SHORT REPORTS

Hyperphosphataemic rickets in an Asian infant

We have recently shown that hyperphosphataemic rickets is associated with hyporesponsiveness of vitamin D to parathyroid hormone. Patients with this disorder have extremely low basal excretions of phosphate in their urine; urinary phosphate and cyclic adenosine monophosphate increase only marginally after challenge with parathyroid hormone. After treatment with vitamin D plasma phosphate concentration becomes normal and urinary phosphate excretion increases. This hyperphosphataemic variant of rickets has hitherto not been described in an infant. We describe one such infant with severe deficiency of vitamin D. So far as we know this is the first reported case of hyperphosphataemic rickets in an infant.

Case history

A baby boy was born to healthy unrelated Asian parents after a full term, non-eventful pregnancy. Both parents were vegetarian and the mother had received only folate and iron supplements during her pregnancy. The infant was breast fed. At 13 days of age he developed projectile vomiting and shortly after admission to hospital he had a twitching episode lasting four minutes. Results of investigations were: plasma calcium concentration 1.26 mmol/l (3.5–4.0 mmol/l); plasma phosphorus concentration 3.2 mmol/l (0.8–1.4 mmol/l); plasma creatinine 280 (9–18 µmol/l); plasma alkaline phosphatase activity 1507 (280–1020 IU/l); plasma total calcium 2.6 mmol/l (3.5–4.6 mmol/l); plasma albumin 35 g/l (35–46 g/l); plasma electrophoretic albumin fraction 96% (18%–90%); plasma cholesterol 3.2 mmol/l (3.5–5.0 mmol/l); plasma creatine kinase 55 (20–200 IU/l); plasma lactate dehydrogenase 178 (20–210 IU/l); plasma sodium 146 mmol/l (135–145 mmol/l); plasma potassium 4.8 mmol/l (3.5–5.5 mmol/l); plasma bicarbonate 32 mmol/l (22–30 mmol/l); plasma glucose 5.2 mmol/l (4.0–6.0 mmol/l); plasma lipase 180 (10–80 IU/l); plasma α-fetoprotein 0.2 (0–2.0 IU/l); plasma uric acid 1.5 mmol/l (0.2–0.7 mmol/l); plasma glucose 5.2 mmol/l (4.0–6.0 mmol/l); plasma lipase 180 (10–80 IU/l); plasma α-fetoprotein 0.2 (0–2.0 IU/l); plasma uric acid 1.5 mmol/l (0.2–0.7 mmol/l); plasma glucose 5.2 mmol/l (4.0–6.0 mmol/l); plasma lipase 180 (10–80 IU/l); plasma α-fetoprotein 0.2 (0–2.0 IU/l); plasma uric acid 1.5 mmol/l (0.2–0.7 mmol/l); plasma glucose 5.2 mmol/l (4.0–6.0 mmol/l); plasma lipase 180 (10–80 IU/l); plasma α-fetoprotein 0.2 (0–2.0 IU/l); plasma uric acid 1.5 mmol/l (0.2–0.7 mmol/l); plasma glucose 5.2 mmol/l (4.0–6.0 mmol/l)

The patient was readmitted six days later (age 28 days) with a recurrence of twitching. Plasma calcium concentration was 1.56 mmol/l (3.5–4.0 mmol/l); plasma phosphorus concentration 2.9 mmol/l (0.8–1.4 mmol/l). Oral calcium supplements and alfalcaldiol 1.25 µg twice daily were begun. Three generalised grand mal convulsions then necessitated a further admission (age 40 days). Plasma calcium concentration was 1.76 mmol/l (3.5–4.6 mmol/l) and alkaline phosphatase activity 268 IU/l. He was treated with oral calcium supplements and phenobarbitone. Electroencephalography, radiography of skull, cranial ultrasound examination, and metabolic and infection screens all gave negative results. The parathyroid hormone concentration on day 52 was raised at 86 nmol/l (86–6 µmol/l). He was discharged from hospital (age 57 days) taking alfalcaldiol 1 µg twice daily and multi-vitamin drops 1 ml twice daily. Plasma calcium concentration was 2.95 mmol/l (0.8–2.6 mmol/l), phosphorus 2.84 mmol/l (1.8–2.6 mmol/l), and alkaline phosphatase activity 134 IU/l. Alfalcaldiol was discontinued at 108 days of age. At 6 months he was thriving and taking no medication. Calcium concentration was 2.4 mmol/l (9.6–13.0 mmol/l), phosphorus 2.2 mmol/l (6.8–10.0 mmol/l), alkaline phosphatase activity 360 IU/l, and parathyroid hormone concentration 36 pmol/l (3–6 pmol/l). A chest radiograph on day 40 was reported as normal and on retrospective examination showed severe sparing and rarefaction of the anterior ends of the ribs.

Comment

This infant’s biochemical abnormalities were accounted for by severe vitamin D deficiency; the features were low calcium concentration; raised alkaline phosphatase activity; non-detectable 25-hydroxyvitamin D in both the infant and the mother; raised parathyroid hormone concentration; and, finally, response to an antirachitic dose of vitamin D in multivitamin drops, which increased his calcium concentration from 1.26 to 1.76 mmol/l (5.0 to 7.0 µmol/l) before the introduction of alfalcaldiol. Such a dose of vitamin D is unable to raise the plasma calcium value in patients with hypoparathyroidism and pseudohyypoparathyroidism. The only unusual biochemical feature in this patient was the greatly increased plasma phosphate concentration, which initially led to considerable confusion about the diagnosis. It was only in retrospect that we arrived at the diagnosis of “hyperphosphataemic rickets.” Review of the chest radiograph at that time showed severe sparing and rarefaction of the anterior ends of the ribs. These changes could have heralded the formation of a rachitic rosary. Hyperphosphataemia in association with rickets has recently been shown by us to be due to severe vitamin D deficiency and a severely diminished end organ (especially renal tubular) response to parathyroid hormone. These patients require large doses of vitamin D, at least initially, since their vitamin D reserves are totally depleted.

These data emphasise that hypovitaminosis D is the commonest cause of hypocalcaemia in Asian neonates. Thus even in the presence of the unusual feature of a raised plasma phosphate concentration, vitamin D deficiency must be considered as the primary cause of hypocalcaemia.
The association of neonatal hypocalcaemia with hypovitaminosis D in Asians was described 14 years ago, and it is tragic that we still see pregnancy related complications of hypovitaminosis D: neonatal secondary hyperparathyroidism and maternal pathological fractures.1

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Transient urinary tract dilatation associated with hypokalaemia

 Pronounced weakness of skeletal or smooth muscle accompanying hypokalaemia of recent onset can result in general paralysis, gastric dilatation, or paralytic ileus.1 A disturbance of neuromuscular excitation, arising from a change in the ratio of extracellular:intracellular fluid potassium concentrations on which transmembrane electrical potential gradient depends is the cause. We report a case of dilatation of the upper and lower urinary tract, with transitory azotaemia, associated with hypokalaemia, which subsequently resolved when serum potassium concentration returned to normal.

Case report

A 73 year old woman continually suffered bouts of depression and confusion but comprehensive investigation had not provided a reason. No biochemical abnormality had been detected two years earlier. She suddenly lost her appetite for eight weeks and became confused, restless, and weak. Her general practitioner requested serum electrolyte concentrations: sodium (Na+) concentration was 140 mmol/l (normal 135-145), potassium (K+) 2-6 mmol/l (normal 3-5), chloride (Cl-), bicarbonate (HCO3-) and inorganic phosphate concentrations were within normal limits. Her serum creatinine concentration was 105 mmol/l (normal 40-130), glucose 6-0 mmol/l (normal 3-6-10), and blood urea concentration was 7-19 mmol/l (normal 2-8-7). On admission the patient was mildly confused but not dehydrated. Blood pressure was 130/80 mm Hg; serum Na+ concentration 135 mmol/l, K+ 3-0 mmol/l, Cl- 107 mmol/l, HCO3- 12 mmol/l, urea 35-6 mmol/l (214 mg/100 ml), creatinine 694 mmol/l (7-9 mg/100 ml), albumin 23 g/l, calcium (corrected) 2-05 mmol/l (2-1-2-5 mg/100 ml), inorganic phosphate 1-62 mmol/l (1-50 g/l). Urine volume was 640 ml/24 hours, and K+ excretion 10 mmol/24 hours. Haemoglobin concentration was 8-9 g/dl, serum folate 6-9 mmol/l, vitamin B12 299 ng/l, and ferritin 302 mmol/l. Erythrocyte sedimentation rate was 68 mm falling in the first hour.

Urine microscopy showed 150 leucocytes and 80 red blood cells/high power field. Culture grew Escherichia coli with a colony count of >105 organisms/ml.

Glomerular filtration rate was 11-3 ml/min/1-73 m², and effective renal plasma flow 71-6 ml/min/1-73 m². An antibiotic given from the second day sterilised the urine by the sixth day. The erythrocyte sedimentation rate then decreased to a 4 mm fall in one hour. Bladder catherisation on the second day produced 100 ml urine. Intravenous fluids were given, initially containing potassium, so that urine volume increased to 1-2-1-7 24 hours. The cather was removed on the fifth day but reinset on the seventh day and 150 ml of urine was removed. Serum creatinine concentration had fallen to 427 mmol/l (4-85 mg/100 ml) by the seventh day; serum K+ was 3-1 mmol/l, and HCO3- 18 mmol/l. Intravenous urography performed on the seventh day showed delayed contrast excretion from bilaterally enlarged hydronephrotic kidneys associated (figure: top) with hydrourerter dilated to the bladder, which was also enlarged. Lumbosacral spine x-ray films were normal.

Cystoscopy (Mr K C Vaughton) showed that the urethra was not tight on a 21 F gauge. The bladder was trabeculated but otherwise normal. Ureteric catheterisation was unsuccessful. Vaginal examination under anaesthesia did not indicate pelvic or faecal masses.

Appetite and food intake gradually improved, her depression abated, and confusion disappeared. The bowels were not opened often, but the stools were not hard and nor were they palpable in the abdomen. Serum creatinine concentration had fallen to 112 mmol/l (12-7 mg/100 ml) by the 14th day, when serum K+ was 3-3 mmol/l and HCO3- 23 mmol/l.

A month later haemoglobin was 11-4 g/dl, serum albumin 35 g/l, serum Na+ 145 mmol/l, K+ 3-7 mmol/l, Cl- 113 mmol/l, HCO3- 30 mmol/l, urea 4-2 mmol/l (25-3 mg/100 ml), creatinine 104 mmol/l (1-18 mg/100 ml), glomerular filtration rate 43-8 ml/min/1-73 m², effective renal plasma flow 127-3 ml/min/1-73 m². A repeat intravenous urogram showed a shrunken pyelonephritic appearance on the right side and a normal outline on the left side with normal pelvicical pattern (figure: bottom).

During several months of follow up serum creatinine and K+ concentrations remained normal and renography showed no sign of an obstructive excretory pattern.

Comment

Hypokalaemia was probably related to poor intake of food, resulting in depression and confusion and depressed neuromuscular activity throughout the smooth muscle of the whole urinary tract. Consequently the pathophysiology of bilateral hydronephrosis and hydrourter dilated periureteric fibrosis, in which peristaltic ureteric contractions are diminished in the absence of physical ob-