

## Fibrochondrogenesis—A Lethal, Autosomal Recessive Chondrodysplasia With Distinctive Cartilage Morphology

The lethal neonatal osteochondrodysplasias are a heterogeneous group of disorders that can be distinguished from each other by radiologic and histopathologic criteria. Fibrochondrogenesis, a neonatally lethal, short-limbed skeletal dysplasia, was first described in 1978 in a single patient who was the offspring of a consanguineous mating. This disorder was named "fibrochondrogenesis" because of a distinctive fibrosis of the growth plate cartilage. In these two articles, four more patients with this syndrome are described and the clinical, radiographic, and morphologic features are defined.

The main clinical features were short-limbed, rhizomelic-type neonatal dwarfism, a relatively large head, a round flat face with prominent eyes, cleft palate (in two of four patients), and a small chest. All four were sporadic, nonconsanguineous cases.

Radiographically, the long bones were short and dumbbell shaped, with broad metaphyses. The ribs were short and cupped. The iliac bones were small and rounded. Dif-

fuse platyspondylia was present, with superior-inferior clefting defects and pear-shaped bodies.

Histological examination of chondro-osseous tissue revealed peculiar pathognomonic abnormalities of the cartilage. The resting cartilage was hypercellular, with round or spindle-shaped fibroblastic-appearing cells. The matrix appeared to be fibrous, with dense septae. At the growth plate, the cells were clustered in irregular nests within a fibrous matrix. The bone appeared normal in structure. Transmission electron microscopy of the cartilage revealed a fibrous matrix surrounded by round or fibroblast-like chondrocytes. The fibrous-appearing matrix was composed of thick-banded, densely packed collagen fibers. Proteoglycan granules were deficient in these areas.

These findings suggest either a defect of Type II collagen synthesis or structure, or an abnormality in the aggregation of collagen fibers secondary to a deficiency or abnormality in proteoglycans. Although this disorder was first distinguished on the basis of the peculiar morpho-

logic cartilagenous abnormalities, the radiographic features have now been recognized as quite distinctive.

Whitley CB, Langer LO, Ophoven J, et al: *Am J Med Genet* 1984;19:265-275; and Eteson DJ, Adomian GE, Ornoy A, et al: *Am J Med Genet* 1984;19:277-290.

**Editor's comment**—*The 1983 Conference for International Nomenclature of Constitutional Disease of Bone (Paris) enumerated ten lethal osteochondrodysplasias identifiable in the newborn period. Several new osteochondrodysplasias are identified each year. An accurate diagnosis must be made to provide meaningful prognostic information and appropriate genetic counseling. The differential diagnosis of these disorders depends on clinical, radiographic, and/or morphologic criteria, since their basic biochemical defects have not yet been elucidated.*

*Most of the severe neonatal disorders can be diagnosed prenatally by careful serial ultrasound examinations during the second trimester.*