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Transient hyperphosphatasemia in a child with nephrolithiasis and severe prematurity

Hiperfosfatasemia transitoria en un niño con nefrolitiasis y antecedentes de prematuridad severa

Dear Editor,

Transient hyperphosphatasemia of infancy and early childhood (THI) is a benign, usually accidentally detected condition characterised by transiently increased activity of serum alkaline phosphatase (S-ALP) in children under five years of age, without any signs of metabolic bone disease or hepatopathy corresponding with the increased S-ALP.[1–4] When detected in a child with either chronic bone, liver or kidney disease, THI might may raise significant concerns.[4–6]

A 13-months' old boy with a complicated perinatal history (severe prematurity – 26th week of gestation, birthweight 1085 g, respiratory distress syndrome, reanimation, neonatal sepsis, pneumonia, artificial ventilation, necrotising enterocolitis, anaemia, hypophosphataemia and osteopathy of prematurity) and resulting bronchopulmonary dysplasia (with consequent furosemide treatment in the infantile period), was hospitalised because of renal colic manifested by painful crying with gross haematuria. Abdominal ultrasound revealed renal stones in each kidney, diameter 3 mm on the left and 6 mm on the right, respectively. The serum values of blood urea nitrogen (BUN), creatinine, potassium (S-K), sodium (S-Na), calcium (S-Ca), phosphate (S-P), magnesium (S-Mg), alanin-aminotransferase (S-AST), apartate-aminotransferase (S-ALT), parathyroid hormone (S-PTH) were all within normal reference range, same as the urinary concentrations of Ca, P, Mg and urinary calcium/creatinine ratio (U-Ca/U-cr). However S-ALP was 34 μkat/L (normal 2.5–9.5 μkat/L). Wrist X-ray was normal without any signs of rickets. As rickets was ruled out, vitamin D levels were not assessed. The only possible relationship between vitamin D and urolithiasis could have been either vitamin D overdosage or hypophosphatemic rickets with hypercalciuria. As S-Ca, S-P and U-Ca/U-cr were all normal and rickets was ruled out, these possibilities were out of question. Hematuria resolved within 3 days. As there were neither laboratory nor clinical signs of liver or bone disease, THI was considered as the most likely diagnosis. Concerning the kidney stones management, conservative approach including periodic ultrasound assessment was decided. The boy was dismissed on day 4 and checked 28 days later. At that time the S-ALP dropped to normal value of 9.2 μkat/L. S-Ca, S-P were also normal. Therefore the patient fulfilled the criteria for THI. There were no further increases in S-ALP and the patient, who is currently 18 months old, remains stable and is periodically checked on an out-patient basis.

Our patient had a history of prematurity, and according to the hospital records, hypophosphatemia occurred throughout 3rd and 4th month of age, thus indicating history of resolved osteopathy of prematurity.

Osteopenia or osteopathy of prematurity (metabolic bone disease of preterm infants or metabolic bone disease of prematurity) is defined as decreased bone mineral content that occurs mainly as a result of lack of adequate phosphate and calcium intake in extrauterine life. The incidence of metabolic bone disease of prematurity among infants born before 28 weeks of gestational age is as high as 30% and it usually occurs between 6 and 12 weeks of age, however the laboratory signs of impaired mineral metabolism can be detected as early as in the 3rd or 4th week of life. The principal cause of disturbed mineral metabolism and metabolic bone disease of prematurity is phosphate depletion, manifested by hypophosphatemia.[7,8] The infant tends to retain maximum amount of phosphate, this resulting in hypophosphaturia and high renal tubular phosphate reabsorption. Due to phosphate depletion, the PTH secretion is low. Furthermore, the calcium accretion in the skeleton is also impaired, which might result in hypercalcemia and, in particular, in hypercalciuria with consequent urolithiasis.[9] Furthermore, treatment with furosemide in the infantile period could have also increased calciuria in our patient. Transient hyperphosphatasemia is a benign condition with good prognosis, that has been so far reported in more than 800 subjects, both sick and healthy children. The basic diagnostic criteria include an age of less than 5 years; variable, unrelated symptoms; no bone or liver disease noted on physical examination or from laboratory investigations; isoenzyme and isoform analysis showing elevations in both bone and liver activity, and a return to normal S-ALP values within four months.[1–6,10] The incidence of THI has been estimated at 2.8%.[10] THI is rather a laboratory than clinical finding and can cause some concern in patients with metabolic bone disorders, kidney or liver disease.[2–6] Normal bone turnover was previously observed in children with THI.[3–6] Our patient with bilateral nephrolithiasis and a history of severe prematurity presented with high S-ALP, initially suggestive of disturbed bone metabolism. However, the normal values of S-Ca, P, Mg, PTH, U-Ca/U-cr and normal wrist X-ray ruled out this possibility and pointed to the diagnosis of THI, which was further confirmed by the normalisation of S-ALP within one month. The present nephrolithiasis was considered as a result of previous hypercalciuria in osteopathy of prematurity, that has already resolved without causal relationship to transiently increased S-ALP.

In conclusion, children with THI should be spared from unnecessary frequent diagnostic procedures and therapeutic interventions.

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