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Prenatal Treatment of Fetal Goitrous Hypothyroidism by Intraamniotic Thyroxine

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ABSTRACT:

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We present the management of a case of fetal goitrous hypothyroidism (FGH) referred to our centre on completion of the 31th week with a view to prenatal treatment. The fetus displayed an anterior neck mass recognizable as thyroid by location and texture. The mother had normal thyroid function tests and no antithyroid antibodies. A cordocentesis was performed to reveal hypothyroid status, also checking the fetal karyotype which was a normal male. Intraamniotic injections of L-thyroxine 500 µg were carried out weekly. After six applications of the dose the pregnancy reached 38+5 weeks when normal delivery ensued, the newborn presenting a euthyroid status. He grew up to a healthy boy, now seven years of age, with completely normal motor and intellectual development.

The rationale behind diagnosis, prenatal treatment and appropriateness of such management is discussed in this article.

Key words: *Congenital Hypothyroidism, Fetal Goiter, Fetal Therapy, Prenatal Diagnosis, Cordocentesis, Amniocentesis.*

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INTRODUCTION

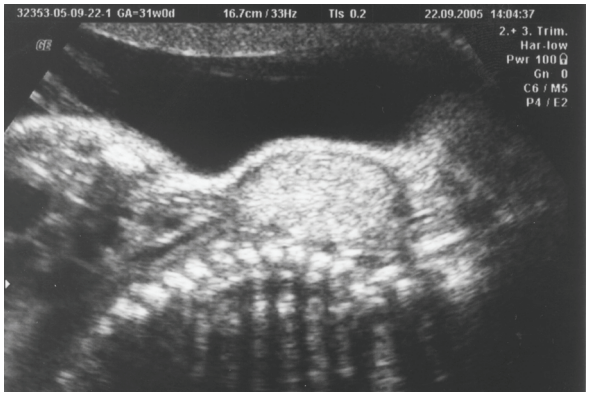
Congenital hypothyroidism (CH) is a relatively rare condition affecting 1 in every 3000 to 4000 newborns (1). When it is but the incidence not only varies with geographic location but has also increased in time due to more accurate testing methods and stricter screening strategy in general (2). The aetiological factors involved are most commonly endemic iodine deficiency, maternal treatment of hyperthyroidism with antithyroid drugs, maternally derived goitrogens and very rarely dyshormonogenesis of the fetal thyroid where the mother has no thyroid disorder (3).

Fetal Goiter can be recognized by a discernible bulky appearance of the gland which may be large enough to keep the fetal neck extended and cause polyhydramnios all of which show with relative ease on a detailed anomaly screen or even on a routine prenatal ultrasound examination. Apart from polyhydramnios, malpresentation, dystocia and even asphyxia and death at delivery may result from upper airway compression. Quantitative assessment of the size (4) can be utilized to show measurements above the 95th percentile for the gestational age or biparietal diameter (BPD). To assess the fetal thyroid status elucidating or confirming the nature of the goiter and carrying out other tests as deemed necessary like karyotype, a cordocentesis is appropriate if prenatal therapy is intended. CH has been treated only after birth for a long time but even very early treatment of the newborn leaves many individuals with intellectual impairment and motor or cognitive deficiencies (1,5). Hence prenatal treatment seems to be most desirable if such outcome is to be avoided. As the placenta is relatively impermeable to thyroid hormones the administration of the drug must be targeted to immediate fetal environment, namely the Amniotic Fluid.

CASE REPORT

A 28 year old primigravida in the 31st week of her pregnancy was referred to our unit from a hospital where the fetus was suspected to have thyroid enlargement from the 25th gestational week onwards. The patient was not on any relevant medication and had no significant personal history of thyroid or other medical disease. Family history included her mother with "toxic goiter" and a brother with "hypoparathyroidism".

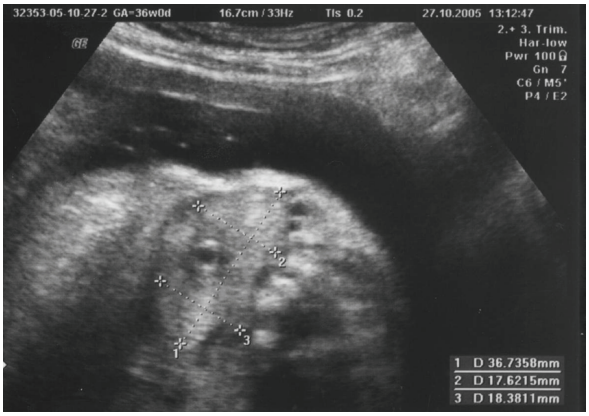
Figure 1. Longitudinal sonogram shows the enlarged thyroid of fetus from the 31 weeks' gestation.



The examination of the fetus revealed a goiter (Figure.1) measuring 41 mm in the transverse plane, 18x17 mm left lobe, 16x16 mm right lobe and 16 mm isthmus. There were no other abnormal findings in the detailed scan, no polyhydramnios was present. The physical examination and ultrasound scan of the mother's thyroid was normal and a laboratory screen was carried out. The thyroid hormones and routine biochemical tests were normal, anti- thyroglobulin (anti-Tg) and anti-thyroid peroxidase (anti-TPO) antibodies were negative, serum thyroxine-binding globulin level was 36 mcg/ml (normal: 15-34 mcg/ml). A free-loop cordocentesis was performed as the placenta was posterior and fetal blood values were obtained. These were: Free triiodothyronine (fT3) 1.29 pg/ml (normal: 2.57-4.43), free thyroxine (ft4) 1.51 ng/ml (normal: 0.932-1.71), thyroid stimulating hormone (TSH) 5.04 mIU/L (normal: 0.270-4.20), hemoglobin 13.5 g/dl, hematocrit 38.8%, platelet count 186,000/µL. A karyotype was also processed from the cord blood sample which revealed a normal male (46, XY).

The treatment was carried out on a once weekly basis, by intraamniotic injection of 500 mcg of L-thyroxine (Henning) via a 21 gauge amniocentesis needle. A total of six injections were performed from 32 to 38th weeks. The course was uneventful and the fetus presented good growth. An ultrasound examination of the fetal thyroid at the 36th week revealed dimesions of 18mm left lobe, 17mm right lobe (AP) and 36 mm in the transverse plane (Figure.2).

Figure 1. The thyroid function measurements which were monitored during the neonatal period.



Maternal thyroid screen was repeated and turned out to be normal at this stage. Spontaneous labour ensued by 38+5 weeks resulting in normal delivery of a healthy male infant weighing 3410 grams. Apgar scores were 9 at 1 minute and 9 at 5 minutes. On examination by the attending paediatrician the thyroid was found to be enlarged but there were no clinical signs of hypothyroidism or of airway obstruction. The examination of a blood sample from the newborn revealed the following values: TSH 2.05 mIU/L (normal: 1.7-9.1), fT3 2.68 pg/ml (normal: 2.9-6.8), fT4 4.35 ng/ml (normal: 1.1-2.0). Infant metabolic screen and thyroid antibody profile were also normal. The mother was discharged the next day and the baby after a further day's stay at the hospital to allow for evaluation by the paediatric endocrinologists. The thyroid function was monitored closely during the neonatal period (Table 1).

Table 1. The thyroid function measurements which were monitored during the neonatal period.

Day of life	4th	8th	10th	30th	Normal Values
TSH (mIU/L)	**0.09**	**0.36**	1.59	**0.53**	1.7-9.1
fT3 (pg/ml)	**2.30**	**2.20**	4.18	4.24	2.9-6.8
fT4 (ng/ml)	**2.46**	1.99	1.97	1.61	1.1-2.0

On the 8th day of life the ultrasound examination of the newborn's thyroid recorded measurements of 14x15x28 mm left thyroid lobe, 16x10x28 mm right thyroid lobe, and an isthmus of 5 mm. The parenchymal echo was normal, no cysts or nodules were detected. The gland was defined as "hyperplastic" by the radiologist.
At the last follow-up visit the "patient" was described as a healthy boy, now 7 years old, on no medications and showing normal bodily growth with normal neurological and cognitive functions.

DISCUSSION

Fetal goitrous hypothyroidism (FGH) if unrecognized prenatally and not acted upon soon enough after birth is associated with retarded skeletal development, mental retardation, hearing defects, poor visuomotor abilities, delayed speech and language development, selective neuromotor deficiencies, and poor attention and memory skills (6). Even though screened CH children are markedly improved by neonatal diagnosis, they are still at risk for subtle irreversible deficits (5). Fetal thyroid gland could be measured by ultrasound reliably from 20 weeks onwards. FG may be easy to miss during routine antenatal visits ultrasonographically and most cases are discovered when a detailed anomaly scan is performed after this week. The case discussed in this report was actually suspected to have a goitre at the 25th week but was referred to us after 30th week of gestation. The differential diagnosis of FG should contain all anomalies of the anterior nuchal area, including cystic hygromas, thyroglossal duct cysts and teratomas (2,7).

Congenital hypothyroidism (CH), also appears to be associated with an increased risk of congenital malformations. In one study, extra thyroidal congenital malformations, the majority of which was cardiac, had a prevalence of 8.4% (8). There were no congenital anomalies in our patient. A large fetal goitre (FG) may cause hyperextension of the neck of the fetus, inducing malpresentation and complicating all stages of labor and delivery (9). In our case where the goitre was not judged to be too large at term . Hence spontaneous onset of labour was awaited, when the head engaged and flexed uneventfully and a normal vaginal delivery ensued. Fetal goiter may present in a hyperthyroid, hypothyroid or even a euthyroid status, so it is imperative to determine the fetal thyroid status before considering therapy in utero. In utero treatment may obviate not only various neurological sequela but also mechanical complications mentioned above. Invasive diagnostic methods should preferably utilised to this end as typically, measurement of amniotic fluid thyroid hormone levels are not reliable showing no correlation with fetal serum thyroxine (10). The fetal thyroid status can be accurately assessed by fetal blood sampling. Some minor or major complications of this invasive procedure are often stressed upon but cordocentesis for prenatal therapy should only be undertaken in centers with expertise where such procedures are routine, hence "high risks" should not be an issue here. There were no minor or major complications associated with the cordocentesis or the intraamniotic procedures that followed in our case.

Many methods of treatment were proposed in different centers with usually 250-500 mcg of L-thyroxine (range 150 to 800 mcg) per injection (corresponding to 3–23 mcg/kg estimated fetal weight/injection), one to six injections, and 1 to 4 week between injections into the amniotic fluid (2). Treatment, we selected, was every week by the injection of 500 mcg of L-thyroxin into the amniotic fluid at 32 between 38 week of gestation.

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