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Case Report

Alveolar rhabdomyosarcoma in children with histomorphological review

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ABSTRACT

Rhabdomyosarcomas (RMS) are aggressive malignant neoplasm of mesenchymal origin, related to skeletal muscle lineage. These are the most common soft tissue tumors in children. The diagnosis is made by microscopic analysis and ancillary techniques like immunohistochemistry, electron microscopy, cytogenetics and molecular biology. We encountered a case of a 03 years old child who presented with a tender, reddish, soft swelling over cheek for three weeks. The FNAC was reported as a small round cell tumor, Probably Primitive Neuroectodermal Tumor (PNET). The biopsy of tumor revealed a small round cell tumor with an alveolar pattern. Tumor giant cells were absent and mitotic figures were infrequent. Hence, differentials of alveolar rhabdomyosarcoma and PNET were rendered. Immunohistochemistry (IHC) demonstrated desmin positivity. Thus, a final diagnosis of alveolar rhabdomyosarcoma was offered.

Keywords: Alveolar rhabdomyosarcoma (ARMS), Primitive neuroectodermal tumor (PNET), Immunohistochemistry (IHC), Fine needle aspiration cytology (FNAC)

INTRODUCTION

Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma of childhood, with an annual incidence of 4 to 7 per million children below 15 years of age. Approximately 65% of cases are diagnosed in children less than six years of age with remaining cases noted in the 10 to 18 year age group.[1] RMS is a highly malignant tumor and is thought to arise from primitive mesenchymal cells committed to develop into striated muscle.[2] In children and young adults, RMS tends to occur in the head and neck, extremities, and genitourinary tract. In contrast, ARMS rarely occurs in head and neck but commonly presents as truncal and extremity tumors.[3] Hence this case is being reported as it involved paranasal region, a rare site.

Overall more than 25% of patients have metastatic spread at the time of diagnosis, with the most common sites include lungs, lymph nodes, bone, and bone marrow.[4] The differential diagnosis of RMS includes 2 categories: the small round cell tumors of childhood and myogenic tumors of various types.[5] In their study, Tsung et al. have reported only 15% paediatric RMS presenting with metastasis in whereas more than 60% adult RMS have regional metastasis at diagnosis.[6]

Herein, we discuss the cytological and histopathological features of small round cell tumors in children with reference to index case we encountered. A diagnosis of ARMS needs to be confirmed by ancillary techniques.

CASE REPORT

Three years old child reported to the Out Patient Department (OPD) of otolaryngology department with the chief complaint of swelling over right cheek and right lateral aspect of nose for three weeks. The swelling was soft, non-fluctuant and mildly tender, measured 5x5 cm. The skin over the swelling was erythematous with raised local temperature (Figure 1).

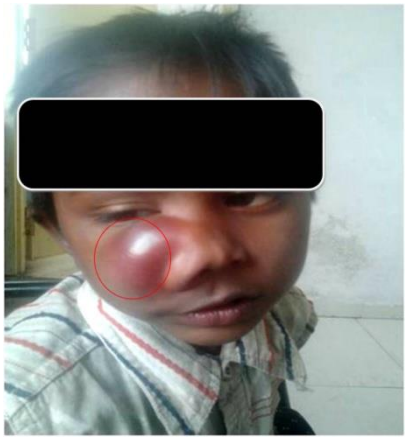

Figure 1: Reddish pink swelling over right cheek and ala of nose.

The CT scan of paranasal area revealed well defined enhancing soft tissue mass with uniform density, occupying right infraorbital and paranasal area. No bony involvement was seen (Figure 2). He was referred to the Cytology lab for FNAC. The aspirate was mixed with blood.

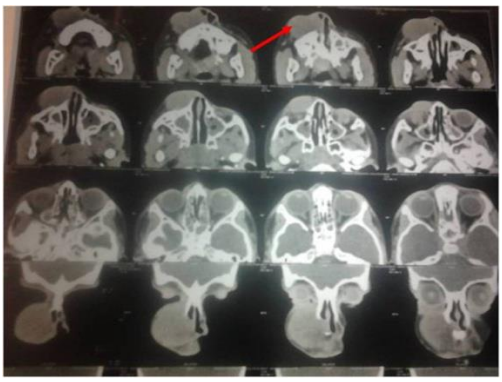

Figure 2: CT scan showing an enhancing soft tissue mass (arrow).

FNAC smears revealed highly cellular tumor, showing monomorphic cells. The cells were predominantly present solitary; few of them were seen in sheets and trabeculae. Some cells were present in loosely cohesive clusters. At places, pseudo-rosettes were noticed (Figure 3). The cells had bare nuclei with mild anisokaryosis. The nuclei had open chromatin and showed condensation at the margins with one to three prominent nucleoli. Mitotic figures were infrequent (Figure 4).

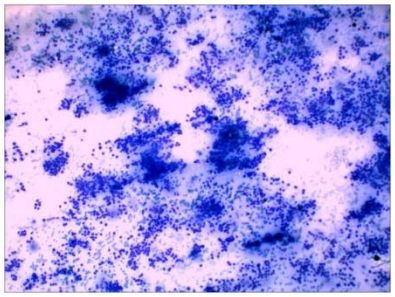

Figure 3: FNAC showing highly cellular smear with monomorphic population of cells in sheets and loosely cohesive clusters. (MGG stain) X100.

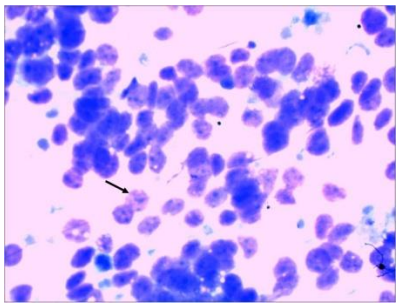

Figure 4: FNAC smear showing cells with bare nuclei and multiple nucleoli. (Arrow) (MGG stain) X 400.

The features were suggestive of small round cell tumor, probably PNET. Biopsy was advised for confirmation.

The biopsy tissue was soft, shiny brown fragment measuring 2.5x1.5x0.5 cm. Multiple sections including the deep part of specimen revealed a highly cellular pattern, composed of small round cells with thick and thin fibrous septa. The cells were clustered in the spaces surrounded by fibrous bands (Figure 5).

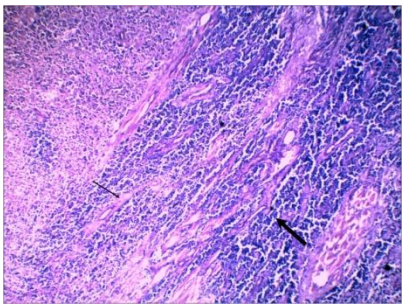

Figure 5: Highly cellular tumor (Thick arrow) with fibrous septa (Thin arrow) (H&E) X100.

The cells were round or oval or spindle in shape with large vesicular nuclei and scanty rim of cytoplasm. Few cells showed prominent nucleoli. Multiple skeletal muscle bundles were seen entrapped within the tumor. Occasional rhabdomyoblast like cells with eosinophilic cytoplasm and eccentric nucleus were also seen within tumor cells. No tumor giant cells were seen. Mitoses were infrequent (Figure 6).

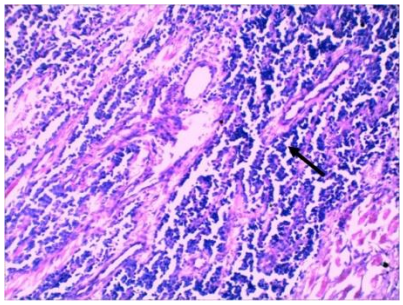

Figure 6: The cells appear clustered in the spaces surrounded by fibrous bands (arrow) (H&E) X400.

The diagnosis was offered as a "high grade malignant small round cell tumor" with a differential diagnosis of a) Alveolar/embryonal rhabdomyosarcoma and b) PNET. Immunohistochemistry was advised to reach a final diagnosis.

The immunohistochemistry was performed on tissue sections with available limited panel consisting of S-100, desmin, vimentin & cytokeratin. A few tumor cells revealed strong immunopositivity for desmin in cytoplasm. Intact skeletal muscle fibers within the tumor were also strongly immune-positive for desmin and showed prominent striations (Figure 7). However, S-100 vimentin & cytokeratin were negative. The tests for detection of myogenin, muscle specific actin (HHF-35) and marker for lymphoma were not done.

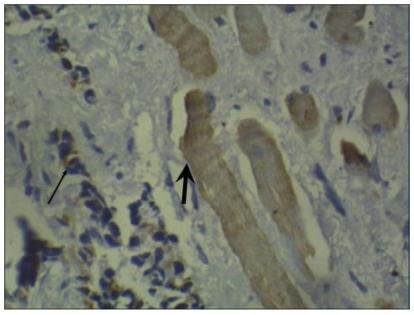

Figure 7: Immunopositivity in skeletal muscle cell cytoplasm (Thick arrow) and tumor rhabdomyoblast (Thin arrow) (Desmin) X400.

DISCUSSION

The cytological diagnosis for all small cell tumors is difficult unless the cytomorphology exhibits specific differentiation. The cytological diagnosis in this case was PNET as the tumor cells had small, round hyperchromatic nuclei, coarse chromatin, scant cytoplasm and occasional rosette formations. Alveolar RMS was ruled out due to absence of cells resembling rhabdomyoblast like eosinophilic cytoplasm and tumor giant cells.

RMS, a tumor derived from mesenchymal tissue, was first described by Weber in 1854.[3] Histomorphologically, pediatric RMS are classified as embryonal RMS (66% of cases), which is characterized by pronounced cellular pleomorphism, alveolar RMS (28%), undifferentiated RMS (4%) and anaplastic RMS (2%). In addition, embryonal RMS are subdivided into botryoid and spindle cell subtypes.[7]

In this case, the tumor cells in ARMS were relatively small with scant cytoplasm. They had regular round nuclei with a monotonous chromatin pattern. The cells where in aggregates and were interrupted by fibrovascular septa. Within these aggregates, areas of discohesion were seen, resulting in spaces that resembled pulmonary alveoli. Similar features were described by Barr et al in a case report.[8] Tumors that appear alveolar under the microscope, but do not have an identifiable PAXFOXO1 translocation, should be classified as embryonal.[9] WHO defined rhabdomyosarcoma as a highly malignant tumor of rhabdomyoblasts in varying stages of differentiation with or without cross-striation.[10]

Immunohistochemically, desmin, muscle specific actin and myogenin are considered to be of diagnostic value in RMS.[10] Our case showed strong immunopositivity with desmin.

The diagnosis of malignant small cell tumors is rather difficult as FNAC cannot differentiate between EWS, PNET and alveolar RMS. The cytological diagnosis of these tumors is usually based on clinical profile, cytology and routine microscopic examination.[11] In our case, the FNAC was very characteristic, which showed rosettes like structures with a few filaments inside these rosettes. The site, age and clinical presentation were indicating PNET/EWS. Alveolar RMS was considered even though tumor giant cells and eosinophilic cytoplasm were absent. A number of studies have addressed the issue of diagnosis of EWS/ PNET by FNAC based on immunohistochemistry.[12] Few authors have recommended that ancillary facilities may not be available in developing countries, hence tissue diagnosis may be offered often based on cytomorphological features of FNAC, as a life saving measures in seriously ill patients.[13] In the indexed case, though FNAC revealed PNET, the authors proceeded with tissue biopsy.

Microscopically, EWS/PNET is composed of uniform small round cells with round nuclei containing fine chromatin, scanty, clear or eosinophilic cytoplasm and indistinct cytoplasmic membranes. The term PNET has been used for tumors that demonstrate neuroectodermal features. PNET shows more frequent nucleoli, mitotic activity as well as necrosis and Homer-Wright rosettes. EWS/PNET is characterized by immunoreactivity for the surface antigen CD99/MIC2, which is expressed in up to 97% of cases.[14] The term Ewing's sarcoma is used for tumors which do not exhibit neuroectodermal differentiation. Use of myogenic markers, particularly myogenin, may be helpful in identifying few cases of EWS/PNET, noting that desmin positivity may occur in

rare peripheral neuroectodermal tumors. CD99, often used as a Ewing's tumour marker, may be positive in RMS.[5]

Some recent studies suggest that for diagnosing alveolar RMS, morphology should be coupled with fusion confirmation. All tumors that have histologic evidence of alveolar features (cytologically and/or architecturally) should be always evaluated with FISH technique. Astekar M et al. (2012) have found that hamotoxylin and eosin morphology and ultra-structure are needed to classify RMS, whereas immunohistochemistry acts only as auxiliary investigation.[10]

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