Case Report

"Primitive myxoid mesenchymal tumor of infancy" - A rare childhood soft-tissue tumor of the mandible

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Abstract

Primitive myxoid mesenchymal tumor of infancy (PMMTI) is an extremely rare soft-tissue tumor of childhood. We report a case of an 18-month-old male child diagnosed with PMMTI of the mandible. Till now <30 cases had been reported in the English literature. Histologically, the tumor consists of primitive spindle/polygonal cells dispersed in a myxoid background with delicate blood vessels. Immunohistochemically, tumor cells are positive for vimentin and negative for all other myoid, neural, epithelial, vascular, and neuroendocrine markers. This tumor was previously included under the diagnostic categories of congenital infantile fibrosarcoma or infantile fibromatosis. Increased awareness of this novel entity is a must as its biological and chemosensitive nature is vastly different from its differentials. Recent immunohistochemical stains and cytogenetic studies have helped to differentiate PMMTI from the other tumors of similar morphology.

Keywords: Fibromatosis, fibrosarcoma, infancy, mesenchymal, primitive

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INTRODUCTION

Soft-tissue tumors are rare in infancy and constitute <6% of the childhood tumors. The common soft-tissue tumors in the 1st year of age are the embryonal rhabdomyosarcoma, congenital infantile fibrosarcoma (IFS), Ewing sarcoma/primitive neuroectodermal tumor, and the undifferentiated sarcoma. Primitive myxoid mesenchymal tumor of infancy (PMMTI) represents a new category of the pediatric fibroblastic myofibroblastic tumor. Herein, we report an 18-month-old male child with PMMTI of the mandible with a better outcome. The macroscopic, microscopic, and molecular study is used to further discuss the distinct clinicopathologic features, differential diagnosis, and prognosis of PMMTI.

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CASE REPORT

An 18-month-old Arab male child who presented with a swelling in the mandible of 1-year duration, was referred to the department of head and neck surgery, in our institution with a biopsy diagnosis of fibrosarcoma from abroad.

Clinically, the swelling was an expansile lesion, involving the anterior mandible with bicortical expansion extending into the soft tissue of the chin area. The swelling was soft and compressible externally. The skin was free.

Hemogram showed hemoglobin of 10 gm/dl, red blood cell -5.16 cells/l, hematocrit-33.3, mean corpuscular volume-64.5 l/cell, mean corpuscular

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hemoglobin-19.8 gms/dl, mean platelet volume-6.41, mean corpuscular hemoglobin concentration-30.6 gms/dl, PLT-391 cells/cmm.

The patient underwent segmental mandibulectomy with anterior skin resection. Grossly, the tumor was 4.5 mm × 3 mm × 3 cm, unencapsulated and firm. The cut surface was gray-white, nodular and gelatinous, with specks of hemorrhage [Figure 1].

Microscopically, the tumor was infiltrative and composed of primitive spindle, polygonal, and round cells arranged in fascicles, bundles and vague nodular patterns in a myxoid background. Periphery showed increased cellularity and a collagenized stroma. A delicate vascular network was seen in some areas in the background [Figure 2]. The tumor cells had bland uniform nuclei with even chromatin, inconspicuous nucleoli, and variable amounts of pale eosinophilic cytoplasm [Figure 3]. Some cells had vesicular nuclei and prominent nucleoli. Mitosis of 3-5/10 hpf was identified and there was no necrosis.

Immunohistochemistry showed diffuse and strong positivity for vimentin [Figure 4] and a Ki-67 proliferative index of 20%–25% in the hot spots. CD34, S100, smooth muscle actin (SMA), desmin, My4, CK, CD99, synaptophysin, and beta-catenin were negative.

The diagnosis was confirmed by a negative ETV6/NTRK3 gene fusion and associated t (12;15) translocation. The above mutation is specific for congenital IFS which is a close differential of PMMTI.

The boy is being followed up and is doing fine for the past 5 years.

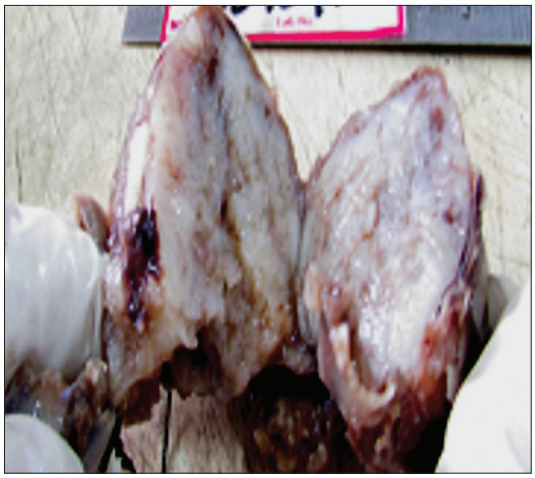

Figure 1: Grossly the tumor was 4.5 cm × 3 cm × 3 cm. Nonencapsulated with a multinodular appearance. The cut surface was Gray (American), gelatinous, with specks of hemorrhage

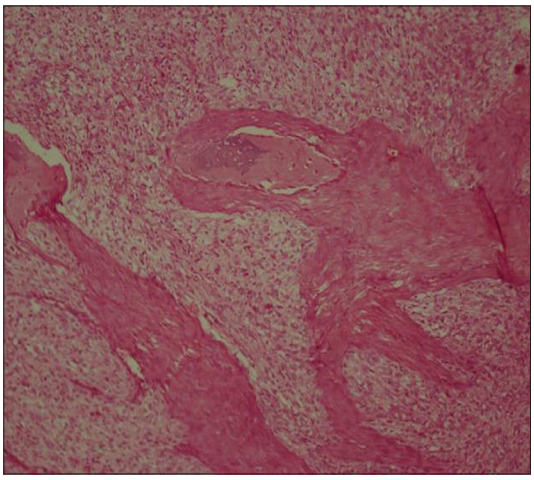

Figure 2: Microscopically, the tumor was infiltrative and composed of primitive spindle, polygonal, and round cells arranged in fascicles, bundles and vague nodular patterns in a myxoid background

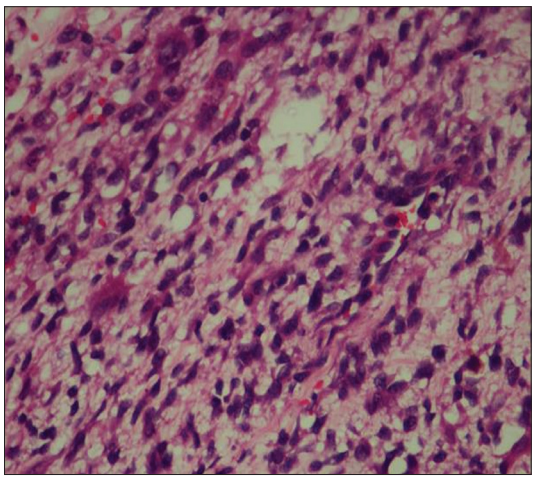

Figure 3: The tumor cells had bland uniform nuclei with even chromatin, inconspicuous nucleoli, and variable amounts of pale eosinophilic cytoplasm

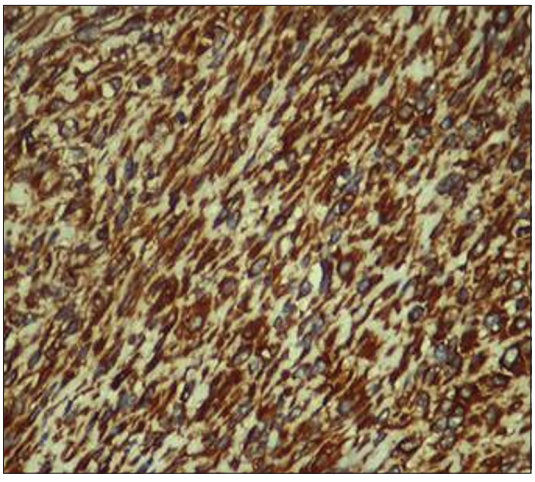

Figure 4: Immunohistochemistry - Vimentin showed strong and diffuse positivity

DISCUSSION

PMMTI, a locally aggressive rare childhood mesenchymal tumor was described in 2006 by Alaggio *et al*.[1] It represents an end spectrum of fibroblastic-myofibroblastic tumors. The tumor has a clinicopathological overlap with a congenital IFS and infantile fibromatosis.[1] Before its description as a distinct entity, most cases of PMMTI were diagnosed as congenital IFS. The histological distinction of this rare entity is crucial, as there is a remarkable difference in the biological behavior and chemosensitivity as compared to its differentials.

PMMTI usually occurs in infancy, rarely up to 5 yearsThe common sites being trunk, head, and extremities. Cases involving the abdominal cavity and vertebrae have also been reported. The tumor has a long, indolent course often complicated by relapse. It is a locally aggressive tumor and with a potential to metastasize. A case with brain metastasis has also been reported.[2]

Grossly, the tumor is unencapsulated, characterized by multinodular growth pattern and local infiltration. Size ranges from 2.5 to 15 cm. Cut surface is gray-white and fleshy with a myxoid/gelatinous appearance in central areas and a firm periphery.[1]

Histologically, the tumor is characterized by low to moderate cellularity, with increasing cellularity towards the periphery. Occasionally, vague nodular architecture and herringbone pattern have been observed. The cells are primitive mesenchymal, which vary in shape from the spindle, polygonal to round. The tumor cells have bland uniform nuclei with fine chromatin, inconspicuous nucleoli, and pale to eosinophilic cytoplasm. The cells are seen embedded in a myxoid stroma with delicate vasculature and focal small cystic spaces. The mitotic rate is variable. Usually <10/hpf. Atypical mitosis is typically absent. Necrosis has not been described. Increased cytological atypia has been noted in recurrent tumours.[3]

Differential diagnosis

1. Congenital-IFS: The tumor is not so myxoid. Increased mitosis and necrosis is seen. It shows (12; 15) (p13; q25) translocation resulting in the ETV6-NTRK3 gene fusion product
2. Infantile fibromatosis: The diffuse mesenchymal type resembles PMMTI but differs in showing interspersed adipose cells, peripheral lymphocytes, higher cellularity, and greater mitotic activity. Beta-catenin (CTNNB1) gene mutation is present
3. Low-grade fibromyxoid sarcoma: This usually occurs after the age of 2 years. There are both fibrous and myxoid zones, an apparent curvilinear vasculature, and giant collage rosettes. A t (7; 16) (q32-34; p11) translocation results in a chimeric FUS/CREB3 L2 gene
4. Myofibrosarcoma: Very rare in infancy. A myxoid background is not seen. The cells are positive for desmin, SMA, and muscle-specific actin
5. The myxoid variant of Dermatofibrosarcoma protuberans: Typically in adults and rarely in the pediatric population. Characterized by the honeycomb trapping of adipose tissue and is positive for CD34
6. Myxofibrosarcoma: This occurs in the elderly and a high-grade spectrum of the tumor.

Immunohistochemically, PMMTI is diffusely positive for vimentin. Variably positive for CD99, CD117, S100, and cyclin D1 and is typically negative for SMA, MSA, desmin, beta-catenin, CD34, CK, EMA, Synaptophysin, and NSE.[4]

Recently, PMMTI tumors have been found to harbor BCOR exon 16 ITD and YWHAE-NUTM2B fusions.[5] BCOR internal tandem duplication (ITD) is the same genetic alteration detected in clear cell sarcoma of the kidney.[5] Previously, the cytogenetic studies revealing an absence of the t (12; 15) ETV6-NTRK3 fusion gene and a lack of mutation in CTNNB1 gene characteristics of congenital IFS and infantile fibromatosis respectively, was taken as confirmatory.[3]

The management is by surgical excision with negative margins. Cases with extensive metastasis can be treated by chemotherapy.[6]

CONCLUSION

PMMTI is a rare soft-tissue tumor of infancy, occurring mainly in the soft tissue of the trunk, head and neck region, and the extremities. It represents a separate entity in the spectrum of fibroblastic-myofibroblastic lesions with at least intermediate (borderline) or low-grade malignant biologic potential. It is characterized by a high rate of local recurrence if incompletely excised. Metastasis and tumor-related death may occur, albeit very rarely.

Increased awareness of this novel entity will help avoid misinterpreting the lesion as a variety of other infantile mesenchymal neoplasms, including congenital fibrosarcoma and infantile fibromatosis.

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Conflicts of interest

There are no conflicts of interest.

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