

Prenatal Diagnosis of Fetal Goiter in a Euthyroid Mother

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Congenital fetal goiter is a very rare pathology, is sometimes difficult to diagnose when there is no maternal history or the goiter size is moderate. We report a case of prenatally diagnosed fetal goiter in a euthyroid mother. A 28-year-old woman was referred to our clinic at 38⁺² weeks of gestation. Ultrasonographic examination revealed a fetal goiter. The maternal history and thyroid function tests, including antithyroid autoantibody tests, were unremarkable. Cesarean section was performed, and the thyroid profile of the neonate was consistent with congenital hypothyroidism. Thyroxine therapy was immediately started. Fetal thyroid function must be determined when a goiter is detected. Cordocentesis is a more reliable but riskier diagnostic tool than amniocentesis. Intra-amniotic injection of thyroxine is relatively safe and an easier management option for fetal hypothyroidism. To develop more noninvasive and safe methods for therapeutic efficacy monitoring, a large-scale study is necessary.

Key Words: Congenital hypothyroidism, Goiter, Prenatal diagnosis

Fetal goiter is a very rare phenomenon with a worldwide incidence of about 1:40,000. Overtreatment of maternal Graves' disease, inappropriate maternal thyroid replacement and, rarely, congenital hypothyroidism can cause fetal goiter. Fetal goiter may accompany with hypothyroidism, hyperthyroidism or euthyroid state.¹

Fetal thyroid disorders are often unrecognized when there is no maternal history of thyroid disease. Fetal goiter is also sometimes difficult to diagnose by ultrasound when only moderately sized. However,

the consequences of undiagnosed impaired fetal thyroid function are serious. Fetal hypothyroidism is associated with mental retardation and delayed bone maturation.^{2,3} Hyperthyroidism is also dangerous, with an increased spontaneous abortion rate due to fetal cardiac failure. Goiter itself, may also result in dystocia or neonatal airway obstruction due to its mass effect.^{4,5} Therefore, fetal thyroid function must be determined when a goiter is detected.

We report a prenatally diagnosed case of fetal goiter in a euthyroid mother, and review crucial points in the management of fetal thyroid disease.

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Case Report

A 28-year-old primigravida was referred to our antenatal clinic at 38⁺² weeks of gestation due to an incidentally detected fetal neck mass. Ultrasonographic examination revealed a symmetrical bilobed mass with peripheral blood flow flushing measuring 34.4×17.4

mm at the anterior portion of the fetal neck, suggestive of thyroid goiter (Figs. 1, 2). Estimated fetal weight and amniotic fluid index were within normal range. Hyperextension of the fetal head was not observed. Other findings of the fetus were unremarkable.

The previous medical history and antenatal course were unremarkable. No signs suggestive of maternal thyroid disease were found. Maternal thyroid function test and antithyroid autoantibody test values were within normal range: TSH level $0.8 \mu\text{U/mL}$ (reference range: $0.4\text{--}4.7 \mu\text{U/mL}$), free T4 0.99 ng/dL ($0.8\text{--}1.9 \text{ ng/dL}$), T3 1.21 ng/mL ($0.8\text{--}2.0 \text{ ng/mL}$), TSH receptor antibody $<0.66 \text{ IU/L}$ ($<1.22 \text{ IU/L}$), Thyroid microsomal

antibody 2.1 IU/mL ($<10 \text{ IU/mL}$), Thyroglobulin antibody 13.6 IU/mL ($<100 \text{ IU/mL}$).

We decided to deliver the fetus for immediate evaluation and treatment. Cesarean section was performed at 39^{+2} weeks of gestation because of dystocia, and a female infant was delivered. Postnatal airway obstruction was not found and the Apgar scores were 8 at 1 minute and 10 at 5 minutes. Neonatal height was 50 cm ($50\text{--}75$ percentile), body weight was 3.28 kg ($25\text{--}50$ percentile) and head circumference was 35 cm ($75\text{--}90$ percentile).

The thyroid profile of the neonate on her first day of life was consistent with congenital hypothyroidism, with a markedly elevated TSH, slightly decreased free T4, and normal T3 level. (TSH $>100 \mu\text{U/mL}$, free T4 0.7 ng/dL , and T3 0.9 ng/mL). Antithyroid autoantibody tests were within normal range (TSH receptor antibody $<0.30 \text{ IU/L}$, thyroid microsomal antibody 3.0 IU/mL , thyroglobulin antibody 20.7 IU/mL).

Oral thyroxine therapy was immediately initiated at $50 \mu\text{g}$ daily (approximately $15 \mu\text{g/kg}$). The TSH level was still elevated, but the levels of free T4 and T3 were normalized by the third day of life (TSH $>100 \mu\text{U/L}$, free T4 1.37 ng/dL , and T3 1.83 ng/mL). On the fifth day of life, a thyroid scan (with Tc99m free pertechnetate) showed no abnormality, dyshormogenesis of thyroid was suggested to be a cause of congenital goitrous hypothyroidism. The newborn's goiter shrank after thyroxine treatment and she was discharged on the sixth day of life. Oral thyroxine therapy was continued after discharge. TSH levels dropped to $0.2 \mu\text{U/mL}$ on the 48th day of life. Follow-up of the infant for 6 months revealed a slightly hypotonic trunk but normal growth and development. Infantile height was 67.6 cm ($50\text{--}75$ percentile), body weight was 7.7 kg ($50\text{--}75$ percentile). The infant showed complete head control and rolling over.



Fig. 1. Sagittal ultrasonogram shows a symmetrical bilobed mass measuring $34.4 \times 17.4 \text{ mm}$ at the anterior portion of the fetal neck.

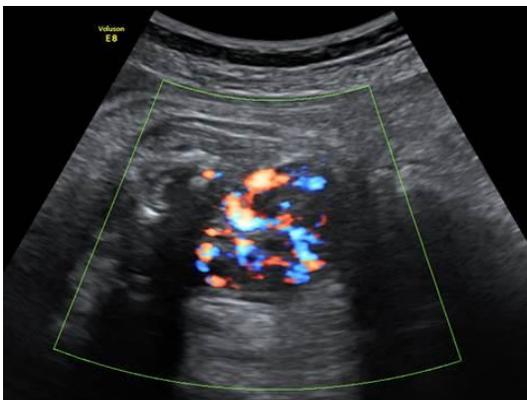


Fig. 2. Sagittal ultrasonogram of the fetal neck shows a goiter with peripheral flushing.

Discussion

Fetal goiter accompanying congenital hypothyroidism is seen in 10–15% of fetuses with congenital hypothyroidism. Fetal hypothyroidism is associated with motor and cognitive defects, delayed bone maturation, and impaired neurological development. Even with immediate postnatal evaluation and replacement of thyroid hormone, some degree of neurologic impairment persists. The impairment degree of IQ score, memory or learning abilities are associated with the severity and duration of the hypothyroidal state.^{6–8}

Fetal thyroid disorder is often undetected when there is no maternal history of thyroid disorder or thyroid medication. Sometimes, a fetal goiter is difficult to detect by ultrasound when the condition is not severe, and must be carefully examined during routine evaluation. When a fetal goiter is detected during antenatal examination, a detailed evaluation including maternal history and maternal physical examination (heart rate, heat intolerance, weight change, exophthalmos, etc.) is necessary. Maternal laboratory evaluation such as baseline thyroid function and antithyroid autoantibody tests should be performed. The following characteristics can be used to identify a fetal goiter: a solid and lobulated mass in the anterior fetal neck, anterior to the trachea, and surrounded by cervical vessels. Reference values for fetal thyroid volume based on estimated fetal weight and thyroid growth rate can be used for the evaluation of the fetal thyroid state.⁹ Color Doppler is also helpful in detecting the fetal thyroid.¹⁰

Fetal thyroid status can be diagnosed via amniocentesis or cordocentesis. Amniocentesis is useful for the TSH level. However, many studies have expressed doubt about its reliability because amniotic fluid

thyroid hormone levels do not accurately reflect fetal hormonal status.¹¹ Cordocentesis is a more reliable diagnostic tool, but riskier, with a fetal bleeding or loss rate of about 0.5–1%.¹²

Management of fetal hyperthyroidism is relatively simpler, via maternal administration of propylthiouracil (PTU). In contrast, fetal hypothyroidism cannot be treated by maternal thyroxine administration because thyroxine cannot pass through the placenta. The only treatment method is injection of thyroxine into fetal muscle or a blood vessel, or into the amniotic fluid. Injection into the fetus itself risks injury and may require several puncture attempts. Intra-amniotic injection of thyroxine is a relatively safer and simpler management option than other methods, and has a long treatment interval. Accordingly, in recent years, intra-amniotic injection of thyroxine has been the most common therapeutic option for congenital hypothyroidism.^{3, 13, 14} Recent study summarized the in utero treatment of fetal goitrous hypothyroidism data in their report.¹⁵

Repeated cordocentesis is hazardous; therefore, monitoring therapeutic efficacy is a matter of concern.¹⁶ Studies suggest that serial ultrasonographic monitoring of fetal goiter size is helpful.¹⁰ Studies on the thyroid vascular pattern using color Doppler are under investigation. A vanishing or diminishing Doppler signal and fetal heart rate variability pattern were suggested to reflect improvement in thyroid function, but a large-scale study is necessary to confirm this.^{10, 17, 18}

To the best of our knowledge, this is the first report about fetal goiter in a euthyroid mother. In our case, there was no polyhydroamnios or fetal neck hyperextension and the size of fetal goiter was not remarkable. Main diagnostic clue was Color Doppler findings with peripheral blood flow flushing of fetal

thyroid. Our case was diagnosed in late pregnancy leaving no time for management. Therefore, we decided on immediate delivery rather than attempting a risky invasive procedure. Although in utero treatment was impossible, our prenatal diagnosis was helpful for immediate postnatal therapy.

In conclusion, even though fetal goiter accompanied by congenital hypothyroidism is a rare disorder, especially in a euthyroid mother, the thyroid must be evaluated during antenatal evaluation. In early pregnancy, in utero evaluation and management is essential, and requires careful and experienced hands. In late pregnancy, postnatal evaluation after should also be considered. Color Doppler will be helpful for initial diagnosis of fetal thyroid disease and monitoring. A large-scale study is necessary for monitoring therapeutic efficacy and long-term prognosis.

References

- 1) Blumenfeld YJ, Davis A, Milan K, Chueh J, Hudgins L, Barth RA, et al. Conservatively managed fetal goiter: an alternative to in utero therapy. *Fetal Diagn Ther* 2013;34:184-7.
- 2) Göktolga U, Karaşahin KE, Gezginç K, Fidan U, Ergün A, Başer I. Intrauterine fetal goiter: diagnosis and management. *Taiwan J Obstet Gynecol* 2008;47:87-90.
- 3) Koyuncu FM, Tamay AG, Bugday S. Intrauterine diagnosis and management of fetal goiter: a case report. *J Clin Ultrasound* 2010;38:503-5.
- 4) Stewart CJ, Constantatos S, Joolay Y, Muller L. In utero treatment of fetal goitrous hypothyroidism in a euthyroid mother: a case report. *J Clin Ultrasound* 2012;40:603-6.
- 5) Uhrmann S, Marks KH, Maisels MJ, Kulin HE, Kaplan M, Utiger R. Frequency of transient hypothyroxinaemia in low birthweight infants. Potential pitfall for neonatal screening programmes. *Arch Dis Child* 1981;56:214-7.
- 6) Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *N Engl J Med* 1999;341:549-55.
- 7) Rovet J, Daneman D. Congenital hypothyroidism: a review of current diagnostic and treatment practices in relation to neuropsychologic outcome. *Paediatr Drugs* 2003;5:141-9.
- 8) Song SI, Daneman D, Rovet J. The influence of etiology and treatment factors on intellectual outcome in congenital hypothyroidism. *J Dev Behav Pediatr* 2001;22:376-84.
- 9) Ho SS, Metreweli C. Normal fetal thyroid volume. *Ultrasound Obstet Gynecol* 1998;11:118-22.
- 10) Volumenie JL, Polak M, Guibourdenche J, Oury JF, Vuillard E, Sibony O, et al. Management of fetal thyroid goitres: a report of 11 cases in a single perinatal unit. *Prenat Diagn* 2000;20:799-806.
- 11) Hollingsworth DR, Alexander NM. Amniotic fluid concentrations of iodothyronines and thyrotropin do not reliably predict fetal thyroid status in pregnancies complicated by maternal thyroid disorders or anencephaly. *J Clin Endocrinol Metab* 1983;57:349-55.
- 12) Simsek M, Mendilcioglu I, Mihci E, Karaguzel G, Taskin O. Prenatal diagnosis and early treatment of fetal goitrous hypothyroidism and treatment results with two-year follow-up. *J Matern Fetal Neonatal Med* 2007;20:263-5.
- 13) Agrawal P, Ogilvy-Stuart A, Lees C. Intrauterine diagnosis and management of congenital goitrous hypothyroidism. *Ultrasound Obstet Gynecol* 2002;19:501-5.
- 14) Corbacioglu Esmer A, Gul A, Dagdeviren H, Turan Bakirci I, Sahin O. Intrauterine diagnosis and treatment of fetal goitrous hypothyroidism. *J Obstet Gynaecol Res* 2013;39:720-3.
- 15) Mastrolia SA, Mandola A, Mazor M, Hershkovitz R, Mesner O, Beer-Weisel R, et al. Antenatal diagnosis and treatment of hypothyroid fetal goiter in an euthyroid mother: a case report and review of literature. *J Matern Fetal Neonatal Med* 2015; 28:2214-20.
- 16) Hanono A, Shah B, David R, Buterman I, Roshan D, Shah S, et al. Antenatal treatment of fetal goiter: a therapeutic challenge. *J Matern Fetal Neonatal Med* 2009;22:76-80.
- 17) Huel C, Guibourdenche J, Vuillard E, Ouahba J, Picketty M, Oury JF, et al. Use of ultrasound to distinguish between fetal hyperthyroidism and hypothyroidism on discovery of a goiter. *Ultrasound Obstet Gynecol* 2009;33:412-20.
- 18) Shoham I, Aricha-Tamir B, Weintraub AY, Mazor M, Wiznitzer A, Holcberg G, et al. Fetal heart rate tracing patterns associated with congenital hypothyroidism. *Am J Obstet Gynecol* 2009;201:48.e1-4.