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PERINATAL HYPOPHOSPHATASIA: PRINCIPLES OF MANAGEMENT AND LESSONS LEARNED

Tyler Peikes, University of Manitoba; **Jyoti McGregor**, University of Manitoba; **Nan Hatch**, University of Michigan; **Camelia Stefanovici**, University of Manitoba; **Cheryl Rockman-Greenberg**, University of Manitoba

Background:
Hypophosphatasia (HPP) is a rare inherited disorder of bone mineralization caused by errors ("mutations") in the *ALPL* gene coding for the tissue nonspecific form of alkaline phosphatase (TNSALP). This disorder clinically ranges from a lethal neonatal presentation to a milder adult presentation. Until recently, there was no approved, effective treatment for HPP but enzyme replacement therapy (ERT) with bone-targeted alkaline phosphatase (asfotase alfa, Alexion Pharma) has changed the prognosis for neonates, infants and children with HPP.

Objective:
The purpose of this case report is to illustrate our local experience with management of a baby with life threatening perinatal HPP.

Methods:
Chart review of the baby's clinical course and special pathological studies were done on bone fragments from skull surgeries

Results:
The baby, diagnosed in utero as having HPP, was born at 34 weeks with virtually no bony mineral evident on her skeletal x-rays and a very narrow chest. ERT was started immediately and a very complicated course ensued including 2 surgical procedures for severe craniosynostosis (premature fusion of the skull bones) that occurs in some individuals with HPP. She was discharged home at age 1 year, only on supplemental oxygen. Special studies done on bone fragments from her skull surgeries, ruled out a dual diagnosis of Crouzon syndrome, a known craniosynostosis syndrome affecting her father who does not have HPP.

Conclusion:
Goals and principles of management of infants with perinatal HPP are complex requiring careful consideration, including indications for instituting and withdrawal of ERT, the role of late preterm delivery, aggressive invasive ventilation from birth and management of lung hypoplasia, treatment of manifestations of HPP known not to respond to ERT such as craniosynostosis, and ethical issues. Clinical practice guidelines for our management of newborns with life-threatening HPP were developed, approved by WRHA neonatal teams and are now posted on the WRHA website.