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# Achondrogenesis: A Case Report.

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**ABSTRACT**

Achondrogenesis is a lethal chondrodystrophy characterized by extreme micromelia, short trunk, and a disproportionately large head. It has an autosomal recessive pattern of inheritance. It occurs in approximately 1 in 40,000 births. Achondrogenesis has been sub classified into Type 1A, 1B, and Type 2, based mainly on clinical and radiological criteria such as pattern of ossification, deficiency, and deformity of ribs.The prevalence of this disease is 0.23/10,000 live births, and lethality among perinatal deaths is 1:539.

**Keywords:** Achondrogenesis Ossification Cartilage Pathology Skeletal Disorders

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## INTRODUCTION

Achondrogenesis, which occurs in approximately I in 40,000 births [3], belongs to lethal forms of chondro- dysplasia. Clinically it is characterized by a severe short— limbed dwarfism, and affected infants die in utero or shortly after birth. Achondrogenesis has been subclas- sifted into type IA, IB and type II, based mainly on clin- ical and radiological criteria such as pattern of ossification deficiency and deformities of the ribs [1-4].

Achondrogenesis type II was initially described by Langer et at. [5] and Saldino [6]; the disorder is also called Langer—Saldino achondrogenesis. The clinicopath- ologic features of this lethal dwarfism has recently been more completely delineated by others [7, 8], and the major clinical features include short trunk with prom- inent abdomen, striking micromelia and hydropic appear- ance. The basic radiographic findings are severe under- ossification of the vertebral bodies, a typical configuration of the iliac bones with concave medial and inferior bor- ders, and nonossification of the ischial and pubic bones. The tubular bones are short, and the metaphyses are splayed and cupped, with irregular ends and spur for- mation [5—8].

## CASE REPORT

Mrs. Suganya, 21 wks, Gravida 3 Abortion 2 , GestationalAge: 21+ 3 days weeks LMP:19.12.14, EDD:25.9.15. Came for regular antenatal checkup first visit in SBMCH. Menstrual history is Regular Cycles. Marital history is Married Since 3 Years, NCM.

**Obstetric history:**

1st pregnancy- conception soon after marriage, Spontaneous abortion at 6weeks . MTP done. 2nd pregnancy- conception, Spontaneous abortion at 6weeks . MTP done. 3rd pregnancy- 1st trimester: Spontaneous conception, Pregnancy was confirmed by UPT, Folic acid was taken. Dating scan was done , NT scan was not done. No h/o fever with rashes , drug intake , radiation exposure, bleeding p/v. Patient was started on susten and ecosporin outside. 2 nd trimester: Inj. TT 2 doses was taken, Iron and calcium was taken, Quickening not felt, No h/o lower abd pain / bleeding p/v. Past History is not a known case of DM,HT, BA, TB, Thyroid, seizures. Personal History is nil Relevant. Family History is Patient had polydactyl in the left hand and patients mother had Right preauricular tag and deafness since birth.

On General examination: moderately built & well nourished. Vitals : BP :110/80 mmhg, PR: 70/min, Temp : Normal, No Pallor, No Pedal Edema, CVS:S1S2+, RS:NVBS+, P/A : Uterus -18 weeks, Fetal pole+.Patient was then advised to take routine blood investigations Including HB,PCV, ESR-80, BLOOD GROUPING & TYPING-O+ve, FBS, PPBS, FT3, FT4, TSH -8.83, HIV,HbsAg, RPR, URINE R/E

**USG – ANOMALY SCAN.**

USG Shows: SLIUG. Thoracic Circumference is smaller than the abdomial circumference, crowding of ribs present, Placenta Anterior Dipping Into The LS, UL: Both Forearm Bones Absent, LL: Femur Absent On Both Sides, Tibia & Fibula Absent On One Side & Present On The Other, Both Feet Shows Club Foot Deformity – Talipes Equines / Varus Deformity.

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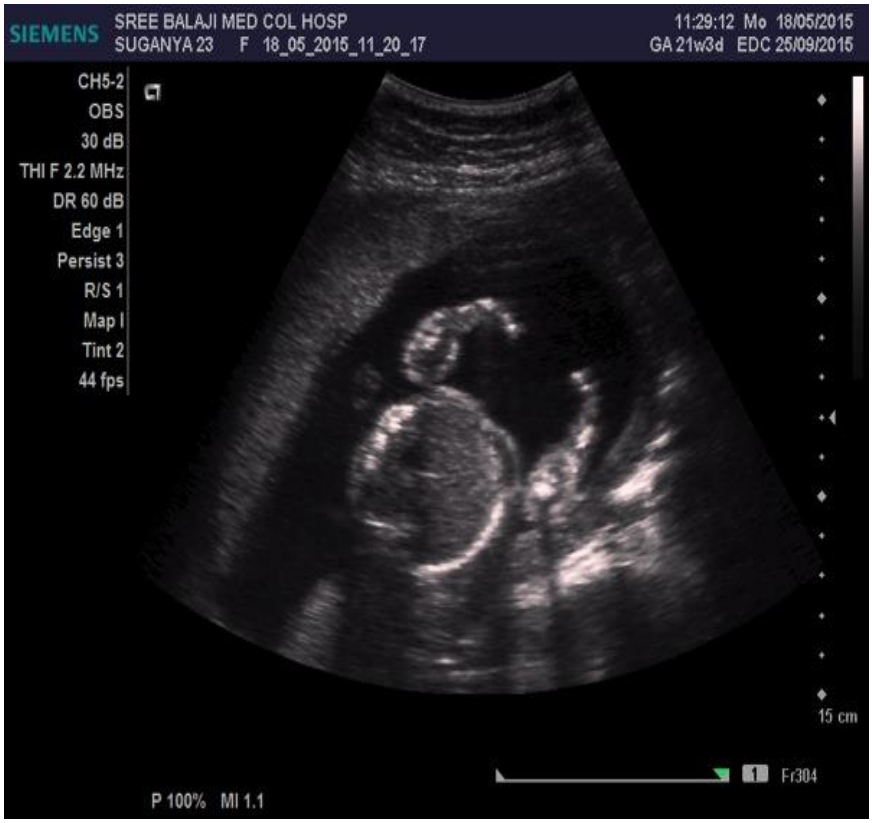
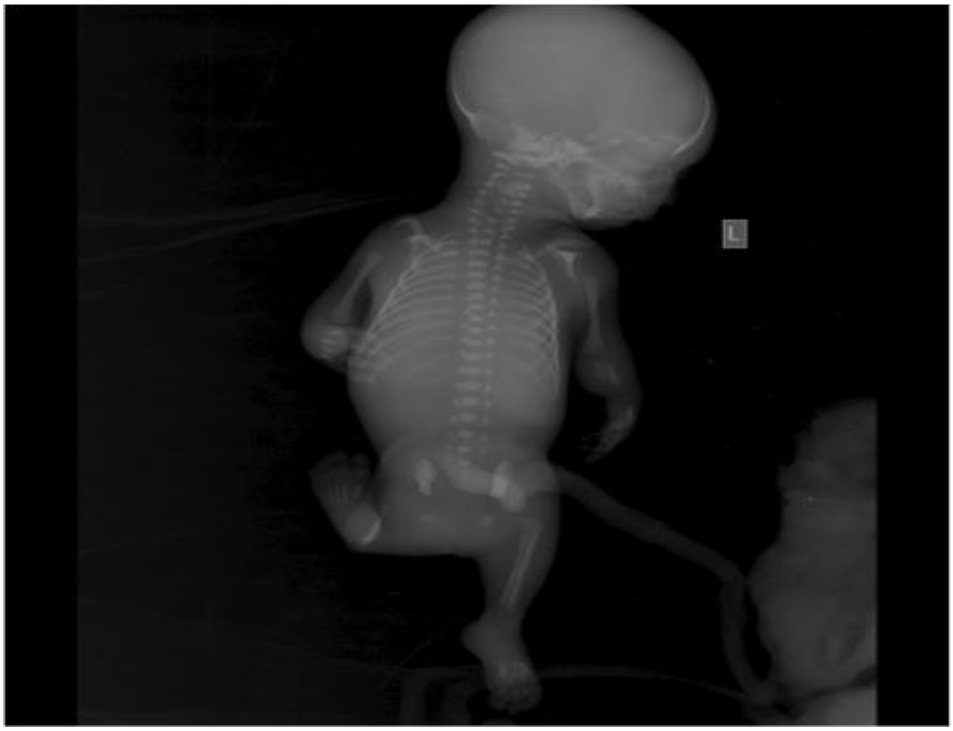
**ACHONDROGENESIS Of The Fetus**

**SHORT UPPER LIMBS**




**X RAY SHOWS THE ABSENCE OF FEMUR BONES :**



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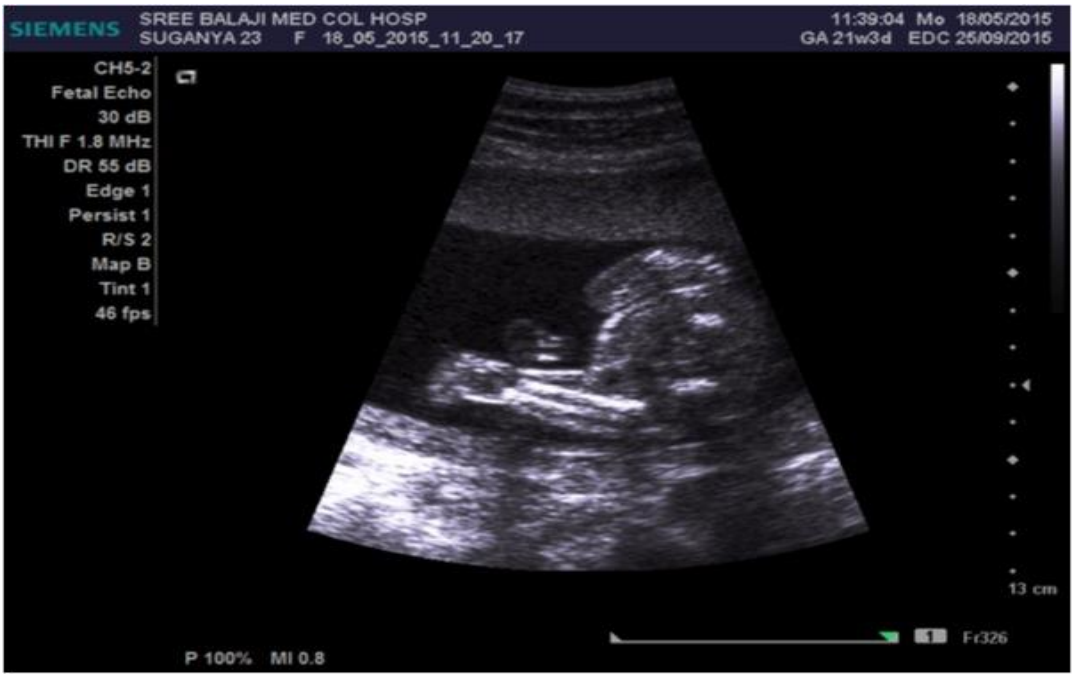
**TIBIA & FIBULA PRESENT:**




MTP Was Done. Spontaneous Expulsion Of The Dead Fetus Dead born fetus, 50gms, on 25.5.15

**DISCUSSION**

HISTORY: Marco Fraccaro first described achondrogenesis in 1952.[1] He used the term to describe a stillborn female with severe micromelia and marked histological cartilage changes. The term was later used to characterize the most severe forms of chondrodysplasia in humans, which were invariably lethal before or shortly after birth. By the 1970s, researchers concluded that achondrogenesis was a heterogeneous group of chondrodysplasias lethal to neonates

INCIDENCE : It occurs in 1: 40000 births. Males and females are equally affected.Type I results in stillbirth more frequently than type II

It was classified under 3 types : Type I A - Houston-Harris type, Type 1B - Parenti-Fraccaro type, Type II - Langer-Saldino type were distinguished on the basis of radiological and histological criteria.Type 1A : autosomal recessive type mutations gene is TRIP11 gene. This helps in the production of a protein called GMAP-210. This protein plays a critical role in the Golgi apparatus. Mutations in the TRIP11 gene prevent the production of functional GMAP-210, which alters the structure and function of the Golgi apparatus.Type 1B: autosomal recessive mutant gene is diastrophic dysplasia sulfate transporter gene (SLC26A2), Type 2: autosomal dominant mutations of the type II collagen gene (COL2A1).Clinically presentation may be Hydrops Fetalis, Breech, Polyhydramnios

TYPE -1: Growth - Lethal neonatal dwarfism, mean birth weight of 1200 g. Craniofacial - Disproportionately large head, soft skull, sloping forehead, convex facial plane, flat nasal bridge, small nose, often with anteverted nostrils, long philtrum, retrognathia, increased distance between lower lip and lower edge of chin double chin appearance (often), Neck – extremely short, Thorax - Short and barrel-shaped thorax, lung hypoplasia, Heart -PDA , ASD , VSD are the most common associated anomalies, Abdomen – Protuberant, Limbs - Extremely short (micromelia), much shorter than type II; flipper-like appendages

TYPE -2: Growth - Lethal neonatal dwarfism, mean birth weight of 2100 g.Craniofacial - Disproportionately large head, large and prominent forehead, flat facial plane, flat nasal bridge, small nose with severely anteverted nostrils, normal philtrum, micrognathia. Neck - Extremely short, Thorax - Short and flared thorax, bell-shaped cage, lung hypoplasia, Abdomen – Protuberant, Limbs - Extremely short (micromelia).

PRE NATAL DIAGNOSIS : USG , Molecular studies. USG features include: polyhydramnios, large head, nuchal edema, reduced rump length, poor ossification of vertebral bodies and limb tubular bones.

Molecular Study includes: Mutation Analysis of the genes,By Chorionic Villous Sampling, Amniotic membrane Sampling in the 1st & 2nd trimesters respectively

In Type IB, both alleles of DDST should be characterized beforehand, and the source parent of each allele identified. Theoretically, analysis of sulphate incorporation in chorionic villi might be used for prenatal diagnosis, but experience is lacking. In Type II, the affected fetus usually has a new dominant mutation of the COL2A1 gene.

**Achondrogenesis type I (Fraccaro-Houston-Harris type)**

Skull - Varying degree of deficient cranial ossification consisting of small islands of bone in membranous calvaria.Thorax and ribs - Short and barrel-shaped thorax; thin ribs with marked expansion at costochondral junction, frequently with multiple fractures. Spine and pelvis - Poorly ossified spine, ischium, and pubis; poorly ossified iliac bones with short medial margins. Limbs and tubular bones - Extreme micromelia, with limbs much shorter than in type II; flipper-like appendages; prominent spike-like metaphyseal spurs; femur and tibia frequently presenting as bone segments. Subtype IA (Houston-Harris type) - Poorly ossified skull, thin ribs with multiple fractures, unossified vertebrae, arched ilium, hypoplastic but ossified ischium, wedged femur with metaphyseal spikes, short tibia and fibula with metaphyseal flare, "rectangular bones". Subtype IB (Fraccaro type) - Adequately ossified skull, absence of rib fractures, ossified posterior vertebral pedicles, crenated ilium, unossified ischium, trapezoid femur, stellate tibia, unossified fibula, arms and legs shorter than in type IA

**Achondrogenesis type II (Langer-Saldino type)**

Skull - Normal cranial ossification, relatively large calvaria Thorax and ribs - Short and flared thorax; bell-shaped cage with broader, shorter ribs without fractures. Spine and pelvis - Relatively well-ossified iliac bones with long, crescent-shaped medial and inferior margins.Limbs and tubular bones - Short, broad bones, usually with some diaphyseal constriction and flared, cupped ends; metaphyseal spurs usually smaller than type I; disproportionately long fibula; mushroom-stem bones

Other Tests Include: Skin And Cartilage Biopsies For Fibroblast And Chondrocyte Cultures Allow Study Of Sulphate Incorporation.

HISTOLOGICAL FINDINGS:Type IA :Normal Cartilage Matrix. Vacuolated Chondrocytes, Intrachondrocytic Inclusion Bodies (Periodic Acid-schiff Stain [PAS] Positive, Diastase Resistant), Extraskeletal Cartilage Involvement, Enlarged Lacunas, Woven Bone.Type Ib : Cartilage shows dense collagen rings. Reduced Staining with Toluidine Blue due to Deficiency In Sulfated Proteoglycans.TYPE II : Lobulated Epiphyseal Cartilage.The cartilaginous matrix is markedly deficient. Balloned Chondrocytes is present

**MANAGEMENT**

Achondrogenesis Can Be Detected At 12 Weeks In NT Scan .Pregnancy Should Be Terminated By MTP.

COUNSELING : Parents Should be given genetic counseling regarding the Recurrence rates for the next child
RECURRENCE RATE: Achondrogenesis type IA and type IB are inherited as autosomal recessive disorders. For a couple who has an affected child, the recurrence risk is 1 in 4 (25%). This risk is markedly higher than the recurrence risk for achondrogenesis type II, which is usually caused by a new dominant mutation.

**CONCLUSION**

Achondrogenesis is the lethal skeletal anomaly .NT scan plays an important role in the early detection of the anomaly .If the anomaly is found the early 1$^{st}$ trimester MTP can be done which has less morbidity .Chromosomal analysis of maternal & paternal blood should be done to find out the carrier state.

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