A case of thanatophoric dysplasia

Veira BRM, Menezes MOA, Raupp VA, Suzana TC, PritsiVelis C, Braga JRS, Faleiro EC, Lima RPC, Antunes CA
Maternidade Escola da Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

Objective
The Thanatophoric Dysplasia (TD) is a congenital syndrome, rare and potentially lethal. Epidemiological records vary to one in 20,000 – 50,000 births. It also shows no predilection for sex. Clinically, it is characterized by macrocephaly, facial dysmorphism, narrow chest with short ribs, micromelia, brachydactyly and hypotonia. We present a case report of a pregnant woman whose fetus was diagnosed with TD, the management of the patient and the baby's symptoms and findings after birth.

Methods
We follow a pregnant woman admitted at our fetal medicine service with a fetus diagnosed with (DOENÇA) by ultrasound findings during her prenatal care and hospitalization until birth.

Results
A. R. S., a thirty year old pregnant woman of 29 weeks and 4 days of gestation, was referred to our Fetal Medicine service due to findings in ultrasound, showing shortening of long bones -humerus and femur. On the first appointment at our fetal medicine department, the patient confirmed to be previously healthy, with no report of drug abuse and no use of regular medication. Gestation was planned and the patient attended five prenatal care appointments. Ultrasound imaging at 17 weeks of gestation showed evidence of shortened femur, with a length compatible with 13 weeks. Second trimester morphology ultrasound suggested thanatophoric dysplasia evidenced by limbs smaller than expected. It was suggested to the patient to start counseling at our psychology department, when she was informed about the main different diagnosis and the poor prognosis. A new fetal assessment through ultrasound was made on January 2015, when the patient was 31 weeks of pregnancy. This ultrasound showed polyhydramnios, shortened long bones (below percentile 5 for gestational age), macrocephaly (cephalic circumference above percentile 95) and narrow chest, short ribs, underdeveloped lungs. In 4 February of 2015 the patient needed to be submitted to an invasive procedure: an amniocentesis in order to provide a respiratory relief to the fetus. 2100 ml of clear liquid was drained at the occasion, with no complications and there was no need for further similar procedures. Doppler evaluation was never altered. In March 10 of 2015, when she was 37 weeks and 3 days of gestation the patient was admitted in labor at our hospital. After a caesarean due to pelvic presentation, the patient gave birth to a hypoactive, non-reactive and bradycardic newborn. The baby’s aggar was 2/4, and needed to receive reanimation right after birth. The newborn was admitted to the neonatal intensive care unit, evolving with desaturation - in spite of mechanical ventilation - and died five hours after birth. Post mortem evaluation showed pulmonary hypoplasia as the cause of death due to Thanathophoric Dysplasia.

Conclusion
Thanatophoric dysplasia was first identified by Maroteaux, in 1967. However, the most oldest case report was made by Maygrier, in 1898. [1, 2] The DT is the most common and lethal type of chondrodysplasia and, usually, the death of the fetus occurs during the perinatal period due to respiratory failure. DT is an autosomal dominant disease, caused by a mutation in the gene FGFR3 (fibroblast growth factor receptor -3; OMIM 187600). Clinically, it is characterized by macrocephaly, facial dysmorphism, narrow chest with small ribs, micromelia, brachydactyly and hypotonia. Radiological tests show skull in cloverleaf like format, platyspondyly, rhizomelic shortening and irregularities in the metaphysis of long bones, shortening femur and abnormalities in central nervous system, such as dysplasia of temporal bone (prominent suture lines and radially directed gyrations ). This is considered the defining pathological features of DT. The diagnosis of DT may be defined during prenatal or perinatal period. On the first trimester, the ultrasound can show shortening of long bones and increase of nuchal translucency. On second and third quarters, we are able to see polyhydramnios, poor growth of the limbs, skull in cloverleaf like format, macrocephaly, ventriculomegaly, narrow chest, platyspondyly and shortened femur. There are two subtypes with relative incidence: Type I - 80% and Type II - 20%. The two subtypes can be differentiated by the skull shape and femur morphology. TD type I is characterized by curved and short femur which is in a telephone receiver like configuration and no cloverleaf shaped skull. The fetuses with type II TD are reported to have cloverleaf skull which means a trilobed skull. The premature closure of coronal and lambdoid sutures is commonly seen with the cloverleaf skull. This diagnosis can be confirmed by amniocentesis between 15 to 18 weeks of pregnancy, or by chorionic villus sampling between 10 to 12 weeks. Differential diagnosis of TD includes homozogous achondroplasia, achondrogenesis (bones demineralization that are most marked), campomelic dwarfism, rhizomelic chondrodysplasia punctata, severe hypophosphatasa and severe osteogenesis imperfect. Most of the fetuses with TD die in utero. The cause of death is due to respiratory insuficiency which may be secondary to the narrow chest cavity and hypoplastic lungs, brain stem compression by the narrow foramen magnum or a combination of both. Surviving neonate is almost always ventilator dependent and mentally deficient.

A. R.

15th World Congress in Fetal Medicine

Vieira BRM, Menezes MOA, Raupp VA, Suzana TC, PritsiVelis C, Braga JRS, Faleiro EC, Lima RPC, Antunes CA
Maternidade Escola da Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

Objective
The Thanatophoric Dysplasia (TD) is a congenital syndrome, rare and potentially lethal. Epidemiological records vary to one in 20.000 – 50.000 births. It also shows no predilection for sex. Clinically, its characterized by macrocephaly, facial dysmorphism, narrow chest with short ribs, micromelia, brachydactyly and hypotonia. We present a case report of a pregnant woman whose fetus was diagnosed with TD, the management of the patient and the baby’s symptoms and findings after birth.

Methods
We follow a pregnant woman admitted at our fetal medicine service with a fetus diagnosed with (DOENÇA) by ultrasound findings during her prenatal care and hospitalization until birth.

Results
A. R. S., a thirty year old pregnant woman of 29 weeks and 4 days of gestation, was referred to our Fetal Medicine service due to findings in ultrasound, showing shortening of long bones -humerus and femur. On the first appointment at our fetal medicine department, the patient confirmed to be previously healthy, with no report of drug abuse and no use of regular medication. Gestation was planned and the patient attended five prenatal care appointments. Ultrasound imaging at 17 weeks of gestation showed evidence of shortened femur, with a length compatible with 13 weeks. Second trimester morphology ultrasound suggested thanatophoric dysplasia evidenced by limbs smaller than expected. It was suggested to the patient to start counseling at our psychology department, when she was informed about the main different diagnosis and the poor prognosis. A new fetal assessment through ultrasound was made on January 2015, when the patient was 31 weeks of pregnancy. This ultrasound showed polyhydramnios, shortened long bones (below percentile 5 for gestational age), macrocephaly (cephalic circumference above percentile 95) and narrow chest, short ribs, underdeveloped lungs. In 4 February of 2015 the patient needed to be submitted to an invasive procedure: an amniocentesis in order to provide a respiratory relief to the fetus. 2100 ml of clear liquid was drained at the occasion, with no complications and there was no need for further similar procedures. Doppler evaluation was never altered. In March 10 of 2015, when she was 37 weeks and 3 days of gestation the patient was admitted in labor at our hospital. After a caesarean due to pelvic presentation, the patient gave birth to a hypoactive, non-reactive and bradycardic newborn. The baby’s aggar was 2/4, and needed to receive reanimation right after birth. The newborn was admitted to the neonatal intensive care unit, evolving with desaturation - in spite of mechanical ventilation - and died five hours after birth. Post mortem evaluation showed pulmonary hypoplasia as the cause of death due to Thanathophoric Dysplasia.

Conclusion
Thanatophoric dysplasia was first identified by Maroteaux, in 1967. However, the most oldest case report was made by Maygrier, in 1898. [1, 2] The DT is the most common and lethal type of chondrodysplasia and, usually, the death of the fetus occurs during the perinatal period due to respiratory failure. DT is an autosomal dominant disease, caused by a mutation in the gene FGFR3 (fibroblast growth factor receptor -3; OMIM 187600). Clinically, it is characterized by macrocephaly, facial dysmorphism, narrow chest with small ribs, micromelia, brachydactyly and hypotonia. Radiological tests show skull in cloverleaf like format, platyspondyly, rhizomelic shortening and irregularities in the metaphysis of long bones, shortening femur and abnormalities in central nervous system, such as dysplasia of temporal bone (prominent suture lines and radially directed gyrations ). This is considered the defining pathological features of DT. The diagnosis of DT may be defined during prenatal or perinatal period. On the first trimester, the ultrasound can show shortening of long bones and increase of nuchal translucency. On second and third quarters, we are able to see polyhydramnios, poor growth of the limbs, skull in cloverleaf like format, macrocephaly, ventriculomegaly, narrow chest, platyspondyly and shortened femur. There are two subtypes with relative incidence: Type I - 80% and Type II - 20%. The two subtypes can be differentiated by the skull shape and femur morphology. TD type I is characterized by curved and short femur which is in a telephone receiver like configuration and no cloverleaf shaped skull. The fetuses with type II TD are reported to have cloverleaf skull which means a trilobed skull. The premature closure of coronal and lambdoid sutures is commonly seen with the cloverleaf skull. This diagnosis can be confirmed by amniocentesis between 15 to 18 weeks of pregnancy, or by chorionic villus sampling between 10 to 12 weeks. Differential diagnosis of TD includes homozogous achondroplasia, achondrogenesis (bones demineralization that are most marked), campomelic dwarfism, rhizomelic chondrodysplasia punctata, severe hypophosphatasa and severe osteogenesis imperfect. Most of the fetuses with TD die in utero. The cause of death is due to respiratory insuficiency which may be secondary to the narrow chest cavity and hypoplastic lungs, brain stem compression by the narrow foramen magnum or a combination of both. Surviving neonate is almost always ventilator dependent and mentally deficient.