

## GROWTH FAILURE IN CHILDREN WITH END STAGE RENAL FAILURE ASSOCIATED ADRENOGENITAL SYNDROME

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### Abstract

**Objectives:** To emphasize the negative role of chronic kidney disease in impaired growth and development of a female 7 year old patient, with chronic renal failure associating sexual developmental disorder - adrenogenital syndrome.

**Methods:** The patient came to monthly follow-ups for the evaluation of her the anthropometric, nutritional and biological status. She was treated with a replacement therapy comprising of growth hormones and cortisone.

**Results:** The girl was diagnosed at birth with polycystic kidney disease and sexual development disorder, karyotype 46XX - adrenogenital syndrome, salt-losing form. Cortisone replacement therapy was initiated in the neonatal period, under hormonal monitoring. At the age of 4 she had a creatinine clearance (Schwartz formula) of 17 ml/min/m<sup>2</sup>, height: H2009 = 83 cm, weight: W2009 = 8 kg and the therapy with growth hormones was initiated. In the following years, the increase in height was 12 cm and in weight 3 kg (H2010 = 95 cm, W2010 = 11 kg), while requiring the initiation of peritoneal dialysis. Currently, H2013 is 104 cm and W2013 is 13 kg.

**Conclusions:** Progression of chronic kidney disease causes retardation of growth and development by: inadequate production of erythropoietin with secondary anemia, bone and mineral disease secondary to renal dysfunction, chronic metabolic acidosis and disruption of the hypothalamic-pituitary growth hormone axis. Adrenogenital syndrome association is an additional factor for impaired growth and development.

**Keywords:** chronic renal insufficiency, adrenogenital syndrome, growth hormone.

### Background

A multitude of modifications in the body's homeostasis are characteristic to chronic kidney disease.

Chronic acidosis causes an increase in protein degradation, a decrease in albumin synthesis, the demineralization of the bones, as well as inhibition to growth hormone secretion. (1-4)

Renal anemia, together with mineral and bone disease secondary to renal dysfunction lead to the alteration of the patients' nutritional status.

In populations with chronic renal disease, the term *malnutrition* should be replaced with *protein-caloric loss*, since the imbalance is caused by metabolic and inflammatory modifications. (5)

A child with chronic kidney disease, uremic stage, may benefit from extrarenal purging techniques or transplantation. Peritoneal dialysis is to be preferred when attempting an extrarenal purge in children, as the circumstances allow it. It can achieve a constant control of uremia, less restrictions of the child's diet, as well as an extra source for calories due to glucose absorption from the dialysis fluid. (6-8)

The clinical assessment of the peritoneal dialysis's efficiency should be made considering the following parameters:

- Hydration status
- Nutrition status
- Intake of calories, proteins, salt, mineral
- Acid-base balance
- Control of anemia
- Control of blood pressure
- Mental growth and development
- Psycho-social rehabilitation
- The patient's well-being

### Objective

To emphasize the negative role of chronic kidney disease in impaired growth and development in children.

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**Case report**

*History*

This is the presentation of a 7 year old female patient held under medical surveillance in the Nephrology Department of the „Louis Turcanu” Children’s Emergency Hospital Timișoara. The child’s parents are young and not consanguine. There is no relevant family history.

The girl is initially diagnosed during her first month after birth with abnormal sexual development, 46XX

karyotype (fig. 1), adrenal-genital syndrome, salt losing type. Biologically, with the exception of her hydric, electrolytic and acid-base imbalance, she has shown high serum levels of urea and creatinine.

The ultrasonography showed bilateral polycystic kidney disease (fig. 2), confirmed by uroMRI (fig. 3). Chronic renal failure is well documented by renal scintigraphy. (fig. 4)

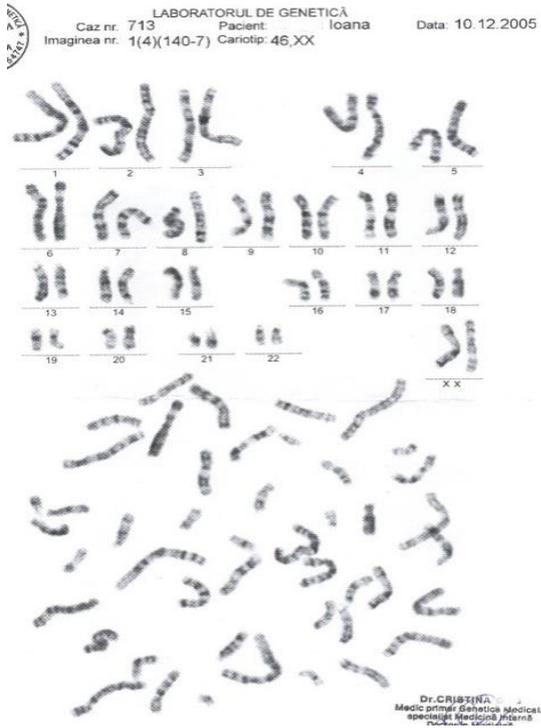


Figure 1. 46XX karyotype.

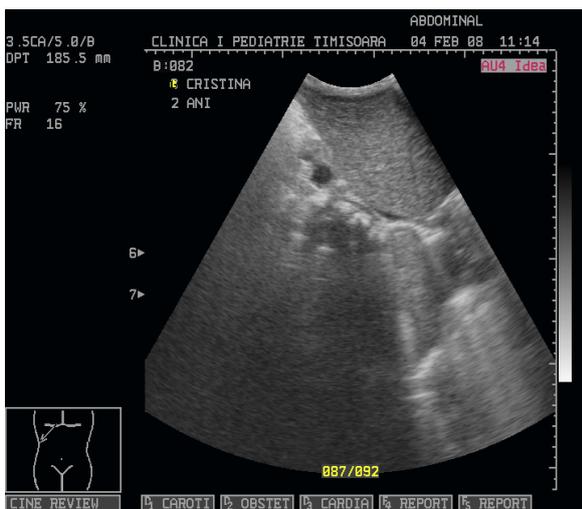


Figure 2 Abdominal echography.

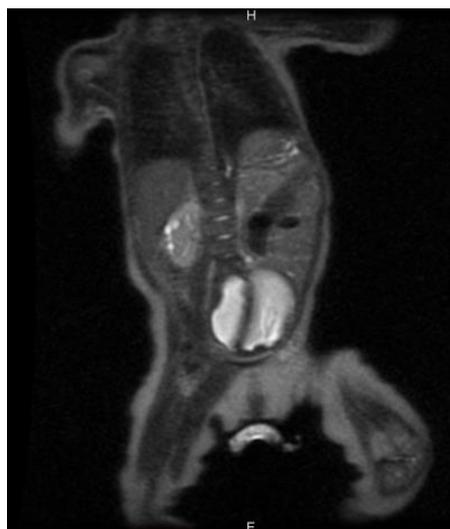


Figure 3 UroMRI aspect.

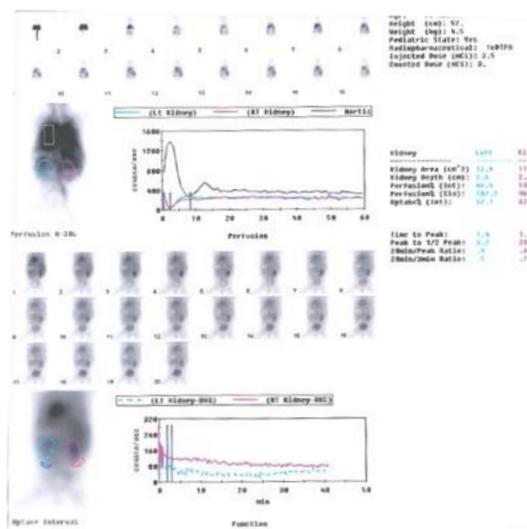


Figure 4 Renal scintigraphy.

At the age of 4, when the chronic kidney disease had reached level 4, the patient had suffered afebrile generalized tonic-clonic convulsions, with no hydric, electrolytic or acid-base imbalance. Also, there was a modification in her EEG but a normal cerebral MRI.

#### Clinical examination

Currently, she is severely underweight (Weight =13 kg, height = 104 cm, below the 3<sup>rd</sup> percentile for age WHO, BMI=12, 01 kg/m<sup>2</sup>). She is pale with an abdominal scar due to the peritoneal dialysis catheter insertion. Her blood pressure is normal for her gender, age and height. Ambiguous genitalia with clitoromegaly. Diuresis is 3.5 ml/kg/h. The patient presented multiplanar *deformities* of the upper and lower *limbs*, *bilateral coxo-femoral subluxation*, while walking was only possible with braces. The clinical examination showed otherwise normal results.

#### Blood work:

- ⊙ KT/V (fractional clearance of urea) = 2.84
- ⊙ Creatinine clearance 16.72 ml/min/1.73 m<sup>2</sup>
- ⊙ Normal serum levels of protein and albumin
- ⊙ Constant level of Hb at 12.2 g/dl.
- ⊙ ↑ Serum cholesterol
- ⊙ Normal serum levels of calcium, phosphorus, normal levels of Ca x P
- ⊙ FAL ↑↑↑, PTH ↑↑↑
- ⊙ Normal acid-base balance

#### Consults

The endocrinologist concluded she has sexual developmental disorder – adrenal-genital syndrome, salt-losing type. The patient required substitution with cortisone. For her growth deficit, within the context of chronic kidney disease, growth hormone therapy is initiated.

The neurologist introduces carbamazepine in her therapy in order to manage the afebrile convulsive episodes.

The nephrologist underlines the complications of end-stage chronic kidney disease: renal anemia, mineral and bone disease secondary to renal dysfunction, chronic metabolic acidosis. Continuous manual peritoneal dialysis improves her nutritional status and her growth. The velocity of the growth process in these patients is strongly related to creatinine clearance, residual GFR, fractional clearance of urea - Kt/V urea. (9) The increase in Kt/V urea is associated with a low serum level of albumin, suggesting that the increase of the dialysis dose can reach a level where benefits are annulled, with a loss of albumins in the dialysis fluid. (10)

#### Treatment and follow-up

The patient undergoes a substitution treatment with cortisone during the first month after birth. Periodic hormone evaluation shows a satisfactory control of the adrenal-genital syndrome: no clinical evolution; biologically: normal electrolytes, glycaemia, gas analysis (BGA).

An optimal level of hemoglobin is reached by substitution treatment with erythropoietin, vitamin and iron supplements.

Mineral and bone disease secondary to renal dysfunction is progressive, despite an appropriate diet, treatment with vitamin D and analogues, calcimimetics.

Growth hormone therapy has led to a somatic growth of 12 cm in height throughout the first year (at the age of 4). The initiation of peritoneal dialysis at the age of 5 caused an improvement in the patient's growth. (fig. 5)

Currently, H<sub>2013</sub> is 104 cm and W<sub>2013</sub> is 13 kg.

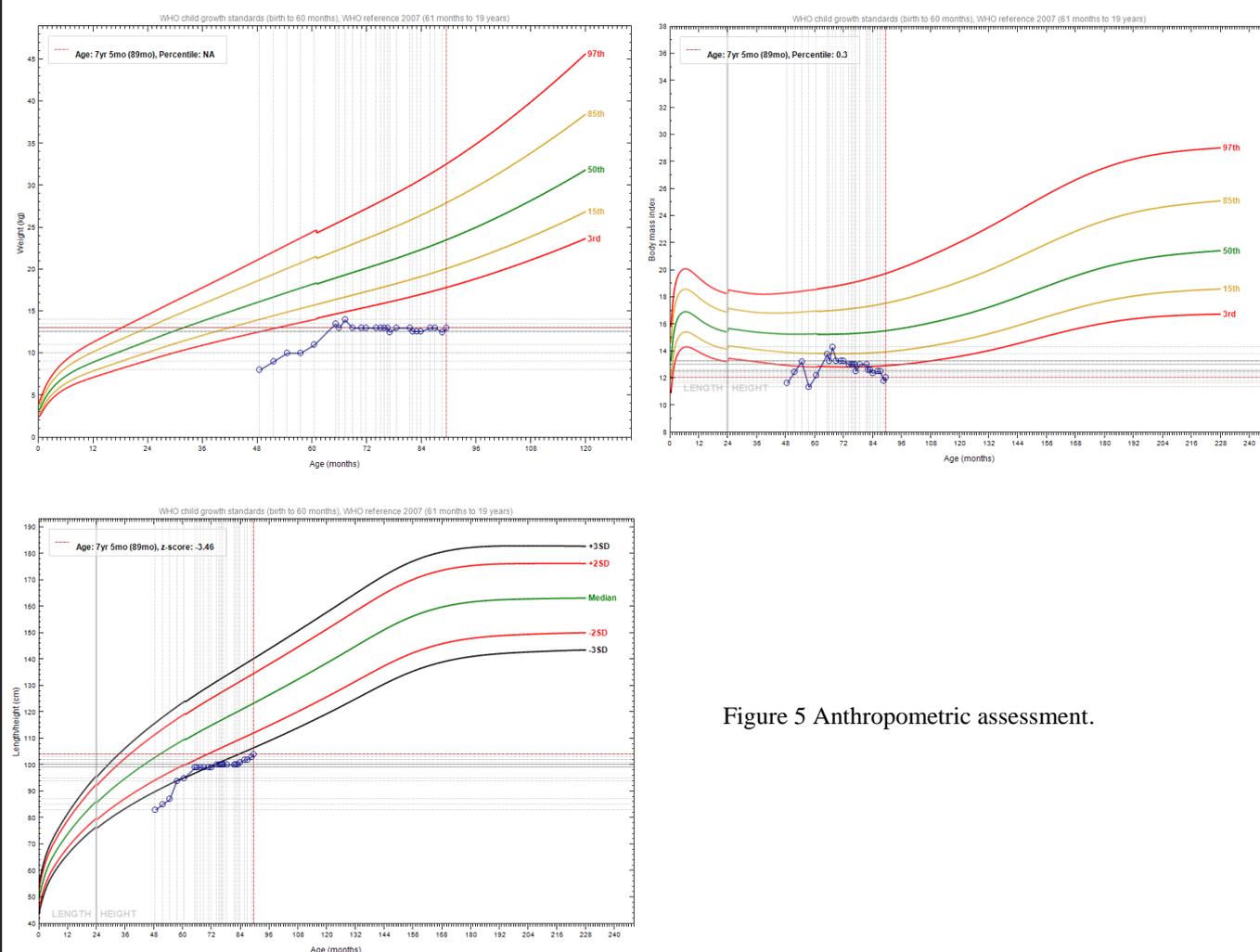


Figure 5 Anthropometric assessment.

### Conclusions

Secondary anemia, metabolic acidosis caused by chronic kidney dysfunction, as well as mineral and bone disease secondary to renal dysfunction lead to impaired somatic growth. The disruption of the hypothalamic-pituitary growth hormone axis is associated. This child has achieved somatic growth based on the growth hormone treatment and on the initiation of peritoneal dialysis as a

means of extra-renal purging. The patient needed periodic hormone monitoring due to her adrenal-genital syndrome.

### Ethical considerations

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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