Lipoblastoma

Appreciation of an Expanded Spectrum of Disease Through Cytogenetic Analysis

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Lipoblastomas are rare soft tissue tumors that predominantly affect the pediatric population. We describe a lipoblastoma of the right hand in a 16-month-old boy. Radiographically the tumor appeared large but fairly well circumscribed and composed primarily of fat. Pathologic evaluation revealed variably sized lobules of adipose tissue and myxoid immature mesenchymal tissue separated by prominent fibrous trabeculae. Cytogenetic analysis showed a clonal chromosomal rearrangement with a breakpoint involving chromosome 8q11.2, confirming the diagnosis of lipoblastoma and thus helping to expand the clinicopathologic spectrum of tumors in this diagnostic category.

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REPORT OF A CASE

The patient was a 16-month-old, otherwise healthy boy who presented with an enlarging right hypothenar mass. His parents first appreciated the mass 4 months earlier and believed it to have nearly doubled in size. There was no recollection of trauma or infection. Physical examination revealed a healthy-appearing boy with an approximately 4 × 2-cm soft mass apparently based in the right hypothenar region and distorting the whole ulnar aspect of the hand; there was no discoloration, infection, or ulceration (Figure 1, A).

RADIOLOGIC FINDINGS

Ultrasound examination showed a heterogeneous mass with multiple echotextures. It was well defined and encapsulated with no demonstrable increased Doppler signal. Magnetic resonance imaging demonstrated a fairly well-defined enhancing mass lateral to the fifth metacarpal (Figure 1, B). It was heterogeneous with some central vacuolated areas. The mass was 3 cm in greatest diameter and involved the entire hypothenar region, extending through Guyon canal along the flexor retinaculum, as well as into the carpal canal along the flexor tendons.

PATHOLOGIC FINDINGS

Gross examination of an incisional biopsy specimen revealed 3 fragments of yellow-tan fibroadipose tissue admixed with firmer white tissue. Histologic examination revealed a fibrofatty lesion consisting of variably sized lobules of adipose tissue separated by fibrous septa (Figure 2, A through D). The lobular tissue consisted of variably sized adipocytes in a moderately myxoid background. Within myxoid areas the nuclei took on a stellate to slightly spindled configuration. Occasional cells showed cytoplasmic vacuolization causing indentation of the nucleus. The septa were moderately cellular, containing fibroblasts with narrow to stellate nuclei and abundant collagen. In several locations the boundary between the septa and the adipose tissue was difficult to discern, as the adipocytes appeared to be intermixed with the septa. Blood vessels varied in size with the largest vessels restricted to septa. Immunohistochemical staining was performed on paraffin-embedded sections; the stellate to spindled cells within the myxoid matrix were positive for S100, CD10, desmin, fascin, vimentin, glial fibrillary acidic protein, CD34, and bcl-2 and negative for glut-1, CD68, CD99, smooth-muscle and muscle-specific actins, and myogenin. NKIC3 was positive in fibroblasts only. Of note, a consultant with expertise in soft tissue pathology offered a diagnosis of lipofibromatosis.

CYTOGENETIC FINDINGS

Cytogenetic analysis of the biopsy specimen revealed 9 of 20 cells with the following karyotype: 46,XY, add(4)(q31),add(8)(q11.2),add 17(q21) (Figure 3). Fluorescence...
Figure 1. A, A large hypothenar mass distorted the right hand. B, Magnetic resonance imaging showing a heterogeneously enhancing mass expanding the tissue lateral to the fifth metacarpal bone.

Figure 2. A, Low magnification shows adipose tissue traversed by fibrous septa of variable thickness (hematoxylin-eosin, original magnification $\times 10$). B, Area of mature adipocytes comprise the majority of the lesion (hematoxylin-eosin, original magnification $\times 60$). C, Occasional myxoid areas are present (hematoxylin-eosin, original magnification $\times 60$). D, Desmin positivity is seen in elongated spindle cells with tapered cytoplasm (original magnification $\times 100$).

Figure 3. Giemsa-banding analysis of metaphase chromosomes shows a rearrangement in 8q11.2 (arrow), characteristic of lipoblastoma. Brackets identify the derivative chromosome 4 and additional material on chromosome 17.
We have described a 16-month-old boy with a large hypothenar lesion histologically and cytogenetically consistent with lipoblastoma/lipoblastomatosis. Lipoblastomas are benign pediatric soft tissue masses characterized by genetic alterations involving the PLAG1 oncogene located on chromosome 8. These lesions, seen mostly in boys younger than 3 years, tend to occur primarily on the extremities. The diagnosis or exclusion of lipoblastoma by histologic examination alone is difficult given the diverse histologic patterns seen in this lesion. Lipoblastomas may show a range of maturation, with immature lipoblasts easily distinguishing a lesion as lipoblastoma, whereas more mature lesions may have histologic overlap with lipoma, fibrolipoma, and lesions of fibrofatty overgrowth syndromes (eg, macroactyly or Proteus syndrome). Myxoid soft tissue tumors such as neurothekeoma, myxoid lipo-sarcoma, or low-grade fibromyxoid sarcoma may also enter the differential diagnosis, particularly with more myxoid variants of lipoblastoma. The small nature of some incisional biopsies may add to the diagnostic difficulty. A further diagnostic problem is the recent innovation of the term lipofibromatosis as a diagnosis for a range of pediatric fibro fatty lesions (including some overgrowth syndromes) most often occurring in the hands. Histologically, lipofibromatosis has been described as consisting of a high proportion of adipose tissue with a fibromatosis-like growth of fibroblasts partitioning lobules of fat. A few of the reported cases have had lobules with a myxoid appearance as may be seen in lipoblastoma. Proponents of the category of lipofibromatosis note that the degree of cellularity in the fibroblastic component is generally greater in lipofibromatosis than in lipoblastoma. Emerging data show that desmin immunostaining, highlighting septal and paraseptal spindle cells in lipoblastoma, is a sensitive marker and appears helpful diagnostically in separating lipoblastoma from its mimics.

The diagnosis of lipoblastoma can be confirmed with cytogenetic testing because these tumors are cytogenetically unique, for the most part containing clonal chromosomal rearrangements involving the 8q11-13 region. Some lipoblastomas have been reported to contain a polysomy for chromosome 8 but lack a specific translocation. In recent studies of lipomatous tumors, 8q11-13 rearrangement was found in a broader spectrum of adipose lesions than would have been predicted by histologic examination alone.

The case presented herein illustrates the evolution of diagnostic surgical pathology, which has recognized “signature” genetic alterations in many tumors. Identification of cytogenetic abnormalities has been incorporated into diagnostic practice, yielding an appreciation of a broader histologic spectrum of individual tumors. The case also illustrates how a diffuse lesion of the hand that might have been labeled by some as a lipofibromatosis clearly falls within the category of lipoblastoma.

**References**