 as a consistent finding in embryonal RMS[1].

RMS poses the biggest challenge inroutine histopathology . The evidence of skeletal muscle differentiation may not be discernable in sections stained with H & E [18] .Moreover , the embryonal subtype of RMS can be exceedingly difficult to distinguish from other poorly differentiated round and spindle cell sarcoma like Ewing's sarcoma, neuroblastoma, peripheral primitive neuroectodermal tumors , and malignant lymphomas[1,18]

Immunohistochemistry is of great help in this context and several markers have been applied to diagnose rhabdomyosarcoma, but their diagnostic value, sensitivity and specifity vary substantially. The markers that are positive in RMS are desmin, myoglobin, myosin, vimentin, muscle specific actin (HHF 35), sarcomeric actin, smooth muscle actin, and Troponin-T[1]. Occasionally, S100 protein

and cytokeratin may also be positive[18]. Thus, only vimentin is present in the cytoplasm of the most primitive cells, and desmin and actin are acquired by developing rhabdomyoblasts [2,5,11]. Several histochemical stains were key in arriving at this conclusion [19]. indicating the presence of muscle cells . Desmin is an intermediate filament protein present in smooth muscle cells, striated muscle cells and myocardium. A positive reaction for vimentin confirms a mesenchymal derived tumor [20] and desmin indicates muscular differentiation [11] . These both histochemical stains were positive in present case. Thus, histopathological analysis confirmed that the tumour was embryonal rhabdomyosarcoma. Desmin is among the earliest muscle structural gene to be expressed in myotome of embryo. It has been regarded as the best single marker for the diagnosis of poorly differentiated RMS [22] Desmin is very sensitive and is identified in as much as 75-100% of RMSs. However, it is not very specific for skeletal muscle, i.e., although desmin can recognize the myogenic phenotype, they do not distinguish between skeletal and smooth muscle differentiation. Myoglobin on the other hand appears to be specific for skeletal muscle, but it has average sensitivity[18]. The management of rhabdomyosarcoma is multidisciplinary approach with optimal integration of surgery, radiotherapy and chemotherapy. Dramatic survival rates have been achieved with multimodal treatment approach.

Conclusion: Our case was embryonal RMS of mandible in an young female patient. The diverse histologic pattern of RMS posed a challenge to the diagnosis but with aid of special stains, suggestion for skeletal muscle neoplasm was obtained. Finally, the use of immunohistochemical markers such as desmin and vimentin ruled out other differential diagnosis and the tumor was categorized as embryonal RMS.

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