Rhabdomyosarcoma (RMS) is a malignant tumor of myogenic origin and originates from embryonal mesenchyme. It accounts for 4%–8% of all pediatric age group malignancies and 50% of childhood sarcomas.[1] Incidence is highest in children between 1 and 4 years of age and is more common in males. Common sites of involvement include the head-and-neck region, genitourinary, retroperitoneum, and extremities.[2] The tongue is most commonly involved in the head-and-neck region with the lip being an uncommon site.[3] Histopathologically, RMS is of three subtypes: embryonal, alveolar, and pleomorphic.[4] Embryonal type is the most common and is further subdivided into botryoid and spindled variants. Anaplastic RMS is an uncommon subtype and can be seen with either of the histomorphology. With this background, we report a case of anaplastic RMS of the upper lip in a female child.

Case report
A 3-year-old female was brought to the hospital with a fungating mass over her upper lip [Figure 1a]. The lesion was present since birth and rapidly increased in size in 4 months. No previous medical records were available. There was neither any swelling elsewhere in the body nor any history of headache or weight loss. Examination revealed a 6 cm × 4 cm × 3 cm exophytic, firm, and tender mass with surface ulceration. A provisional diagnosis of pyogenic granuloma was made. Frozen section was not performed. An excisional biopsy was done and histopathology revealed a markedly cellular tumor composed of sheets and nests of large round cells with an eccentrically placed large hyperchromatic nucleus, opened up chromatin, and prominent nucleolus. Numerous typical and atypical mitotic figures were also seen [Figure 2a-c]. The anaplastic features were present diffusely. The tumor expressed MyoD1 [Figure 2d], desmin, vimentin and was negative for CD 99, cytokeratin, CD 45, synaptophysin, and S-100. A final diagnosis of anaplastic variant of RMS was rendered and the patient was started on adjuvant chemotherapy, which led to a significant reduction in size. Post this, she underwent a complete surgical excision with 0.5 cm margin was done followed by the repair of the primary defect. Follow-up of 4 years has shown no recurrence so far [Figure 1b].

Discussion
RMS is a malignant soft-tissue tumor of the pediatric age group showing skeletal muscle differentiation. Exact etiopathogenesis of RMS is not known. It is known to be associated with certain genetic disorders such as neurofibromatosis (NF-1) and Li-Fraumeni syndrome.[3] The median age of anaplastic RMS is 40 months. The term congenital RMS is used for cases that arise within 1 month of age and accounts
for 0.4% of all RMS cases.\textsuperscript{5} Genitourinary and head and neck are common sites of involvement. Head-and-neck RMS is divided into three types depending on the propensity for central nervous system involvement and site involved: parameningeal, orbital, and nonorbital nonparameningeal. The parameningeal RMS is usually associated with the worst prognosis, and it involves the pterygopalatine, infratemporal fossa, paranasal sinuses, and middle ear. The nonorbital nonparameningeal sites show a good prognosis and include the scalp, face, and oral cavity. Oral cavity RMS is rare with the lip being a very uncommon site of involvement.\textsuperscript{6} Magnetic resonance imaging is the best imaging modality for soft-tissue tumor size and extension, whereas computed tomography helps determine metastasis in cases of RMS.\textsuperscript{1,3}

In 1958, Horn and Enterline divided the RMS into various histological types: embryonal, alveolar, botryoid, and pleomorphic subtypes.\textsuperscript{7} Following this, Intergroup RMS Study Pathology Committee made changes to the system with alveolar RMS diagnosis being based on the presence of alveolar pattern. The presence of 50% or more of alveolar pattern is no longer a criterion for the diagnosis. Furthermore, new subtypes like sarcoma undifferentiated, RMS with rhabdoid-like features made entry into IRS protocols.\textsuperscript{8} It led to different classification systems based on histomorphology and molecular studies.\textsuperscript{6}

RMS is a type of small round cell tumor and depending on the site, histomorphology differs substantially. The majority of the genitourinary region’s RMS is either embryonal or botryoid, and the extremities are alveolar or embryonal. Before the designation of separate entity, anaplastic RMS was reported as alveolar or embryonal RMS with anaplastic features depending on histological picture. Among its various histological subtypes, anaplastic RMS is not so common. In RMS, the prognosis depends on the histological type: botryoid associated with the best prognosis, whereas alveolar and anaplastic subtypes show poor prognosis. embryonal subtype associated with an intermediate prognosis.\textsuperscript{8} The prognosis of RMS with rhabdoid-like features is unclear. Hence, anaplastic RMS is separately grouped due to poorer prognosis as compared to classical embryonal or alveolar RMS.\textsuperscript{9}

However, anaplasia is very uncommon among children. The International Classification of RMS has now included anaplastic RMS.\textsuperscript{10} The anaplastic features in other pediatric malignancies such as medulloblastoma, Wilms’ tumor have been known to associate with poor prognosis. In one of their reviews, the Children’s Oncology Group discussed that anaplasia may affect the clinical outcome and might be more common than previously reported by some studies.\textsuperscript{10} Anaplasia in RMS can be focal or diffuse. Type I are tumors with focal anaplasia and are characterized by the presence of anaplastic cells scattered among the nonanaplastic cells, whereas diffuse sheets or clusters of anaplastic cells characterize type II tumors with diffuse anaplasia.\textsuperscript{4} According to a study done by Qualman et al.,\textsuperscript{10} the presence of either focal or diffuse anaplasia in RMS negatively influenced the
tumor-free survival rate on univariate analysis (63% vs. 77% at 5 years) and overall survival (68% vs. 82% at 5 years) rates.

Molecular studies are done to classify RMS based on genetic differences between various subtypes. RMS with PAX7-FKHR shows a better prognosis than PAX3-FKHR translocation.\(^9\)

Recently, Alaggio et al. described a novel VGLL2 gene rearrangement in congenital or infantile spindle cell RMS. Other genetic alterations like NCOA2 gene fusion have also been defined and when seen along with VGLL2, show favorable clinical behavior.\(^11\) The anaplastic variant is characterized by cells with hyperchromatic nuclei (three times larger than neighboring nuclei), multipolar mitotic figures, TP53 mutations, and p53 protein overexpression.\(^12\)

Clinical differential diagnosis of RMS includes hemangioma, hematomata, neuroblastoma, and other sarcomas. In the current case, clinical differential diagnosis of pyogenic granuloma was made due to the pedunculated and vascular nature of the swelling along with overlying slough and reddish hue. The histopathological features of RMS range from undifferentiated small round cell tumor to rhabdomyoma. The most characteristic feature for RMS diagnosis is the presence of embryonic myogenesis, which is usually identified on histopathology, ultrastructural, and immunohistochemical examination.\(^10\) The phosphotungstic acid hematoxylin and iron hematoxylin were used to demonstrate the striated muscle origin of RMS before the development of immunohistochemistry.\(^9\)

Among immunohistochemical markers, myogenin is a more specific marker than desmin and muscle-specific actin. Furthermore, it is a very sensitive marker with sensitivity even more than myoglobin.\(^4\) MyoD1 and myogenin expression, nuclear transcription factors that initiate myogenesis, precede the expression of cytoplasmic striations, myosin-ribosome complexes, myoglobin, and muscle-specific actin.\(^10\) The final histological diagnosis was of anaplastic RMS based on classical histomorphology and immunohistochemistry.

Treatment options include surgical excision, chemotherapy, and radiotherapy. Out of these, complete surgical excision is the most effective treatment. However, multimodality is the treatment of choice and increases survival to 70%.\(^4\) In some cases, delay in correct diagnosis or nonsurgical management in the first instance can increase morbidity and mortality associated with this tumor.\(^7\) Hence, an early surgical intervention can be a great help in preventing mortality as well as recurrences.

The case has been presented here because of an extremely uncommon site (lip) and that too of anaplastic variety, which makes it further rare. Rapid increase in the size of lesion should alarm the clinician and pathologist for aggressive workup and management. The case report also highlights the successful multimodal treatment of a challenging case.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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