

**METASTATIC RHABDOMYOSARCOMA DIAGNOSED BY FINE NEEDLE  
ASPIRATION CYTOLOGY OF THE AXILLARY METASTASIS: A CASE REPORT**Tuba Kara<sup>\*1</sup>, Rabia Bozdogan Arpacı<sup>1</sup>, Ebru Serinsoz<sup>1</sup>, Didar Gursoy<sup>1</sup>, Caglar Citak<sup>2</sup>, Ayşe Polat<sup>1</sup>,<sup>1</sup>Department of Pathology, School of Medicine, Mersin University, Turkey.<sup>\*2</sup>Department of Pediatric Oncology, School of Medicine, Mersin University, Turkey.**\*Corresponding Author: Tuba Kara**

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Article Received on 19/07/2016

Article Revised on 10/08/2016

Article Accepted on 01/09/2016

**ABSTRACT**

Rhabdomyosarcoma (RMS) is the most common soft tissue tumor in childhood. The aim of the present case is to assess the role of fine needle aspiration cytology (FNAC) in the management of childhood RMS. A 17 year-old female patient was referred to the doctor due to a mass 10 cm in diameter on the left forearm and a palpable mass in the axilla. In microscopic examination of the biopsy from forearm a tumor having features consistent with alveolar RMS was observed and immunohistochemistry confirmed the diagnosis. FNAC was performed to the lesion in the axilla. Cytologically the cells were small and lymphocyte-like, with eccentrically located hyperchromatic nuclei and cytoplasmic vacuoles. The lesion was diagnosed as small round cell tumor, consistent with RMS with these findings. After a neoadjuvant chemotherapy protocol, transcondylar amputation was performed to the left forearm. After 11 months breast metastasis was confirmed pathologically in permanent histological sections.

**KEY WORDS:** Alveolar rhabdomyosarcoma; fine needle aspiration cytology; pediatric; metastasis.**INTRODUCTION**

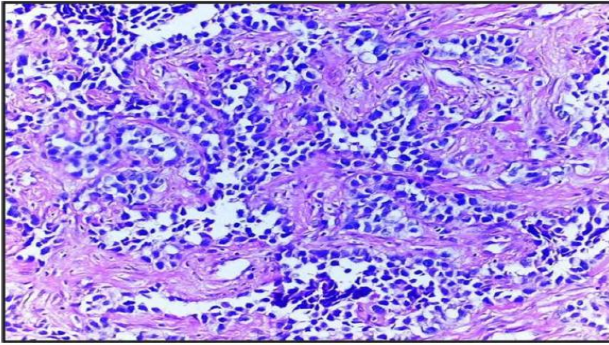
Rhabdomyosarcoma (RMS) is a malignant tumor which originates in the primitive mesenchymal cells- precursors of the striated skeletal muscle. The sites most affected by this tumor are the head and neck, trunk and the extremities.<sup>[1]</sup> It's one of the most common soft tissue sarcomas under the age 15, but is also common in adolescents and young adults. The most common metastatic sites are bone, bone marrow, lung and lymph nodes. However, the breast can be the site of the primary tumor or metastasis in some cases. Fine needle aspiration cytology (FNAC) acquired an important role in providing morphological diagnosis. It is quick, economical, and carries minor risks compared to surgical biopsy such as: infection, bleeding, pain and often considerable delay in diagnosis.<sup>[2]</sup> With this report our aim was to assess the role of FNAC in the management of childhood RMS.

**CASE REPORT**

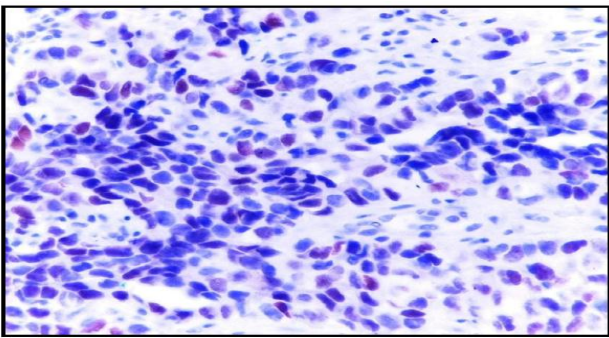
A 17 year-old female patient was referred to the department of orthopaedics due to a painful mass 10 cm in diameter on the left forearm and a palpable mass in the axilla about the last three months. Incisional biopsy was performed with a preliminary diagnosis of malignant fibrous histiocytoma. In microscopic examination the tumor was composed of ill defined aggregates of round or oval tumor cells which formed irregular alveolar spaces

(Figure 1). There was loss of cellular cohesion. The tumor cells showed immunohistochemical reactivity for vimentin, desmin, myogenin (Figure 2), S100; while they were negative for LCA, pancytokeratin, synaptophysin and chromogranin A. These findings were consistent with alveolar RMS. After the diagnosis of RMS, USG guided FNAC was performed to the lesion 5.5 cm in diameter in the axilla. Smears were air dried and stained with Giemsa and some were also wet fixed for Papanicolaou staining. The smears were cellular. The cells were small and lymphocyte-like with eccentrically located hyperchromatic nuclei and cytoplasmic vacuoles (Figure 3,4). The tumor cells showed immunocytochemical positivity for myogenin (Figure 5). A diagnosis of small round cell tumor, consistent with RMS was made with these findings. Treatment according to the Intergroup Rhabdomyosarcoma Study Group protocol (VAC: vincristine, actinomycin-D, and cyclophosphamide) was started. Transcondylar amputation was performed to the left forearm due to limited tumor regression after chemotherapy. Macroscopically the tumor mass was 12x5x3cm and consisted mostly of necrotic tissue. Microscopically, the tumor was composed mostly of differentiated rhabdomyoblasts which were positively immunostained with desmin and myogenin. After 11 months a lesion 47x22 mm in size was detected in the left breast which was suspicious for metastasis and tru-cut biopsy was

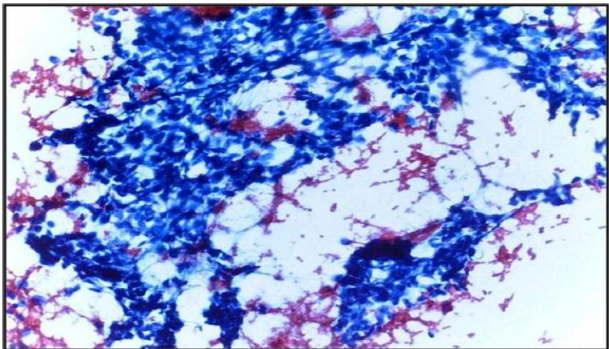
performed for diagnosis and RMS was confirmed pathologically in permanent histological sections.



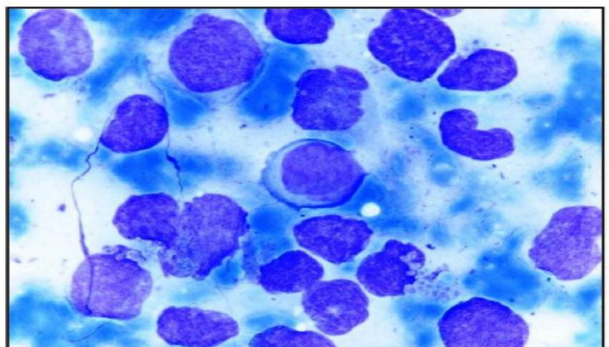
**Figure 1. Aggregats of round or oval, small and lymphocyte like tumor cells (HE, x200)**



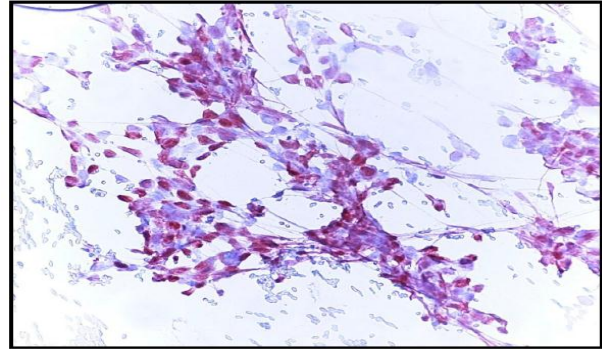
**Figure 2. Strong immunoreactivity with myogenin (Myogenin, x400)**



**Figure 3. Groups of small and primitive tumor cells (PAP, x200)**



**Figure 4. Small tumor cells with hyperchromatic nuclei (MGG, x1000)**



**Figure 5. Immonureactivity with myogenin in cytologic material (Myogenin, x 400)**

## DISCUSSION

Tumors originating in the soft tissues represent only 6% of all pediatric malignancies and 53% of these are rhabdomyosarcomas, which constitute 3.5% of all cancers in children under 14 years of age and 2% of cases in the 15-19 year age group.<sup>[3]</sup> The sites most affected by this tumor are the head and neck (44%), the trunk (41%) and the extremities (14.6%) and less commonly orbital cavity, intrathoracic and retroperitoneal regions.<sup>[1]</sup> There is a slight male predisposition for this tumor. Our patient was an adolescent female with lesions located in her left forearm and axilla.

With new treatment protocols using preoperative chemotherapy, the need for a quick, minimally invasive, and accurate diagnostic procedure has arisen.<sup>[4]</sup> Usually cytologic subclassification of adult soft tissue sarcomas is not possible, in fact this has no influence on initial therapy. In contrast, cytologic subtyping of pediatric sarcomas by FNAC seems highly accurate and is necessary for appropriate therapy.<sup>[5]</sup>

FNAC has been widely accepted as a reliable diagnostic modality in the pediatric population, and the value of FNAC in diagnosing childhood tumours has been documented in several reports.<sup>[4]</sup> Several authors have reported accuracy rates of FNAC ranging from 92–97% in distinguishing between benign and malignant lesions in children. Data on the accuracy of specific diagnosis are lower and range between 76–81% for childhood tumors.<sup>[2]</sup> Larger series are needed to support the cytological findings.

RMS belongs to the small blue round cell tumor family which includes lymphoma, neuroblastoma, primitive neuroectodermal tumor, Ewing sarcoma, Willm's tumor and small cell tumor. The clinical findings such as the site of the primary tumor and the age of the patient are important in differential diagnosis. These tumors can be classified as embryonal, alveolar and pleomorphic. The subtype has also predictive role in prognosis; alveolar and pleomorphic type having a less favorable prognosis than the embryonal type.<sup>[6]</sup>

Cytological findings; large, cytoplasm rich, tadpole or ribbon like tumor cells seen together with predominantly small and primitive tumor cells in the smears help distinguishing RMS from other small round cell tumors.<sup>[6]</sup> Cells with eccentrically located nuclei and abundant cytoplasm with multinuclear tumor giant cells in a background of mucosubstance help in the diagnosis. In addition presence of binuclear cells is an important clue for the diagnosis of alveolar subtype RMS.

On the other hand RMS exhibits a variety of morphologic pictures regarding cellular morphology and architectural patterns, even within the same histologic subtype. Therefore, a reliable subclassification into alveolar and embryonal RMS cannot always be made from FNAC smears. However, all cases suspected to be RMS must always be confirmed immunocytochemically since they could be confused even with some benign and malignant tumors with similar morphology.<sup>[7]</sup> FNAC material may be used for immunocytochemistry (cell block), conventional cytogenetic analysis, flow cytometry, and image analysis, and even for research purposes, with informed consent of the patient.<sup>[5]</sup> Desmin is positive even in the poorly differentiated rhabdomyoblasts, whereas myoglobin is positive almost entirely well differentiated rhabdomyoblasts.<sup>[8]</sup> Hence desmin is a more useful marker in the diagnosis of RMS than myoglobin which is more specific for rhabdomyoblastic differentiation.<sup>[6]</sup> Myogenin is also extremely sensitive and specific in defining rhabdomyoblastic lineage especially in alveolar subtype.<sup>[9]</sup>

Distant metastases are discovered at diagnosis in approximately 20% of children, more frequently in lungs, bone marrow, bones, and distant lymph nodes. Breast location of RMS is uncommon and has been reported in up to 6% of patients with metastasis.<sup>[10-12]</sup> In different series less than 40 cases with breast metastasis were reported.<sup>[11-13]</sup> The reported patients share common characteristics: most of them are adolescent girls with alveolar RMS like our case. The gender and age range support the hypothesis that the physiologic state of the breast might be a determining factor in the development of breast metastases. Howarth et al. suggested that the increased vascularity of the breast, due to the pubertal development phase, typical of the adolescent age, is responsible for the increased risk of hematogenous metastases in this specific site.<sup>[11]</sup> The predominance of alveolar histology may be explained by its propensity to develop metastatic lesions and higher frequency in adolescence, but may also represent a distinctive pattern of dissemination. Another characteristic of the reported series seems to be the location of the primary tumor in the extremities, as was the case in our patient. This association was more evident in the report by Howarth et al., in which all seven patients had the primary tumor located in the extremities.<sup>[11]</sup> Similar to the IRS study<sup>[12]</sup>, the site of primary RMS was confined to the extremities in 8 of 19 cases with breast metastases, at the time of the

diagnosis or at first relapse. Since breast investigation is not part of the usual diagnostic work up for patients with RMS, this information is important to include a specific recommendation for adolescent females in clinical protocols. Mammography has rarely been found helpful because of the poor image quality due to the dense fibroglandular structure of breasts in young girls; therefore ultrasound should be preferred to search for breast lesions and MRI should be the preferred imaging technique if further investigation is needed.<sup>[14]</sup> Unfortunately, the breast was not an isolated site of metastasis in our case, as the patients presented with two or more organs involved in disease dissemination. This may be related to a delay in diagnosis, but also to an intrinsic tumor aggressiveness. The poor prognosis, in spite of aggressive chemotherapy, confirms the need to explore different treatment strategies in these patients. In the meantime more aggressive local modalities of surgical treatment and/or radiotherapy of the breast lesions should be recommended.

In conclusion, FNAB is a safe method of establishing the diagnosis of RMS without delay and often can replace histology for pre-treatment diagnosis in the presence of reliable clinical data. Further experiences will make it possible to subclassify RMS with FNAC alone. Although breast metastasis in RMS patients is a rare event, an accurate clinical and radiographic or ultrasound evaluation of the mammary region, should be part of the usual diagnostic work up in adolescent girls with alveolar histology especially if the primary tumor arises in the extremities.

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