THE SALT-WASTING TYPE OF 21-HYDROXYLASE DEFICIENCY: A CASE STUDY

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Abstract
The 21-hydroxylase deficiency is a monogenic disease, with a recessive autosomal transmission, which causes the disturbance of the synthesis of suprarenal corticoids.

We present the case of a newborn, aged 17 days, male, timely delivered, mother’s fourth child, with a mixed feeding, who was admitted to the 2nd Pediatric Clinic of the Emergency Hospital in Craiova with lack of weight gain progress and agitation. The baby presented, the following day after admission, severe dehydration syndrome with a hypovolemic shock, without any signs of fever, vomiting or diarrheic stools. We suspected the salt-wasting syndrome, which was later confirmed. Although the mother initially declared that her other three children were healthy, she later admitted that her first child, a girl, was diagnosed with 21-hydroxylase. Following an emergency treatment, of hydro-electrolytic balancing, and continued with a specific treatment, the evolution was favorable.

Key words: 21-hydroxylase deficiency, salt-wasting, newborn, male

Introduction
The 21-hydroxylase deficiency is a disease with recessive autosomal transmission, which causes the disturbance of the synthesis of corticosuprarenal steroids (1, 2). The dysfunction of the 21-hydroxylase enzyme causes an inefficient synthesis of cortisol and aldosterone and an androgenic overproduction (1, 2).

The disease presents three clinical types: two classic types (the salt-wasting and the simple virilizing ones) and a non-classic type with late onset (1). The two classic types are characterized by the virilization of the external genitalia, early, heterosexual pseudo-puberty and sterility in girls, and by isosexual, precocious pseudo-puberty in boys, together with a hypo-height tendency in boys and girls alike. To these changes which are present in the salt-wasting type, we can also add metabolic decompensations which present polyuria, hypotonic dehydration, hyperkalemia and metabolic acidosis, with an unfavorable evolution if no specific treatment (2).

Description of case
The newborn R.F., aged 17 days, was admitted to the 2nd Pediatric Clinic of the Emergency Hospital in Craiova (Medical History 44971/2011) accusing lack of weight gain progress, scleral- tegumentary jaundice and agitation.

Heredocolateral antecedents: young, healthy parents; three siblings: two brothers aged 10 respectively 8 years, and a sister aged 11 years and 6 months, who were healthy, without any chronic diseases within their family.

Personal physiologic antecedents: the fourth child, full-term delivery at the Emergency Hospital in Craiova, normal birth, head-down position, 3,500 g in weight, 52 cm in height, with no sufferance at delivery, Apgar score 9, presenting jaundice three days after birth; sent home when three days old, 3,200 g in weight, with a mixed feeding after two weeks of life (adapted milk powder formula); vaccinated in the hospital BCG and antihepatitis B; he received Vigantol Oil (2 drops per day), as a prophylactic measure.

Life conditions: a house in the urban area, adequate conditions, 7 rooms, 12 people.

Anamnesis. The mother notices her son’s lack of weight gain progress after she leaves the hospital, the persistence of the tegumentary jaundice, agitation, and she decides to return to hospital.

At admission the newborn had no fever, with a fair general state, G=3,200 g, T=53 cm, SC=0.14 m², teguments and mucosae with intense jaundice, elements of folliculitis on an erythematous ground at the upper abdominal level, abdominal cutaneous creases with diminished elasticity, perioral cyanosis, nasal obstruction, the presence of bilateral vesicular murmur, feeble, slow heart beats, cold extremities, lingual mycotic deposits, normotensive anterior fontanelle 2.5/2 cm, the presence of the Munro reflex, a light, generalized hypotony, breastfed, without congenital malformations when objective exam.
with the diagnosis of 21-hydroxylase deficiency. The mother was once again asked if, within her family, there were relatives with 21-hydroxylase deficiency, and this time she admitted that her first child, a girl aged 11 years and 6 months, who was diagnosed with 21-hydroxylase deficiency, virilization type, was monitored by the Medical Genetics Department of the Emergency Hospital for Children in Cluj-Napoca.

We continued the investigations for the serum ionogram (table 1), the Astrup method and other specific tests in order to diagnose the 21-hydroxylase deficiency. Astrup parameters: pH= 7.39-7.26; pCO₂= 36.2-32.4 mmHg. 17-OH progesterone= 9.01 ng/ml (normal values= 0.8-5 ng/ml). Testosterone= 348 μg/dl (newborn normal values= 75-400 μg/dl). Aldosterone= 316 pg/ml (newborn normal values= 5-160 pg/ml). Cortisol= 2.09 ng/dl (newborn normal values = 3-20 ng/dl). Diuresis= 310-420 ml. On the basis of the anamnestic data, (a sister diagnosed with 21-hydroxylase deficiency), the clinical picture (lack of weight gain progress and the onset of an acute dehydration syndrome, without vomiting and diarrheic stools), and the paraclinic data: ionogram with hyperpotassemia, hyponatremia, hypoglycemia, metabolic acidosis, combined with other specific data (highly increased 17-OH progesterone, low serum cortisone), we set the diagnosis of salt-wasting type of 21-hydroxylase deficiency to a male newborn (with no genitalia anomalies).

### Table 1. Serum Ionogram.

<table>
<thead>
<tr>
<th>Date</th>
<th>Na (mEq/l)</th>
<th>Cl (mEq/l)</th>
<th>K (mEq/l)</th>
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<td>79</td>
<td>7</td>
</tr>
<tr>
<td>11.09.11</td>
<td>105</td>
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<td>5.9</td>
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<td>89</td>
<td>5.5</td>
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<tr>
<td>14.09.11</td>
<td>128</td>
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<td>7.3</td>
</tr>
<tr>
<td>15.09.11</td>
<td>129</td>
<td>90</td>
<td>4.5</td>
</tr>
</tbody>
</table>

The treatment continued with an endovenous perfusion with glucose, NaCl 5.8%, calcium gluconate 10%, and hydrocortisone hemisuccinate i.v., then with Prednisone p.o and Astonin p.o., a treatment which was decided after the telephonic recommendations of Professor Dr. Paula Grigorescu Sido, from the Medical Genetics Department of the Emergency Hospital for Children in Cluj-Napoca.

Under treatment, the general state gradually improved, the newborn accepted to be fed, he gained 150 g in weight, good heart beat, AV=130/min, the tegumentary jaundice gave up (total bilirubin=1.92 mg%, direct bilirubin=0.34%, indirect bilirubin=1.58%). After 14 days of hospitalization, the patient transferred to the Emergency Hospital for Children in Cluj-Napoca, Medical Genetics Department, where the 21-hydroxylase deficiency diagnosis was confirmed. At present, he is under treatment with Hydrocortisone and Astonin p.o., with a favourable evolution.

### Discussions

The classic type of disease appears in 1 out of 15,000-20,000 births for most of the populations; approximately 70% of the affected children present the salt-wasting type (3).

The gene which is responsible for the synthesis of 21-hydroxylase enzyme is located on the short arm of human chromosome 6, next to the genes of the histocompatibility complex (1, 2). The various mutations of the gene cyp-21 lead to faults of variable intensity at the level of the 21-hydroxylase enzyme, and consequently there are types of disease of different severity (3). In the severe, salt-wasting types, both aldosterone and cortisol are deficient because both hormones require 21-hydroxylase for their synthesis (3, 4). The alteration of the negative feedback circuit of the corticosuprarenal leads to disturbance of the corticotropic hypophysis combined with the stimulation of cortisol.
synthesis, proximal to the enzymatic block and with the deviation of the steroid synthesis through alternative pathways and androgenic overproduction, which is responsible for the feminine pseudohermaphroditism (4).

This disease frequently starts in the third week of life, as it happened with our case and, without a quick mineralocorticoid and glucocorticoid substitutive treatment, the evolution is fatal because of the hypovolemic shock or heart failure due to hyperkalemia.

The diagnosis is more difficult to establish in boys because they have their external genitalia clinically healthy; because the evolution of the disease is rapid, the boys who present genital anomalies are more likely to decease than the girls (5). That is why many countries decided to start the newborn screening, for this disease, from the 3rd-5th day of life, through doses of 17-OH progesterone in the capillary blood (6). Finding the heterozygotes is recommended in the families where there is one patient with 21-hydroxylase deficiency (2,6).

**Paraclinic examinations**

The hormonal examinations are necessary both for plasma (17-OH progesterone, ACTH, 21-deoxycorticisol, testosterone, and 17-OHpregnenolon) and for urine (17 cetosteroids). The specific hormonal diagnosis criterion is represented by the increased concentration of 17-OH plasmatic progesterone (the metabolic substrate used by 21-hydroxylase) (6, 7).

Radiologic examinations: the fist x-ray to determine the child’s bone age.

The ultrasound examination visualizes the corticosuprarenal glands, the girls’ internal genitalia and the boys’ testicle.

Genetic examinations: the Barr test and the karyogram which certify the genetic sex.

Genetic molecular examinations to determine the genetic mutation and its severity type (2, 3).

The prenatal diagnosis is possible in the first pregnancy trimester when using the analysis of the DNA which is obtained through the corial vilosities biopsy or in the second trimester through amniocentesis. It is recommended in the families where there is already an affected child and the prenatal treatment could be necessary (8).

**References**


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