THANATOPHORIC DWARFISM: THREE CASE REPORTS

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SYNOPSIS

Thanatophoric dwarfism is a rare and invariably fatal form of dwarfism. This report presents the clinical and sonographic findings of this form of dwarfism based on 3 cases managed in our hospital. The differentiation of this form of dwarfism from other forms are discussed.

INTRODUCTION

Thanatophoric dwarfism was first described by Maroteaux et al in 1967 (1). Although rare, it is the most common of all the forms of lethal dwarfism (2). The name is derived from the Greek word 'thanatophoros' meaning "constantly bearing death". Most affected infants survive from a few hours to a few days, although one mechanically-ventilated baby was reported to survive for 156 days (3). The cause of death in thanatophoric dwarfism is cardiorespiratory failure, secondary to the severely constricted thoracic cages and extremely small lungs (4). The underlying pathogenesis of this distinct form of dwarfism is a generalised failure of endochondral bone formation.

The purpose of this paper is to describe the clinical presentation and obstetric outcome of thanatophoric dwarfs managed in our hospitals, and to point out characteristics which differentiate this condition from clinically similar but non-lethal forms of dwarfism such as achondroplasia or achondrogenesis. This differentiation not only influences antenatal and intrapartum management, but ensures proper genetic counselling in future pregnancies.

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CASE REPORTS

Case One

Mdm HBH was a 38 year old Malay women in her third pregnancy with two previous normal livebirths. she first presented in the third trimester of pregnancy with anaemia, pre-eclampsia, polyhydramnios and breech presentation. Ultrasound examination confirmed the excessive liquor and the breech presentation. It also revealed that the baby had shortened and bowed limbs, a large head, and a constricted chest with a protuberant abdomen. These ultrasonic features were suggestive of thanatophoric dwarfism, and confirmation of the diagnosis was subsequently made with radiology. The patient went into spontaneous labour at 39 week's gestation. Vaginal examination revealed a cord prolapse in early labour with the live foetus still in breech presentation. The poor prognosis was clearly explained to the parents but they insisted that all measures should be undertaken to save their baby. An emergency Caesarean section was performed and a female baby weighing 3480 gms was delivered. The Apgar score was 2 at 1 minute and 3 at 5 minutes. Immediate resusitation was instituted but death was pronounced 49 minutes later.

Case Two

Mdm SGI was a 30 year old primigravida who was well antenatally until 27 week's gestation when she was noted to have polyhydramnios with a uterus larger than dates. Both her parents were diabetics and an oral glucose tolerance test revealed that she had impaired glucose tolerance. She was therefore admitted for control and management of this problem. An ultrasound examination at 29 weeks' gestation showed a footling breech with short femur and humerus, bowed tibia and radius bones, and an abnormally large skull. A diagnosis of thanatophoric dwarfism was suggested and this was confirmed with radiology. She went into premature labour at 30 weeks' gestation and delivered a 1310 gms baby girl by assisted breech delivery after 2 hours of labour. The apgar score was 4 at 1 minute and 5 at 5 minutes. The neonate died after 2 days.

Case Three

Mdm KSY was a 31 year old Chinese gravida 2 para 1 who was first seen at 16 weeks' amenorrhoea because she had gestational diabetes mellitus during her first pregnancy requiring insulin for therapy. Her first baby was born at full term by a normal vaginal delivery and weighed 4120 gms. An oral GTT was urgently repeated this pregnancy and confirmed recurrent gestational diabetes. She was started on insulin therapy. Ultrasonic examination at 35 weeks' gestation showed a breech with a large skull, short limbs with a narrow thorax, a protuberant abdomen and polyhydramnios. Thanatophoric dwarfism was suspected and this was confirmed with radiology. The baby spontaneously reverted to cephalic presentation at 36 weeks. In view of the diagnosis, it was decided at that stage to deliver the baby and the patient was surgically induced at 36 weeks' gestation. A male baby weighing 2440 gms was born by a normal vaginal delivery. Apgar score was 2 at both 1 and 5 minutes, and was pronounced dead after 44 minutes. He had a large hard skull, shortened limbs and a small chest.

SUMMARY OF CASES

The mean age of the patients was 33 years (range 30 to 38 years), while their husbands' age ranged from 32 to 40 years. Two were multiparous while one was a primigravida. None of them had a family history of thanatophoric dwarfism. Polyhydramnios and breech presentation was found in all cases. Spontaneous version occurred in one case, while in one the breech persisted till term. The third delivered prematurely as a breech. Antenatal diagnosis of dwarfism was made by ultrasonic examination in all patients. The diagnosis of thanatophoric dwarfism was confirmed in all by typical findings on radiology (Table 1). Two patients went into spontaneous labour prematurely, while 1 patient had labour induced at 36 weeks' gestation. Two patients achieved normal vaginal delivery while the third required Caesarean section at the patient's request. All had poor Apgar scores at birth and the birthweights ranged from 1310 to 3480 gms. Two died within the hour and the third was dead within 2 days of delivery. Two babies were female and one was male.

DISCUSSION

Thanatophoric dwarfism is a rare form of dwarfism first described less than 2 decades ago (1). Antenatal diagnosis of this condition is important as it is uniformly fatal and its differentiation from non-lethal forms of dwarfism have a direct bearing on management. The quoted incidence of thanatophoric dwarfism varies from 1 in 6,400 (5) to 1 in 10,000 births (6).

The conditions most commonly confused with thanatophoric dwarfism are achondroplasia and achondrogenesis, although one had to bear in mind all the types of dwarfs that have been described (Table 2). Homozygous achondroplasia, in particular, resemble thanatophoric dwarfs very closely, but fortunately examination of the parents will readily exclude the condition if both parents are phenotypically normal. Clinical examination of the babies after birth is not very helpful as many of the clinical features of the different forms of dwarfs are non-specific and may overlap. An exception to this rule is achondrogenesis where the trunk and limbs are uniformly small, in contrast to the other types of dwarfs where the trunk is normal in size and only the limbs are short. One, therefore, has to rely on investigatory procedures such as sonography or radiography for diagnosis. Ultrasound can reliably diagnose dwarfism in the third trimester, but differentiation between achondroplasia and achondrongenesis, as well as diastrophic dwarfism, which also give similar sonographic features (7), is more difficult. A number of recent articles have suggested that sonography can diagnose specific forms of dwarfism (8,9,10). For instance, the absence of spinal echoes, due to poor ossification in the vertebrae, has been said to be diagnostic of achondrogenesis (11). Similarly the clover-leaf skull, a trilobar skull deformity caused by premature fusion of cranial sutures, is said to be diagnostic of thanatophoric dwarfism (10). Although the clover-leaf skull has been described in association with other malformations (12), it has never been described in association with other forms of dwarfism. In the case of camptomelic dwarfism, its unique bowing of the extremity of the long bones (2) is said to be diagnostic, but can still be confused with the bowing found in thanatophoric dwarfs. Other sonographic features have also been described, but they are less distinctive. These include marked soft tissue redundancy secondary to the small thorax and extremities in thanatophoric dwarfs (7,9,13); and the shortening of the femur late in the second trimester seen in heterozygous achondroplasia (14). In practice, it remains difficult to make the sonographic distinc-

TABLE 1
RADIOLOGICAL FEATURES OF THANATOPHORIC DWARFISM

GENERAL APPEARANCE

Normal sized trunk with short limbs
Narrow thorax
Small, square scapulae
Airless lungs

VERTEBRAL BODIES

Extremely flat, wide intervertebral disc spacs
Inverted 'U' appearance

PELVIS

Short & broad
Rectangular ilia
Spurring of ischium
Flat & horizontal acetabular roofs

LIMBS

Short, broad & bowed
'Telephone receiver' appearance of femora — due to pear-shaped translucencies of proximal femora, and cupped & flarred metaphysis

SKULL

Prominent frontal bone
Depressed root of nose
Good mineralisation
Short skull base
'Cloverleaf appearance' — due to premature fusion of the coronal & lambdoidal sutures
Small facial bones

TABLE 2
TYPES OF CONGENITAL SHORT-LIMBED DWARFISM

LETHAL

Thanatophoric dwarfism
Homozygous achondroplasia
Achondrogenesis (Fraccaro-Parenti & Houston-Harris type)
Chondrodysplasia calcificans congenita punctata (lethal rhizomelic recessive form)
Campomelic syndrome
Hypophosphatasia (congenital lethal type)
Osteogenesis imperfecta (recessive thick bone type)

NON-LETHAL

Achondroplasia
Diastrophic dwarfism*
Spondyloepiphyseal dysplasia congenita
Metatrophic dwarfism
Chondroectodermal dysplasia
Asphyxiating thoracic dysplasia*
Metaphyseal chondrodysplasia (McKusick type)
Mesomelic dwarfism

* May be lethal

tion between thanatophoric dwarfism and other forms of dwarfism if the clover-leaf deformity is absent. The definitive diagnosis usually rests with radiological examination, which is still the most consistent means of differentiation and the original basis by which the nomenclature of dwarfisms was first described (2). The radiological features of thanatophoric dwarfs are listed in Table 1, and the features which distinguish it from achondroplasia and achondrogenesis are listed in Table 3 (4).

diabetes is characteristically associated with sacral agenesis, another malformation involving bone, and the association of maternal diabetes to thanatophoric dwarfism has not been reported on in other reviews (4,15,20). None of the 3 cases reported here had the clover-leaf skull and diagnosis had to be confirmed with radiography. Once the diagnosis is confirmed, it is advisable to expedite delivery as continuation of pregnancy may result in obstructed labour due to the large hard skull (17).

TABLE 3
RADIOLOGICAL DIFFERENTIATION BETWEEN THANATOPHORIC DWARFISM (T.D.), ACHONDROGENESIS (A.G.) AND ACHONDROPLASIA (A.P.)

	T.D.	A.G.	A.P.
Micromelia	+ + +	+ + +	+ +
Maximal shortening	proximal	both	proximal
Metaphyseal flaring	+ +	+ + +	+
Spinal column short	+/–	+ +	+/–
Narrow sacrosciatic notch	+	–	+
Iliac bones flattened	+	+	–
Short ribs	+ +	+ + +	+

FEATURES SPECIFIC TO THANATOPHORIC DWARFISM:

Inverted "U" or "H" shaped vertebral bodies (AP view); bony spurs on the proximal femur & anterior face of L1; and metaphyseal & ischial spicules.

FEATURES SPECIFIC TO ACHONDROGENESIS:

Deficient ossification of vertebrae; absent ossification of pelvic bones; and rib fractures.

The genetics of thanatophoric dwarfism is still unknown. Although there are a number of reports of thanatophoric dwarfs occurring in families (5,16,17,18), they have been disputed (4,15). Early cases reported as thanatophoric siblings were later shown to represent achondrogenesis instead (5). Chemke et al (18) published a report of two thanatophoric children born to consanguineous parents and were originally criticised for being unsupported by radiographs (15). They have since published a complete report (16), and this remains the only confirmed case of familial thanatophoric dwarfism. In review of the reported cases of thanatophoric dwarfism, Pena & Goodman (19) concluded that the data favour a polygenic mechanism, with some cases due to autosomal recessive inheritance, and suggested an empirical recurrence risk of 1:50.

In our experience, the most consistent clinical presentation of thanatophoric dwarfism was polyhydramnios associated with a breech presentation. In a recent review, polyhydramnios was reported in 71% of cases (15). The excessive liquor appeared to be the underlying cause for the complications encountered in our patients, that is, the breech presentations, the cord prolapse in one patient and the premature deliveries in two others. Caesarean section was resorted to in one case when ideally it should have been avided as the prognosis is invariably fatal. This, however, was performed at the patient's insistence. Advanced paternal age did appear to be a contributory factor in our cases as the oldest father was but 40 years of age. Although the female : male ratio was 2:1, there are too few cases for any conclusion. An interesting feature in or three cases is the presence of gestational diabetes mellitus in one patient and impaired glucose tolerance in another. Gestational

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