Maternal Iodine Exposure: A Case of Fetal Goiter and Neonatal Hearing Loss

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A 27-year-old gravid 1 at 27 weeks 6 days with a history of hypothyroidism had an ultrasound that demonstrated a 3.9 × 3.2 × 3.3-cm well-circumscribed anterior neck mass, an extended fetal head, and polyhydramnios. Further characterization by magnetic resonance imaging (MRI) showed a fetal goiter. During her evaluation for the underlying cause of the fetal goiter, the patient revealed she was taking nutritional iodine supplements for treatment of her hypothyroidism. She was ingesting 62.5 times the recommended amount of daily iodine in pregnancy. The excessive iodine consumption caused suppression of the fetal thyroid hormone production, resulting in hypothyroidism and goiter formation. After the iodine supplement was discontinued, the fetal goiter decreased in size. At delivery, the airway was not compromised. The infant was found to have reversible hypothyroidism and bilateral hearing loss postnatally. This case illustrates the importance of examining for iatrogenic causes for fetal anomalies, especially in unregulated nutritional supplements.
identified. The differential diagnosis for these ultrasound findings included a teratoma, lymphangioma, goiter, branchial cleft cyst, and vascular malformation such as hemangioma.

The patient’s pregnancy was complicated by hypothyroidism. She was taking Armour Thyroid, a natural thyroid hormone, which is equivalent of 38 μg thyroxine (T4). After the diagnosis of the fetal neck mass, maternal thyroid function was assessed. Her thyrotropin (TSH) was 2.73 μIU/mL (normal: 0.4–3.6 μIU/mL), total T4 was 8.3 μg/dL (normal: 7.5–10.3 μg/dL), free T4 was 0.67 ng/dL (normal: 0.6–1.0 ng/dL), and total triiodothyronine was 2.0 ng/mL (1.8–3.7 ng/mL). She was also negative for thyroid-stimulating immunoglobulins, thyroid peroxidase antibodies, and thyroglobulin antibodies.

The patient underwent a fetal MRI to better characterize the neck mass. On MRI at 29 weeks gestation, the mass measured 3.4 × 2.2 cm with the morphologic appearance of an enlarged thyroid gland, consistent with a fetal goiter (Fig 2). The trachea was surrounded by the mass but appeared patent.

Upon further questioning of the patient, we discovered that as part of her hypothyroid treatment by a naturopathic provider, she was taking 2 pills per day of Iodizyme-HP dietary supplement (2.5 mg iodine and 3.75 mg iodide = 6.25 mg total in each pill). Her supplemental iodine and natural thyroid hormone replacement were immediately discontinued. She was placed on Synthyroid 75 μg daily instead.

Given the ultrasound and MRI findings, there was concern about airway patency at delivery. A multidisciplinary team was formed involving perinatology, neonatology, pediatric anesthesiology, and pediatric otolaryngology. An ex utero intrapartum treatment (EXIT)
procedure was planned for delivery to allow for appropriate management of the neonatal airway.

One month after discontinuing the supplemental iodine, the fetal goiter decreased in size to 2.7 × 2.4 × 2.3 cm. The fetal neck was less extended and the polyhydramnios resolved (Fig 3). A follow-up MRI also showed the mass was smaller (1.5 × 2.1 cm) with a patent trachea. The multidisciplinary team reviewed these findings and agreed to proceed with a primary cesarean delivery scheduled with the pediatric anesthesiologist, pediatric otolaryngologist, and neonatologist in attendance to manage a potentially difficult airway but without a planned EXIT procedure.

At 39 weeks gestation, the patient presented for a primary cesarean delivery. A male infant weighing 3230 g with Apgar score of 8 at 1 minute and 9 at 5 minutes was delivered with some degree of difficulty given the fetal head position. The infant cried at time of delivery. Pediatric anesthesiology, pediatric otolaryngology, and neonatology evaluated the neonate. At birth, there was no airway compromise and only blow by oxygen was required. On examination, no neck mass was visualized or palpated but the neonate was noted to maintain his head to the left due to in utero positioning. The infant at birth was 30th percentile for weight, 71st percentile for length, and 54th percentile for head circumference. At 8 hours of life, the infant developed respiratory distress, requiring intubation for surfactant. The neonatology team intubated him without difficulty on the first attempt and extubated him the next day.

Serial thyroid function testing during the 8-day hospitalization was normal without any intervention. Just after delivery, the infant’s TSH was 22.6 μIU/mL (normal 0–3 days old: 5.17–14.6 μIU/mL) and free T4 was 1.9 ng/dL (normal 0–3 days old: 0.66–2.71 ng/dL). His TSH and free T4 decreased over his hospital course. On day of life (DOL) 2, the TSH was 5.97 μIU/mL and the free T4 was 2.65 ng/dL. On DOL 6, the TSH was 1.53 μIU/mL (normal 4–30 days old: 0.43–16.1 μIU/mL) and free T4 was 2.58 ng/dL (normal 4–30 days old: 0.83–3.09 ng/dL). A neck ultrasound showed a diffusely enlarged thyroid without focal abnormality (Fig 4). The remainder of the neonatal hospital course was relatively unremarkable except for hyperbilirubinemia and failing a hearing screen. Brainstem auditory evoked response testing demonstrated bilateral moderate peripheral auditory abnormality for the 500- to 4000-Hz frequency range, likely sensorineural. The infant was discharged from the hospital on DOL 8. At 5 weeks old, he was alert without constipation or difficulty feeding. He was euthyroid (TSH 1.57 μIU/mL [normal 31 days to 12 months old: 0.62–8.05 μIU/mL] and total T4 11.0 μg/dL [normal 1–12 months old: 7.2–15.6 μg/dL]). He was fitted for bilateral hearing aids.

**DISCUSSION**

Fetal goiters are an uncommon prenatal finding. In cases in which thyroid-stimulating antibodies are absent in the mother and causes of dyshormonogenesis are excluded, other etiologies for a fetal goiter must be investigated. This case illustrates the importance of examining for iatrogenic causes for fetal abnormalities. Our patient was taking a natural thyroid supplement that is equivalent to 62.5 times the recommended daily allowance of iodine in pregnancy. The excessive iodine supplementation caused the fetal goiter and hypothyroidism.

During pregnancy, iodine crosses the placenta via active transport. Iodine is concentrated in the thyroid gland and is essential for the synthesis of thyroid hormones. The recommended daily allowance for pregnant women is 200 μg iodine.
Iodine toxicity can develop when consuming >1.1 mg daily. In healthy subjects, excessive intake of iodine acutely inhibits thyroid hormone secretion and temporarily inhibits thyroid biosynthesis. After prolonged exposure to excessive iodine, organification and thyroid hormone biosynthesis resume in a normal fashion. This is also known as escape from the Wolff-Chaikoff effect. Unlike children and adults, the immature fetal and neonatal thyroid gland cannot decrease intracellular iodine transportation. The fetus therefore remains hypothyroid. This effect resolves when the excessive iodine supplementation is removed.

It is important that clinicians examine all patient medications, including nutritional supplements. As nutritional supplements are not subject to standardized regulations by the Food and Drug Administration, patients may be unknowingly consuming supratherapeutic doses of potential fetal teratogens. A recent study by de Vasconcellos et al described 8 children with neonatal goiters secondary to a compounded prenatal vitamin. The vitamin contained 400 times more than the recommended dose of iodine in pregnancy. The goiters were identified both prenatally and confirmed by ultrasound after delivery. In all cases, thyroid function returned to normal after delivery or when exposure to excessive iodine was discontinued.

With regard to the bilateral hearing loss, it is difficult to say whether this is a consequence of the transient fetal hypothyroidism. Deafness is a known consequence of untreated hypothyroidism. The risk of hearing loss seems to be closely associated with the severity of hypothyroidism and is particularly relevant in children with in utero onset of hypothyroidism. In 1 cohort of patients with congenital hypothyroid detected by neonatal screening at 8 to 22 years of age, there was mild and subclinical hearing impairment in approximately 25% of patients, despite early and adequate replacement treatment. The critical period for development of the cochlea starts at the end of the first trimester of pregnancy and continues to the first year of postnatal life. Thyroid hormone has been shown to regulate cochlear development. Neonates diagnosed with fetal goiter and suspected in utero hypothyroidism warrant careful follow-up over the first few decades for hearing loss.

Fetal neck masses, such a goiter, can compress the trachea, leading to airway compromise at delivery. As in this case, a fetal MRI may serve as an adjunct to ultrasound to better characterize soft tissue masses, the impact of masses on the trachea, and the cartilaginous structures of the upper airway. Furthermore, a multidisciplinary team, including pediatric anesthesiologist, pediatric otolaryngologist, and neonatologist, should be involved in delivery planning. An EXIT procedure is used to secure the neonatal airway while fetal-placental circulation is preserved in cases of airway obstructions (eg, congenital airway obstructions, laryngeal atresia, micrognathia, fetal neck masses, and intrathoracic masses). An EXIT procedure is associated with increased maternal hemorrhagic morbidity and risk of cesarean hysterectomy. However, it should be considered and can decrease the mortality of neonates when airway compromise is possible.

Excessive maternal iodine supplementation is a rare but reversible cause of fetal goiter. This case illustrates the importance of examining patients’ use of medications during pregnancy, including naturopathic supplements, as it may reveal the underlying cause of a fetal anomaly and help determine clinical management.
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