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Case report-Olgu sunumu

A successful pregnancy in a patient with acromegaly under octreotide-LAR treatment: a case report

Oktreotid-LAR tedavisi alan akromegalik bir hastada başarılı gebelik: olgu sunumu

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Abstract

The patient was a 30 -year-old female acromegaly patient who was operated for pituitary macroadenoma. The response to postoperative oral glucose tolerance test (OGTT) after operation was insufficient. For this reason, Octreotide-LAR (OCT-LAR) treatment was started. On 15 months after the therapy, the patient presented with failure of menstruation for four months, so pregnancy test was performed and pregnancy was diagnosed. The patient had used OCT-LAR during the period without knowing that she was pregnant. Since it has been shown with magnetic resonance imaging (MRI) that the pituitary adenoma did not grow, we stopped the OCT-LAR treatment. The patient delivered a healthy newborn girl of 2650 g in weight and 50 cm in length at the 37 weeks of gestation. MRI was performed for postpartum macroadenoma assessment and the lesion did not grow during this period. Two months after the delivery, the response of growth hormone to OGTT was evaluated. OCT LAR treatment was started again because the suppression was not seen. We believe that the size of the adenoma must be checked by MRI to make a decision in discontinuing or continuing treatment as the most suitable approach, when pregnancy develops in acromegalic patients. Furthermore, we think that OCT-LAR should be discontinued during pregnancy until more safety data are obtained.

Key words: Acromegaly, pregnancy, octreotide

Özet

Hipofizer makroadenom nedeniyle opere olan 30 yaşındaki bayan hastanın operasyon sonrası yapılan oral glukoz testine GH cevabı yetersizdi. Bu nedenle Octreotide-LAR (OCT-LAR) tedavisi başlandı. Tedavinin 15. Ayında, 4 aydan beri adet görmemesi nedeniyle yapılan gebelik testinde gebelik olduğu tespit edildi. Hasta bu dönemde gebe olduğunu bilmediği için OCT-LAR tedavisi almıştı. Hipofiz manyetik rezonans görüntülemede (MRG) adenomda büyüme olmadığı görüldüğü için OCT-LAR tedavisi kesildi. Hasta gebeliğin 37. haftasında 50 cm boyunda ve 2650 gr ağırlığında sağlıklı bir kız doğurdu. Postpartum dönemde adenoma değerlendirmek için yapılan hipofiz MRG'de büyüme olmadığı görüldü. Doğumdan 2 ay sonra yapılan OGTT'ye büyüme hormon supresyonu yetersiz olduğu için OCT-LAR tedavisi yeniden başlandı. Akromegali hastalarında gebelik oluştuğunda tedaviye devam etme veya bırakma kararını vermek için adenoma boyutunun hipofiz MRG ile kontrol edilmesi gerektiğinin en uygun yaklaşım olduğuna inanıyoruz. Ayrıca daha güvenli veriler elde edilinceye kadar gebelik sırasında OCT-LAR tedavisi kesilmesi gerektiğini düşünüyoruz.

Anahtar sözcükler: Akromegali, gebelik, oktreotid

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Introduction

Pregnancy is very rare in acromegalic women due to decrease in fertility in these patients[1]. Impairing gonadotropin secretion and hypophysis disfunction may be responsible for infertility. In addition, hyperprolactinemia occured in acromegalic patients might contribute to infertility by causing function disorder in hypothalamic-pituary-ovarian axis [2]. Infertility or miscarriages at early stages of the pregnancy may associated the mentioned factors.

Due to the effects of either recent developments in microsurgical methods or somatostatin analogues, ensuring ovulation in these patients boosted frequency in pregnancy with acromegalic women [3]. This study presents the course and the consequence of pregnancy in an operated acromegalic female patient whose octreotide long acting repeatable (OCT-LAR) treatment was discontinued.

Case

The 30-year-old woman operated because of pituitary macroadenoma (2.5x1.5 cm) causing acromegaly disease had insufficient suppression response of growth hormone in postoperative oral glucose tolerance test (OGTT). Preoperative levels of GH (Growth hormone) and IGF-1 were 50.8 mIU/L and 1110 ng/mL respectively while the postoperative IGF-I was 450 ng/mL. OCT-LAR (10 mg for every 4 weeks subcutaneous) treatment was commenced. After 3 months, the dose was increased to 20 mg because of treatment failure. In the 15th month of therapy, the patient presented failure of menstruation for four months, then a pregnancy test was performed and pregnancy was diagnosed. The patient used OCT-LAR during the period without knowing that she was pregnant. Since the hypophysis gland was established as shrunk secondary to operation and any tumor was non-existent by the hypophysis MR performed immediately before pregnancy (Figure 1), we terminated OCT-LAR.

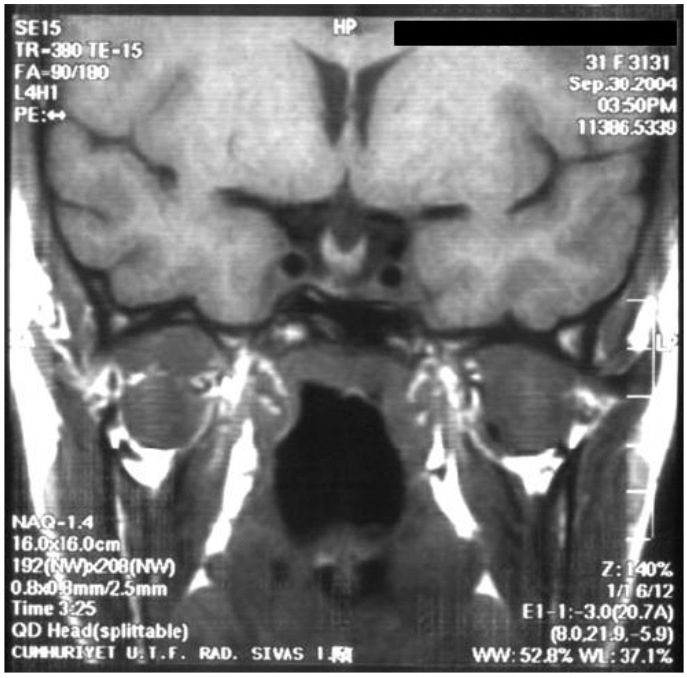

Figure 1. Pituitary MRI from pre-pregnancy.

Gestational diabetes mellitus was not established in OGTT performed at 24th gestational week. The patient normally delivered a healthy newborn girl at the 37th gestational week, with newborn weighing 2650 grams and with a length of 50 cm. No malformation and metabolic imbalance were observed in the newborn. MRI was used for postpartum macroadenoma assessment and it did not demonstrate any growth during this period. Postpartum MRI showed empty sella (Figure 2).

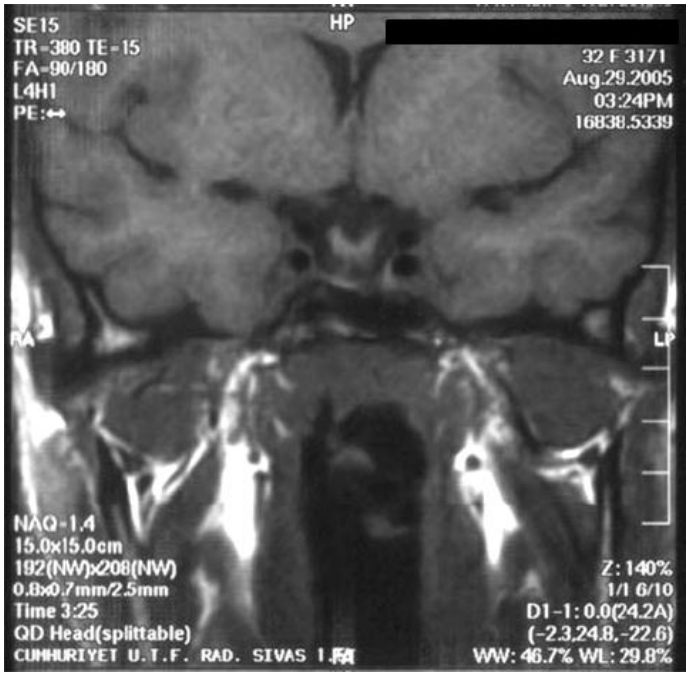

Figure 2. Pituitary MRI from postpartum period.

Two months after the birth, OGTT was done. Serum samples were collected at 0, 30, 60, 90, and 120 min for GH and responses to the glucose load were as follows: 7.16, 2.56, 2.53, 3.33, and 3.80 mlU/L, respectively. Because of insufficient suppression response of growth hormone to OGTT, OCT LAR treatment was restarted.

Discussion

In normal pregnancy, the placental GH variant steadily replaces pituitary GH after the first trimaster. From the second trimester until delivery, pituitary GH is suppressed and IGF-1 levels rise, whereas in pregnant acromegalic patients, pituitary GH secretion is not diminished, and IGF1 increases in the second trimester as in normal pregnancy [4]. Optimal treatment approaches must be discussed in active acromegalic pregnant women with no post-operation remission, and thus, treated with octreotide. During the pregnancy, progressive growth at hypophysis tumors has been reported [5]. There is limited knowledge on the use of octreotide in pregnancy. Nineteen acromegaly cases ongoing treatment of somatostatin during pregnancy were reported in literature [6]. In 15 of these cases, while the treatment was terminated after the pregnancy was confirmed, 4 of them continued the treatment. In our case, since tumor was not established in the MRI scan performed before pregnancy, octreotide treatment was discontinued and the patient was followed up carefully until the term for headache and loss of sight - the symptoms that are related with both clinical findings and tumor growth. In our patient, no pathologic finding was observed during that period. The post-pregnancy hypophysis MR found no growth in tumor. Since, the studies demonstrated that octreotide passed through placenta [7] the use of this medicine during pregnancy was thought to have negative impact on the fetal development. However, permanent fetal growth retardation was not observed throughout

the course of pregnancy in cases continuing the treatment [6]. Because very few cases were reported on octreotide use during pregnancy, having a precise opinion on the issue is not possible at least for the time being.

OCT-LAR that constitute one of the treatment options in acromegaly affects somatostatin receptors subtypes 2 and 5 and shrinks the size of tumor, it eliminates such symptoms as headache, malaise, and arthralgia, and decreases the levels of GH and IGF-I [8]. GH produced during pregnancy was established to have predominately synthesized. It was suggested that octreotide did not inhibit GH secretion because somatostatin receptors subtype 4 exist in placenta, and thus fetal growth retardation did not occur in patients receiving the treatment at the early stages of pregnancy [9]. Although our subject did receive octreotide in the first four-month period, significant fetal growth retardation did not occur during the intrauterine stage and any fetal growth issue was not observed in postpartum phase. Its reason may be octreotide not reducing placental GH secretion. Another issue that needs attention in pregnant acromegalic women that do not go through any treatment is gestational diabetes mellitus. GH is known to have a powerful insulin antagonist effect [10]. Both acromegaly itself and the increased insulin resistance in advanced phases of pregnancy [11] may cause the development gestational diabetes. In our case, gestational diabetes was not observed despite the termination of treatment.

We believe that checking the size of the adenoma to make a decision in discontinuing or continuing the treatment is the most suitable approach, if pregnancy develops in acromegalic patients. Furthermore, we think that OCT should be discontinued during pregnancy until more safety data are obtained.

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