

Solid alveolar rhabdomyosarcoma with multiple cutaneous site presentation in a child

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ABSTRACT

Rhabdomyosarcomas (RMS) are the most common childhood soft-tissue tumors. Case reports of RMS presenting at multiple cutaneous sites simultaneously are extremely rare and most of these have been reported as of embryonal type which is the most common RMS in childhood. We present here a rare case of a 2-year-old child who presented to us with multiple cutaneous swellings that had grown over the past 6 months. Fine-needle aspiration cytology was performed from all the swellings and diagnosis of small round blue cell tumor was made. Biopsy from one of these swellings showed features of alveolar RMS (ARMS) (solid variant) that was confirmed on immunohistochemistry. ARMS are associated with a poorer prognosis compared to other RMS with higher rates of dissemination and mortality even after an initially good response to chemotherapy; hence, it becomes important to be aware of their unusual histological variants and accurately diagnose them.

Key words: *Atypical sites, Blue tumors, Muscle tumors, Pediatric neoplasms*

Soft-tissue tumors (soft-tissue sarcomas [STS]) are responsible for 6% of all childhood tumors and 53% of these are rhabdomyosarcomas (RMS), which are seen mostly in the head-and-neck regions, genitourinary system, and extremities [1]. Multiple cutaneous presentations of RMS are extremely rare and very few cases have been reported in the literature affecting predominantly males [2]. Alveolar RMS (ARMS) is usually found in adolescents and typically arises in the deep musculature of the extremities, unusual primary sites being head, neck, trunk, pelvis, and retroperitoneum [3]. Few cases, however, have been reported in newborns and neonates, with a female predominance, multiple cutaneous presentations and more aggressive course [4]. Here, we report a case of ARMS in a 2-year-old girl child with an unusual presentation (multiple cutaneous lesions) and unusual histopathology (a solid variant of ARMS [SARMS]).

CASE REPORT

A 2-year-old girl child presented to the department of pediatrics with complaints of multiple cutaneous swellings in the right thigh, left and right supraclavicular, and the right temporal region that had grown over the past 6 months one by one with the thigh swelling being the first one to be noticed. Her family history was insignificant. On examination, the swellings were firm, mobile, and non-tender and ranged from 0.5×0.5 cm to 1.5×1.5 cm in size, the thigh swelling being the largest (Fig. 1).

Her general condition and hematological profile were within normal limits. She was advised to get a cytological examination done. Fine-needle aspiration cytology (FNAC) was attempted from all of the above sites and showed similar cellular morphology. Smears were hypercellular with cells arranged in sheets and pseudopapillary fragments. The cells were small and medium-sized, uniform, round to ovoid, had hyperchromatic nuclei, high N: C ratio, granular chromatin, prominent nucleoli, and scant basophilic cytoplasm showing occasional vacuolations. Focal areas showed spindle cell morphology. Numerous bi and multinucleated tumor cells, mitotic figures, occasional rosettes, and few strap cells were also seen. The smears prepared from the thigh swelling showed additionally a markedly dense fibrillar background (Fig. 2). The findings were suggestive of a small round blue cell tumor (SRBT) and histopathological examination for confirmation was advised.

We received a biopsy from the thigh swelling in the form of multiple, small, and irregular gray-white tissue pieces. On histopathology, slides showed thick fibro-collagenous cores that were surrounded by sheets and clusters of small round cells which at few places showed a loose alveolar pattern and frequent perivascular rosetting. Cells showed mild pleomorphism with a round to ovoid nuclei, hyperchromatic nuclei with inconspicuous to single prominent nucleoli and a scant amount of cytoplasm. Occasional multinucleated cells and numerous mitotic figures were noted. Some sprinkling of atypical spindle cells was noted. Necrosis was also seen (Fig. 3).

The differentials considered were the SARMS and synovial sarcoma (SS). Immunohistochemistry (IHC) for myogenin, Myo D1, and transducin-like enhancer of split 1 (TLE 1) was done. Myogenin and Myo D1 were diffusely and strongly positive while TLE 1 was negative (Fig. 4). The case was thus finally diagnosed as a SARMS. On follow-up, we got to know that the patient had not undertaken any treatment and at the time of writing this paper had developed many more swellings.

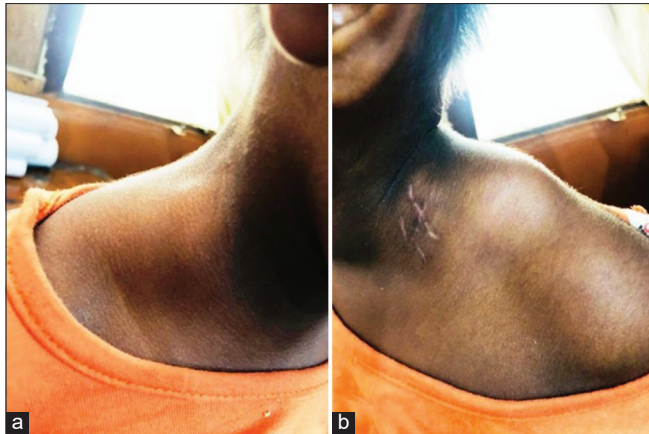


Figure 1: (a and b) Photograph of the patient showing right and left supraclavicular swellings

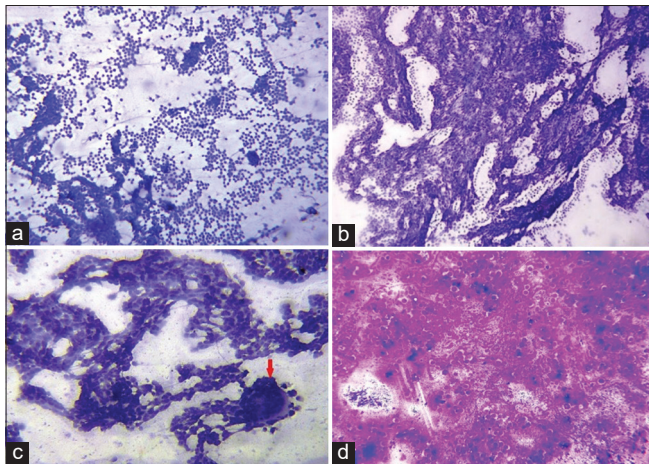


Figure 2: (a) Smears showing cellular small round tumor cells predominantly in sheets (PAP×10); (b) section showing areas of tumor cells predominantly in tight clusters (PAP×40); (c) sections (arrow) showing a multinucleated cell (PAP×40); (d) sections from the thigh swelling showing tumor cells lying in a dense collagenous background (May-Grünwald-Giemsa×10). PAP: Papanicolaou

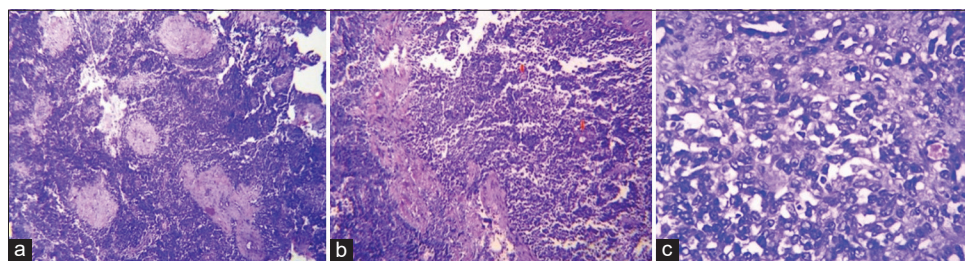


Figure 3: (a) Sections showing sheets of small round blue tumor cells densely adhered to thick collagenous cores (hematoxylin and eosin [H and E] ×4); (b) a high power view showing frequent perivascular rosetting (arrow) (H and E×10); (c) tumor cells having round to slightly oval nuclei, vesicular chromatin, prominent nucleoli, and scant eosinophilic cytoplasm with ill-defined cell borders (H and E×40)

DISCUSSION

RMS are thought to derive from myogenic precursor cells and belong to the group of SRBTs, which accounts for 4–8% of all STSs in children mostly occurring between the ages of 3 and 12 years [1,3]. Infants and young children tend to have embryonal RMS (ERMS), adolescents and young adults tend to have ARMS, and older adults tend to have pleomorphic RMS, although there is some overlap [5]. ARMS tends to show a bimodal peak, one in children <6 years of age and another in adolescents and young adults with a mean age of 15–20 years. ARMS typically arise in the deep musculature of the extremities and comprise approximately 50% of all extremity RMS. Unusual primary sites are the head, neck, trunk, pelvis, and retroperitoneum [3].

However, few cases have been reported in newborns and neonates, with a female predominance, cutaneous site presentations, and more aggressive course [4]. While congenital ERMS is often localized and has the same behavior as that observed in older children with a good prognosis, congenital ARMS is a highly malignant tumor, often occurring as the disseminated disease with a dismal prognosis. Moreover, ARMS often evolves with the development of brain metastases despite an initial good response to chemotherapy; hence, accurate identification is very important [6].

Cutaneous/subcutaneous presentation of RMS is rare with very few cases being reported till date in the literature, most of which were of an embryonal type and very few of alveolar type [2]. Among the non-RMS STS, SS are the most common STS affecting children with an estimated incidence rate of 2.75/100,000 [7]. Its occurrence as a cutaneous lesion is rare [8], even rarer in the head-and-neck region, where the common sites are the hypopharynx and parapharyngeal spaces. It is reported that childhood-onset SS bears a better prognosis as compared to adulthood-onset ones [9].

In the present case, FNAC smears showed a SRBT with cells arranged in discohesive sheets and pseudopapillary fragments; cytoplasm was showing occasional vacuolations; focal areas had spindle cell morphology; numerous bi and multinucleated tumor cells were seen; occasional rosettes and strap cells were seen. The smears prepared from the thigh swelling showed a markedly dense fibrillar background. In spite of the presence of rosettes and cytoplasmic vacuolations seen, the existence of frequent bi and multinucleated tumor cells seen ruled out the possibility

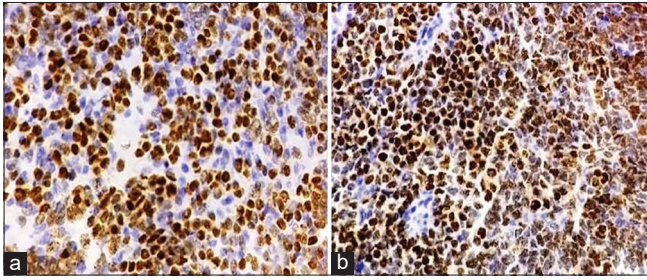


Figure 4: (a) Tumor cells showing strong positivity for myogenin (IHC×40); (b) tumor cells showing strong positivity for Myo D1 (IHC×40). IHC: Immunohistochemistry

of an extra-skeletal primitive neuroectodermal tumor (PNET). The fibrillar background and presence of occasional strap cells favored an RMS. However, in view of the focal spindle cells seen, a possibility of SS was also kept. Although vacuolations are not a feature routinely described in the cytology of RMS, in a study of pediatric ARMS, these have been mentioned [10].

Cases with multiple cutaneous lesions, as noted in the present case, are extremely rare and represent a diagnostic challenge since there are no clinical characteristics that differentiate this condition from other pathologies. A small round cell sarcoma in a child in a cutaneous/subcutaneous location calls for the differential diagnosis among ERMS, neuroblastoma, PNET/Ewing's sarcoma, lymphoma, granulocytic sarcoma, monophasic SSs, melanotic neuroectodermal tumors, etc. Factors to be considered are complete clinical data and results of hematological and radiological findings. Multiple sections need to be studied for specific features such as alveolar structures, rhabdomyoblastic differentiation, rosettes, and intracytoplasmic glycogen/pigment, etc. [11].

On histology, ARMS is highly cellular and often contains densely populated fields of small round blue cells. When this is the predominant or sole feature then the term “solid variant” applies. This variant tends to occur in younger children as compared to a classical variant which tends to occur in older children and adolescents. In the present case, this was the predominant arrangement of tumor cells with very focal areas showing an alveolar pattern. Similar to ours, Buch *et al.* have documented a case of solid ARMS in a 6-month-old baby with patent ductus arteriosus [11]. There are a few other case reports that mention SARMS diagnosed in children [12]. Rekhi *et al.* have described a mixed alveolar – ERMS in a 2-month-old child with multiple rapidly progressing cutaneous masses [13].

Separating solid foci of ARMS from the dense portion of ERMS are difficult. Cytologically, ERMS cells tend to have oblong shapes with oval nuclei and relatively bland chromatin, whereas ARMS cells tend to be larger and contain round, Ewing tumor like nuclei with central nucleoli and less cytoplasm [5]. According to Klijanienko *et al.*, on the fine-needle aspiration, alveolar subtypes are more cellular than the non-alveolar ones, exhibit more of alveolar structures, multinucleated giant cells with nuclei in wreath-like configuration, mitotic figures, and cytological atypia. Inversely, spindle-shaped cells and rhabdomyoblastic cells are more frequently seen in non-ARMS [10].

Neuroblastoma, another small cell tumor characterized by a diffuse pattern of small round cells and the presence of rosettes/pseudorosettes with pale eosinophilic material, is quite similar to ARMS. The frequently elevated level of urinary catecholamines and positivity for chromogranin/synaptophysin on IHC aids in the differential diagnosis [14]. Soft-tissue Ewing's sarcoma smears are highly cellular, have a tigroid background and comprise large pale cells with vacuolated cytoplasm and small dark cells with scant cytoplasm along with occasional rosette-like structures, but never show bi-multinucleate cells and are CD 99 positive.

Non-Hodgkin lymphoma comprises monomorphic malignant lymphoid cell population, and background shows lymphoid globules. It is leukocyte common antigen positive. Granulocytic sarcomas are generally associated with organomegaly and can be clinched on peripheral blood smear/bone marrow examination. SS smears comprise two morphologically distinct cell populations of epithelial and spindle sarcomatous cells. However, poorly differentiated forms can mimic a SRBT. Most cases are positive for TLE 1 and epithelial membrane antigen. Clear cell sarcoma (malignant melanoma of soft tissues) smears show dispersed round, polygonal, or spindle-shaped cells with a prominent nucleolus, binucleate or multinucleated giant cells with intranuclear cytoplasmic pseudo inclusions and clear to pale staining cytoplasm. Most cases are strongly positive for S-100 protein and HMB-45 [12].

Translocation t(2;13)(q35;q14) occurs in 60% of ARMS, and translocation t(1;13)(p36;q14) occurs in approximately 20% of ARMS. These translocations result in the expression of chimeric transcription factors PAX3-FKHR (PAX3-FOXO1) or PAX7-FKHR (PAX7-FOXO1), respectively. However, approximately 20% of ARMS are translocation negative [15] and more likely to be SARMS [11]. Such cases respond to an intensive chemotherapy regime, but their outcome remains unfavorable. Documentation of more such cases with treatment and clinical outcomes would be useful.

CONCLUSION

The SARMS is an uncommon tumor of pediatric age group, with only a handful of cases reported at multiple cutaneous locations. On cytology and histology, many SRBTs enter their differential diagnosis due to the absence of the specific alveolar pattern. SARMS, unlike conventional ARMS, are usually t(2;13)/(1;13) negative making their identification all the more challenging. A diligent search for certain specific RMS features and the typical IHC positivity for myogenin and Myo D1 may be helpful. ARMS are associated with a poorer prognosis compared to other RMS; hence, the importance of diagnosing them timely and accurately cannot be overemphasized.

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