JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH

How to cite this article :
VERMA A, MOHAN S, KUMAR S. THANATOPHORIC DYSPLASIA. Journal of Clinical and Diagnostic Research [serial online] 2007 August[cited: 2007 August 6]; 4:308-310. Available from
http://www.jcdr.net/back_issues.asp?issn=0973-709x&year=2007&month= August &volume=1&issue=4&page=308-310&id=76

CASE REPORT

Thanatophoric Dysplasia: Case Report and Review of literature

ASHISH VERMA, SUYASH MOHAN, SUNIL KUMAR

ABSTRACT

Thanatophoric Dysplasia (TD) is the most common, congenital, sporadic, usually lethal skeletal dysplasia characterized by shortening of the limbs, small conical thorax, platyspondyly and macrocephaly. TD is divided into 2 clinically defined subtypes type 1 and 2 with some clinical overlap between the 2 subtypes. Autosomal dominant mutations in the fibroblast growth factor receptor 3 gene (*FGFR3*), which has been mapped to chromosome band 4p16.3, results in both subtypes. The vast majority of cases are due to de novo mutations. This condition has characteristic sonographic features that suggest the diagnosis prenatally, although distinction from other short-limbed dysplasia syndromes may be difficult. To date, over 100 cases have been described. Thanatophoric fetuses usually die within the first 48 hours of life from pulmonary hypoplasia caused by a narrow thorax. We report a case of type 1 TD with typical imaging findings, along with a short review of the available literature.

Key Words: Thanatophoric Dysplasia; Cloverleaf skull; telephone receiver femora

Introduction:

Thanatophoric Dysplasia (TD) is a congenital, sporadic, usually lethal skeletal dysplasia characterized by shortening of the limbs, small conical thorax, platyspondyly and macrocephaly. Its incidence is 1 in 64000 to 1 in 100000 of the total live births. It is of two major subtypes viz. a short curved femur characterizes type 1, while a straighter femur with clover leaf skull characterizes type 2 [1]. It was first described by Maroteaux et al in 1967 [2]. The name of this dysplasia is derived from a Greek word 'Thanatophores' which means constantly bearing death. The term 'clover leaf skull' has been used synonymously to Kleeblattschlader syndrome [3]. From India Gupta and Bhargava [4] have reported a still born fetus of this type of dysplasia. Because of the rarity of this condition we report this case with a short review of the available literature.

Dr. Sunil Kumar, MD, Professor, Department of Radiodiagnosis, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Raebareily Road, Lucknow, 226014, UP, INDIA.
E-mail: anitasunilk@yahoo.co.in , drsuyash@gmail.com ;
Telephone: + 91 522 2668700 Extn. (O) 2565, (R) 2566 **Fax:** + 91 522 2668017.

Case Report:

A still born male fetus (gestational age approximately 32 weeks) delivered by Caesarean section was evaluated radiologically followed by autopsy. The mother was from a rural background and did not have any antenatal ultrasonographic

evaluation. There was one day old history of per vaginal leaking. In the absence of adequate obstetric history, the attending obstetrician took her up for emergency Caesarean section with a provisional diagnosis of non progression of labour. The fetal weight at birth was 1800 gms. On autopsy, the findings were suggestive of Thanatophoric dysplasia and pulmonary hypoplasia was labeled as the most probable cause of death. The plain skiagrams of the baby revealed a large sized skull with short base, small face and a H shaped configuration of the vertebral bodies. Clavicles showed the typical 'bicycle handle appearance' while both the humerii and femora revealed the 'telephone receiver appearances'. The thorax was narrow with horizontally placed ribs. Brachydactyly with absence of the carpal and tarsal bones were noted on the X-rays (Figure 1).

Discussion:

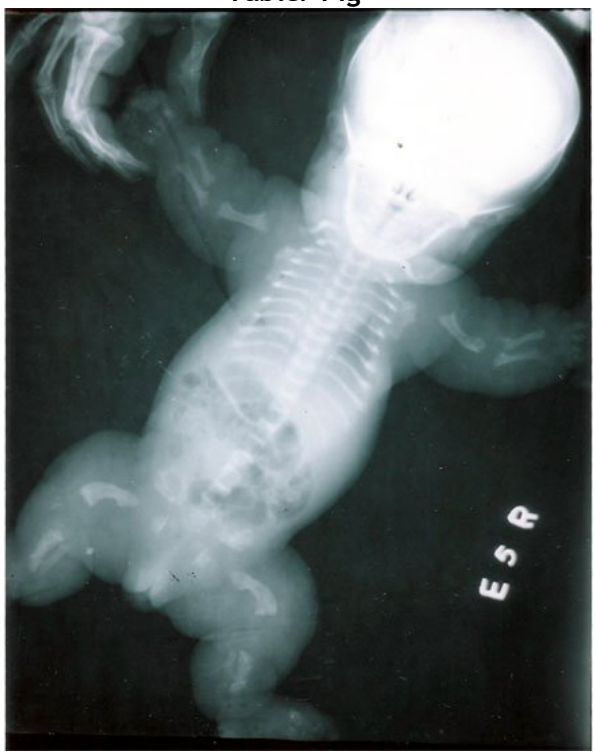
Thanatophoric Dysplasia is a condition of unknown etiology with the majority of case reports being sporadic. Some authors have reported a dominant gene mutation to be associated with this condition. Maternal Rubella infection has been proposed to be a probable etiological factor [5]. Molecular analysis of the fibroblast growth factor III receptor gene (FGFR 3) in both subtypes suggest that this is a genetically homogenous disorder. This usually leads to in-utero death of the fetus; the longest survival however has been reported to be of 9 years [6]. Males are affected more than females. The case reported here was a male fetus delivered by Caesarean section and remained alive for twenty four hours only.

Short limb dwarfism is usually of two types: type 1 presenting with polyhydramnios, macrocephaly, short limbs, narrow thoracic cage and curved short femur (the typical telephone receiver appearance) but without a cloverleaf skull. Type 2 is characterized by short limbs, narrow thoracic cage, straight short femora, hydrocephalus, and cloverleaf skull [1, 7]. However the other reported varieties are Torrance, San-Diego, and Luton types. The present case belongs to type 1 with the 'telephone receiver appearances' of both the humerii and femora. The thorax was narrow with horizontally placed ribs along with brachydactyly and absent carpals and tarsals. Association of soft tissue syndactyly of fingers and toes was for the first time reported by Brodie et al [8]. Other associated anomalies are accessory pelvis ossification centers, skin disorders, like acanthosis nigricans and cerebral anomalies including that of temporal lobe gyri and hippocampus, neuroglial heterotopias, fibre tract hypoplasia, dysplasia of deep nuclei etc. Kyphosis and lordosis has also been observed. Bowing of tubular bones may be explained by diminished mechanical stability. Impaired endochondral ossification is more prominent towards the periphery of the metaphysis leading to tongue shaped osseus cones directed towards the epiphyses. The perichondral spurs and linguiform endochondral growth plates result in 'Maple leaf like' contour of metaphyses of tubular bones and acetabular roof [9].

Death usually occurs either as a result of conical thorax and pulmonary hypoplasia (as seen in the present case) or due to cervical cord compression at a narrowed foramen magnum associated with posterior arch anomaly [10].

Antenatal sonography in second trimester not only confirms the diagnosis but also differentiates it from the other non lethal dysplasias. Three dimensional ultrasound is able to visualize the thickened redundant skin fold, limb and craniofacial anomalies more clearly [11]. Nevertheless X-ray examination must be performed after birth to confirm various findings which along with the autopsy diagnosis helps in counseling of the parents [12].

Table/ Fig



Plain skiagram showing typical X-ray appearances of skeletal abnormalities related to skull, clavicle, thorax, vertebrae, humerii, and femora in a case of Thanatophoric Dysplasia. (Consent from family obtained)

References

[1] Chang TK, Wang Y, Liu AM, Tung JC. Thanatophoric dysplasia type 1. Acta Pediatr Taiwan 2001;42(1):39-41.

[2] Maroteaux P, Lamy M, Robert JM. Le nanisme thanatophore. Presse Med 1967;75:2519-2524.

[3] Young RS, Pocharzetsky R, Leonicas JC, Wexley H. Thanatophoric dwarfism and cloverleaf skull (kleeblastscadel). Radiology 1973;106:401-405.

[4] Gupta R, Bhargava SK. Thanatophoric Dwarfism. Ind J Radiology 1976; 30: 223-228.

[5] Widding K, Steinhoff R, Guenther H. The cloverleaf skull syndrome. Zentrablatt fur Allgeeine Pathologic and Pathologische anatomie 1974;118(4): 358.

[6] Baker KM, Olson DS, Harding CO, Pauli RM. Long term survival in typical thanatophoric dysplasia Type 1. Am J Med Genetics 1997;70:427-436.

[7] Chen CP, Chern SR, Stuh JC, Wang W, Yeh LF, Chang TY, Tzen CY. Prenatal diagnosis and genetic analysis of type 1 and 2 thanatophoric dysplasia. Prenat Diag 2001; 21:89-95.

[8] Brodie SG, Kitoh H, Lachman RS, Nolasco LM, Mekikian PB, Wilcox WR. Platyspondylic lethal skeletal dysplasia, San Diego type is caused by FGFR3 mutation. Am J Med Genetics 1999;84:476-480.

[9] Weber M, Johannisson T, Thompson M, Rehder H, Neithard FU. Thanatophoric dysplasia type 1: new radiologic, morphologic and histologic aspects towards the exact definition of the disorder. J Pediatr Orthop B 1998;7:1-9.

[10] Faye-Peterson OM, Knisely AS. Neural arch stenosis and spinal cord injury in thanatophoric dysplasia. Am J Dis Child 1991;145:87-89.

[11] Garjian KV, Pretorius DH, Budorick NE, Cantrell CJ, Jhonson DD, Nelson TR. Fetal skeletal dysplasias: three dimensional ultrasound – Initial experience. Radiology. 2000; 214: 717-723.

[12] Sauer I, Klein B, Leeners B, Cotarelo C, Heyl W, Funk A. Lethal osteochondrodysplasias – prenatal and postnatal differential diagnosis. Ultraschall in der Medizin 2000;21:112-121.