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BRIEF COMMUNICATION

A Case of Dichorionic Twin Pregnancy with Maternal Propylthiouracil Induced Hypothyroid Goiter in Both Fetuses Treated with Intramniotic Levothyroxine

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Abstract Fetal hypothyroid goiters are observed in 1:40,000 births. They are usually attributed to underlying thyroid glandular dysgenesis, dyshormonogenesis, or an adverse effect of maternal anti-thyroid drugs. The objective of the present case report is to outline the details of a twin gestation with hypothyroid goiter in both fetuses managed by intramniotic levothyroxine administration. The index pregnancy was of dichorionic twin gestation in which the mother was receiving oral propylthiouracil. Fetal goiters were first detected in ultrasound performed at 31 weeks of gestation. The hypothyroid nature of goiters was confirmed by cordocentesis from both sacs. Intramniotic administration of 100 μg of levothyroxine into both sacs was performed twice at the interval of two weeks. The response to treatment was assessed by amniotic fluid thyroid hormone levels, and serial measurement of thyroid gland volume. Emergency cesarean section was performed at 35 weeks due to preterm labor. Both fetuses were euthyroid at birth and were discharged in good health.

Keywords Fetal goiter · Fetal hypothyroidism · Intramniotic levothyroxine · Amniocentesis

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Introduction

The fetal hypothyroid goiters depict a physical expression of underlying thyroid glandular dysgenesis, dyshormonogenesis, or the undesirable effect of maternal anti-thyroid drugs [1, 2]. Observed in 1:40,000 births, they are uncommon prenatally compared to the ten times greater incidence of congenital hypothyroidism [3]. The objective of the present article is to elucidate the salient aspects of a twin gestation with hypothyroid goiter in both fetuses, managed by intramniotic Levothyroxine. To the best of authors' knowledge, this is the first ever reported case of both fetuses of a twin pair treated simultaneous for hypothyroid goiter.

Case Report

A 29-years-old Indian nullipara underwent a multifetal pregnancy reduction (triplets to twins) from authors' fetal medicine unit at the 12th gestational week. Routine maternal investigations revealed hyperthyroidism, triggering her obstetrician to initiate oral propylthiouracil (PTU) therapy without undertaking an etiological workup. An ultrasound scan performed at 26^{+0} weeks of gestation revealed polyhydramnios, and intertwin growth discordance. A review scan at 31^{+1} weeks confirmed the progression of polyhydramnios, development of goiter in both fetuses, and growth restriction in one of the twin due to placental insufficiency (Fig. 1). The hypothyroid nature of the goiters was confirmed by cordocentesis from both the fetuses. The mother was admitted, and the PTU therapy promptly discontinued. Following deliberations within the institutional review board, a decision for intramniotic instillation of levothyroxine into both the sacs was taken.

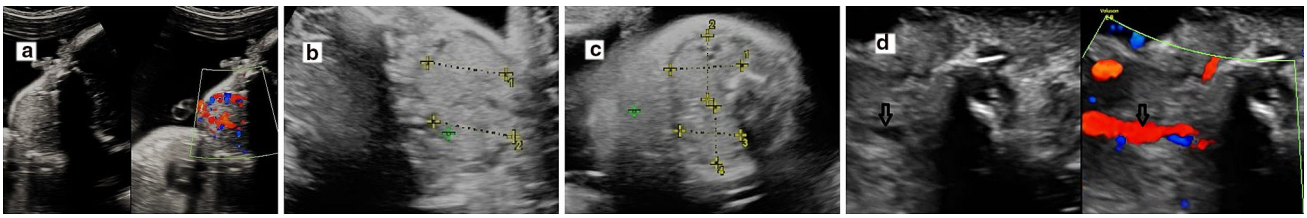

Fig. 1 Ultrasound images of hypothyroid goiter of fetus 1. **a** Sagittal image showing the goiter with demonstration of increased vascularity on color Doppler. **b** Longitudinal measurements of each lobe of the thyroid gland, and **c** Antero-posterior and transverse width of each lobe. **d** Shrinkage of the same thyroid gland following two doses of levothyroxine with relief of pressure on the trachea (*open arrow*). The movement of fluid inside can be visualized on color Doppler

The pertinent treatment details are outlined in Table 1. After the second instillation at the 33rd gestational week, maternal antenatal steroids were administered. Weekly ultrasound scans for fetal wellbeing and cervical assessment were performed. Finally, an emergency cesarean section was performed at 35^{+0} weeks for advanced preterm labor and podalic presentation. The babies were euthyroid and did not require levothyroxine. The knee X-rays of both neonates failed to demonstrate distal femoral epiphyses (DFE). Eventually, they were discharged in good health.

Discussion

The first case of fetal therapy for hypothyroid goiter was described in 1980 [4]. The cases reported thereafter have consistently improved our understanding regarding the entity. Though the beneficial role of intramniotic levothyroxine is not explicit, the available evidence currently favors therapy [5]. Furthermore, information on fetal goiters in twin gestations is generally lacking. Reynolds et al. reported goiter in both fetuses of a twin pair in which treatment was not undertaken considering the risks, and the late gestation at diagnosis [6]. Saini et al. reported goiter in one of the twins' fetus which was treated with intramniotic levothyroxine [7].

The European Society of Pediatric Endocrinology mentions cordocentesis as the method of choice for the diagnosis of fetal hypothyroidism without any recommendation on treatment [8]. Untreated fetal hypothyroidism has been associated with impaired language, perceptual motor and visual spatial development deficits [9, 10]. Labor dystocia and mechanical obstruction to breathing are potential intrapartum and postpartum complications, respectively [5]. Therefore, prenatal therapy with levothyroxine seems prudent. The recommended dose is 10–15 μg/kg body weight weekly [2].

In the index case, factors against invasive treatment were risk of iatrogenic preterm birth, and probable spontaneous resolution of goiters after withdrawal of PTU. The factors favoring therapy were the uncertainty regarding probable neurological sequelae from untreated hypothyroidism, reduction of polyhydramnios enabling prolongation of the pregnancy, and shrinkage of the neck mass subverting respiratory embarrassment at birth [8, 11]. The authors eventually opted for a smaller dose of levothyroxine (100 μg), and a biweekly regime. Despite the treatment, the presence of residual thyromegaly at birth in present case suggests the likely circumvention of mechanical obstruction by the goiters on the upper airway. The non-appearance of DFE postnatally in index case, raises concerns regarding the likely impact of the period of untreated hypothyroidism on fetal skeletal and brain maturation. The presence of knee epiphyses at birth correlates with the future intellect [12].

The fetal goiters can be functionally hypothyroid, hyperthyroid or euthyroid [2]. Hypothyroid goiters are suspected in prenatal ultrasound by the increased peripheral vascularity on color Doppler, and paradoxical excessive fetal movements [13]. The diagnosis is confirmed by cordocentesis and assessing fetal thyroid hormones [2]. Amniocentesis is avoided for the primary diagnosis of fetal thyroid function as the amniotic fluid thyroid hormone levels represents combined maternal and fetal contributions [2]. The treatment response should be judged by serial sonographic thyroid volume measurement as recommended by Ho and Metreweli [14], and estimation of amniotic fluid TSH and free T4 levels [5, 15]. The authors recommend sonographic reappearance of fluid movement across fetal trachea following relief of tracheal compression as a sign of treatment response (Fig. 1).

In conclusion, the intricacies of index case contributes to the existing literature by presenting an alternative, predominantly conservative treatment regime. It underscores the potential impact of maternal drugs on fetal physiology, and the need for strict adherence to the standard evidence based guidelines in managing maternal conditions.

Table 1 Treatment, surveillance and outcomes following intramniotic levothyroxine in index case of twin gestation

Parameters		FETUS 1					FETUS 2[a]				
Gestational weeks	Events	TSH IU/L	FT4 pmol/L	FT3 pmol/L	Thyroid volume (cm^3)	Scan	TSH IU/L	FT4 pmol/L	FT3 pmol/L	Thyroid volume (cm^3)	Scan
31^{+1}	Cordocentesis both fetuses	61.45	0.849	–	15.4	EFW = 1717 g SVP = 15 cm	47.89	0.807	–	8.8	EFW = 1090 g SVP = 9 cm
31^{+5}	Amniocentesis from both sacs	1.92	0.32	–	Not measured	–	1.7	0.28	–	Not measured	–
31^{+5}		Levothyroxine 100 μg administered intramniotically					Levothyroxine 100 μg administered intramniotically				
32^{+0}	Amniocentesis from both sacs	0.94	1.11	–	8.3	–	0.5	0.61	–	5.5	–
32^{+0}		Levothyroxine 50 μg administered intramniotically					Levothyroxine 50 μg administered intramniotically				
33^{+0}	Amniocentesis from both sacs	0.564	1.34	–	Not measured	EFW = 2224 g SVP = 12 cm	0.330	0.78	–	Not measured	EFW = 1150 g SVP = 6 cm
35^{+0}	Emergency cesarean section performed at 35 weeks for advanced preterm labor with podalic presentation Neonate 1 (male) weighed 2334 g; Neonate 2 (female) weighed 1232 g, required NICU care for 7 days										
Day 3 postpartum		2.39	9.69[b]	0.982[c]	Mild enlargement		3.79	15.47[a]	1.47[c]	Mild enlargement	

Normal fetal blood thyroid hormone levels—TSH = 3.9–9.7 IU/L, FT4 = 11.5–14.7 pmol/L

Normal amniotic fluid thyroid hormone levels—TSH = 0.04–0.5 IU/L, FT4 = 1.29–9.93 pmol/L

Normal thyroid volume (cm^3) = 0.24 ± 0.10

Normal day 3 thyroid profile levels: TSH = 0.43–16.1, T4 = 5.24–23.2, T3 = 0.6–2.43

FT4 Free T4; *FT3* Free T3; *EFW* Estimated fetal weight; *NICU* Neonatal intensive care unit; *SVP* Single vertical pocket *TSH* Thyroid stimulating hormone

[a]Fetus 2 had growth restriction due to placental insufficiency

[b]Total T4 and not free T4

[c]Total T3 and not free T3

Compliance with Ethical Standards

Conflict of Interest None.

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