Pseudohypoaldosteronism type 1 in an infant

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Introduction

Pseudohypoaldosteronism (PHA) type 1 is a rare but serious abnormality characterised by mineralocorticoid resistance causing hyperkalaemia and hyponatraemia [1]. There are two clinically distinguishable entities of PHA type 1, an autosomal recessive severe variant with multiple target organ involvement and an autosomal dominant less severe variant with isolated renal involvement. Autosomal recessive PHA type 1 is due to defective epithelial amiloride sensitive sodium channels. We report an infant with autosomal recessive PHA type 1 associated with cholelithiasis and hypocalcaemia who was successfully treated with 6% saline, G solution and calcium polystyrene sulphonate resins.

Case report

A six-week old baby boy was referred from a local hospital where he had presented at 4 weeks of age with vomiting, poor feeding and lethargy of two weeks duration. He was the 2nd child of consanguineous parents. Maternal polyhydramnios had been noted antenatally. He had been collapsed on admission to the local hospital with severe dehydration. Examination had shown a fair complexioned child with a weight of 2.83 kg which was 450g lower than the birth weight. Examination of the systems was unremarkable with normal male external genitalia. His initial serum electrolytes were: Na^+ 97 mmol/l, K^+ 9.7 mmol/l and Cl^- 84 mmol/l. Blood glucose was 7.3 mmol/l, pH 7.43 and bicarbonate 20.6 mmol/l. CRP was negative, blood cultures sterile and 2D echocardiogram was normal. A tentative diagnosis of salt-losing congenital adrenal hyperplasia had been made and treatment commenced with hydrocortisone and fludrocortisone. Response to therapy was poor after 2 weeks of treatment and as the 17 hydroxy progesterone done on the 28th day of life was normal at 9.8 ng/ml (29.4nmol/l) he was transferred for further management.

On admission to our ward at 45 days of age he was dehydrated with a weight of 2.85 kg and length and head circumference of 54 cm and 37 cm, which were on the 25th and 10th percentiles respectively. His blood pressure was 70/40 Hgmm. We optimised his treatment with hydrocortisone and fludrocortisone and further investigations were done. Polyuria was observed at 7-10 ml/kg/hour. His serum electrolytes on several occasions showed a persistent hyponatraemia ranging from 111 mmol/l to 121 mmol/l and hyperkalaemia ranging from 7.0

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mmol/l to 9.4 mmol/l. Urinary sodium was 123 mmol/l (normal < 20 mmol/l). Serum creatinine was 56 µmol/l (normal < 88µmol/l), blood pH was 7.5 and bicarbonate was 20.6 mmol/l. Ultrasound scan of the abdomen revealed multiple gall bladder calculi, normal kidneys and normal adrenal glands. Serum calcium was 1.82 mmol/l (normal 2.1-2.7). Urine calcium to creatinine ratio showed hypercalciuria of 1.9 (normal < 0.4). Repeat 17 hydroxy progesterone done on the 48th day of life was also normal at 0.4 ng/ml (1.2 nmol/l). The lack of clinical response and the persistent biochemical abnormalities in spite of adequate replacement therapy prompted us to revise the diagnosis to pseudohypoaldosteronism type 1.

His serum sodium was corrected and maintained with a very high sodium intake (30-35 mmol/kg); initially intravenously and later with oral 6% saline. Hyperkalaemia was treated with frequent salbutamol nebulisations and oral K binding resins (calcium polystyrene sulphonate resin 1g qds). Hydrocortisone and fludrocortisone were omitted. Hypocalcaemia responded to intravenous calcium gluconate and did not recur. His serum aldosterone level was very high at 26054 pmol/l (normal 28-445) which favoured the diagnosis of PHA type 1.

He was sent home after 2 weeks on oral 6% saline, G solution (mixture of sodium chloride and sodium bicarbonate containing 1.34 mmol of sodium per millilitre) and calcium polystyrene sulphonate resin. After 10 days polyuria had settled and a weight gain of 300g was seen and serum electrolytes remained normal with a normal blood pressure. At the last review after 2 months the baby weighed 4.8 kg and was developing normally and had normal serum electrolytes and blood pressure of 90/60 Hgmm. The early age of onset and severity of disease were in favour of the autosomal recessive variant of pseudohypoaldosteronism type I.

Discussion

PHA type I is a rare disease which requires a high index of suspicion for diagnosis [2]. The persistent electrolyte abnormalities with dehydration inspite of adequate treatment with hydrocortisone and fludrocortisone, absence of hyperpigmentation, normal 17 OHP values on two occasions, no evidence of adrenal hyperplasia or renal anomalies on ultrasonography and very high serum aldosterone level were pointers to the diagnosis of pseudohypoaldosteronism type 1 in this child. Presence of parental consanguinity, early age of onset and severity of disease were in favour of the autosomal recessive variant of pseudohypoaldosteronism type I.

Association between PHA type 1 and cholelithiasis is very rare. There were only two previous cases reported [3,4]. This unusual association was seen in our patient. Salt-wasting and dehydration are assumed to be the pathogenetic mechanisms leading to gallstone formation possibly beginning in fetal life [4]. Cholelithiasis is uncommon in infants and is usually due to secondary causes [5]. Therefore it would be advisable to screen infants with cholelithiasis for pseudohypoaldosteronism when the first line investigations are negative.

Hypercalciuria which was seen in our patient has been previously reported to be associated with PHA type 1 [6]. Our patient had a transient hypocalcaemia needing treatment with intravenous calcium gluconate, which has not been reported previously in association with PHA. The most likely explanation for hypocalcaemia would be the hypercalciuria which was detected in our patient. Although hypocalcaemia was transient, the serum calcium and urinary calcium will be repeated during follow up.

Management of pseudohypoaldosteronism is challenging. There are reports where it had been extremely difficult to correct the electrolyte imbalance [7]. The ideal resin to counteract the hyperkalaemia in PHA is sodium polystyrene sulphonate which is not available in Sri Lanka. Our patient was successfully managed and discharged after 2 weeks on oral 6% saline, G solution and oral calcium polystyrene sulphonate resin and showed a remarkable improvement on return. At 4 months of age he was thriving with a weight of 4.8 kg and developing normally.

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