Congenital Pseudohypoaldosteronism: Early Acute Onset in a Saudi Child

Hussein Salman, Ahmed M. Abanamy, Ghassan Basset, Devebrata Roy


This paper reports congenital pseudohypoaldosteronism in a 9-day-old Saudi girl presenting as an acute salt loss syndrome with severe hyperkalemia and cardiac rhythm disorders. The patient responded only to cation exchange resin and high salt supplementation. Attention is drawn to this entity particularly in Saudi Arabia where consanguinity is common and where salt replacement may be difficult because of the hot environment.

Pseudohypoaldosteronism is a rare congenital disorder due to an end-organ (mineralocorticoid receptor) defect. Familial occurrence (with male predominance) is not uncommon but sporadic cases have been described. Clinical features are very variable from an early severe form to progressive, or chronic and even asymptomatic forms (in adults).

We report congenital pseudohypoaldosteronism in a 9-day-old Saudi girl who was recently admitted to our hospital and presented with acute salt loss syndrome and severe metabolic acidosis, sudden hyperkalaemic phase and severe cardiac rhythm disorders, and who did not respond to high dose of fludrocortisone acetate but only to cation exchange resin and to high dose salt supplementation. To our knowledge, no such case has been reported from Saudi Arabia. We would like to draw the attention of local paediatricians to this entity among the other metabolic and hormonal disorders which are not uncommonly seen in this country.

Case Report

The child was admitted at the age of 9 days with complaints of poor feeding and lethargy for 1 day, and skin rash for 3 days. Pregnancy, delivery, birth parameters and the perinatal period had been normal. The family history was insignificant apart from first degree parental consanguinity.

On admission, the patient was afebrile, mildly dehydrated, irritable, grunting, tachypneic with a disseminated pustular skin eruption, left purulent conjunctivitis, sluggish reflexes, normal female genitalia, and a normal heart examination with a regular rate at 150/min.

Initial investigations showed a severe metabolic acidosis (with a PH of 7.05, PCO₂ of 20, HCO₃ of 7.8), a high urea of 55 mmol/l and high creatine of 188 µmol/l (gradually normalized), a low sodium of 121 mEq/l, a high potassium level ranging from 8.6 mEq/l to 12 mEq/l with a mean of 9.6. Random urine electrolytes showed a high sodium (mean of 186 mmol/l/day and a low potassium (mean of 4 mmol/l/day). Blood culture was positive for Staphylococcus aureus. Other investigations including CSF study, blood glucose, ultrasound of abdomen and kidneys were normal.

A provisional diagnosis of neonatal septicemia with renal failure, with possible adrenal insufficiency was made and the child was started on intravenous (i.v.) liquids, i.v. antibiotics, and i.v. sodium bicarbonate, under cardiorespiratory monitoring. Two hours after admission, the patient developed lethargy, shallow breathing, dropped heart beat, and cardiac arrhythmia with brady-cardia and tachycardia. The ECG showed a wide QRS
Congenital Pseudohyposalteronism

complex, prolonged PR interval, absence of P waves and LBBB. The child was then started on antihyperkalaemic measures on which she was stabilized. Further samples to evaluate adrenal function were taken and showed a normal serum cortisol, concentration of 358 nmol/l (N165–744), a normal ACTH, 69 miU/l (N14–100) but very high levels of plasma aldosterone (8320 then 13900 pmol/l (N110–960), and renin 888 pmol/l/h (N13–104 pmol/l/h). The patient was then started on i.v. then oral hydrocortisone (10 mg/kg/day) and intramuscular (i.m.) DOCA (1 mg/kg/day) then oral fludrocortisone acetate (initially 50 μg/day), and salt supplementation of 2 g/day at first through i.v. liquids and then via a nasogastric tube. Despite the gradual increase over 1 week of fludrocortisone acetate to 200 μg orally per day (associated with 4 mg daily i.m. of DOCA), and of salt supplementation (4 g/day), the child remained hyponatraemic and hyperkalaemic. Hydrocortisone and DOCA/fludrocortisone acetate were progressively stopped and salt supplementation was increased over 2 weeks to 8 g/day using saline solutions and common salt in bottle feeds. Transient polyuria was noted at this time but the patient improved gradually and maintained her serum sodium concentration at more than 130 mEq/l, and her potassium at less than 7 mEq/l. Her clinical condition (hydration, activity, feeding, weight) improved significantly with a daily salt supplementation of 3–5 g/day. Family screening (parents and siblings) was negative. The serum concentrations of 17-OH progesterone <15 nmol/l) and testosterone were normal. The final diagnosis was congenital pseudohyposalteronism.

Discussion

Congenital pseudohyposalteronism is an uncommon disorder related to an end-organ (mineralocorticoid receptor) defect. Apart from the classical familial occurrence (autosomal recessive, autosomal dominance with variable expressivity), there are reported sporadic cases. In our case there was family history of parental consanguinity. The disorder seems more frequent in males (58%). Its clinical features are variable from a fulminant presentation in a preterm infant, (early progressive or severe salt-loss) to a chronic salt-wasting with failure to thrive, lethargy, vomiting, and poor feeding. In our 9-day-old female patient, the onset of the disease was characterized by its early age, its acute hyperkalaemic phase with cardiac rhythm disorders and severe metabolic acidosis with azotaemia. There was no vomiting, no diarrhoea, and the external genitalia was normal. Asymptomatic forms have been described in adults and even in siblings or parents of a patient. In our case, family screening (parents, siblings) was negative. The diagnosis of the disease is based on a high plasma aldosterone level and high renin plasmatic activity, normal ACTH and cortisol levels, normal renal function and unresponsiveness to the administration of mineralocorticoids (DOCA, fludrocortisone acetate) as shown in our patient. The serum cortisol level is normal in patients with congenital pseudohyposalteronism. However, it should be high during acute stress. In our patient the blood sample for this investigation was taken on the second day after admission after stabilization of the patient under antihyperkalaemic measures and other symptomatic therapy. This could explain the normal level.

Pseudohyposalteronism is characterized by unresponsiveness to mineralocorticoids. Previously, a high dose of fludrocortisone (as high as 300 μg) was tried with success. Our patient did not respond to 200 μg/daily of fludrocortisone acetate orally associated with DOCA 4 mg daily as an i.m. injection, but only to salt supplementation as described previously. However, we had to use 8 g sodium chloride per day before attaining a normal serum sodium level. Indomethacin was not used in our patient because of its potential side-effects, especially in long-term depression of renin activity and renal insufficiency.

There is spontaneous clinical improvement with advancing age despite persistence of biochemical features. (This is unexplained but probably related to proximal tubular maturation and the tendency of the child to ingest more salt.) The parents of our patient received explanations about the condition and the favourable long-term prognosis. Stress was laid on the need for salt supplementation for several years (to avoid growth retardation) before eventually being able to discontinue therapy.

In summary, congenital pseudohyposalteronism should be considered in the differential diagnosis of disorders with metabolic acidosis and a salt losing state. In a country like Saudi Arabia, with its hot environment and excessive sweating, these children might need higher doses of sodium than those usually prescribed elsewhere.

References


