PERINATAL JOURNAL

Case(s)

Perinatal Journal 2024;32(2):128-131

Prenatal diagnosis of fetal goiter and successful treatment with intraamniotic levothyroxine: a case report

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Abstract

Objective: Fetal goiter is rare and may cause polyhydramnios, fetal growth restriction, and congenital hypothyroidism. We aimed to report a rare case of fetal goiter complicated by polyhydramnios in a pregnant woman.

Case(s): A 32-year-old woman with a 32-week pregnancy was referred to us because of polyhydramnios. Ultrasound examination revealed fetal asymmetric growth restriction and severe polyhydramnios. The fetal stomach was smaller, and pharyngeal dilatation and approximately 50x45 mm fetal neck mass (goiter) were observed. Also, mild hypothyroidism was detected in maternal thyroid function tests. In-utero treatment was initiated with 200 µg of levothyroxine injected into the amniotic sac. This treatment was repeated every 10 days for 2 doses following the initial dose. After levothyroxine treatment, fetal goiter and amniotic fluid volume completely recovered until birth.

Conclusion: Fetal goiter can be successfully treated with an intraamniotic injection of levothyroxine.

Keywords: Fetal goiter, prenatal diagnosis, intrauterine treatment, levothyroxine

Introduction

Fetal goiter, or thyromegaly, is a diffuse enlargement of the fetal thyroid gland and a rare clinical condition that causes fetal and maternal complications. The incidence of fetal goiter is extremely rare and ranges from 1 in 30.000 to 1 in 50.000 live births.[1] The most common form of congenital hypothyroidism is primary hypothyroidism with elevated thyroid-stimulating hormone (TSH) levels due to thyroid dysgenesis (80% cases) or dyshormonogenesis in 20% of cases. Hypothyroidism causing fetal goiter not only carries a significant risk of psychomotor impairment but can also lead to fatal intrauterine and obstetric complications. Compression of the esophagus and tracheal can lead to polyhydramnios, growth retardation, preterm labor or peripartum asphyxia, and neck hyperextension due to a cervical mass may cause dystocia during labor.[2] In fetal iodine deficiency (hypothyroidism), it can cause motor or cognitive deficits or impaired mental development during childhood.[3] Although intravascular and intramuscular administration is available for direct administration of the drug to the fetus, intraamniotic L-thyroxine injection by absorption through the fetal gastrointestinal system and reaching the fetal circulation has become the standard treatment for fetal goiter hypothyroidism due to its ease of administration, low complication rate and prolonged intervals.[4] The diagnosis of fetal goiter may be possible with careful antenatal ultrasound examination. Grayscale (2D), 4D and colour Doppler sonography are useful in diagnosing a fetal neck mass. When a fetal neck mass is detected, it

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How to cite this article: Yalınkaya A, Oğlak SC, Gündüz R, Ağaçayak E, Yayla M. Prenatal diagnosis of fetal goiter and successful treatment with intraamniotic levothyroxine: a case report. Perinatal Journal 2024;32(2):128-131 DOI: 10.59215/prn.24.0322007

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should also be examined in terms of pharyngeal dilatation, stomach pocket and polyhydramnios. When fetal goiter and its symptoms are detected, levothyroxine treatment should be initiated immediately to prevent fetal and maternal complications.[5] In this study, we aimed to present the diagnosis and treatment approach of fetal goiter.

Case(s)

A 32-year-old woman with a 32-week pregnancy was referred to our clinic because of polyhydramnios. Ultrasound examination revealed mild fetal growth restriction (FGR) and severe polyhydramnios. The bilobal thyroid gland's mass was measured as 50 x 45 mm (goiter) on the fetal neck. It was also seen that the pharynx was dilated, and the stomach was small (Figures 1 and 2). It was thought that fetal goiter was compressing the esophagus, preventing fetal swallowing, and causing polyhydramnios. Maternal thyroid function tests (TFT) were performed; thyroid-stimulating hormone (TSH) 4.26 mIU/mL, free T3 (FT3), and free T4 (FT4) were observed slightly low. Fetal thyroid function in the amniotic fluid was not tested. Also, fetal blood sampling was not performed to analyze fetal thyroid functions. Oral Levothyroxine (Euthyrox) 100 mcg/day was administered for maternal hypothyroidism. Levothyroxine injectable form was obtained within two weeks from abroad for fetal treatment. At the end of the two weeks, maternal thyroid hormones were regressed to normal values. Also, fetal goiter and amniotic fluid volume were minimally improved. Levothyroxine 100 mcg vial 1x200 mcg direct intra-amniotic injections were performed three times at 10-day intervals for fetal treatment. Fetal goiter's volume reduced rapidly after the first injection, amniotic fluid returned to the normal level, and also fetal growth significantly improved. In the last ultrasound examination before the birth, the bilobal thyroid gland was measured as 26x11 mm. Indication of previous cesarean section, a male fetus, 3050 g, with 8/9 APGAR scores was delivered by cesarean section at the 39th week of gestation. No abnormalities were found in the examination and TFT results of the newborn (Figure 3). Neonatal thyroid hormone levels were within the normal ranges: FT3 was 4.2 ng/dL (reference range between 1.57-4.4 ng/dL), FT4 was 1.29 ng/dL (reference range between 0.71-1.96 ng/dL), and TSH was 4.77 mIU/mL (reference range between 1.12-8.21 mIU/mL). The mother and baby were discharged on the first postoperative day. The patient has consented to the submission of the case report to the journal.

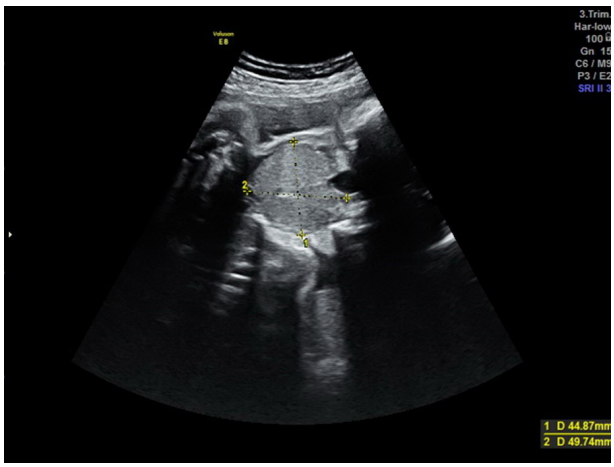

Fig 1. Bilobal thyroid gland's mass was measured as 50 x 45 mm (goiter) on the fetal neck

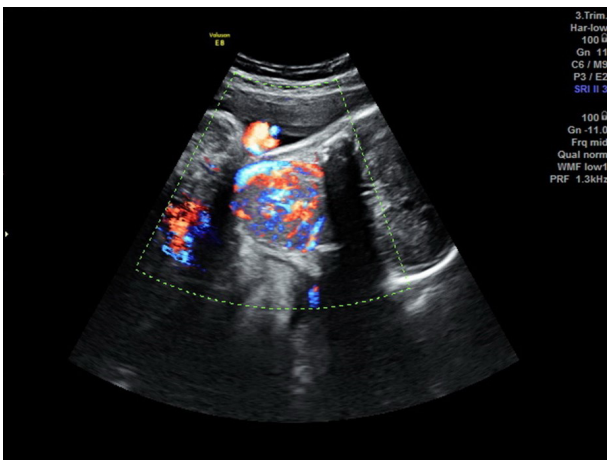

Fig 2. Color Doppler imaging of the fetal thyroid gland

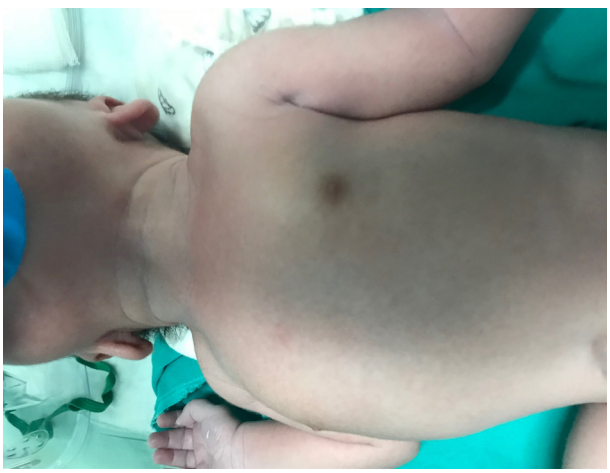

Fig 3. The newborn delivered at 39w

Discussion

Fetal goiter can occur as part of a hyperthyroid, euthyroid, or more frequently hypothyroid state. It is usually diagnosed on ultrasound examination in the second and third trimesters of pregnancy. Magnetic resonance imaging (MRI) is also useful in the diagnosis of fetal goiter .[1,6] This case was referred to our center at the 32nd week of gestation due to polyhydramnios. At the first ultrasound examination, a fetal neck mass (goiter) was diagnosed. Grayscale and C Doppler Ultrasound are sufficient for the diagnosis of fetal goiter. Therefore, there is no need for expensive imaging diagnostic tools such as MRI. Dyshormonogenesis usually causes fetal goiter; the impairment of hormone biosynthesis leads to an increase in the fetal TSH level, resulting in the formation of fetal goiter. Fetal goiter may cause hyperextension of the neck, pressure on the vascular structures, polyhydramnios and edema. Mental and motor retardation in fetal hypothyroidism cases have been reported.[7] Therefore, early diagnosis of fetal hypothyroidism and appropriate hormone replacement therapy are important.

Experienced clinicians may suppose fetal thyroid hormone status by describing the fetal goiter appearance (thyroid diameter, vascularization) and bone maturation at ultrasound examination. Fetal hyperthyroidism may be considered when there is oligohydramnios, accelerated bone maturation or fetal tachycardia.[8,9] In difficult cases, the American Thyroid Association recommended that the direct measure of fetal umbilical cord blood sample is the gold standard diagnostic method.[10] In our case, fetal thyroid hormones were not studied, because fetal thyroidism symptoms and signs were very prominent, and it would not change our treatment option. Also, possible risks of cordocentesis were avoided. However, fetal goiter may be caused by maternal Graves' disease, Hashimoto's thyroiditis, iodine uptake, propylthiouracil and methimazole exposure. On the other hand, fetal goiter may also be caused by primary fetal hypothyroidism.[11] There were not any drug administrations or thyroid diseases until the third trimester of this gestation in our patient's medical history. The prevalence of congenital hypothyroidism presenting with thyroid enlargement is approximately 1 per 40 000 and is found in only 10% to 15% of all cases of congenital hypothyroidism.[12] The excessively large fetal thyroid gland may cause polyhydramnios by compressing the trachea and esophagus.[13] In our case, fetal goiter caused pharyngeal dilatation, polyhydramnios and a small stomach by compressing the esophagus and making it difficult for the fetus to swallow fluid. As reported in a systematic review and meta-analysis, maternal subclinical hypotroidism is associated with FGR.[14] In our case, mild FGR was detected due to this condition and rapidly improved by levothyroxine treatment until the delivery. At the same time, amniotic fluid volume was also decreased to normal level rapidly. Intrauterine Levothyroxine in doses ranging from 150 to 500 mcg and administrations varying every 7 to 14 days are available in different studies.[15] In a study[16], it has been reported that repeated 200 µg and over doses direct intra-amniotic levothyroxine injection in the third trimester of gestation is effective in fetal therapy and has no adverse effects. Additionally, after confirming fetal hypothyroidism with cordocentesis, the thyroid hormone levels can be evaluated by serial amniocentesis. Amniocentesis to assess the TSH levels in the amniotic fluid could be useful for analyzing fetal thyroid metabolism, which is safer than cordocentesis.[17] Previous studies reported that the amniotic fluid TSH levels reflect fetal rather than maternal thyroid function since TSH does not cross the placenta.[18] In our patient, maternal mild hypothyroidism was treated with oral Levothyroxine. Fetal TFTs were not performed in fetal blood or amniotic fluid since amniocentesis or cordocentesis was not performed. However, Levothyroxine 200 mcg was injected directly into the amniotic fluid three times at 10-day intervals for fetal treatment. After the first dose of levothyroxine injection, amniotic fluid volume and fetal goiter size were reduced rapidly, and fetal growth restriction became normal. Also, all of the hypothyroidism symptoms and signs were improved until the delivery. The patient was delivered two weeks after the last drug dose. The infant's TFTs were normal in the early postpartum period and until the six-month period.

Conclusion

Fetal goiter should be considered in patients with polyhydramnios and fetal growth restriction. In all polyhydramnios patients, the fetal thyroid gland should be evaluated by ultrasound examination. In the case of fetal goiter, thyroid function tests should be performed to determine maternal hypothyroidism and oral levothyroxine should be initiated if necessary. In cases with fetal goiter, to prevent prenatal and postnatal hypothyroidism complications, treatment should be started immediately with intra-amniotic levothyroxine injection.

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