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CONGENITAL ADRENAL HYPERPLASIA IN ADOLESCENTS AGE 18 YEARS

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Abstract

Congenital adrenal hyperplasia is an autosomal recessive genetic disorder that results in deficiency of enzymes required for steroidogenesis in the cortex of the adrenal glands. The incidence of CAH is rare and it can occur in both males and females. Generally, CYP21 mutations lead to deficiency of the 21-hydroxylase enzyme and failure of adequate cortisol synthesis. Congenital adrenal hyperplasia (CAH) is classified into two types, namely classical and nonclassical types. The patient's clinical manifestation was genital ambiguity in female infants. The aim of this case report is to share our experience of CAH in adolescents in West Sumatera. We report a case of congenital adrenal hyperplasia in an 18 year old girl. The patient was referred to the Urogynecology Obstetrics and Gynecology Department, Dr. M. Djamil Padang with chief complaint of clitoral enlargement since the age of 5 years. On physical examination, vital signs were within normal limits, chest examination revealed Tanner Stage 3 breasts, genital examination revealed an enlarged clitoris with a size of 3x1 cm without the presence of a vaginal canal. Investigations that support the diagnosis are 17-hydroxy progesterone laboratory with a result of 90.2 nmol/L. On ultrasound examination of the abdomen within normal limits with the results of chromosome 46,XX analysis. The patient had not had an adrenal crisis for 18 years. The patient was diagnosed with clitomegaly and the cause of congenital adrenal hyperplasia. The patient was given hydrocortisone therapy at a dose of 20 mg in the morning, followed by a dose of 15 mg at night and planned to undergo clitororeduction surgery by carrying out the perioperative and postoperative hydrocrotisone therapy protocol. The patient's family was given counseling, carried out regular monitoring of the patient and hydrocortisone therapy. Congenital adrenal hyperplasia is a disease caused by genetic disorders that require multidisciplinary management. Enforcement of diagnosis, appropriate management, and counseling are needed to optimize patient growth and development.

Keywords: congenital adrenal hyperplasia, girl

Introduction

Congenital adrenal hyperplasia (CAH) or congenital adrenal hyperplasia is an autosomal recessive disorder due to mutations or deletions of CYP21A that causes defects in steroidogenesis in the production of glucocorticoids, mineralocorticoids, or sex steroids. This disorder generally causes a deficiency of 21-hydroxylase production and results in reduced synthesis of the hormones cortisol and aldosterone, followed by an excessive increase in androgen production. Excessive androgen production causes changes in the development of primary or secondary sex characteristics in infants, children, and adults (Dhyani, Batubara, Handryastuti, & Prayitno, 2016; Utari, 2016).

CAH cases were classified into classic (salt wasting and simple virilizing) and non-classical types. The classic type of salt wasting is caused by a 2110 C>T mutation in exon 8 which results in a change in the amino acid arginine to tryptophan (R356W), the classic simple virilizing type is caused by a 1001 T>A mutation in exon 4 which results in a change in the amino acid isoleucine to aspargine (I172N), while the non-classical type is caused by a 1685 G>T mutation in exon 7 which results in a change in the amino acid valine to leucine (V281L) (Indradjaja A, Suryawan IWB, 2014).

The incidence of CAH cases is estimated at 1:13,000 to 1:15,000 in 6.5 million newborns worldwide. It is estimated that 75% of patients have a salt-wasting phenotype. In America, cases of CAH usually occur in the Yupik Eskimo and American races. Because CAH is an autosomal disorder, both male and female can occur equally (Widodo et al., 2016).

Clinical manifestations in cases of inadequate mineralocorticoids due to low cortisol levels, the patient will experience vomiting due to sodium deficiency which can lead to dehydration, hypovolemia, shock, and death. In the case of androgen oversecretion, men will have more facial hair and a standard penis size that is functional but does not produce sperm, or in women who have clinical genital ambiguity, irregular menstruation, infertility, enlarged clitoris, and a shallow vagina (Momodu, Lee, & Singh, 2021).

Early diagnosis of CAH is needed to prevent worsening of the adrenal crisis, get proper treatment, have normal growth and development, and reduce the psychological burden of gender confusion (Das, Rakib, Khanam, Pillai, & Islam, 2019).

Research Methods

Patient An. D is an 18-year-old woman who was referred to the Urogynecology Obstetrics and Gynecology Clinic at Dr. RSUP. M. Djamil Padang on October 11, 2021 with the chief complaint of clitoral enlargement since the age of 5 years. However, the patient was only brought to Solok Hospital for treatment when he was 9 years old. The patient denied any complaints of abdominal pain, abdominal enlargement, and vaginal bleeding. The patient denied bowel and bladder complaints. Menarche history of menarche at the age of 13 years with regular cycles for 5-6 days in each cycle, the patient usually changes 2-3 pads every day without menstrual pain. The patient is not

married. In order for the patient to receive further examination and treatment, the patient was referred to Dr. RSUP. M. Djamil.

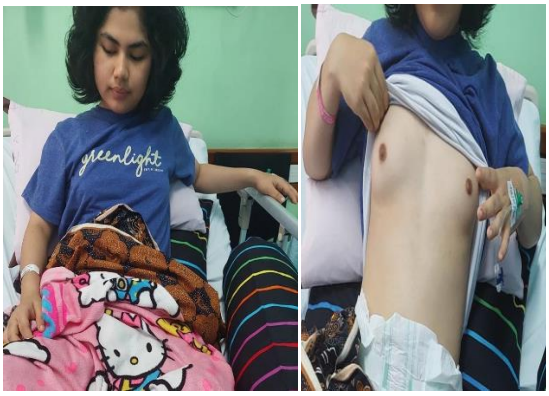

Figure 1
Patient An. D, 18 years old with genital ambiguity

The patient's family history of ambiguous genitalia was denied. There was no history of the use of hormonal therapy and genetic disorders in the family. There was also no family relationship between the patient's mother and father.

On physical examination obtained through examination of vital signs and general survey. Vital signs found were good general condition, cooperative awareness of compos mentis, blood pressure 128/89 mmHg, pulse 88x/minute, respiratory rate 19x/minute, and temperature 36.9. The patient's body weight (BB) is 51 kg, the patient's height (TB) is 155 cm with a Body Mass Index (BMI) of 21.2 kg/m2 with the impression of normoweight.

On general survey examination, skin turgor was found to be good. On skin examination, there were no hyperpigmentation, petechiae, purpura, pallor, cyanosis, jaundice, edema, and no enlarged lymph nodes (KGB). On examination of the head there is black hair, the conjunctiva is not anemic and icteric, pupillary reflexes are normal. On examination the lungs and heart were within normal limits. On chest examination, there were breasts with Tanner Stage 3. On abdominal examination there was no tenderness, hepatomegaly and splenomegaly. On examination of the external genitalia, it was found that there was pubic hair, the size of the clitoris was 3x1 cm, without the presence of the vaginal canal. There was no edema in the extremities.

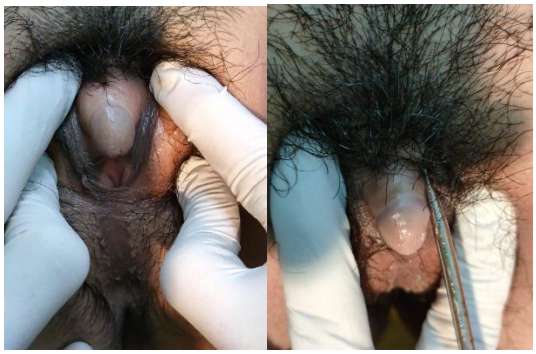

Figure 2
Enlargement of the patient's clitoris.

Investigations carried out to confirm the patient's diagnosis were complete blood counts, blood glucose, electrolytes, 17-OH progesterone, abdominal ultrasound, and chromosomal analysis.

On investigation, the results showed hemoglobin (Hb) 12.9 g/dL, leukocytes 12.090/mm3, hematocrit 39%, platelets 347.000/mm3, and GDS 151 mg/dL., albumin 4.5 g/dL, globulin 2.6 g/dL, SGOT 12 U/L, SGPT 12 U/L, total bilirubin 0.4 mg/dL, urea 13 mg/dL, creatinine 0.8 mg/dL, calcium 9.7 mg/dL, sodium 139 mmol /L, potassium 3.7 mmol/L, and chloride 105 mmol/L. Anti-HIV and non-reactive HBsAg examination. The chest X-ray appeared normal with no abnormalities in the heart and lungs.

The patient also underwent an ultrasound examination with the impression of the internal genitalia not finding any abnormalities. The results of the patient's chromosomal analysis (9 May 2011) obtained from heparin peripheral blood and then studied through 20 cells using the G-Banding technique were 46,XX and no major structural abnormalities were seen. Then, 17-hydroxy progesterone was examined (15 January 2015) to confirm the diagnosis and the result was 23.47 ng/dL with the impression in accordance with Tanner stage 3, then the 17-hydroxy progesterone laboratory was repeated (26 January 2015) with a result of 90.2 nmol/L.

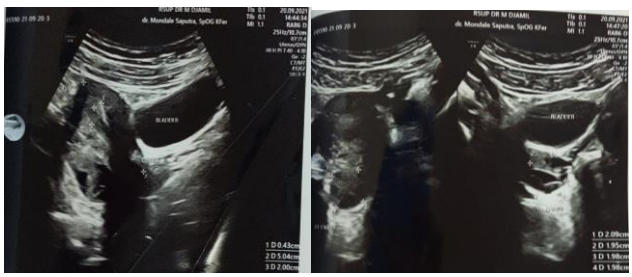

Figure 3
The results of the patient's ultrasound examination

Based on the history, physical examination, and supporting examination, the patient was diagnosed with clitomegaly and the cause of congenital adrenal hyperplasia. The history that supports the diagnosis of CAH is the main complaint of clitoral enlargement since the age of 5 years. Physical examination that supports the diagnosis is

an enlargement of the clitoris with a size of 3x1 cm without the presence of the vaginal canal. Investigations that support the diagnosis are 17-hydroxy progesterone laboratory with a result of 90.2 nmol/L.

The patient was managed by giving hydrocortisone at a dose of 20 mg in the morning, followed by a dose of 15 mg at night. In addition, clitoral reduction (clitorreduction) was performed by carrying out perioperative and postoperative hydrocrotisone therapy protocols. Prior to surgery, the patient will be examined for GDR and then given intramuscular hydrocortisone 120 mg IM 1 hydrocortisone na-succinate 8x25 mg IV on the first day, hydrocortisone na-succinate 8x12.5 mg IV on the second day, hydrocortisone 40 mg orally on the third day, and hydrocortisone 20 mg orally (10-5-5 mg) on the fourth day.

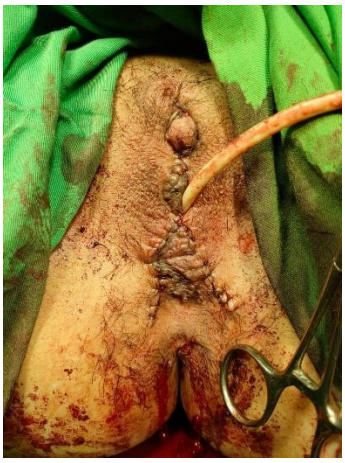

Figure 4
Patient's clitororeduction surgery

Result and Discussion

Confirmation of the diagnosis is obtained from the history, physical examination, and supporting examinations. The female patient aged 18 years, weighing 51 kg, was referred from Solok Hospital to the Urogynecology Obstetrics and Gynecology Clinic at Dr. RSUP. M. Djamil Padang was accompanied by his family on October 11, 2021 with the main complaint of clitoral enlargement since the age of 5 years.

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder caused by defects in steroidogenesis. Cortisol production in the zona fasciculata of the adrenal glands is mediated by five major mediators. This disorder causes 21-hydroxylase production deficiency, 11-hydroxylase deficiency, 3-hydroxysteroid dehydrogenase deficiency, 17-hydroxylase deficiency, and Steroidogenic acute regulatory (StAR) protein mutations. In CAH, enzyme deficiency occurs which results in impaired cortisol synthesis and hyperplasia and oversecretion of defective enzyme precursors. The blockade of cortisol synthesis will lead to stimulation of the adrenal cortex and the accumulation of cortisol precursors which will be converted into sex hormone biosynthesis. Impaired production of cortisol and aldosterone can cause severe salt insufficiency and adrenal crisis, which usually occurs in the first week of life. The

occurrence of virilization of female external genitalia is caused by excessive production of adrenal androgens (Kazmi et al., 2017).

Baby girls with classic CAH (salt wasting or simple virilizing) generally show clinical conditions of genital ambiguity. This external genitalia will vary from minimal clitoromegaly to close to the picture of the male external genitalia but no testes are palpable. In male infants with CAH will show clinical hyperpigmentation with normal external genitalia (Krishnan & Yahaya, 2018).

In patient An. D complains of an enlarged clitoris. Prader stage and external genitalia virilization is stage III. On the external genitalia visible enlargement of the clitoris with a size of 3x1 cm without the vaginal canal. Chromosomal examination showed 46, XX in each cell. The laboratory result of 17-hydroxy progesterone is 90.2 nmol/L.

Management of CAH requires multidisciplinary management. Every child with genital ambiguity requires psychological counseling regarding gender identity and family roles related to the patient's growth and development.

The management of CAH is differentiated based on the age of the patient. In infants and children, management aims to prevent adrenal crisis, early virilization, promote normal growth, avoid electrolyte disturbances, and dehydration. In adolescents and adults, the goals of treatment are to achieve normal reproductive and reproductive function and to avoid chronic medical complications such as Cushing's syndrome (Dabas et al., 2020; Nidal et al., 2020).

The principle of CAH management is:(Makiyan, 2016)

1. Medical

   Administration of glucocorticoids to reduce hyperplasia and oversecretion of androgens and mineralocorticoids. Patients with CAH require high doses of steroids in the setting of trauma, surgery under general anesthesia, and gastroenteritis who are at risk of dehydration. The right dose of medication will help prevent adrenal crisis, reduce virilization (masculinization) so that optimal growth and development can be achieved. Glucocorticoid in infancy is hydrocortisone with a maintenance dose of 10-15 mg/body surface area/day divided into 3 doses. Hydrocortisone has the least adverse effect on bone density compared to dexamethasone, prednisolone, or prednisone. In infants with salt wasting CAH, additional NaCl 1-2 g/day can be given.

2. Surgery

   Surgery was performed on infants with genital ambiguity that required correction. Surgery is not necessary if the patient has mild clinical virilization. Genital surgery consists of vaginoplasty, clitoroplasty, and labia surgery. Bilateral adrenalectomy is not indicated in children with CAH.

3. Long term monitoring

   Monitoring of side effects of glucocorticoid and mineralocorticoid therapy is necessary. Patients with CAH require screening for metabolic and cardiovascular disorders.

This patient had no clinical adrenal crisis for the past 18 years, but clitoral enlargement began to appear since the age of 5 years. The new patient was brought to the hospital when he was 9 years old, then the patient regularly took corticosteroids before the planned surgery.

Reconstructive surgery on genital ambiguity has been performed on CAH patients since the early 20th century. In patients with severe cases (Stage Prader C3), clitoral and vaginal surgery can be performed from infancy. Genital organ surgery performed on infants aged 2-6 months can be performed on female infants with the classic type of CAH. This surgery consists of cytoscopic genito-plasty, clitoroplasty, and clitororeduction to maximize anatomical function in sexual function. The clitoris is innervated by sensory nerves that pass through the dorsalis clitoris and pudendal nerves from segments S2-S5. Incision of the glans clitoris and corpus cavernosum on the clitoro would have the risk of damaging the innervation resulting in disturbances in orgasmic sensation, decreased sexual sensitivity, loss of clitoral tissue, and cosmetic problems. Thus, in this patient a clitororeduction procedure was planned which had no impact on innervation because it only incised the corpus cavernosum.

Conclusion

Congenital adrenal hyperplasia is a disease caused by genetic disorders that require multidisciplinary management. In this case, the patient was diagnosed with clitomegaly and the cause of congenital adrenal hyperplasia. The patient was treated with hydrocortisone therapy and clitoro-reduction reconstructive surgery. Enforcement of diagnosis, appropriate management, and counseling are needed to optimize patient growth and development

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