ADRENOGENITAL SYNDROME: POSITIVE DIAGNOSIS, EVOLUTION AND PROGNOSIS

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Abstract

The adrenogenital syndrom is a group of autosomal recessive diseases which causes the disturbance of the synthesis of suprarenal corticoids.

We present the case of a newborn, age 2 days, female, born prematurely, gestational age 36 weeks, with a malformation of the external genitalia, which shows at age of 1 week deterioration of general condition, loss of appetite, weight loss, severe dehydration syndrome, hyponatremia, hyperkalemia. We suspected the adrenogenital syndrome, which was later confirmed. With a specific treatment the evolution was favorable.

Key words: adrenogenital syndrom, newborn

Introduction

Congenital adrenal hyperplasia or adrenogenital syndrome is a group of autosomal recessive disorder caused by deficiency of one or more enzymes involved in normal synthesis of steroids (aldosterone, cortisol and sex hormones) .In all forms there is decreased production of cortisol leading to an increased synthesis of pituitary ACTH, resulting in excessive adrenal stimulation with its hyperplasia, associated with hypersecretion of steroids and their metabolites.(1)

The most common cause of congenital adrenal hyperplasia (90-95% of cases) is the result of a deficiency of 21-hydroxylase. Depending on the clinical manifestations, adrenogenital syndrome can be divided into a classic tipe, with neonatal onset, which is divided into variant associated with salt-waste, and without salt -waste (simple virilizing variant), and anon-classical tipe, with late-onset.

The classic tipe of adrenogenital syndrome has an incidence of 1 in 15,000 to 20,000 births of live fetuses. About 75% of infants affected associates aldosterone deficiency which causes loss of salt (Debra and Fibiger described formin newborn and infant),associated with cerebriform adrenal hyperplasia ,withthe masculinization of external genitalia in girls. Clinical symptoms occur during the first 2 weeks of life: hyponatremia, hyperkalemia, blood volume depletion, hypotension, hypotonia, psychomotor agitation, stationary or declining growth rate, and acute dehydration syndrome in severe forms.Non-classical tipe occurs in childhood or young adulthood with hirsutism, amenorrhea and infertility, and has an incidence of 1 in 1,000 births of live fetuses. (2,3)

Description of case

Newborn, aged 2 days, coming from monitored pregnancy, GII PII, birth by caesarean section, premature ruptured membranes, gestational age 36 weeks, birth weight 2480g, 47cm waist, with satisfactory early neonatal adaptation, IA = 8 / 1', mother with negative Rh without antibody titer, at clinical examination are seen a malformed genitalia (clitoris hypertrophy) and suspected a malformation of the urinary tract (urine passing through the vagina).

The clinical status at admission is relatively good, balanced cardio-pulmonary, renal lodges free diuresis present, urine passing through the vagina; external genital organs - hypertrophy of the clitoris, labia majora pseudoscrotal looking.

In evolution, at age of 1 week, the overall condition of the newborn deteriorates, with drowsiness ,inability of feeding, weight loss. ASTRUP index reveals hyponatremia (sodium minimum values of 118,7mmol / l) and hyperkalemia (potassium maximum values 7,3mmol / l). (tab.1)

It raises the suspicion of adrenogenital syndrome and completed the laboratory investigations.

Genetic exam: ambiguous appearance of external genitals, intersexual stage Prader III, normal female karyotype: 46 XX

Abdominal and pelvic ultrasonography: liver without expansion of intra and extra hepatic biliary, normal size; currently gallbladder; normal spleen size; kidneys with echogenic and normal size; full bladder; uterus and vagina viewable ultrasound (fig. 1), ultrasound undetectable ovaries; bilateral adrenal glands hypertrophy (fig.2,3). Conclusion: Bilateral congenital adrenal hyperplasia.

Transfontanelar ultrasonography: interhemispheric fissure normally, lateral ventricles 2mm, V3-V4 normally, normal brain tissue, periventricular formations at the base of the lateral ventricles bilateral.Conclusion: bilateral subependymal hemorrhage.

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Tab.1 -laboratory investigations at admission.

17-α-hidroxiprogesteron (VN< 8,000)	33,670ng/ml
Androstendion (VN=0,2000-1,1000)	>10,000 ng/ml
Cortizol (VN=171-536)	307,1 nmol/L
Estradiol	50,4pg/ml
LH	<0,100mUI/ml
Progesteron	39,95ng/ml
Testosteron (VN=75-400 μg/dl)	6,00 ng/ml
TSH (VN=0,43-16,1)	1,36 pUI/ml
FT3 (VN=3,08-8,1)	5,09 pmol/l
FT4 (VN=10,6-39,8)	18,5 pmol/l

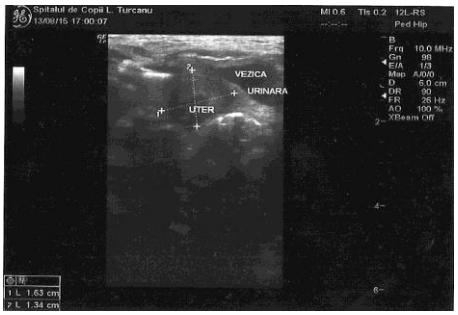

Fig. 1 Ultrasonograhyc appearance – uterus.

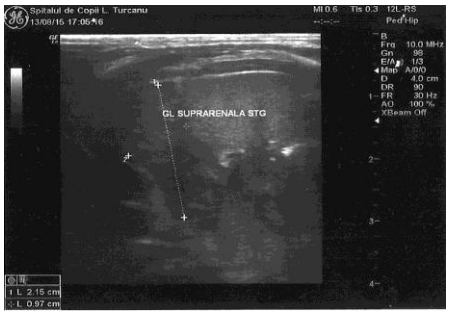

Fig. 2 Ultrasonograhyc appearance – left adrenal gland.

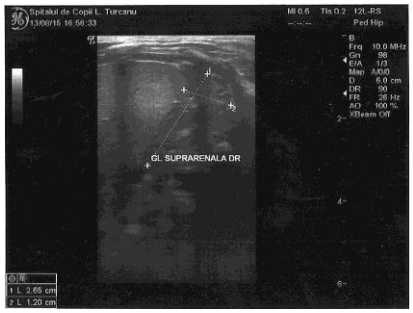

Fig. 3 Ultrasonograhyc appearance – right adrenal gland.

Pediatric endocrinologic exam: hypertrophy of the clitoris, labia majora pseudoscrotal looking intersexual Prader-stage III / IV; it's recommended to start Astonin and Hydrocortisone treatement.

We start *the treatment* with Astonin (fludrocortisone) 0.05 mg / day; initial hemisuccinat corticosteroid hydrocortisone intravenously with 10mg / kg / day in 4 doses, then oral Hydrocortisone 20mg / m2 in 3 doses; rebalancing hydroelectrolytic infusion (with additional sodium) and acid-base status. The sodium in the diet was supplemented.

Under treatment, the general state gradually improved, with normalization of sodium, potassium and hormonal values.

Discussions

Although the prognosis is good with proper treatment, however, the infant mortality rate of newborns with congenital adrenal hypertrophy undetected through neonatal screening is 11.9%.

Most often under diagnosed or late diagnosed cases are those of the males, which presents more discreet virilising signs than women. However we can not make a parallel between the degree of virilization of the external genitalia and severity of the disease in women. It can meet the appearance of female pseudohermaphroditism, where there is a structure and normal position of internal genitalia, and external genital abnormality that can be quantified as Prader's scheme. Female pseudohermaphroditism of 21-hydroxylase deficiency is the most common leading cause of intersex newborn.

Among infants affected by 21-hydroxylase deficiency, approximately 75% present the salt-waste tipe of the disease. This occurs about 2 weeks old, later to the breastfed infants and earlier ato the premature babies.

At the time of occurrence of salt-waste syndrome the diagnosis is facilitated, but treatment is urgent need to establish, in its absence the circulatory collapse, shock and death occur inevitable. In some cases of congenital adrenal hypertrophy there are brain damage caused by shock, and distance learning and cognitivedifficulties.(4,5) To the male newborns salt – waste occurs much later and adreno-genital syndrome diagnosis often is not done in the first year of lifeAt the time salt-waste apears, most likely it is a congenital adrenal hypertrophy.

In the absence of neonatal screening and without a family history of the disease, all male infants and a small percentage of the female remain undiagnosed until adrenal crisis. In many countries began the screening of newborns between day 3-5 of life by measurement of 17-OH progesterone in capillary blood and antenatal screening by chorionic villi or amniotic fluid molecular genetic testing.

All patients diagnosed with adreno-genital syndrome requires treatment with glucocorticoids for the correction of existing cortisol deficiency: hydrocortisone oral dose of 20 mg / m2 / day in two or three doses.Subjects with salt-waste requires replacement with mineralocorticoids: fluorohidrocortisone 0.1-0.2 mg / day, to normalize the balance of sodium / potassium,and in acute crises of salt-waste is used maximum dose of hydrocortisone intravenously, and sodium supplementation in rebalancing hydroelectrolytic infusions.(6,4)

Once with the ageing the salt-waste syndrome attenuates,treatment is required only in decompensation moments outcome in mistakes in drug therapy, during intercurrent diseases, traumas, intoxications.Whitout proper treatment it can cause short stature because of the early welding of the growth cartilage at the age of 7-8 years, particular phenotype, virilizations, early puberty, cognitive deficits.With a proper treatment the pacients can reach a normal stature, with a psihointelectual evolution and a normal reproductive capacity.Treatment efficiency can be verified by periodic dosing of the 17-hidroxiprogesterone, androstenedione and testosterone, by the rithm of the growth, bone age,blood pressure in salt-waste type.(4)

Female patients with external genitals abnormality can have a reconstructive surgery.

Psychotherapy is necessary for a better understanding of the disease, chronic treatment, so there is a better evolution of the disease

Prophylactic treatment consists in administering dexamethasone 20 mg / kg in 2-3 intakes at-risk pregnant women in the first 6 weeks of pregnancy.It prevents virilization and sexual ambiguity to the female fetus, but the chronic substitution treatment to the affected child will still be necessary.(7,2)

Conclusions:

• positive diagnosis is relatively easy to determine when external genitalia are modified and salt-waste syndrome occurs

• onset diseases is more quickly (in the first week of life) in premature born compared with term born baby

• for positive diagnosis requires a multidisciplinary team (pediatrician, endocrinologist, geneticist)

• Long-term evolution of the case depends on the rigor with which treatment is administered, and adjust it according to biological and hormonal investigations

• a good parents education in understanding disease, chronic treatment and need periodic investigations is very important

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