LETHAL NEONATAL DWARFISM: A CASE OF ACHONDROGENESIS

MASOOD K AFZAL
CHOO KENG EE

SUMMARY

Achondrogenesis is a lethal neonatal chondrodysplasia with extreme micromelia and marked discrepancy between the relatively large head and the decreased trunk length. The affected neonates are usually delivered prematurely, and are stillborn or die soon after birth. Polyhydramnios is frequently present. It is an inherited autosomal recessive disease. The radiographic features are diagnostic.

INTRODUCTION

OUR interest in neonatal dwarfism was aroused by the presentation of a deformed neonate with short upper limbs and flapper-like lower limbs. We were unable to diagnose that baby. That was three years ago, since then we have seen one case of short rib polydactyly syndrome, one case of chondrodysplasia puncta or Conradi's disease and one of neonatal osteopetrosis. Our most recent addition is a case of achondrogenesis which we present here. The aim of this article is to alert paediatricians and obstetricians of neonatal dwarfism so that genetic counselling to parents can be done. More often than not, in pratice, such babies are diagnosed as "still birth", "preterm baby with congenital deformities" or "preterm with achondroplasia".

CASE REPORT

A baby girl was prematurely delivered at 28 weeks gestation on 18.10.1979 to a thirty-year-old mather (K bt. A.H.). This was her fourth pregnancy, she had one previous abortion. Three other children are alive and well. The parents are well and healthy. There was no history of congenital abnormalities. There was no antenatal history of drugs or illness. The baby was delivered gasping and died shortly afterwards. At birth the baby weighed 2 lb 8 oz and the Apgar was 2 at 1 min. The neonate had a disproportionately large head, short neck, distended abdomen, thorax and reduction deformities of all limbs. The baby was markedly oedematous, (Fig. 1). Head circumference was 28.5 cm, crown-rump length 20 cm and crown-heel length 25 cm. The thoracic circumference at the nipple was 21 cm. Post-mortem of the baby was not granted and we were also unable to obtain blood for chromosomal and viral studies.

The radiographic features in this neonate are seen in Fig. 2. There is absent ossification of the lumbar vertebrae and sacrum. The ischium and pubic bones are also unossified. The iliac bones are small with concave inner and inferior margins. The tubular bones are markedly shortened and show metaphyseal widening and cupping. The thorax is small and barrel-shaped, the ribs are short. The small non-ventilated thoracic cage contrasts with the bulging abdomen. The skull shows good ossification and appears very large in comparison with the marked shortening of trunk and limbs.

The clinical and radiographic features in this newborn baby are characteristic of Achondrogenesis type 2(Langer-Saldino-Fraccara). The absent ossification of the lumbar vertebrae, sacrum, ischium and pubis with the characteristic small iliac bones with concave inner and inferior margins (Fig. 3) are diagnostic of achondrogenesis. The normal ossification of the skull and the radiographic appearance of the limbs are features consistent with type 2 (Yang, 1974). The abnormality in type 2 appears to affect cartilage and tubular bones but not membraneous bones.

Masood K. Afzal, MBBS, DMRD,
Radiologist, University Hospital, University of Malaya, Kuala Lumpur.

Choo Keng Ee*, MBBS, MRCP (UK)
Paediatrician, General Hospital, Seremban

*Presently, Paediatrician, General Hospital, Kuala Trengganu.

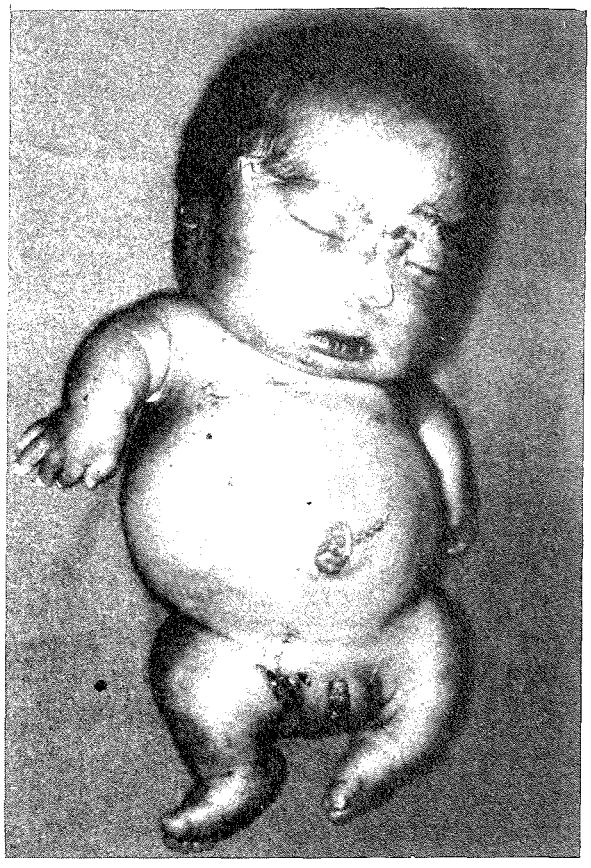

Fig.1 Photograph of achondrogenic newborn showing large head, short thick trunk and marked micromelia.

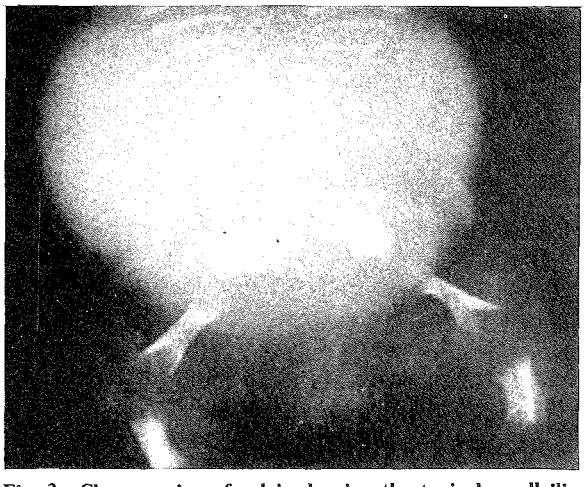

Fig. 3 Close-up view of pelvis showing the typical small ilia with concave inner and inferior margins which is diagnostic of achondrogenesis.

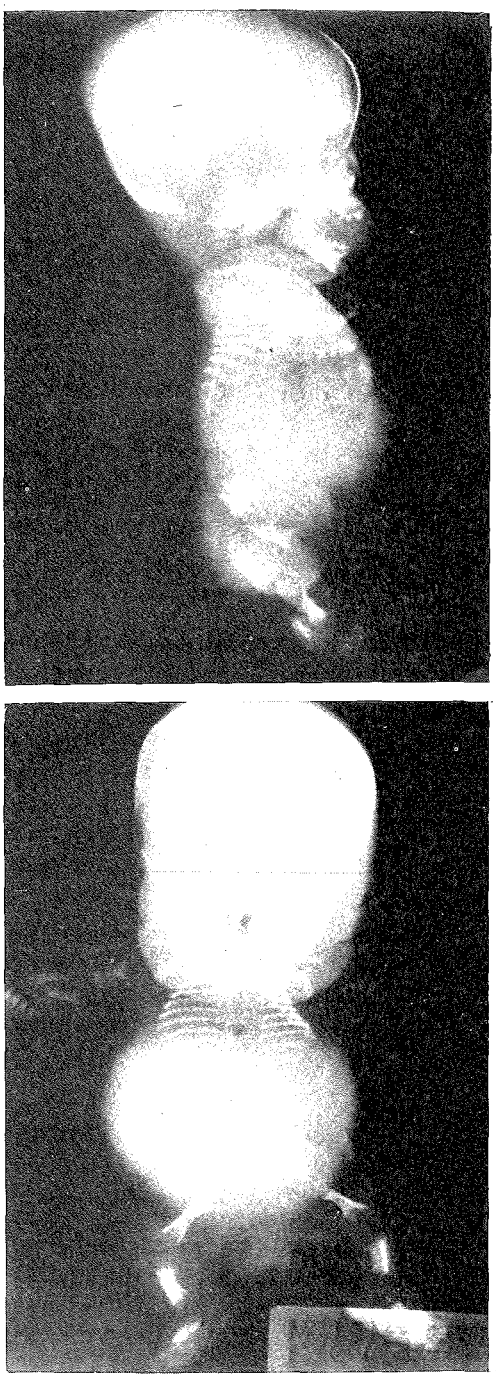

Fig. 2 Achondrogenesis: anterior and lateral radiographs showing non-ossification of vertebrae and pelvic bones; small ilia with concave inner and inferior margins; small thorax with short ribs; prominent abdomen and large head with normal ossification of skull. The tubular bones of the limbs are short and show characteristic metaphyseal widening and cupping.

DIFFERENTIAL DIAGNOSIS

Achondrogenesis type 1 is characterised by poor ossification of the skull, multiple rib fractures and very short, broad bones of the extremities with marked bowing. In short rib polydactyly syndrome and thanatophoric dysplasia there is ossification of the vertebral column and pelvis. The bones of the extremities have a different appearance than in achondrogenesis. Severe hypophosphatasia is differentiated by the absent or severely delayed ossification of the skull and the delicate appearance of the tubular bones with characteristic metaphyseal ossification defects (Spranger, 1974). Histologically achondrogenesis type 1 is probably a primary disorder of connective tissue and shows severe retardation of chondrocytic proliferation in the physeal cartilage. On the other hand, achondrogenesis type 2 is probably a disoder representing degeneration of proliderating epiphyseal cells with extremely dificient matrix (Yang, 1976). Further discussion on the differential diagonsis may be found in Saldino (1971) and Xanthakos *et al.* (1973).

GENETICS

Saldino, 1971 mentions of two families in which multiple siblings were affected, one of these parents were consanguinous. He also mentions a case where one of a pair of twins was affected while the other was normal. This strongly suggests that achondrogenesis, both types, are genetically determined disorders with an autosomal recessive mode of transmission. There is, therefore, one in four risk of recurrence for each subsequent child of parents who have produced an affected infant. However, the lethality of the condition should be stressed when counselling parents who are contemplatihg procreation. Equally it should be emphasised that there is a three out of four chance that any further offspring will be normal.

DISCUSSION

An underlying skeletal dysplasia should be suspected in the differential diagnosis of any baby who is short for gestational age, any baby who has disproportionate shortening of the limbs or trunk, and in any baby with multiple congenital abnormalities. There are several different conditions that may produce low birth weight or short length for gestation infant. These include placental insufficiency, foetal-maternal endocrine defect, chromosomal abnormalities, dysmorphology syndrome, intrauterine infection, skeletal dysplasia, etc (Sillence, 1978). In the assessment of the small infant details of the pregnancy, delivery, obstetric and family history and the initial examination of the neonate and its placenta may provide a clue to the underlying cause. An accurate assessment of gestation is necessary to interpret measurements of length, weight and head circumference in the newborn. The mother's menstrual history may be the only reliable index of gestational age. Having established that an infant is disproportionately short, one must determine whether the shortening primarily affects the trunk or the limbs and if the latter whether it is proximal (rhizomelic) middle segment (mesomelic) or distal (acromelic) or a combination of these.

If skeletal dysplasia is suspected a proper work-up would include:-

1. History: Family and maternal obstetric history.
2. Clinical examination
3. Clinical photographs
4. X-ray examination: skeletal survey - babygram
5. Morphological studies of chodroosseous tissue: biopsy, autopsy.
6. Other: Chromosome study, immune function, biochemistry etc.

The evaluation of a baby with skeletal dysplasia requires a multidisciplinary approach utilising clinical, radiographic, genetic and morphological findings. Although we still do not have a satisfactory classification of skeletal dysplasia, the present one based on clinical and radiographic features has evolved a concept that is invaluable for proper family counselling and for

the medical care of the children affected, and enables a fairly prompt and accurate diagnosis in most cases. This is the International Nomemclature for Constitutionsl Diseases of Bone which was adopted in 1970 and further revised in 1977. This classification (Rimion, 1978) divides the skeletal dysplasias into two major groups: The *chondrodysplasias* (abnormal growth and deveiopment of cartilage and/or bone) and the dysostoses (malformations of individual bones, singly or in combination). The short-limbed dwarfisms or chondrodysplasias are subdivided into those disorders that are manifest at birth and those that become apparent later in life. Neonatal chondrodysplasias are again subdivided into those disorders that are almost always lethal (stillborn or die soon after birth) and those in which the baby usually survives the neonatal period.

The disorder that comprise lethal neonatal dwarfism are:-

1. Achondrogenesis type 1 (Parenti-Housten-Harris).
2. Achondrogenesis type 2 (Langer-Saldino-Fraccare).
3. Thanatophoric dysplasia type 1.
4. Thanatophoric dysplasia type 2 (clover leaf skull).
5. Short rib polydactyly syndrome type 1 (Majewski).
6. Short rib polydactyly syndrome type 2 (Saldino -Noonan).
7. Short rib polydactyly syndrome type 3 (Naumoff).
8. Asphyxiating thoracic dystrophy (ATD) or Juene syndrome.
9. Chondroectodermal dysplasia or Ellis van Creveld syndrome (EVC).
10. Campomelic dysplasia.
11. Achondroplasia homozygous type.
12. Chondrodyplasia punta rhizomelic type.
13. Osteogenesis imperfecta type 2 (lethal preinatal type).
14. Hypophosphatasia (severe).
15. Congenital osteopetrosis.

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