Heterogeneity of Chondrodysplasia Punctata*

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Summary. Based on the experience of the Kiel registry of bone dysplasias and on an extensive review of the literature, the clinical and genealogic data of two major types of Chondrodysplasia punctata are presented and discussed.

The Conradi-Hünermann type of C.p. with predominantly epiphyseal, frequently asymmetric calcifications and dysplastic skeletal changes was reported in combination with cataracts in 17% and with skin changes in 28% of cases. It has a relatively good prognosis and is possibly caused by a dominant mutation. Genetic heterogeneity and the influence of environmental factors cannot be excluded in this type.

The rhizomelic type of C.p. with severe, symmetrical proximal shortening of the extremities, and marked metaphyseal changes was reported to be combined with cataracts in 72% of the cases and with skin changes in 28%. It seems to be a lethal condition leading to death usually before the end of the first year of life. It is probably caused by the homozygous state of an autosomal gene.

Other types of Chondrodysplasia punctata possibly exist.

Chondrodysplasia punctata has been confused particularly with Zellweger's cerebro-hepato-renal syndrome and with multicentric epiphyseal ossification in multiple epiphyseal dysplasia.

Zusammenfassung. Auf der Grundlage der Erfahrungen des Kielers Knochendysplasie-Registers sowie auf Grund einer ausführlichen Literaturübersicht werden die klinischen und genetischen Daten von zwei Haupttypen der Chondrodysplasia punctata dargestellt und diskutiert.


2. Rhizomeler Typ: Schwere, symmetrische, proximale Verkürzung der Extremitäten sowie deutliche Veränderungen der Metaphyse in Kombination mit Katarakt in 72% und

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Möglicherweise gibt es noch weitere Typen der Chondrodysplasia punctata.

Die Chondrodysplasia punctata wurde mit dem cerebro-hepato-renalen Syndrom (Zellweger) sowie mit den multizentrischen epiphysalen Ossifikationen bei der multiplen epiphysären Dysplasie verwechselt.

Introduction

Chondrodysplasia punctata (C.p.) commonly has been regarded as a single nosologic entity characterized by the presence of punctate epiphyseal and extraepiphyseal calcifications in roentgenograms of newborns and infants. A variety of names has been attached to this condition such as chondrodystrophia calcificans, chondroangiopathia calcarea, dysplasia epiphysealis punctata or Conradi-Hünermann disease.

In contrast to the traditional assumption of apparent clinical and genetic homogeneity of C.p. the present review sets out from the following hypotheses:

A. Punctate intra- and extracartilaginous calcifications in infants are non-specific. They may be found in a variety of hereditary and nonhereditary conditions. Numerous cases with such calcifications have been erroneously diagnosed and published as examples of C.p.

B. The term “chondrodysplasia punctata” seems to have been applied to more than one entity. There exist two and possibly more diseases which resemble each other but can be distinguished by the radiologic appearance of their bone changes and to some extent on the basis of clinical and histopathologic features.

C. Different phenotypes of C.p. may in fact correspond to different genotypes.

Nomenclature

Following a suggestion of the European Society for Pediatric Radiology (Maroteaux et al., 1970) the term “chondrodysplasia punctata” is preferred to other synonyms. One type of C.p. is called the “Conradi-Hünermann type” because it shows the features described by these authors. A second type of C.p. is called the “rhizomelic type” because one of the conspicuous features of this disease is the striking shortening of the humeri, the femora or all of these.

Source of Data

The following analysis is based on data from 8 patients of the bone dysplasia register of Kiel and on a review of 128 cases reported in the literature. 6 personal patients and 94 cases from the literature are listed in Tables 2 and 3 as examples of chondrodysplasia punctata. 2 personal and 7 literature cases have been omitted from the discussion because they possible represent a different entity (see Results III). In 9 cases the diagnosis of C.p. probably was incorrect (Table 1). 18 cases in which the radiologic documentation did not allow a definite diagnosis were omitted from this review.

1 Asanti and Heikel, 1963, cases 4, 5; Bergstedt and Kahlen, 1954, case 1; Delobel, 1961, case 1; Dietrich, 1915; Fritsch and Manzke, 1963, case 1; Josephson and Cratti, 1961; McKaith, 1967; Palitzsch, 1964; Robertson, 1967, case 2; Swoboda and Pichler, 1966, case 2; Tasker et al., cases 1—4; Thiel et al., 1969, cases 2, 3; Wiskott, 1929.