

Fetal Goiter: A Case Presentation*

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The association of hyperthyroidism and pregnancy is a rare but potentially serious condition that occurs in 0.2% of pregnancies (1). However, during pregnancy, hyperthyroidism is frequently seen as a maternal endocrine disease; Graves' disease is the most frequent one in etiology (1-2). Maternal Graves' disease and the antithyroid drugs used to treat hyperthyroidism in pregnant women can affect fetus causing hyperthyroidism or hypothyroidism and goiter (3). Fetal hypothyroidism may be caused by transplacental passage of either maternal thyrotropic-binding inhibitory immunoglobulin antibodies or maternal treatment with antithyroid drugs during pregnancy (4). Congenital hypothyroidism is seen in 1 in every 3500 neonates (5-6). We present a case of fetal goiter caused by maternal usage of propylthiouracil during pregnancy that was diagnosed on a prenatal ultrasonography.

KEY WORDS Fetal goiter, neonatal hypothyroidism

Case Presentation

Mrs. AK, 27 years old, born in Giresun, G₅ P₃ A₁, applied to the hospital with the onset of labor. At the vaginal examination, the cervix was found 80% effaced, 3 cm. dilated. The pregnant was hospitalized since she was in active labor. History revealed that she was being followed by an obstetrician during the antenatal period and according to her history, the gestational age should have been 39 weeks. Her first pregnancy resulted in a stillbirth at 8 months. The second aborted at 10th weeks and the last two pregnancies ended consecutively at 30 and 24 weeks of gestation. She has no child at home. Physical examination revealed a 1+ goiter and pretibial edema. Proteinuria was detected as >300 mg/dl.

At ultrasonographic assesment the fetus was found in 32 weeks of gestation inappropriately of her last menstrual period (Fig. 1). Amniotic fluid index was 4 cm. (<5% percentile), and at umbilical

artery Doppler flow study, the absence of end-diastolic flow (AEDF) and bradyarrhythmia was detected (Fig. 2). During the examination, fetal neck was seen always hyperextended although fetal body movements were not rare. Fetal anatomy examination revealed bilobulated, hyperechogenic well defined masses of 49 mm. diameter in fetal neck (Fig. 3). History of the pregnant revealed that she had goiter for three years, had used propylthiouracil (PTU) 150 mg/day in the first six months of pregnancy and 300 mg/day in the last 4 weeks. Assesment of the history and ultrasonographic findings led to a final diagnosis of fetal goiter and intrauterin fetal growth retardation (IUGR).

Because of the absence of end-diastolic flow at umbilical artery and late decelerations on cardiotocography, cesarean section was planned with indication of acute fetal distress. The male infant, 2650 g, was delivered with Apgar scores of 5 and 5 at first and fifth minutes. Due to the respiratory distress caused by the mass at the neck, the newborn was immediately sent to the neonatal intensive care unit (NICU) (Fig. 4). At NICU, the examination of the newborn revealed poor general

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Figure 1. A bilobulated hyperechogenic mass of 49 mm. diameter was seen at the neck of the fetus.

Figure 2. The biometric measurements of fetus.

Figure 3. At the umbilical artery doppler flow analysis, the absence of end-diastolic flow was detected.

status, negative suckling reflex, positive Moro and catching reflexes, a large mass at the neck, presternal edema and dispnea. Pulse rate was 124/min and respiratory rate was 80-86/min. In the first

Figure 4. The neonate at NICU, with a large mass at the neck.

24 hours, complete blood count and endocrine analysis were performed to determine thyroid status. The results were as hemoglobin 11.5 g/dL, T_3 : 20 ng/dL (normal ranges were 89-256 ng/dL), T_4 : 1.0 μ g/dL (12-22 (g/dL), TSH: 128 mIU/L (1-39 mIU/L). The neonate was considered hypothyroidic and 1/4 tablet/day of levothyron was started through a nasogastric tube. The vital status of the neonate was deteriorated on the second day of life. On the third day, due to septicemia, pulmonary and intraventricular hemorrhage early neonatal death was occurred.

Discussion

Normal thyroid function in pregnancy is essential for normal growth and maturation of the fetus (7). Any disturbance of thyroid function, either from disruption of the hypothalamic-pituitary-thyroid axis or from non thyroid disease can have a profound effect on this process. Women who have hyperthyroidism should be euthyroidic before they are allowed to become pregnant (7).

Since congenital hypothyroidism is sporadic and since there is no current method for easily screening all pregnancies for hypothyroidism, the thrust in fetal diagnosis and therapy has been in those pregnancies suspected of having a hypothyroid fetus when a fetal goiter is detected by ultrasonography or in a hyperthyroid mother who may be on antithyroid therapy (8,9). Ultrasonography is useful for assessing fetal growth and for the detection of fetal goiter, which is reported in

mothers who receive excessive doses of anti-thyroid drugs (ATD) (10).

Antithyroid treatment is the therapy of choice in pregnancy. Thionamids are the most common agents used. They include carbimazole, methimazole (MMI) and propylthiouracil (PTU). These drugs have two actions. First they inhibit thyroid hormone synthesis. This is achieved by the competitive blocking of the peroxidase enzyme, preventing the release of iodine from circulating iodides. The enzymes responsible for the iodination of tyrosine and the coupling of iodothyronine molecules are also inhibited. The second action is to cause a reduction in the levels of circulating autoantibodies. PTU has the additional effect of inhibiting the peripheral conversion of T_4 to the more active T_3 (7,11). MMI and PTU rapidly cross the placenta; MMI is slightly bound to the serum albumin and therefore, crosses the placenta faster than PTU. In general, it is recommended to use the lowest dose of ATD effective in controlling maternal hyperthyroidism in order to avoid fetal hypothyroidism and goiter (12). The initial dose of PTU is 150 mg every 8 hours, or 20 mg of MMI twice a day. The dose may vary from 50-200 mg of PTU every 8 hours or equivalent amount of MMI, 10-60 mg a day according to patient symptomatology. The therapeutic dose is determined by the regression of clinical symptoms of hyperthyroidism and the evaluation of free T_4 level. PTU is given to achieve free T_4 level at the upper limit or just above it. The cessation of PTU treatment a few weeks before delivery and keeping the daily dose below 50 mg reduces the risk of neonatal hypothyroidism (10,13). In the presented case, history shows that the patient had been used PTU at a dose of 150 mg in the first two trimesters and 300 mg in the last trimester until delivery; however, in the literature, it is reported that even the lowest dose that achieves maternal euthyroidism may cause fetal hypothyroidism (14,15). For this reason, in suspected pregnancies, sonographic diagnostic clues of fetal hypothyroidism such as goiter, hyperextended neck, bradycardia, decreased fetal movement, subcutaneous edema, polyhydramnios due to difficulty in swallowing, intrauterine growth retardation (IUGR) and even umbilical hernia should be screened carefully (14-16). Further-

more, the only reliable way to establish prenatal diagnosis of fetal hypothyroidism is percutaneous fetal umbilical cord blood sampling, since amniotic fluid levels do not properly represent the fetal thyroid function (18,19). We couldn't achieve a chance to perform percutaneous fetal umbilical cord blood sampling in our case because of acute fetal distress developed in a short time after diagnosis and the infant was delivered by cesarean section immediately. In the first 24 hours, blood analysis was done, in order to reanalyse at the fourth day, to explain fetal thyroid status. As we know, at the time of parturition, in response to neonatal (cold) extrauterine exposure, there is an acute release of thyroid-stimulating hormone (TSH) mediated by thyroid-releasing hormone (TRH), and serum concentration of TSH peaks at mean level approximating 70 mU/L at 30th minute. Circulating TSH remains moderately elevated for 2-3 days after birth. But we could not repeat the analysis as the infant died at the third day.

Another important complication that accompanies fetal hypothyroidism is IUGR (16,17). In our case, besides the growth retardation, oligohydramnios and AEDF at the umbilical artery were found at ultrasonographic examination. Although polyhydramnios often accompanies fetal goiter due to difficulty in swallowing, the occurrence of oligohydramnios in our case might be explained by the presence of IUGR. In this case, the presence of both IUGR and AEDF in umbilical artery point to uteroplacental insufficiency.

In summary, careful attention to the clinical progress of the disease and the proper interpretation of thyroid tests are essential in the management of hyperthyroidism in pregnancy. Patients should be seen at regular intervals, preferably every two weeks at the beginning of therapy and tests should be performed at each visit. Ultrasound should be used to detect fetal goiter from 20 weeks onward when fetal thyroid gland becomes responsive to passively acquired antibodies or ATDs (10). In case of fetal goiter, serious consideration should be given to performing cordocentesis to determine fetal thyroid function. In the treatment of hypothyroidic goitrous fetus, levothyroxine should be administered by intraamniotic injection.

The levothyroxine dose of 250µ weekly has been proved to be effective in the treatment (12). There is considerable evidence for the essential role of thyroxine hormone in the growth and development of the central nervous system. The final outcome of mental development in children with congenital hypothyroidism depends on the severity, the time of onset (in utero), and duration of thyroid insufficiency. Therefore early diagnosis and prompt treatment of fetal hypothyroidism are extremely important to prevent serious perinatal complications.

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