Cutaneous Mesenchymal Tumors in Childhood

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I. Introduction

Cutaneous tumors are relatively common in children, and most are benign. Many palpable superficial nodules are reactive lymph nodes or cysts, and the majority are diagnosable by their clinical features. Only 1-2% of all pediatric skin tumors are malignant. As a group, mesenchymal tumors account for a small proportion of all skin nodules in childhood, but they form a disproportionately large subset (approximately 1/3, with 25% of these being rhabdomyosarcoma) of malignant cutaneous tumors in childhood. The possibility of a cutaneous metastasis of a mesenchymal tumor or an unusual mesenchymal proliferation originating in a congenital melanocytic nevus must also be considered.

II. Learning objectives

Upon completion of this presentation, participants should be able to:
1.) Describe the diagnostic spectrum of cutaneous mesenchymal neoplasms in childhood, exclusive of vascular lesions.
2.) Apply a morphologic pattern-based approach to differential diagnosis, in conjunction with clinical information and adjunct tests.
3.) Diagnose primary cutaneous neoplasms and cutaneous metastases of sarcomas in childhood.

III. Round and epithelioid cell tumors

Cutaneous round and epithelioid cell tumors in children include rhabdomyosarcoma, Ewing sarcoma, clear cell sarcoma of soft parts, myoepithelioma, malignant rhabdoid tumor, epithelioid sarcoma, and epithelioid malignant peripheral nerve sheath tumor. Among these, cutaneous rhabdomyosarcoma is the most common type of cutaneous sarcoma in children and may be primary, metastatic, or disseminated. Alveolar, embryonal, and spindle cell/sclerosing types of rhabdosarcomas can all involve skin. Cutaneous Ewing sarcoma can also be primary, metastatic, or disseminated. Some evidence suggests that primary cutaneous Ewing sarcoma may be a clinically favorable subtype, especially when the tumor is small. Other cutaneous tumors with EWS gene rearrangements may sometimes involve the skin, especially angiomatoid fibrous histiocytoma, myoepithelioma and myoepithelial carcinoma, and clear cell sarcoma. Malignant rhabdoid tumor can occur in the skin as a primary, metastatic, or congenital disseminated form, typically in newborns and infants and with loss of nuclear INI-1 protein expression in most cases. Epithelioid sarcoma in children has a predilection for the head and neck, including the oral cavity, in addition to the more usual sites on the
extremities and perineal region. Other unusual cutaneous mesenchymal epithelioid and round cell tumors include epithelioid malignant peripheral nerve sheath tumor, mesenchymal chondrosarcoma with cutaneous involvement, and a variety of vascular tumors with epithelioid morphology. Useful diagnostic adjuncts include immunohistochemistry (especially MyoD1, myogenin, muscle specific actin, desmin, CD99, synaptophysin, S100 protein, HMB45, Melan A, INI-1, cytokeratin, epithelial membrane antigen, and glial fibrillary acidic protein as well as lymphoid markers), assessment for gene rearrangements (such as \textit{EWSR1, PAX-FOXO, SMARC1BI, SYT} and \textit{FUS}), and in selected cases mutation analysis for \textit{SMARC1BI} or \textit{BRAF}.

IV. Spindle cell and myxoid tumors

Spindle cell and myxoid tumors with cutaneous involvement in children include myofibroma, a variety of cutaneous fibroblastic and myofibroblastic tumors, fibrous histiocytoma and its variants, plexiform fibrohistiocytic tumor, smooth muscle tumors, nerve sheath tumors, and lipoblastoma. Myofibroma is a solitary, multiple, or generalized tumor with an occasional familial pattern and occurs in infancy to adulthood, although most cases occur within the first two years of life. It forms a histologic continuum with myopericytoma and infantile fibrosarcoma, but unlike infantile fibrosarcoma, myofibroma lacks a gene rearrangement of \textit{ETV6-NTRK3}. Cutaneous fibroblastic-myofibroblastic tumors that present particular diagnostic challenges in children include giant cell fibroblastoma, dermatofibrosarcoma protuberans, infantile fibrosarcoma, primitive myxoid mesenchymal tumor of infancy, and low grade fibromyxoid sarcoma. These can usually be distinguished with a combination of clinical and histologic features, immunohistochemistry, and selective genetic tests on tumor tissue. Fibrohistiocytic tumors such as fibrous histiocytoma and its variants, nerve sheath tumors, and atypical fibroxanthoma can occur in children, but are relatively common throughout life and are not discussed in further detail in this presentation. Other spindle cell tumors that offer particular diagnostic challenges in children include plexiform fibrohistiocytic tumor, smooth muscle tumor of uncertain malignant potential (in the context of immunosuppression), dermal nerve sheath myxoma, and lipoblastoma. Useful diagnostic adjuncts include immunohistochemistry (smooth muscle actin, muscle specific actin, desmin, h-caldesmon, myogenin, myo-D1, CD34, MUC4, epithelial membrane antigen, claudin, GLUT1, S100 protein, HMB45, Melan A, and GFAP), gene rearrangement studies (\textit{ETV6-NTRK3, COL1A1-PDGFB, FUS-BBF2H7, ALK, PLAG1}), and EBV in-situ hybridization.

V. Unusual mesenchymal proliferations in congenital melanocytic nevi

Although congenital melanocytic nevi are very common, malignant melanoma and other mesenchymal neoplasms originating in melanocytic nevi in childhood are quite rare. The mesenchymal tumors are histologically complex neoplasms that reflect the capacity of the neural crest for divergent differentiation. Histologic patterns encountered in these rare, complex growths include small round cells, spindle cell components with melanin or composed of neural supportive tissue, epithelioid elements with or without melanin, neuronal or ependymal proliferations, specific types of sarcomas, including malignant
peripheral nerve sheath tumor and rhabdomyosarcoma, or other combinations including unclassifiable malignancies. Morphologic criteria for malignancy in this context are not well-defined.

VI. References


