



A Rare Skeletal Dysplasia: Achondrogenesis Type 1

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Abstract

Achondrogenesis is a rare osteochondrodysplasia that is characterized by severe shortness of extremities, a short trunk, macrocephaly and a protuberant abdomen. There are 4 types of achondrogeneses. Achondrogenesis type 1 is an autosomal recessive condition with a fatal course. In this article, we are presenting a case of skeletal dysplasia that was detected during an obstetric ultrasonographic check in the 16th gestational week with clinical and radiological results suggestive of achondrogenesis type 1A (Parenti-Fraccaro). Skeletal dysplasias might be detected as of the beginning of the second trimester. With genetic inheritance and a fatal course, achondrogenesis must be detected prenatally with a view to talking to the family and suggesting the termination of the pregnancy.

Keywords: Achondrogenesis, skeletal dysplasia, prenatal diagnosis.

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Introduction

Musculoskeletal dysplasias are rare conditions with genetic inheritance that

emerge with the abnormal development of bony and cartilaginous tissue. These dysplasias may be general anomalies of bone or cartilage or may be observed in the



form of pathologies limited to a specific bone or extremity segment.

Achondrogenesis is a fatal osteochondrodysplasia that presents with severe shortness (micromelia), macrocephaly and a short trunk that involves both proximal and distal extremity segments. Its incidence is one in approximately 43.000 births [1]. It results from a mutation in fibroblast growth factor receptor 3 (FGFR3) and has a genetic mode of inheritance. It has 4 sub-types, and type 1 (Parenti-Fraccaro) is further divided into two sub-types. Cases of achondrogenesis get a diagnosis on the basis of clinical, radiological and histological characteristics.

Types 1 and 2 have an autosomal recessive inheritance pattern. The family history must be questioned as an absolute necessity in case of prenatally suspected skeletal dysplasia. In this article, we are presenting a prenatally detected case of skeletal dysplasia with postnatal clinical and radiological results suggestive of achondrogenesis type 1A (Parenti-Fraccaro).

Case Presentation

A routine obstetric ultrasonography (USG) performed on a pregnant women with a gravida of 2 and a parity of 1 in the 16th gestational week from the last menstrual period indicated the presence of skeletal dysplasia. There was no defining characteristic in personal or family history. Her laboratory results were in the normal range. The USG gave way to the

observation of a single living fetus consistent with the 17th gestational week in terms of head circumference (HC), biparietal diameter (BPD) and abdomen circumference and with the 12th gestational week in terms of femur length (FL). During the USG, the case was established to have distinct retardation in all long bones when compared to those of the same gestational age in addition to macrocephaly, narrow thorax, protuberant abdomen, reduced thorax/abdomen ratio, reduced vertebral echogenicities, horizontally placed short ribs with irregular cortex and increased echogenicity, pyelectasis, protruding forehead, nasal bone hypoplasia, increased skin thickness, and polyhydramnios. Upon amniosynthesis, the result was suggestive of 46 XX karyotype and normal. The family was provided with genetic consultancy and suggested the termination of the pregnancy. The pregnancy was terminated upon consent given by the family. The post-mortem examination revealed severe micromelia, narrow thorax, wide abdomen, protruding forehead, flat nasal root, hypertelorism, and low-set ears in the fetus. The directed graphs obtained from the fetus in the post-mortem period indicated a picture that was consistent with the prenatal USG findings. They showed almost non-existent ossification in the vertebrae and loss of mineralization in calvarium, as well as distinct shortness of the extremities. As a result of clinical and radiological evaluations, the fetus was diagnosed with achondrogenesis type 1A.



Image 1: Post-termination photograph of the fetus. The long bones of all extremities appear to be short, and macrocephaly, flat nasal root, protruding forehead, low-set ears and narrow thorax are prominent.



Image 2: Nasal hypoplasia, protruding forehead, narrow thorax and protruberant abdomen observed in ultrasonography.



Image 3: Shortness of extremities and reduced ossification in calvarium and vertebrae observed in radiography.

Discussion

The incidence of musculoskeletal dysplasias remains to be unclear. As they can be observed secondary to the ossification of fetal bones in the ultrasonography, musculoskeletal dysplasias start to appear as of the beginning of the second trimester that marks the start of ossification. The most common musculoskeletal dysplasias are tanatrophic dysplasia, achondroplasia, achondrogenesis and osteogenesis imperfecta, respectively [2].

The ultrasonographic findings of achondrogenesis include a flat facial profile, severe micromelia, macrocephaly, narrow thorax, widened abdomen, and poor ossification in calvarium and vertebrae. Furthermore, findings may include fetal hydrops and polyhydramnios [3-5]. A short nose, a very short trunk and a short neck accompanied by a protuberant

abdomen (possibly arising from hydrops) are the other characteristics of achondrogenesis type 1 [6-8]. Achondrogenesis type 1A comes with reduced ossification in calvarium, almost non-existent ossification in vertebral bodies, and possibly thin and broken ribs. Type 1B does not involve rib fractures, and its ossification is better than that in type 1A [9]. In Type II (Langer-Saldino), however, the changes are less distinct and hydropic with short extremities. Ossification in calvarium is better than that in Type 1; however, vertebra corpus ossification is rather poor.

Achondrogenesis might be confused with other musculoskeletal dysplasias, potentially resulting in misdiagnosis. Tanatrophic dysplasia and tanatrophic dysplasia might be distinguished from achondrogenesis on the basis of absence of macrocephaly, presence of flattened vertebra corpuses, a normal trunk height



and a normal calvarial mineralisation. Tanatrophic dysplasia might be accompanied by cardiac and renal anomalies and the shape of a clover on the skull. Non-lethal achondroplasia must also be considered in the differential diagnosis. Achondroplasia indicates a normal body height with rhizomelic shortness of extremities and deformities of the spine. The directed graph indicates an increase in the width of metaphyses, and bone diameter and density [8]. In osteogenesis imperfecta, on the other hand, short and deformed extremities, reduced mineralization in bones and an accordion- or telescope-style appearance might be observed together with the accompanying multiple bone fractures. Devoid of sufficient mineralization, the calvarion becomes easily deformed, thereby facilitating the imaging of cerebral structures [10, 11].

Conclusion

As 90% of congenital anomalies are sporadic, USG is of utmost importance in detection of such anomalies. Identification of musculoskeletal anomalies requires the review of all bones in fetal examination. Detection of skeletal dysplasias in the prenatal period is of paramount importance for early termination of the pregnancy and provision of genetic consultancy to the family for their subsequent pregnancies.

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