# SPINDLE CELL RHABDOMYOSARCOMA OF THE MANDIBLE IN A CHILD: A CASE REPORT AND LITERATURE REVIEW

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## ABSTRACT

Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma of children and adolescents, with the embryonal type being the most common subtype [1]. Spindle cell rhabdomyosarcoma was previously regarded as a rare variant of embryonal rhabdomyosarcoma but now it is considered as a separate entity. It most commonly involves the para testicular region followed closely by the head and neck region and has a predilection for young males. We report a case of a 10 years old female patient diagnosed with spindle cell rhabdomyosarcoma of the mandible

**Key Words:** Spindle cell rhabdomyosarcoma, Myogenic markers, Mandible.

**This case report can be cited as: Zaheer A, Ali Z. Spindle cell rhabdomyosarcoma of the mandible in a child: A case report and literature review. Pak J Pathol. 2021; 3(4): 170-173.**

## INTRODUCTION

Rhabdomyosarcoma (RMS) is a common childhood and adolescent sarcoma exhibiting a varying degree of skeletal muscle differentiation. In 1854 Weber first described RMS. It accounts for 6% of all the malignancies in children under 15 years of age [2]. RMS is further classified into four histological subtypes including embryonal, alveolar, pleomorphic, spindle cell/sclerosing rhabdomyosarcoma. These subtypes are distinguished by their distinct characteristics, and embryonal type accounts for the majority of the cases. Primary site of involvement of RMS includes the genitourinary system, head and neck region, and less commonly extremities [3].

RMS has no clear etiological factors identified to account for its occurrence however there is increasing evidence that suggests genetic abnormalities may play a role in its development. The recent analysis demonstrates an association with MyoD1 mutation [4]. As compared with other subtypes; the spindle cell variant is associated with a favorable outcome in children. The survival rates of RMS patients have steadily improved over the last several decades with the introduction of multimodal therapy. We report a case of Spindle cell rhabdomyosarcoma (SC-RMS) of the mandible in a 10 years old child

## CASE REPORT

A 10-year-old female patient presented to Shifa International Hospital (SIH), Islamabad outpatient department with history of swelling on the right mandible associated with numbness since one month. The swelling was gradually increasing in size but there was no associated pain, fever or discharge. All her initial workup was done from a hospital in Saudi Arabia where she also underwent surgery and a 3.0 x 2.5 x 2.0 cm mass along with teeth was excised. On histopathology differential diagnosis of rhabdomyosarcoma and infantile fibrosarcoma was given. Patient had now came to SIH for chemotherapy and further management.

A CT scan with contrast was performed at SIH that showed a large lobulated soft tissue density mass with extensive lytic destruction of the right mandible extending inferiorly up to the symphysis menti and crossing the midline. She was given four cycles of chemotherapy in SIH but no clinical or radiological response was noted. Surgical intervention was then planned by a multi-disciplinary team and wide local excision with tracheostomy, neck dissection (Level I, II, and III lymph nodes), and extended 2/3$^{rd}$ mandibulectomy was performed followed by reconstruction with vascularized free fibula flap (VFFF). Per op margins were sent for the frozen section that were reported negative for malignancy. Mandibulectomy specimen along with the cervical lymph nodes were then sent for histopathology. On gross examination, the specimen consisted of a mandibular bone measuring 9.0 x 3.5 x 3.0 cm. The over lying soft tissue was serially sectioned to reveal a tan white and firm tumor mass, measuring 8.5 x 2.5 x 2.2 cm. Grossly the tumor had a whorled cut surface (Figure-I). The sections from the tumor showed sheets and fascicles of round to spindle shaped cells with pleomorphic, hyperchromatic nuclei and eosinophilic cytoplasm. Scattered rhabdomyoblasts with eccentric nuclei and

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*Received: 9* ***Sep 2021****; Revised:* ***22 Nov 2021****; Accepted:* ***16 Dec 2021***

ample eosinophilic cytoplasm were also seen with frequent mitotic figures (Figure-II). The submitted lymph nodes showed prominent germinal centers and reactive hyperplasia. A comprehensive panel of immunohistochemistry was applied to these sections including Smooth Muscle Actin (SMA), Desmin, MyoD1, EMA, and Myogenin. Positive staining was demonstrated only for MyoD1 antibody (Figure-III). Based on morphology and immunohistochemistry a final diagnosis of Spindle cell Rhabdomyosarcoma was rendered.

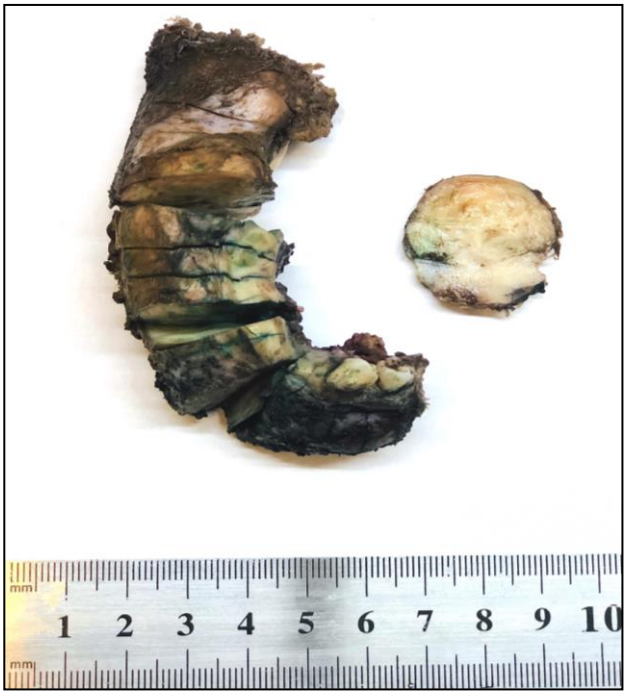


**Figure-I: Gross appearance of the tumor involving the mandible bone with overlying soft tissue and impacted teeth. Cross section of the tumor showing tan grey whorled appearance.**

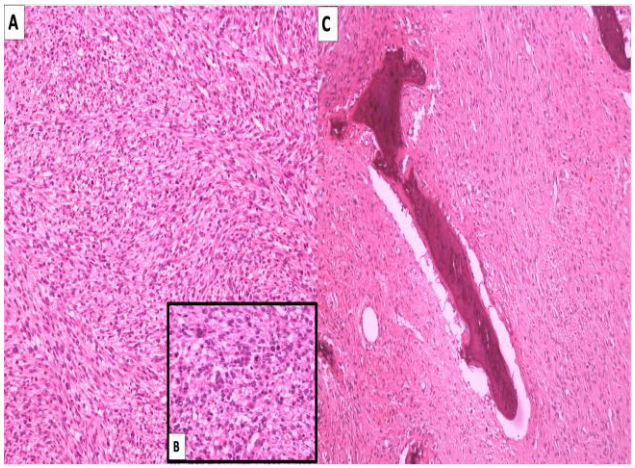


**Figure-II: Spindle cell Rhabdomyosarcoma: (A) and (B) sheets of round to spindle shaped cells arranged in interlacing bundles and fascicles (Hematoxylin and Eosin, magnification x200). Inset showing higher magnification (Hematoxylin and Eosin x400). (C) Tumor infiltrating into the underlying bone (Hematoxylin and Eosin, magnification x200).**

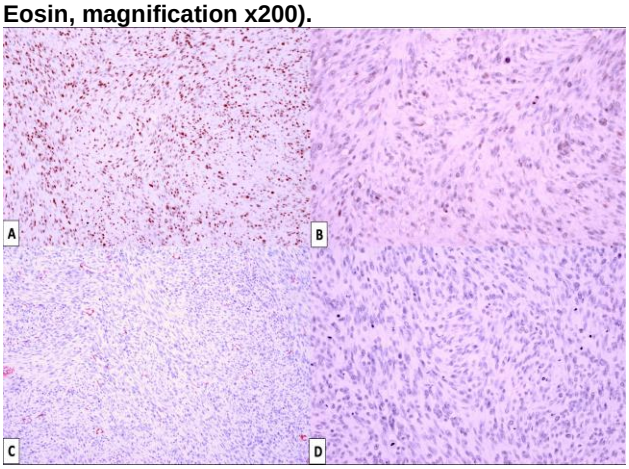


**Figure-III: Immunohistochemistry: (A) MyoD1 immunostain showing diffuse nuclear staining. (B), (C) and (D) Negative immunostaining for Myogenin, ASMA, and Desmin respectively (Immunohistochemistry, magnification x200).**

## DISCUSSION

SC-RMS is a rare mesenchymal tumor but its incidence is relatively high in children and adolescents. The mean age of diagnosis ranges from 3 years to 30 years. It accounts for 5 to 15 percent of all malignant solid tumors and 6 percent of all malignant diseases in children under the age of 15 years [5].

Spindle cell rhabdomyosarcoma (SC-RMS) is one of the four histological subtypes of RMS, frequently affecting young males. Most commonly involved sites include the paratesticular region and head and neck. Rarely subcutaneous and deep soft tissue of the extremities and visceral organs can also be involved. It can typically present as a rapidly growing, painless soft tissue mass with nonspecific symptoms related to the location and impingement on the surrounding structures and nerves. As in our case the patient presented with a painless increasing mandibular mass.

Most RMS cases are sporadic in nature however some association with familial syndromes like neurofibromatosis and the Li-Fraumeni syndrome (LFS) had been described, raising the possibility of its association with p53 germline mutation. A number of other mutations including RAS and MET oncogene have also been described in RMS cell lines. It is not known whether these alterations are involved in RMS tumor pathogenesis or reflect secondary abnormalities that occur during tumor progression [2].

SC-RMS can be well or poorly circumscribed, and there are no distinguishing macroscopic features that differentiate this tumor from other types of sarcomas. The cut surface reveals a firm, tan white

mass with a whorled appearance that may grossly resemble a leiomyoma or leiomyosarcoma. Histologically SC-RMS is predominantly comprised of uniform cellularity of elongated, spindle shaped cells arranged in fascicles and whorls. Individual cells have blunt ends, centrally placed nuclei, small or inconspicuous nucleoli, and eosinophilic fibrillary cytoplasm. Occasionally another cell type known as immature rhabdomyoblast is found admixed with this population, comprising only a minor portion of the tumor. These cells have eosinophilic cytoplasm, eccentric nucleus, and often show cross-striations. Presence of these cells warrants the diagnosis of SC-RMS. In 2000 Mentzel and Katenkamp described the sclerosing variant of SC-RMS for the first time.[4] The sclerosing spindle cell rhabdomyosarcoma (S-Sc-RMS) shares similar clinical, histopathological, and genetic features with SC-RMS except that it has a prominent hyalinized matrix, which can be confused with osteoid and chondroid.

RMS is both clinically and histopathologically a diagnostic challenge due to its varied morphology. The rhabdomyoblasts may exhibit numerous appearances, including small round cells to ribbon- or strap-shaped to large and pleomorphic cells. Further, a benign inflammatory infiltrate if present can sometimes be so dense that it masks the presence of neoplastic cells. A careful histological examination is required to differentiate such lesions from other poorly differentiated round and spindle cell sarcomas such as neuroblastoma, Ewing's sarcoma and malignant lymphomas.

Given the wide range of possible differentials for SC-RMS, immunohistochemistry is critical for diagnosis. Myogenic markers such as desmin, myoglobin, MyoD1 and myf-4 (myogenin) are found consistently positive in SC-RMS. The number of differentiated cells affects the immunostaining for desmin. Desmin immunostain should never be used as a sole diagnostic marker because it can show nonspecific reactivity in smooth muscle cells and myofibroblasts. Myogenic transcription factors such as myogenin and MyoD1 are currently used as a standard approach for diagnosis due to their high sensitivity and specificity [5]. In our case the neoplastic cells showed immunoreactivity solely for MyoD1.

Pediatric SC-RMS has a better long term prognosis as compared to adult RMS due to multimodality approach that has increased the cure rates to 70% [7]. Making correct diagnosis is therefore critically important. The standard treatment protocol includes a combination of chemotherapy and surgical excision with or without adjuvant radiotherapy [8]. It is recommended to completely excise the tumor if not causing any functional loss. Radiotherapy can be used for the local control of the residual disease [9]. In case described although patient received four cycles of chemotherapy prior to excision but no definite chemotherapy response was noted and surgical excision was then planned. Metastases during the disease is present at the time of diagnosis in about 20% of cases. Major metastatic sites include the lung, lymph nodes and bone marrow.

The SC-RMS case reported at our department had a gross resemblance to leiomyoma or a leiomyosarcoma. Diagnosis had been made on the basis of its characteristic histology and immunoreactivity for MyoD1. Patient received a combination of chemotherapy and surgical resection with a successful graft placement. However contrary to the existing theories no response to chemotherapy was noticed. There was no evidence of metastasis.

## CONCLUSION

Mandibular spindle cell rhabdomyosarcoma is a relatively rare entity and has a better prognosis in children than adults. Early identification can help improve the overall prognosis of disease. Judicious use of immunohistochemistry markers like desmin, MyoD1, myogenin, ASMA, and EMA helps in establishing the diagnosis. The treatment of RMS is a multidisciplinary approach that includes surgery, radiotherapy, and chemotherapy.

## AUTHORS CONTRIBUTION

**Amna Zaheer:** Composed and drafted the report, literature review.

**Zafar Ali:** Carried out the conception and assisted in drafting, literature review.

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