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Case Reports

Primary Cutaneous Rhabdomyosarcoma

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We report an unusual case of primary cutaneous embryonal rhabdomyosarcoma presenting as a solitary skin lesion on the anterior chest of a 20-month-old child. The tumor was characterized by small, round to oval, poorly differentiated cells. Immunohistochemically, the tumor was negative for NSE, S-100 protein, LCA, and keratin but positive for muscle-specific actin, myoglobin, desmin, and vimentin, thus indicating the presence of myogenous differentiation. Ultrastructural analysis demonstrated thick and thin filaments. Special studies showed no evidence of a primary rhabdomyosarcoma in the patient at a more typical location, nor was there any evidence of metastases.
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Rhabdomyosarcomas are malignant mesenchymal neoplasms characterized by skeletal myogenic differentiation. Despite this cardinal feature, they are believed to derive from primitive mesenchymal rests rather than from skeletal muscle, and most lesions arise in extramuscular sites. In the past, evidence for skeletal muscle differentiation has depended upon identifying cross-striations or rhabdomyoblasts on hematoxylin- and eosin–stained tissue sections. Hence, only the better-differentiated cases displaying these characteristics could be diagnosed with any real confidence or accuracy. With the advent of diagnostic immunohistochemistry and electron microscopy, detection of earlier and more subtle evidence of myogenic differentiation is possible. Although they have been reported in virtually every location, the majority of these neoplasms occur in the head and neck regions or the genitourinary tract. In lesser numbers, they have been found in the extremities and—rarely—in the thorax, retroperitoneum, and biliary systems (1). Although previous case reports have indicated that rhabdomyosarcomas can arise from subcutaneous tissue, we report an unusual case of primary cutaneous rhabdomyosarcoma arising within the dermis in a 20-month-old child.

CASE REPORT

A 20-month-old male infant presented with a 1.2 × 0.6 cm pink-tan soft plaque containing a 0.6-cm raised nodule located 2.5 cm medial to the left nipple. This lesion began as a hyperpigmented macule that appeared when the patient was 2 months old, and gradually increased in size. The patient was an

otherwise healthy twin delivered at 39 weeks by caesarean section. The other twin is alive and well. The patient's lesion was biopsied and re-exised for diagnosis.

Subsequent to the pathological diagnosis, the patient underwent staging procedures in search of a primary rhabdomyosarcoma at a more common location or evidence of metastatic disease. Contiguous 10-mm axial CT scans from the thoracic inlet through the pelvis, bilateral bone marrow biopsies, and whole-body bone scan all yielded normal findings. The patient received a course of chemotherapy, which was well tolerated. He has remained free of recurrence and without evidence of metastatic disease after 10 months of follow-up.

PATHOLOGY

Tissue was fixed in 10% buffered formalin solution and embedded in paraffin. Additional sections were cut for immunohistochemistry, and an avidin-biotin peroxidase-antiperoxidase technique was applied using commercially available antisera. For electron microscopy, fresh tissue was placed in 1% glutaraldehyde and postfixed with 2% osmium tetroxide. It was then embedded in resin, stained

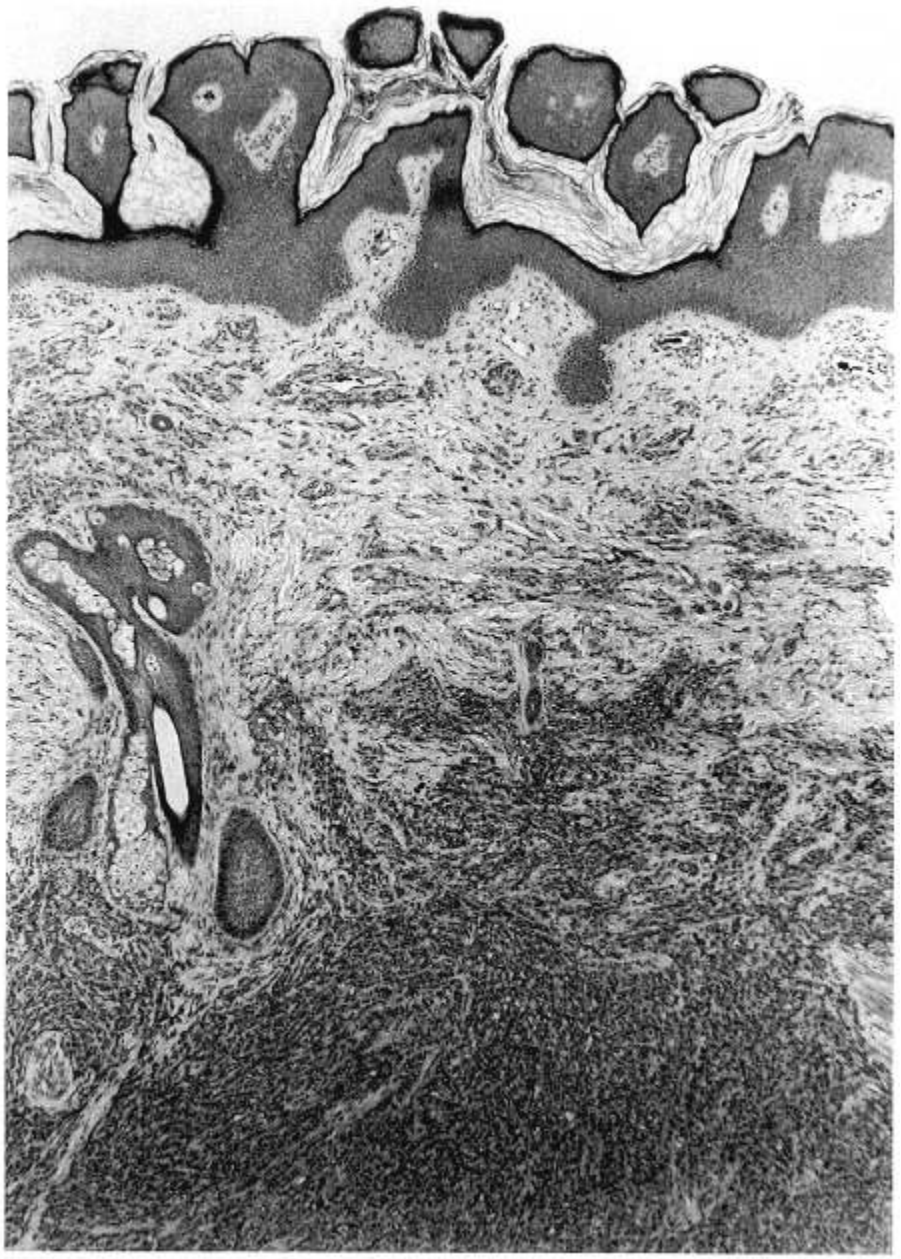

FIG. 1. Biopsy specimen showing epidermal nevus and monomorphous dermal infiltrate of small round cells.

with uranyl acetate/lead citrate, and examined using a JEOL IOO-S electron microscope.

By light microscopy, the biopsy specimen and re-excised tissue demonstrated a diffuse infiltration of the dermis by a monomorphous population of small, round to oval cells (Fig. 1). These cells had a streaming appearance through the more superficial dermal collagen and tended to spare the adnexal structures. Dense collections of neoplastic cells were noted in the deep dermis. Virtually all cells had a prominent, hyperchromatic nucleus and scant cytoplasm. A few isolated cells were surrounded by a rim of eosinophilic cytoplasm without apparent cross-striations (Fig. 2). Mitotic figures were numerous, but cellular anaplasia and pleomorphism were absent. In addition to the findings in the dermis, the overlying epidermis showed moderate hyperkeratosis and papillomatosis (Fig. 1).

Immunohistochemical studies revealed cytoplasmic reactivity for vimentin, muscle-specific actin, myoglobin, and desmin (Fig. 3). Neuron-specific enolase, S-100 protein, leukocyte common antigen, and keratin were all nonreactive in the neoplastic population. Histochemical reaction with chloro acetate esterase (CAE) was also negative.

Small, primitive-appearing cells with regular, rounded nuclei and scanty cytoplasmic organelles were seen on electron microscopy. A minor population of neoplastic cells were somewhat larger and displayed one or more of the following features: disorganized z-bands with thick and thin filaments attached to z-discs (Fig. 4), sarcolemmal-like base-

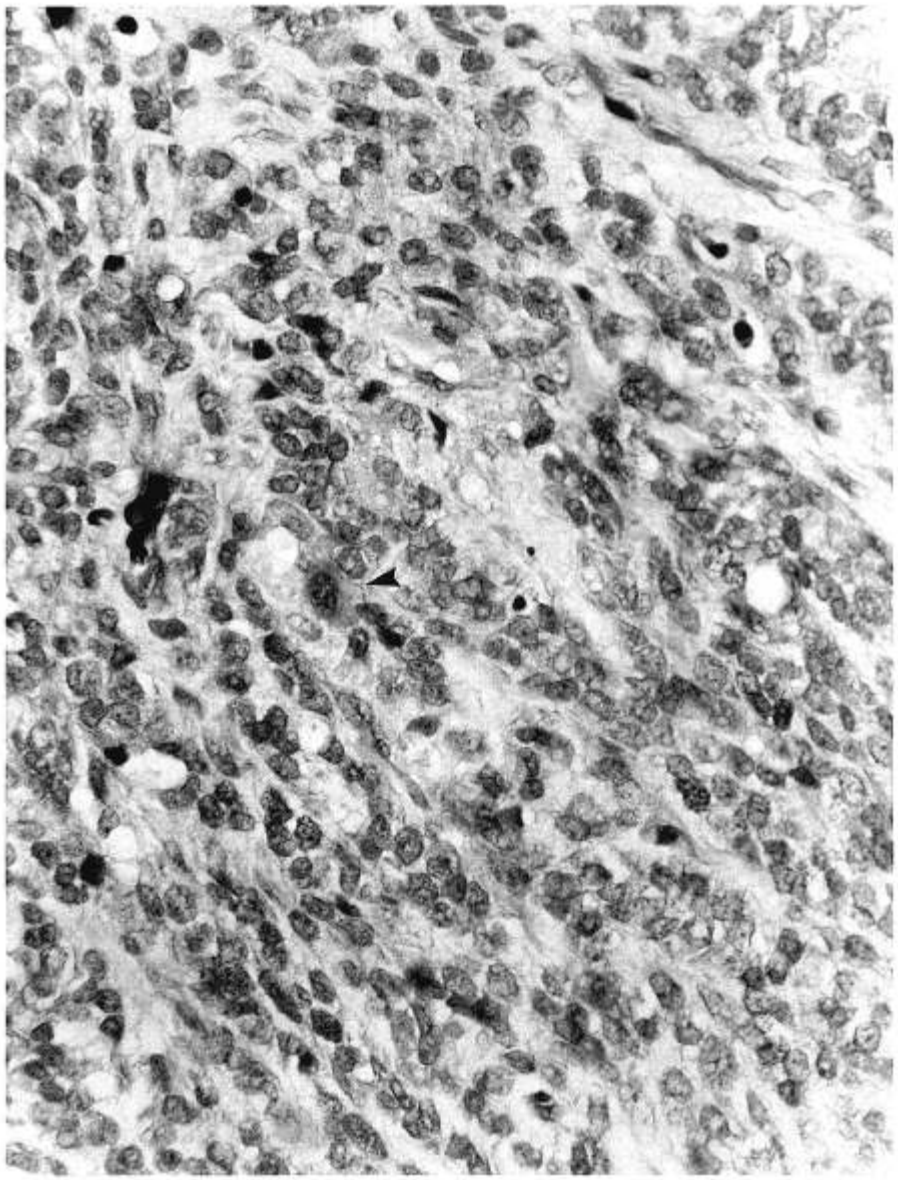

FIG. 2. Rhabdomyoblast (arrow) with eccentrically placed nucleus and abundant eosinophilic cytoplasm.

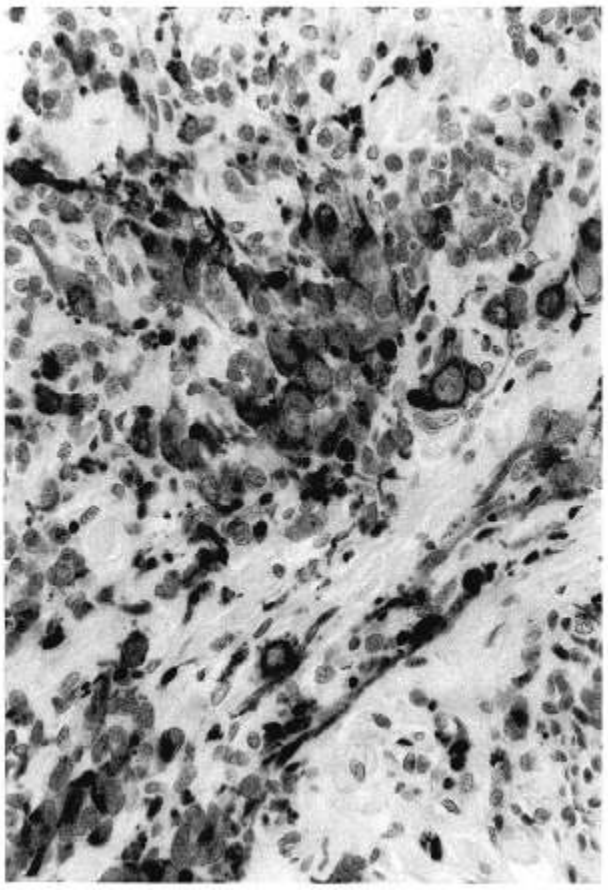

FIG. 3. Tumor cells demonstrating strong desmin positivity in cytoplasm.

ment membrane, or polyribsomes attached to filaments.

DISCUSSION

The clinical presentation of a solitary, nodular, and hyperpigmented cutaneous lesion in this infant was not especially disturbing until histological examination revealed a uniform small-cell infiltrate replacing a large part of the dermis. The epidermal changes of acanthosis and papillomatosis were consistent with an epidermal nevus. However, the monomorphous dermal population yielded the differential diagnosis of a "small, round-cell neoplasm" (4). In a child of this age, the most likely possibilities based upon the histopathologic findings are neuroblastoma or a hematolymphoid infiltrate. However, these neoplastic processes generally have multiple cutaneous nodules. Furthermore, a neuroblastoma metastatic to the skin often fulfills the clinical criteria for stage IV-S disease with bone marrow or hepatic involvement (14). Acute nonlymphoid leukemias of monoblastic or myelomonocytic phenotypes and B- and T-cell lymphomas have been reported in children. In a high proportion of cases, these patients are 1 month through 2 years of age (10,11,18). Other possible small, round-cell tumors include rhabdomyosarcoma, Ewing's sarcoma, and peripheral primitive neuroectodermal tumor. Cutaneous metastases of these tumors are extremely rare.

In addition to the small, round-cell neoplasms, there are also the large mononuclear cellular lesions including histiocytosis X (Langerhans' cell granulomatosis) and the non-Langerhans' cell infiltrates of the dermis. A familiar example of the latter is the juvenile xanthogranuloma with characteristic Touton giant cells (15). Furthermore, there are a number of other histiocytic proliferations of the dermis that have been less readily classifiable in terms of their mononuclear phagocytic or mesenchymal derivation (8). These lesions are more often solitary than multiple in skin. Involvement of deep soft tissues, bone, and organs (lungs, liver) are rare manifestations (14).

Primary cutaneous neoplasms are very uncommon in the pediatric population (6). Sporadically occurring basal cell carcinomas and malignant melanomas are recognized entities in children. They can be associated with the nevoid basal cell carcinoma syndrome, xeroderma pigmentosum, or the dysplastic nevus syndrome. Malignant melanoma and other neural crest–related small-cell and spindle cell neoplasms have been reported in giant congenital melanocytic nevi. Some of these small-cell neoplasms have rhabdomyoblastic elements in addition to melanocytes. Dermal-based, nonepithelial neoplasms in childhood are principally vascular (e.g., hemangioma, lymphangioma), mast cell, fibrohistiocytic, or myofibroblastic in origin.

The present case of a primary embryonal rhabdomyosarcoma in the dermis of a young child is an extraordinary event, as judged by the combined experience of the authors and a review of the literature. Wiss et al. reported two cases of rhabdomyosarcoma involving the dermis of the face in patients 12 months old and 19 years old (17). One lesion was located on the nasolabial fold; the other was on the right cheek. In both cases, several months passed before a pathologic diagnosis was established. Biopsy specimens showed rhabdomyosarcomas with alveolar features: The tumors appeared to arise in the subcutaneous tissues, with secondary extension into the overlying dermis.

In our patient, there was an 18-month interval between the initial appearance of the lesion and biopsy. The development of a small nodule in a soft,

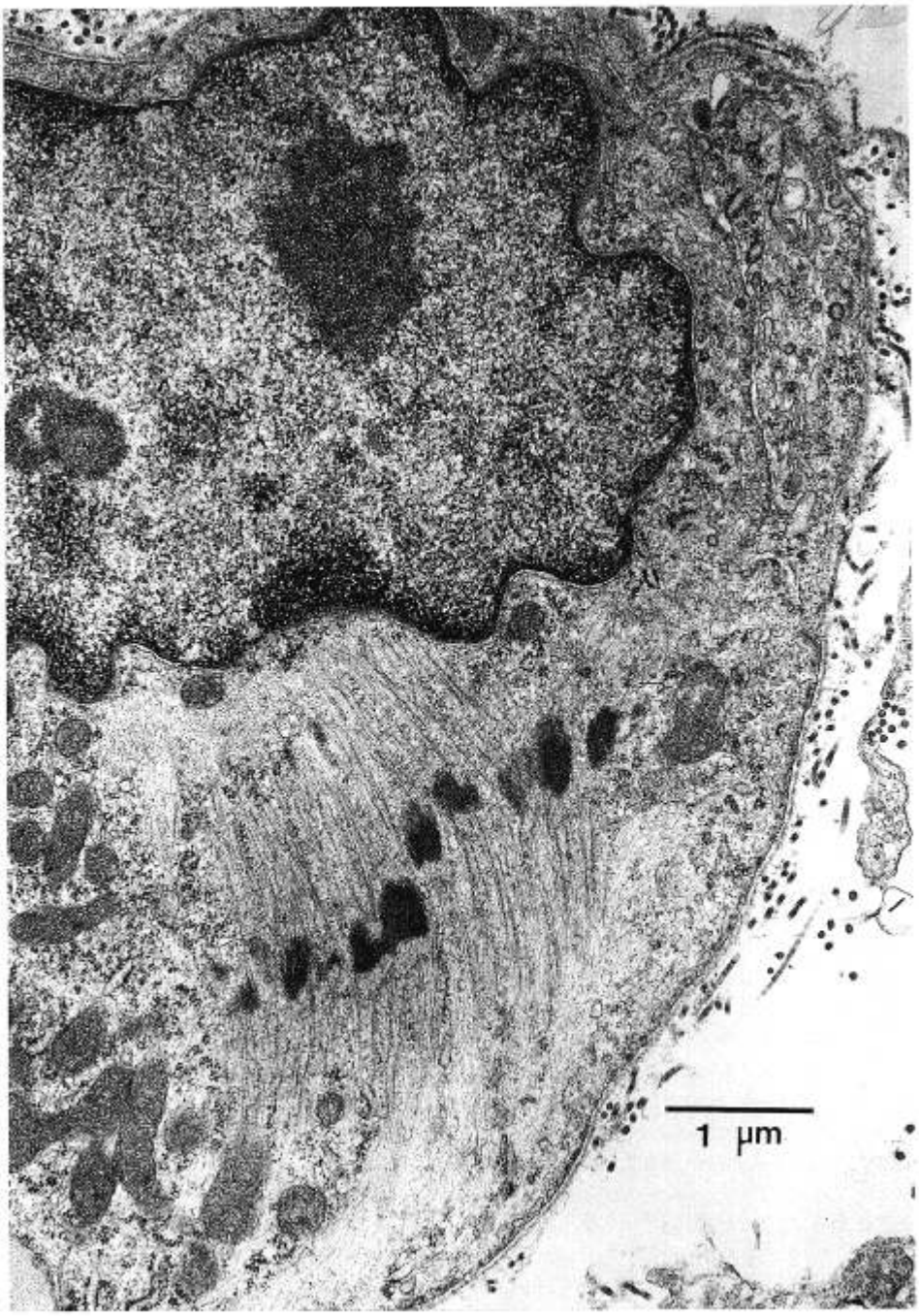

FIG. 4. Large tumor cell containing thick and thin filaments attached to z-discs.

plaque-like lesion was the cause for clinical concern. The neoplasm had features of embryonal rhabdomyosarcoma and was confined to the dermis. The tumor apparently arose in this site, since local resection—including the underlying ribs—disclosed complete absence of tumor in the subcutaneous tissues. From this perspective, our case is unique as a primary rhabdomyosarcoma of the dermis.

One other curious aspect of this case was the presence of epidermal nevus-like changes that probably accounted for the hyperpigmented macule noted at 2 months of age. A histogenetic relationship between an epidermal nevus and a rhabdomyosarcoma is difficult to establish; yet Dimond and Amon (5) described the case of a 15-month-old boy with a large epidermal nevus of the neck and trunk who developed an embryonal rhabdomyosarcoma

of the bladder. Other congenital disorders associated with rhabdomyosarcoma are von Recklinghausen neurofibromatosis and nevoid basal cell carcinoma syndrome (4). The latter syndrome can also be found to coexist with fetal rhabdomyosarcomas (9)—an entity that should be mentioned in light of the fact that immunohistochemical and electron-microscopic findings in this case indicated a rhabdomyoblastic origin. However, the prominent mitotic activity and undifferentiated appearance of this child's tumor would rule against fetal rhabdomyoma.

The diagnosis of rhabdomyosarcoma was established through the combined application of electron microscopy and immunohistochemistry. Some primitive rhabdomyosarcoma may have only basement membrane–like material adjacent to the plasma membrane; however, thick and thin filaments with z-bands were noted in our case.

Various muscle-specific antigens have been evaluated for their specificity and sensitivity in the detection of rhabdomyosarcoma (7,12,13). In our experience, the combination of vimentin, desmin, and muscle-specific actin has proven most useful. Myoglobin was also reactive in this case, but, desmin and myoglobin are less consistently positive in embryonal rhabdomyosarcomas than vimentin and muscle-specific actin in the experience of one of us (L.P.D.). Vimentin reactivity was detected in the small, primitive tumor cells, thus supporting the hypothesis that rhabdomyosarcomas originate from uncommitted mesenchymal cells whether they are present in the bladder, orbit, middle ear, or dermis. Vimentin is known to be present in the early stages of normal muscle cell differentiation, when it is co-expressed with desmin (2). Anomalous expression of other intermediate filaments, keratin, and S-100 protein also has been reported (3), but it was not seen in this case. The present case points out the need for a panel of several markers whenever a small-cell neoplasm is being evaluated, because an unlikely diagnosis such as cutaneous rhabdomyosarcoma may, in fact, emerge. □

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