SHORT COMMUNICATION

ENZYME REPLACEMENT THERAPY IN DIFFERENT CLINICAL PHENOTYPES OF HYPOPHOSPHATASIA – A PRESENTATION OF TWO CASES

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Background
Hypophosphatasia (HPP) is a rare inborn error of bone metabolism due to inactivating mutations in the gene encoding tissue non-specific alkaline phosphatase (TNSALP). It results in a reduced activity of TNSALP and elevation of its substrate. HPP shows a wide clinical spectrum ranging from severe neonatal forms with extreme skeletal hypomineralisation, lung hypoplasia and seizures to milder forms with dental abnormalities. Mortality is high in neonatal and infantile forms. Enzyme replacement therapy with ENB-0040 (Enobia Pharma, USA) a bone-targeted, human recombinant TNSALP fusion protein is being evaluated for the treatment of severe forms in a clinical phase 2 study (ENB010-10).

Case reports
We enrolled two infants in the ENB010-10 study receiving treatment with ENB- 0040, 2-3 mg/kg s.c. thrice weekly. Both patients are compound heterozygous but differ in their clinical phenotype. In the first male patient diagnosis of HPP was made because of respiratory insufficiency due to severe lung hypoplasia, almost no visible bone, craniosynostosis and vitamin B6 dependent seizures in his first days of life. Treatment with ENB-0040 started at the age of 4 months. The second patient, a girl with an infantile form of HPP started treatment with ENB-0040 at the age of 3 years and 3 months. She had a history of failure to thrive, short stature, rickets, nephrocalcinosis, recurrent respiratory infections, complex craniosynostosis with intracranial hypertension and a profound gross motor delay as she was hardly able to crawl. Both patients show an improvement in skeletal mineralization and motor function/activity during the first months of treatment. Ventilatory parameters of patient 1 improved, however further follow up is necessary to determine whether lung hypoplasia is completely reversible.

Conclusion
ERT with ENB-0040 was well tolerated and effective in our two patients differing in the clinical phenotype. ENB-0040 offers a promising therapy in life-threatening as well as in milder but severely debilitating forms of HPP.