Research Paper Medical Science

A Rare case report of fetal autopsy – ACHONDROGENESIS TYPE II (LANGER SALDINO)

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ABSTRACT

Achondrogenesis type II is a type of short trunk osteochondrodyplasia, an autosomal dominant type 2 collagenopathy with an incidence of 1 in 40,000 births and is invariably fatal in perinatal period.

KEYWORDS Autopsy, Achondrogenesis type II (ACG II), Fetus, Lethal genetic skeletal dysplasia, Short long bones.

INTRODUCTION:

Achondrogenesis type II is an autosomal dominant osteochondrodysplasia[1] which can be diagnosed prenatally as early as 12 weeks of gestation by ultra sonographic examination[2]. It is a type II collagenopathy due to mutation in COL2A1 gene located on chromosome 12q3, 1-13.3[3] Clinical features are uaually extremely short trunk and extremities along with cardiac abnormalities like patent ductus arteriosus, atrial septal defects and ventricular septal defects. Hydropic appearance and polyhydromnios is present. The major radiological findings are markedly deficient ossification in the vertebral bodies which are frequently absent in the lumbosacral region and absence of pubic and ischial ossification. ACG II has better ossified ilia and limb bones that exhibit flared and cupped metaphyseal ends with well ossified cranial bones and there are no rib fractures.Histopathologically changes in the resting cartilage are characteristic with deficient matrix, markedly enlarged lacunae[4]and perichondrocytic collagen rings . There is increased population of chondrocytes which may or may not be ballooned out. The canals of the resting cartilage are markedly enlarged, stellate in shape and fibrotic. The growth zone is retarded and disorganised. Immunohistochemical and microchemical studies suggests ACG II is a disorder of type II collagen biosynthesis [5].

CASE REPORT:

A female fetus born to healthy, non consanguinous young couple by terminating in 5th month for multiple abnormalities detected by prenatal sonographic examination. TIFFA scan examination reveals fetus with congenital abnormalities like skeletal dysplasia in form of micromelia, narrow thorax , pulmonary hypoplasia, sub occipital cystic hygroma and subaortic ventricular septal defect(Figure 1) .On autopsy externally fetus shows hydrops, dwarfism, large head, cystic hygroma, short trunk, severe micromelia and distended abdomen.Internal examination showed subaortic ventricular septal defect (Figure 1). bilateral pulmonary hypoplasia(Figure 2). All bones of axial and appendicular skeleton are present within normal limits. All other organs are normal.

Histopathology shows resting cartilage shows significant deficiency of matrix and markedly enlarged lacunae. Chondrocytes are increased in number and shows ballooned out appearance (Figure 2).Cartilage canals are markedly enlarged, stellate in shape and fibrotic. Perichondrocytic collagen rings are seen in resting cartilage.

DISCUSSION :

Marco and Fraccaro first described achondrogenesis in 1952, in 1983 a new radiological classification of achondrogenesis (types I – IV) was given by Whitley and Gorlin. In the late 1980s, structural mutations in collagen II were detected. The severest phenotype of ACG II produced by mutations of COL2AI, is caused by the absence of type II collagen in the cartilage matrix. The type I and III collagens that replace it appear to be unable to compensate for the lack of type II collagen. Spondyloepiphyseal dysplasia congenital, spondyloepimetaphyseal dysplasia and Kniest syndromes are also caused by dominant – negative mutations of COL2AI in which the cartilage contains abnormal type II collagen but no detectable type I or III collagens.6

Lethal genetic skeletal disorders usually result in death within the perinatal period and these disorders often detected by ultrasonography in early mid trimester.7 In our study skeletal abnormalities were detected in 5th month (at 18 weeks) of gestation. Infants with this disorder have short arms and legs, a small chest with short ribs, and underdeveloped lungs. The skull bones may be soft, but they often appear normal on X – ray images. In contrast vertebrae and pelvis donot harden, or ossify. Typical facial features include a prominent forehead, a small chin and in some cases cleft palate. The abdomen is enlarged, and excess fluid builds up in the body before birth a condition called hydrops fetalis. Infants with this disease are usually premature and stillborn or die shortly after birth from respiratory failure. Evidence based diagnostic approach can be done by prenatal sonological examination, infantogram, histopathological study, DNA analysis, mutational analysis and by chondrocyte cultures8.

In our case study a female fetus of 18 weeks gestation prenatally on TIFFA scan was found to have congenital abnormalities like skeletal dysplsia in the form of micromelia,narrow thorax and pulmonary hypoplasia, sub occipital cystic hygroma and sub aortic ventricular septal defect. After termination of pregnancy fetus on radiological examination showed un-

ossified parietal cranial bone, short narrow thorax, short ribs without fractures, unossified lower thoracic, lumbar vertebrae, sacrum and pubic bones, short long bones with diaphyseal constriction and flared, cupped ends. At autopsy fetus is found to have multiple external anomalies like fetal hydrops, dwarfism, large head, cystic hygroma, short trunk, severe micromelia and distended abdomen., internal anomalies like subaortic ventricular septal defect and bilateral pulmonary hypoplasia. On microscopic examination there is deficiency of matrix and enlarged lacunae in resting cartilage, increased chondrocytes with ballooned out appearance, enlarged cartilage canals which are stellate in shape and fibrotic. Perichondrocytic collagen rings are seen in resting cartilage.

In conclusion Achondrogenesis type II is a lethal genetic skeletal dysplasia relies mainly upon radiologic as well as on histologic examination and should be confirmed in genetic studies by mutations in COL2AI gene. An evidence based lethal genetic skeletal dysplasias can be terminated by early midtrimester. No treatment is available for the underlying disorder. Genetic councelling is essential as asymptomatic carriers may be present in the families of the effected patients.

Figure 1:

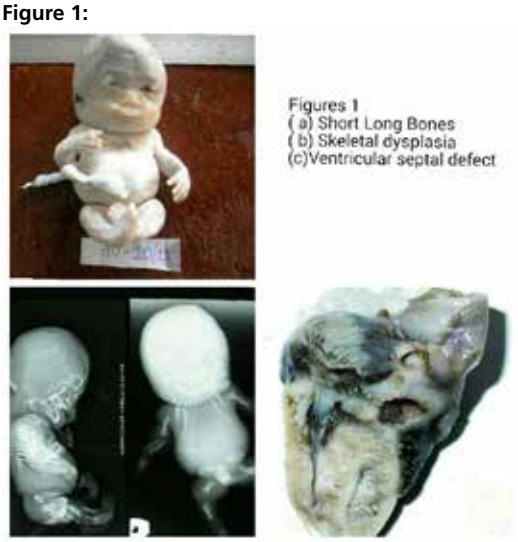
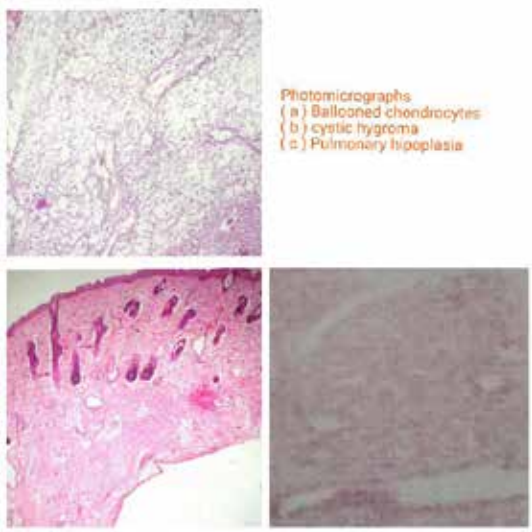


Figure 2:



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