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Hydrops Fetalis Secondary to Maternal Exposure to Propylthiouracil

Maternal Propiltiourasil Maruziyet Sonrası Gelişen Fetal Hidrops
Endokrinoloji ve Metabolizma

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Özet

Tiroid hastalıkları, gebelik esnasında kompleks hormonal değişiklikler nedeniyle yaygın olarak görülür. Fetal hidrops, düşük doğum ağırlığı, fetal distress ve nörofizyolojik gelişme geriliği açısından risklidir. 20 yaşında primigravid gebe hipotiroidizmle başvurdu ve bu esnada propiltiourasil (PTU) 3x1 kullanmaktaydı. Yapılan ultrasonografi (USG)'de hidrops fetalis görüldü ve bunun üzerine PTU tedavisi kesildi. Takiplerinde fT3 2.81 (2.3-4.2) pg/ml, fT4 0.82 (0.88-1.72)ng/dl ve TSH 1.65 (0.57-5.6) µIU/ml olarak tespit edildi. Kontrol US'de fetal hidropsta gerileme olduğu görüldü. Hasta 37+2 haftalık iken sezeryan ile 3150 gr ağırlığında bir kız çocuğu dünyaya getirdi.

Anahtar kelimeler: *Fetal Hidrops, Propilthiourasil*

Abstract

Thyroid disorders are common in pregnancy, due to the complex hormonal changes during pregnancy. Fetal hypothyroidism has been associated with increased risk of low birth weight, fetal distress, and impaired neuropsychological development. A 20-year-old primigravida had no pregnancy-related problem but had hypothyroidism. Propylthiouracyl (PTU) 3x1 had been commenced, on that control visit, ultrasonography (US) revealed hydropsfetalis, and the patient has been referred to our policlinic. We discontinued PTU and on her control visit, fT3 was 2.81 (2.3-4.2) pg/ml, fT4 was 0.82 (0.88-1.72) ng/dl, and TSH was 1.65 (0.57-5.6) µIU/ml; control US revealed regression of fetal hydrops. A normal-birth-weight (3150 gr) female infant born (a cesarean section was performed) at 37+2 weeks'gestational age.

Keywords: *Hydrops Fetalis, Propylthiouracil*

Introduction

Thyroid hormones are essential for fetal neurological development [1]. Fetal hypothyroidism may result from maternal exposure to anti-thyroid drugs (ATD) [2]. Intra-amniotic treatment with levothyroxine normalizes fetal thyroid functions and reduces size of goiter. Fetal hypothyroidism is an uncommon condition in the etiology of hydropsfetalis. Maternal exposure to ATD may additionally lead to congenital anomalies of musculoskeletal system and urogenital system. Herein, we present a pregnant woman with hydropsfetalis secondary to maternal exposure to high-dose propylthiouracil.

Case Report

A 20-year-old primigravida consults her physician for routine control in the 12thweek of first gestation. Meanwhile, she mentions about sweatcomplaint existing for the last one year. Results of laboratory analyses performed accordingly were as follows: free T3:3.76 (2.5-3.9) pg/ml, free T4:1.18 (0.61-1.12) ng/dl,and TSH:0.42 (0.34-5.6) µIU/ml. The patient had been told that she had no pregnancy-related problem but had hypothyroidism. Propylthiouracyl (PTU) 100 mg/day had been commenced and she had been asked to come for control visit after one month. On the control visit after one month, she had been informed that there was no

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problem regarding pregnancy, but the dose of PTU had been increased to 150 mg/day since fT3 was 3.4 (2.3-4.2) pg/ml, fT4 was 1.29 (0.88-1.72) ng/dl, and TSH was 0.13 (0.57-5.6) μIU/ml, and she had been invited for control again after one month. On that control visit, again she had has no pregnancy-related problem, but the dose of PTU had been increased to 300 mg/day since fT3 was 3.32 (2.3-4.2) pg/ml, fT4 was 1.02 (0.88-1.72) ng/dl, and TSH was 0.53 (0.57-5.6) μIU/ml. On the control visit again after one month, results of thyroid function test were as follows: fT3:2.64 pg/ml (2.3-4.2), fT4:0.98 (0.88-1.72) ng/dl, and TSH: 1.77 (0.57-5.6) μIU/ml. However, US revealed hydropsfetalis, and the patient has been referred to our policlinic (Figure 1).

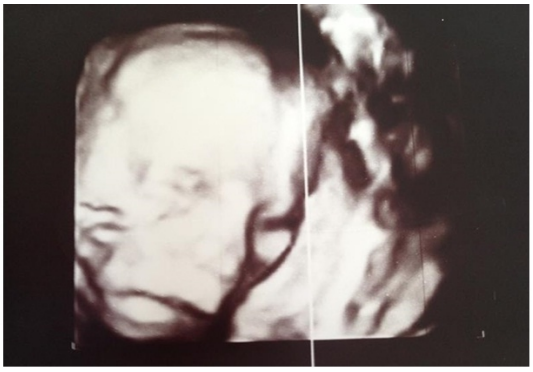

Figure 1
Propilthiouracil after fetal hydrops ultrasonografi appearance

We discontinued PTU; Anti-TG, Anti-TPO, and Thyroid receptor antibodies were found negative and the patients called for control after 15 days. On her control visit, fT3 was 2.81 (2.3-4.2) pg/ml, fT4 was 0.82 (0.88-1.72) ng/dl, and TSH was 1.65 (0.57-5.6) μIU/ml; control US revealed regression of fetal hydrops (Figure 2).

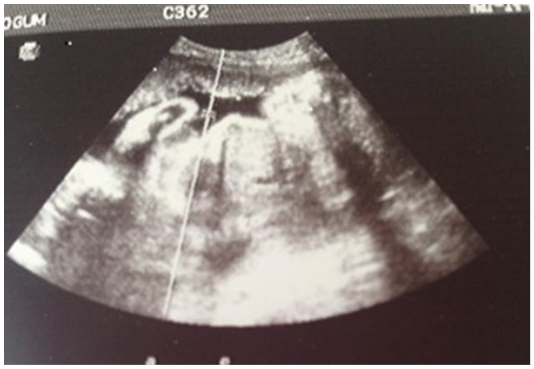

Figure 2
Revealed regression of fetal hydrops

A normal-birth-weight (3150 gr) female infant born (a cesarean section was performed) at 37+2 weeks'gestational age. A euthyroid, non-edematous, non-goitrous neonate was delivered and newborn's psychomotor development was normal.

Discussion

Pregnancy is a time of complex hormonal changes. In women with normal thyroid function, there is an increase in

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thyroxine (T_4) and triiodothyronine (T_3) production, which results in inhibition of thyroid-stimulating hormone (TSH) in the first trimester of pregnancy, due to a high human chorionic gonadotropin (hCG) level that stimulates the TSH receptor because of partial structural similarity[3]. Clinical or subclinical thyroid disorders are usually detected during pre-conceptional counseling or in women who have just conceived and have done tests for thyroid function. According to recent American Thyroid Association (ATA) guidelines, if laboratory-dependent, trimester-specific ranges for TSH are not available, the recommended reference ranges for TSH are 0.1 to 2.5 mIU/L in the first trimester, 0.2 to 3.0 mIU/L in the second trimester, and 0.3 to 3.0 mIU/L in the third trimester. Medical therapy of hyperthyroidism in Grave's disease is limited to two antithyroid drugs (ATD)s, namely PTU and methimazole (MMI). PTU is believed to be somewhat safer for pregnant women than MMI[4]. In the literature, neonatal anomalies due to maternal exposure to ATD are quite common. Maternal side effects of ATDs include toxic reactions such as fever, nausea, pruritus, skin rash and arthralgia and metallic taste and serious complications such as granulocytopenia, agranulocytosis, vasculitis, lupus-like syndrome and hepatitis[5]. ATDs may affect the fetus also. In addition to fetal hypothyroidism and the development of fetal goiter, the use of PTU and MMI has been reported to be associated with congenital anomalies including muscular hypotonicity, cryptorchidism, aortic atresia, hypospadias, congenital dislocation of the hip, aplasia cutis congenita, choanal atresia and syndactyly. However, no effect on long-term cognitive or somatic development has been found in infants exposed in utero to ATDs[6]. The treatment of fetal hypothyroidism involves normalizing maternal thyroid functions, discontinuation of ATDs, as well as possible direct intra-amniotic treatment with thyroid hormone. It is unclear whether intra-amniotic fetal treatment for hypothyroidism is necessary in a euthyroid mother. In most instances, maternal T4 transfer through the placenta will provide for the needs of the fetus[7]. Herein we presented a case, in whichfetal hydrops has been developed secondary to maternal exposure to high-dose PTU. But, intra-amniotic fetal treatment for hypothyroidism is not necessary for our patient. A euthyroid, non-edematous, non-goitrous neonate was delivered and newborn's psychomotor development was normal. However, fetal hydrops secondary to hypothyroidism caused by maternal exposure to ATD is a quite rare condition. Non-immune hydrops has been described previously in a neonate with congenital hypothyroidism delivered to a healthy mother[8.]

Gestational thyrotoxicosis is known to cause thyroid dysfunction. Such changes during pregnancy should be well-known and be intervened accurately. Therefore, these patients should certainly be consulted with endocrinologists.

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Information Presentation

36. Türkiye Endokrinoloji ve Metabolizma Hastalıkları Kongresi