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Successful pregnancy and delivery of a patient with congenital adrenal hyperplasia

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Congenital adrenal hyperplasia (CAH) during pregnancy is a rare condition. Only a few cases have been reported in the literature. CAH patients has lower pregnancy rate compared to normal women. A 27-year-old nulliparous woman, a diagnosed case of 21-hydroxylase deficient simple virilising form of classic CAH visited. She got pregnant spontaneously without any trial of assisted reproductive technology. At the age of 12, she underwent clitoral resection and vaginoplasty. She took dexamethasone or prednisolone after operation. She delivered healthy singleton female baby by cesarean section. Four years later, she delivered healthy singleton female baby by repeat cesarean section. Two female babies have shown normal external genitalia. Here, we report a case of successful pregnancy and delivery in a patient with CAH.

Keywords: Congenital adrenal hyperplasia; Delivery; Fertility; Pregnancy

Introduction

Congenital adrenal hyperplasia (CAH) is a group of diseases in steroid biosynthesis, due to an enzyme lack in the transformation of cholesterol to cortisol. CAH is a monogenic, autosomal recessive disorder [1]. More than 90 percent of CAH is caused by steroid 21-hydroxylase shortage. The classic form generally presents at childbirth with serious virilization and/or salt wasting, however, a late onset of non-classic form of CAH is generally diagnosed at childhood or after adolescence [2]. In classic form of CAH, glucocorticoid (often with mineralocorticoid) treatment is required, on the other hand in the milder non-classic form, treatment is given when patients get symptoms due to hyperandrogenemia such as hirsutism, oligomenorrhea, and infertility. The diagnosis of non-classic form of CAH (NCCAH) is based on increase of 17-hydroxyprogesterone, the metabolite of progesterone and precursor to cortisol, and dehydroepiandrosteronesulfate. Infertility is comparative in NCCAH, though there is a higher occurrence of spontaneous miscarriage [3]. NCCAH women with menstrual dysfunction responds well to adrenocortical inhibition with prednisone, and the significant improvement of menstrual regularity is frequently noted [4]. Here, we report a case of successful pregnancy and delivery in a patient with CAH for the first time in Korea.

Case report

A 27-year-old nulliparous woman, a diagnosed case of 21-hydroxylase deficient simple virilizing form of classic CAH visited our department from the endocrinology department for pregnancy maintenance. Her diagnosis had been identified at eleven years old with a high testosterone level, raised 17-hydroxyprogeterone level , enlarged clitoris and normal karyotype (46, XX).

At the age of 12, she underwent clitoral resection and vaginoplasty at urology department of our hospital. She took dexamethasone (minimum dose 0.5 mg/day to maximum

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dose 1.0 mg/day) after operation. Four months later, her breasts expanded and in six months' time, menstruation began. The treatment sustained without any other complication. The treatment had continued and urology department referred this case to endocrinology department when she was 27 years old. Medication was changed to prednisolone and the endocrinology department had prescribed it (minimum dose 10 mg/day to maximum dose 20 mg/day) before pregnancy.

She married at 25 years old and had a spontaneous abortion at 26 years old. After the abortion, she got pregnant spontaneously without any trial of assisted reproductive technology. At 12+3 week of gestation, she first visited our department. The first trimester screening conducted at the first visit of 12+3 week of gestation was normal and quad test conducted at 16+3 week of gestation was also normal. She was diagnosed with gestational diabetes mellitus as blood sugar was mildly increased than normal range in the 100 g oral glucose tolerance test conducted at 24+6 week of gestation. Lifestyle modification was recommended to the patient and blood sugar was well-controlled without any medication. Ultrasonography was performed at two to four weeks. The development of fetus was appropriate to the gestational age without any sign of intrauterine growth retardation or large for gestational age. During pregnancy, she continued to take prednisolone (minimum dose 7.5 mg/day to maximum dose 20 mg/day) on demand at endocrinology department.

Cesarean section was preferred other than vaginal delivery, as she had cephalopelvic disproportion on examination and history of vaginoplasty. She delivered female weighs 2,990 g by elective cesarean section at 38+4 week of gestation. The baby exhibited normal 7 Apgar score and did not require oxygen or respiratory assistance. The external genitalia was normal and there was a sign of normal karyotype (46, XX) in the result of chromosomal study. After the delivery, the patient had took prednisolone (15 mg/day) consistently for the CAH.

After one time of spontaneous abortion, 3 years later, at the age of 30, she became pregnant of the second baby spontaneously. She was diagnosed with gestational diabetes mellitus due to the mildly increased level of blood sugar at the 100 g oral glucose tolerance test conducted at 23+4 week of gestation, however, the blood sugar was well-controlled by life style modification without medication. The development of fetus was appropriate to the gestational age and antenatal care did not show any particular sign. During this pregnancy, she continuously took the prednisolone (minimum dose 7.5 mg/day to maximum dose 15 mg/day) prescribed by endocrinology department. She delivered 3,250 g female baby at 38+2 week of gestation, by cesarean section. The baby exhibited normal Apgar score and did not require oxygen or respiratory assistance. Four years old baby and eleventh month old bay have shown normal external genitalia and normal development up to now.

Discussion

Since CAH was first described by DeCrecchio in 1865, it has academically confirmed by Wilkins et al. [5]. Due to the genetic deficiency required for biosynthesis of cortisol, the creation of cortisol was decreased and the secretion of ACTH increased as the hypothalamus-pituitary axis reacts to the low level of cortisol. It induces the hyperplasia of adrenal cortex, thus, precursor and testosterone of cortisol was mass-produced and the distinctive clinical symptoms are shown [6]. Therefore, it is cured by supplementary hormone administration [7]. It is known that 21-hydroxylase deficiency is the main cause of CAH in the rate of 90% to 95% [8].

CAH is divided into simple virilizing, salt-wasting, and nonclassical form according to clinical manifestation. Co-occurrence of synthesis disability of cortisol and aldosterone with complete enzyme deficiency is the most severe form. Untreated infants with renal salt-wasting suffer insufficient feeding, body-weight loss, and dehydration which can advance to azotemia, vascular collapse, shock and death. Adrenal crises arise in the newborn period as early as one to seven weeks of life [9]. Therefore, early diagnosis and appropriate cure should be conducted immediately after birth.

Nonclassical CAH, occasionally called late-onset, mild or attenuated, arises when there is only a mild insufficiency of enzyme 21-hydroxylase. These patients do not waste salt, and females are not virilized at birth [10]. In the case of nonclassical 21-hydroxylase deficiency, there would be no specific abnormality at birth, but it has mild symptoms, such as menstrual irregularity, hirsutism, and infertility, around menarche and sometimes it shows masculinization of external genitalia [11,12].

Endocrine test of 21-hydroxylase deficiency suggests that

the high concentration of progesterone and 17-hydroxy progesterone in blood is significant to decide the effect of treatment because progesterone blocks the conversion to the 11-deoxycortisol. The excretion of pregnanetriol and the level of androstenedione and testosterone in urine are elevated caused by the increase of 17-hydroxy progesterone.

Early diagnosis and the treatment are important which gets rid of the excessive secretion of adrenocorticotropic hormone (ACTH), replenishes required hormone, and corrects external genitalia. Long-lasting glucocorticoid replacement treatment is the mainstay of therapy for CAH patients. It reduces 17-hydroxyprogesterone and adrenal androgen by normal range as glucocorticoids replacement replenishes cortisol and inhibits the secretion of ACTH.

Since Blizzard and Wilkins [13] administrated cortisone for the first time, cortisol, cortisone and prednisolone have been used; however, it is known that cortisol has the most significant effects by proving stable physiological supplementing comparatively. Getting pregnant of CAH patients requires several conditions, strict keeping of steroid replacement, appropriate vaginal opening for coitus, and sufficient adrenal suppression during the attempts to get pregnant [14].

CAH patients has lower pregnancy rate compared to normal women, however, cortisol replacement therapy enables the normal pregnancy, and moreover glucocorticoid treatment raises the pregnancy rate of non-classical CAH patients as much as the rate of normal women [15]. When the fetus is at risk for CAH, dexamethasone (20 μg/kg/day in 3 divided doses) is administered to the pregnant womem before the ninth week of gestation, or ideally before the seventh week, blind to the sex or affected state of the fetus. This inhibits fetal hypothalamic-pituitary-adrenal axis, excess adrenal androgen secretion and prevents virilization in affected females [16]. Dexamethasone is used because it crosses the placenta, crossing from the maternal to the fetal circulation.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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