SHORT COMMUNICATION

CLINICOGENETICAL CHARACTERISTICS OF JAPANESE PATIENTS WITH YPOPHOSPHATASIA

Taketani T[1,2], Onigata K[1], Kanai R[1], Kobayashi H[1], Mushimoto Y[1], Mihara A[1], Oyama C[1], Fukuda S[1], Yamaguchi S[1]

[1]Division of Blood Transfusion, Shimane University Hospital, Shimane, Japan, [2]Department of Pediatrics, Shimane University Faculty of Medicine, Shimane, Japan Correspondence to Takeshi Taketani,MD., PhD. Division of Blood Transfusion, Shimane University Hospital, 89-1, Enya, Izumo, Shimane, 693- 8501, Japan. E-mail; ttaketani@med.shimane-u.ac.jp

[Introduction] We examined clinical and genetical characteristics in pediatric Hypophosphatasia (HPP) in Japan. [Methods] We surveyed pediatric HPP using a questionnaire at about 500 pediatric medical institutions in Japan and reviewed 51 patients (pts) with HPP. [Results] There were 34 perinatal (67%), 5 infantile (10%), 9 childhood (18%), and 3 odonto-type (6%) pts. In the perinatal type, 18 pts demonstrated curved or shortened long bones of the extremities in utero (53%), 17 pts required ventilator-associated respiratory impairment (50%), and convulsion was detected in 9 of 34 pts (26%). All infantile pts became symptomatic by the age of 4 months, and were accompanied with failure to thrive and hypercalcemia. In pts in the childhood type, short extremities (4 pts), short stature (6 pts), or premature loss of deciduous teeth (4 pts) were found at diagnosis. Mutation analysis performed in 28 pts (56 alleles) identified revealed 1559delT in 25 alleles (47%) and pF327L mutation in 8 alleles (14%). Seven Pts with 1559delT/1559delT, most frequent mutations, were exclusively perinatal-type. Of 4 pts 1559delT/pF327L (the second frequent mutations), 2 pts were perinal-type, one was infantile-type and the other was childhoodtype. All pts with this mutation survived but had different clinical features. Seventeen Pts with perinatal type and 1 Pts with infantile type died. Respiratory disturbance, hypomineralization, loss of bone, small chest, and 1559delT homozygous mutation were significant poor prognostic factors. The median period of death was 4 months (range 0 to 68 months). The main cause of death was respiratory failure. In contrast, 22 pts with perinatal or infantile type and all pts with childhood and ododo-type have survived. ALP titers of survived perinatal or infantile type tended to gradually increase. However, all surviving pts have physical and/or mental handicaps, most likely resulting from long-bone bowing, bone pain, short stature, premature loss of deciduous teeth, or mental retardation. Five pts with short stature took growth hormone replacement therapy. [Conclusions] We demonstrated natural clinical course and phenotype-genotype correlation of Japanese HPP. Perinatal- and infantile-type patients with respiratory problems or 1559delT homozygous mutations have poor outcome, and all survivors had several handicaps, suggesting that all pts with HPP would require early and curative intervention such as enzyme replacement or cell transplantation.