Carbonic Anhydrase II Deficiency in a Tunisian Girl

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Objective : Carbonic anhydrase (CA) II deficiency or marble brain disease also known as Guibaud–Vainsel syndrome, is a rare autosomal recessive disorder caused by mutation in the CA II gene that leads to osteopetrosis, renal tubular acidosis (RTA) and cerebral calcification.

Case report :

A 11-years-old girl presented to our hospital for asthenia. There wasn't a family history of consanguinity .

She has a normal natal and neonatal period. She was operated for 2 fractures of the forearm and the tibia . she has a history of development delay and growth failure.

Physical examination revealed dehydration signs:persistent skin folds, dysmorphic features with wide forehead, a prominent narrow nose, a small mouth with crowded teeth. Her height and weight were 125 cm and 16 kg, respectively. She had a fluent nasal speech. A central nervous system examination revealed no neurological deficit.

Laboratory investigations showed hyponatremia=128 mmol/l, hypokalemia,2.6 mmol/L; chloride, 156 mmol/L; calcium:1.93 mmol/l. Her venous blood pH was 7.3, PCO2=2.55kPa, HCO3 =14.6 mmol/L. The vitamin D level was 15.2 nmol/L. The urine pH was 6.5 and the urine anion gap was 11 mmol/l, consistent with **renal tubular acidosis** .

A Chest, skull and vertebrae radiographs showed significantly increasing bone density (Fig.1). The CT of the brain was normal.

She was treated by an adequate hydration , with electrolytes replacements, calcitriol and thiazidic diuretics.

Fig.1 Skeletal survey showing generalized increased bone density.

Conclusion : Early recognition of the disease is a key, as an early appropriate treatment institution is essential in order to prevent further complications of this rare syndrome

Discussion :

- Prevalence of this disorder is not known.
- Fewer than 100 cases have been reported to date.
- Many reports involved families of North African and Middle Eastern descent, but cases have been documented worldwide.
- Transmission is autosomal recessive.
- Caused by mutations in the CA2 gene (8q22) encoding carbonic anhydrase II
- Patients present a triad of mild osteoporosis, mixed proximal and distal RTA, and intracerebral calcifications but this third cardinal feature of the disorder, was variable and at times unapparent like our patient.
- clinical manifestations include fractures, growth failure and short stature, developmental delay, intellectual deficit, dental malocclusions/malalignment, cranial nerve compression and hearing impairment.
- Diagnosis is based on radiological findings in the presence of acidosis and intracerebral calcifications, and can be confirmed by molecular genetic testing.
- Antenatal diagnosis is possible if the mutation(s) causing the condition in the family are known
- Management of CAII deficiency syndrome consists of bone marrow transplantation to correct the osteopetrosis and life-long alkaline therapy for RTA electrolytes replacements, calcitriol and thiazidic diuretics.
- Severity is variable but the disorder has a milder course than in patients with classic osteopetrosis