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Case Report

Radiological Features of Achondrogenesis Type 1A: Case Report and Review of the Literature

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Abstract

Achondrogenesis is a rare autosomal recessive disorder presenting with severe shortness of limbs, incomplete vertebral ossification, barrel-like thorax, short extremities, enlarged abdomen and prominent forehead. The diagnosis of skeletal dysplasia could be done as soon as 13th week of gestation on prenatal ultrasonography (US). Early diagnosis is of utmost importance for accurate timing of termination and genetic counseling for future pregnancies. In this study, we illustrate the radiological and clinical findings of achondrogenesis type IA on a case that initially misdiagnosed as achondrogenesis type II on prenatal US at 16th week of gestation. Postmortem examination and pathological findings were also discussed in light of literature.

ABBREVIATION

US: Ultrasonography

INTRODUCTION

Achondrogenesis presents with severe micromelia, macrocranium, a normal to poorly ossified skull, decreased thoracic circumference, pulmonary hypoplasia, decreased bone mineralization and a short trunk that involves both proximal and distal segments of extremity [1]. Achondrogenesis, an autosomal recessive genetic disorder, is the second most common lethal skeletal dysplasia [2]. Its incidence is one in approximately 40.000 births [3]. It has 4 sub-types, and type I (Parenti-Fraccaro) is further divided into A and B sub-types. Unlike achondrogenesis type IB, type IA also includes rib fractures. Both have severe micromelia, partial or complete lack of ossification of the calvarium, vertebral bodies. Achondrogenesis type II (Langer-Saldino) accounts for 80% of achondrogenesis cases. It is characterized by normal calvarial ossification and absent ossification of vertebral column, sacrum, and pubic bones. Of all skeletal dysplasias, achondrogenesis type II has the most complete lack of vertebral ossification [4]. Achondrogenesis is diagnosed base on the clinical, radiological and histological findings. The pattern of mineralization is important in differentiating type I and II cases. When incomplete mineralization involves skull and iliac wings the presumptive diagnosis is type I; If skull appears to be normally mineralized then the presumptive diagnosis should be type II. If incomplete mineralization is detected on prenatal US, a confirmatory X-ray study needs to be performed. Since the recognition of demineralization by ultrasonography (US) is fraught with false negatives, there will be a tendency to over-report the type II form [5]. In this article, we are presenting a prenatally detected case of skeletal dysplasia with post-natal clinical and radiological results suggestive of achondrogenesis type IA. In the present case, demineralization of the skull and iliac wings along with multiple rib fractures that were observed on X-ray image, supported the diagnosis of type IA achondrogenesis. Nonetheless, having seen echogenic calvarial structures on prenatal US, we mistakenly presumed a diagnosis of achondorgenesis Type II.

CASE PRESENTATION

24 –year- old, gravid 2, parity 1 female was referred to our clinic for detailed prenatal fetal US examination. The first child was healthy and the family history of the mother was unremarkable with no history of medical conditions and drug use during pregnancy. Blood panel and regular tests of the mother were within the normal range. A single alive fetus of 17th gestational week with consistent biparietal diameter, head circumference and abdomen circumference measures were observed on US (Toshiba, aplio 300, Japan). However, femur and humerus length were significantly short for gestational age with measures of approximately 12 weeks and 2 days. On US, macrocephaly, short body and extremities, decreased thorax

diameter, disproportionate thorax and abdomen diameters, nasal bone hypoplasia, thickened and edematous skin and polyhidramniosis were evident. Amniotic index was 20 cm. Vertebral column was hypoechoic with overt demineralization. The echogenity of calvarium was low, but unlike vertebra it was not overtly hypoechoic and demineralization was not concieved for this reason.Ribs were short and horizontally aligned with cortical irregularity suggestive of fractures (Figure 1). Amniosynthesis was reported with normal karyotype of 46 XX. The pregnancy was terminated upon consent given by the family. Postmortem evaluation of fetus revealed micromelia, narrow thorax, wide and protuberent abdomen, flat nose base, prominent forehead, hypertelorism and low-set ears. Incomplete vertebral mineralization and micromelia were verified on plain X-ray studies. Additionally, cranium was also radiolucent with incomplete mineralization, unlike what was foreseen on prenatal US (Figure 2). Based on findings on X-ray studies, the fetus was diagnosed with achondrogenesis type IA. In the case we presented here, fetal skeletal dysplasia was detected antenatally on US, but final diagnosis obtained by fetopathological examination and radiographic studies.

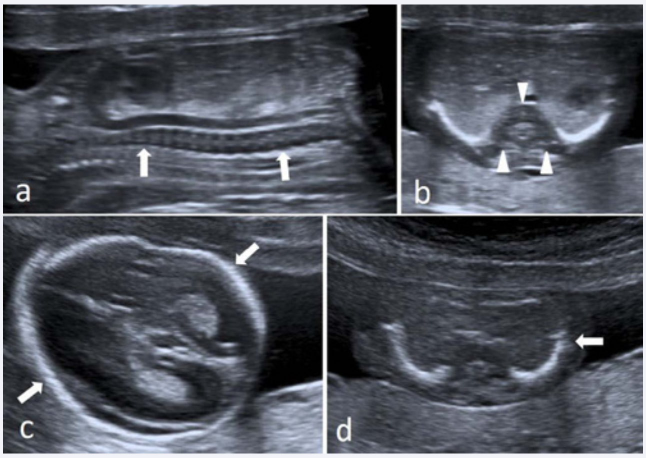


Figure 1 (a) Ultrasound demonstrating hypoechoic vertebral column (arrow) because of demineralization in sagittalplane, (b) in axial planeall three ossification centers are seen hypoechoic due to absence of mineralization (arrow). (c)The echogenity of calvarium is low (arrow), but unlike vertebra it is not overtly hypoechoic and demineralization is not concieved for this reason. (d).Ribsare short and horizontally aligned with cortical irregularity suggestive of fractures (arrow).

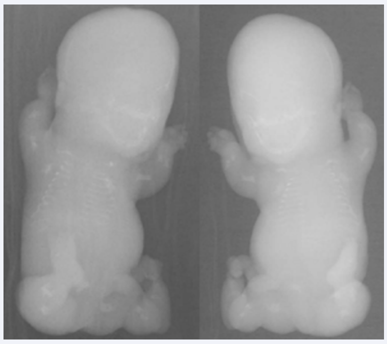


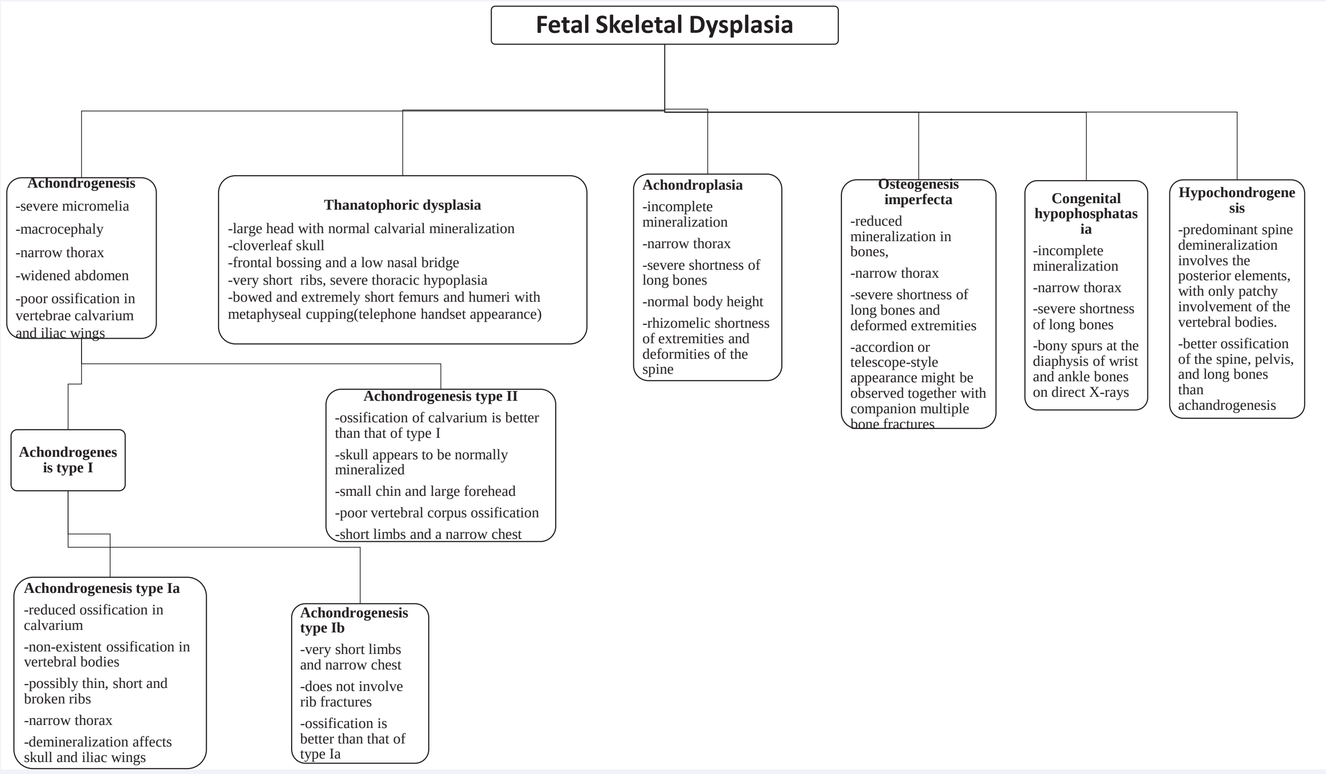
Figure 2 X-ray demonstrating incomplete vertebral mineralization and micromelia. Cranium is radiolucent within complete mineralization. Vertebral column can not be observed due to demineralization. Thorax is seen narrow and abdomen is seen wide and protuberent.

DISCUSSION

Achondrogenesisis a rarely seen autosomal recessive osteocondroplasia. Histologically, achondrogenesis occurs as a result of shape or arrangement disorder of cartilage matrix [6]. Achondrogenesis is diagnosed based on clinical, radiological and histological findings. Fetal skeletal dysplasia detected antenatally with US and final diagnosis is made based on fetopathological examination and radiographic studies in most cases, and molecular testing as deemed necessary [5]. The US findings of achondrogenesis include severe micromelia, macrocephaly, narrow thorax, widened abdomen, poor ossification in vertebrae, calvarium and iliac wings. Characterization of demineralization is important in differentiating type I from type II [3,4]. Achondrogenesis type IA comes with reduced ossification in calvarium, almost non-existent ossification in vertebral bodies, and possibly thin and broken ribs. When demineralization affects skull and iliac wings, the presumptive diagnosis is achondrogenesis type IA [3]. Achondrogenesis type 1B does not involve rib fractures, and its ossification is better than that of type IA. In achondrogenesistype II, ossification of calvarium is better than that of type I; however, vertebral corpus ossification is rather poor. When skull appears to be normally mineralized, the presumptive diagnosis is type II [4,5]. When mineralization is present on US, an X-ray may confirm it. Since the recognition of demineralization by US is fraught with false negatives, there will be a tendency to over-report the type II form [5]. In the case we reported here, we prenatally detected skeletal dysplasia with postnatal clinical and radiological results suggestive of achondrogenesis type IA. In our case, demineralization of the skull and iliac wings and multiple rib fractures observed in radiological images support the diagnosis of achondrogenesis type IA. As a result of echogenic calvarial structures on prenatal US, we mistakenly presumed a diagnosis of achondrogenesis Type II despite visible cortical irregularities and fracture lines in the ribs.

On US, musculoskeletal dysplasias start to appear at the beginning of second trimester, which marks the start of cartilage ossification. The most common musculoskeletal dysplasia are thanatophoric dysplasia, achondroplasia, achondrogenesis and osteogenesis imperfecta, respectively [7]. Achondrogenesis could be confused with other musculoskeletal dysplasias, potentially resulting with misdiagnosis. Achondrogenesis and differential diagnosis of the other muscle-skeletal dysplasias schematized below [Insert Flow Chart].

Thanatophoric dysplasia has similar appearance to achondrogenesis. In thanatophoric dysplasia, calvarial mineralization is normal with infrequent so-called “Four-leaf clover appearance” and vertebras are of normal length with flat corpora. Bowed short femurs seen in thanatophoric dysplasia are known as ‘telephone handset’ appearance [4,8]. Because of existing calvarial and vertebral hypomineralization and no previoulsy described morphological features that



Flow Chart

typically seen in thanatophoric dysplasia, we excluded a diagnosis of thanatophoric dysplasia based on the clinical and radiological findings in the present case. Other differential diagnosis of achondrogenesis is congenital hypophosphatasia, achondroplasia and osteogenesisimperfecta. Incomplete mineralization, narrow thorax and severe shortness of long bones are seen in all three listed skeletal dysplasia [4]. Bony spurs at the diaphysis of wrist and ankle bones on direct X-rays are typical for hypophosphatasia [9]. Achondroplasia presents a normal body height with rhizomelic shortness of extremities and deformities of the spine. In homozygotic achondroplasia there is no calvarial mineralization deficit [10]. Achondrogenesis could be distinguished from other dysplasia with incomplete mineralization of skull, which does not exist in any other skeletal dysplasia. Classically, because of predominant demineralization of the vertebral body, only the two echogenic posterior elements or neural arches appear on US in a transverse image of the spine. This is in contrast to hypophosphatasia congenita, in which the predominant spine demineralization involves the posterior elements, with only patchy involvement of the vertebral bodies. Hypochondrogenesis is phenotypically similar but it is less severe according to achondrogenesis with better ossification of the spine, pelvis, and long bones [4]. In osteogenesis imperfecta, short and deformed extremities, reduced mineralization in bones, and an accordion or telescope-style appearance might be observed together with companion multiple bone fractures [10].

Similar to the other lethal short limb dysplasia, achondrogenesis is lethal due to pulmonary hypoplasia. Affected cases are either still born or die in the neonatal period. Specific prenatal diagnosis by US is helpful for differential diagnosis of lethal skeletal dysplasias, which is necessary for genetic counseling on future risks. The pregnancy can be managed as other pregnancies with fatal outcome and the option of pregnancy termination may be offered at any time after a definitive diagnosis [11].

In conclusion, fetal skeletal structures could be elaborately examined during routine prenatal US and diagnosis of skeletal dysplasia can be made based on these findings. Characterization of mineralization is important in differentiating between Achondroplasia type I and II. Incomplete or vague mineralization on US can be confirmed with additional X-ray studies. Early prenatal diagnosis of rare skeletal dysplasia like achondroplasia is of utmost importance in making decision of pregnancy termination and genetic counseling for potential risks of future pregnancies.

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