

A case of genetically proven carbonic anhydrase II deficiency

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Background: Carbonic anhydrases are a family of 14 Zn containing enzymes with variable distribution in the body, which main function is to catalyze the reaction $\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-$ and thus regulate the acid-base balance.

The only known disease due to deficiency is this of Carbonic anhydrase II. CA II deficiency is extremely rare (<1:1 000 000) autosomal recessive disease, which is characterized by the triad of osteopetrosis, basal ganglia calcifications and renal tubular acidosis. In addition short stature, facial dysmorphism and different degree of mental retardation are possible features. Different mutations of the gene for CAII on 8q21.2 lead to impaired enzyme activity and typical clinical, biochemical and imaging manifestations

Objective and hypotheses: A 5 years old girl, from normal pregnancy of parents, who deny consanguinity was referred to endocrinology department because of short stature, developmental delay and basal ganglia calcifications on CT scan, found incidentally.

Method: Clinical evaluation, laboratory tests of hormones, electrolytes, biochemical indices, acid-base status, infections, kidney ultrasound, radiological examination of bone age, neurologic, ophthalmologic examination and molecular genetic analysis.



Results: Clinical evaluation confirmed mild dysmorphic features, short stature H 93 cm (4 years 7 months old) SDS_H (-2,97), low weight W 10,3 kg, SDS_W (-3,0) and some developmental delay – first words 1 year 6 months, first sentence after 3 1/2 years, walks by herself after 1 y 9 months.

Laboratory testing proved severe decompensated normal anion gap metabolic acidosis: **pH 7,22**, **pCO₂ 36,1 mmHg**, **pO₂ 80,7 mmHg**, **HCO₃⁻ 14,3 mmol/l**, **BE -13**, low normal Ca, Ca²⁺, high P, Cl⁻ and blood urea nitrogen, normal values of intact PTH, ACTH, serum Cortisol at 8 a.m. and 8 p.m., TSH, fT₄.

Congenital infections were also excluded by means of serologic studies

Imaging studies showed extensive basal ganglia calcifications as well as calcifications in the white matter at the border with the gray and some discrete in the cerebellum, delayed by 2 years bone age and increased bone density, as well as mild nephrocalcinosis.

A molecular genetic analysis revealed homozygous mutations c.275A>C, pGln92Pro on the gene for CAII on 8q21.2, which confirmed the clinical diagnosis. Both parents as well as the older sister of the patient are heterozygous carriers of the mutation, without any clinical manifestation. This mutation is found only in two other patients of gypsy origin from Czech Republic and Germany.

Treatment: The child receives oral 8,4 % Sodium bicarbonate for correction of metabolic acidosis at high dose 4x17 ml and showed improvement in clinical manifestations and laboratory data. She grows very well – with 3 cm for 6 months and is with much better emotional and physical condition.

Conclusion: Children with this rare syndrome may come into medical attention for failure to thrive, short stature, developmental delay or brain calcifications. It is crucial for the patient's quality of life and long term prognosis to receive an early diagnosis and efficient treatment, because metabolic compensation provides normal adult height and hematologic and neurologic complications of osteopetrosis are not severe.

Bibliography:

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