Turkish Journal of Endocrinology and Metabolism, (2001) 1 : 43-45 **ORIGINAL ARTICLE**

Pseudohypoaldosteronism Type I: A Report of Two Cases

Enver Şimşek Kenan Kocabay

Department of Pediatrics, Abant İzzet Baysal University School of Medicine, Düzce, Turkey

Pseudohypoaldosteronism (PHA) is characterised by salt wasting and failure to thrive in the newborn because of the resistance of mineralocorticoid receptors to aldosterone. The diagnosis is based on dehydration, hyponatremia, hyperkalemia, high urine sodium, and high serum concentrations of aldosterone and renin. The hyponatremia in PHA is not improved by exogenous mineralocorticoid administration without added sodium chloride. In this paper we reported two cases whose clinical and laboratory findings were compatible with the classical PHA. The hyponatremia of the cases was improved only by exogenous sodium chloride supplementation to their diets.

Key words: Pseudohypoaldosteronism type 1, hydramnios

Introduction

Pseudohypoaldosteronism was first described in 1958 by Cheek and Perry, who reported an infant with severe salt wasting in the absence of any renal or adrenal defect (1). The epithelial Na^+ channel (ENaC) is comprised of three homologous subunits: alpha, beta, and gamma, all of which are required for formation of a fully functional channel (2). ENaC mediates the aldosterone-dependent sodium resorption in the distal nephron and is involved in the regulation of blood pressure. Mutations in genes encoding ENaC subunits can cause human disease by increasing channel function in Liddle's syndrome, a form of hereditary hypertension, or by decreasing channel function in pseudohypoaldosteronism type I (PHA-1), a salt-wasting disease of infancy (2, 3). The diagnosis of PHA-1 is based on dehydration, hyponatremia, hyperkalemia, high urine sodium, and high serum levels of aldosterone and plasma-renin-activation (4, 5). Patients of PHA-1 are resistant to mineralocorticoid administration and the symptoms improve after a period of sodium supplementation (6).

Correspondence address:

Enver Şimşek
Abant Izzet Baysal University, Faculty of Medicine,
Department of Pediatrics, Division of Pediatric Endocrinology,
Konuralp, Düzce - TURKEY
Tel : +90 374 541 41 07
Fax : +90 374 541 41 05

In this paper we reported two cases whose clinical and laboratory findings were consistent with PHA. The second case of PHA was associated with hydramnios during the fetal period. To our knowledge, this is the first reported case of PHA from Turkey associated with hydramnios.

Case Reports

Case 1

A male newborn was admitted to the hospital because of vomiting and diarrhoea on the 14th day of postnatal life. He was the product of the first and uncomplicated pregnancy of a 27-year-old mother and had a birth weight of 3100 g and height of 51 cm. On physical examination on the 14th postnatal day, the patient was pale and severely dehydrated. The temperature was 35.5°C, the pulse was 140, the respiration was 65, and the blood pressure was 50/30 mmHg. The weight was 2900 g. The level of creatinin was 0.9 mg/dl (normal 0.3-1.0 mg/dl) and blood urea nitrogen was 85 mg/dl (normal 3-12 mg/dl). The other biochemical tests, such as glucose, bilirubin, calcium, phosphorus, aspartat aminotransferase, alanin aminotransferase, and microscopical examination of urine were normal. The hormonal analysis is shown in Table 1. Arterial pH was 7.15 (normal 7.35-7.45); PCO_2 was 23 mmHg (normal 27-41 mmHg) and total CO_2, 7 mmol/L (normal 13-22 mmol/L). On the admission day he was treated

Table 1. The results of biochemical, hormonal and urine analysis of the cases on admission.

	Na (mEq/L)	K (mEq/L)	BUN (mg/dl)	PRA ng/ml/saat	ACTH (pg/ml)	Kortizol µg/dl	Aldosteron pg/ml	Urine Na mEq/L
Normal	135-145	3.5-4.5	10-20	< 16.6	25-100	5-23	5-65	<40
Case I	126	7.5	85	49	169	11	986	95
Case II	116	7.2	69	67	97	16	687	78

PRA, Plasma-rennin-activation; BUN, blood urea nitrogen; ACTH, adrenocorticotrophic hormone.

Table 2. The results of biochemical, hormonal and urine analysis of the cases at the second week of mineralocorticoid replacement therapy.

	Na (mEq/L)	K (mEq/L)	BUN (mg/dl)	PRA ng/ml/saat	ACTH (pg/ml)	Kortizol µg/dl	Aldosteron pg/ml	Urine Na mEq/L
Normal	135-145	3.5-4.5	10-20	< 16.6	25-100	5-23	5-65	<40
Case I	129	6.8	32	44	152	17	756	82
Case II	122	6.9	62	59	101	19	623	71

with 0.9% NaCl, 5% dextrose, and bicarbonate infusion. He did not respond to exogenous mineralocorticoid replacement therapy (150µg/24h). Natriuresis remained during mineralocorticoid therapy. Together hormonal analysis and unresponsiveness to mineralocorticoid replacement (9α-flourocortisol) resulted in the diagnosis as a PHA-1. Control levels of urine sodium and hormonal analysis are shown in Table 2. The serum sodium was normalised only by minimum 30-mEq/kg/24 h oral sodium chloride replacement.

Case 2

A three-month-old male was admitted to hospital because of vomiting, weight loss and diarrhoea. He had had vomiting for two months. Diarrhoea began at the age of one month. He had been breast-fed. The parents were healthy and were first-degree relatives. The patient was the product of the third pregnancy of a 29-year-old mother. Because their first child had been diagnosed as having pseudohypoaldosteronism in Germany and had been treated by supplementation sodium chloride in his diet, this last pregnancy had been controlled every three months by ultrasonography. Hydramnios was demonstrated by ultrasound at the 6th month of pregnancy. The temperature was 36.5°C, the pulse was 160, the respiration was 45, and the blood pressure was 70/40 mmHg. Physical examination revealed tachycardia, cool and mottled skin of extremities, prolonged capillary refill and sunken eyeballs and fontanels. The weight was 3600 g (<3rd percentile for age and gender); height was 55 cm (3-10th percentile for age and gender). The results of urine, biochemical and hormonal analysis on admission to our hospital are summarised in Table 1. Arterial pH was 7.05 (normal 7.35-7.45); PCO_2, 17 mmHg (normal 27-41 mmHg) and total CO_2, 11 mmol/L (normal 20-28 mmol/L). He was treated with sodium deficiency replacement, fluid and bicarbonate infusion on the second day. Thereafter exogenous mineralocorticoid replacement therapy was begun. After ten days of mineralocorticoid replacement therapy (150 µg/24h), hyponatremia (131, 129, 126), mEq/L) was revealed again (Table 2). The diagnosis of PHA-1 was made in the same manner as case one. Oral salt replacement in the daily diet was begun. The serum sodium of the patient improved only with minimal 40-mEq/kg/24 h oral sodium chloride replacement.

Discussion

Pseudohypoaldosteronism (PHA) is characterised by salt wasting and failure to thrive in the early period of life, accompanied by high urinary levels of sodium despite hyponatremia, hyperkalemia, elevation of plasma renin activity and high plasma aldosterone levels (1-6). The cases of PHA are characterised by unresponsiveness to external mineralocorticoid therapy because of abnormal or absent mineralocorticoid receptors (2, 3, 6). All of

our cases were consistent with pseudohypoaldosteronism on the basis of clinical and laboratory findings (Table 1). Following the parental therapy, 9-α fluorohydrocortisol (Astonin H, 0.1 mg, Tablet) was begun in both cases as a mineralocorticoid replacement therapy. The urine sodium concentrations of the cases dit not show a tendency to decrease in either case (Table 1). These findings confirmed the diagnosis of PHA-1 in case 1 and case 2. The normal ranges of serum sodium of case 1 and case 2 were maintained only by oral supplemental sodium chloride in doses of 30-mEq/kg/24 h and 40-mEq/kg/24 h, respectively. However with this replacement therapy the serum sodium of case 1 and case 2 were found within the normal range, but the urine sodium excretion continued in a range between 45 and 108 mEq/L. Salt supplement to the diet was often rejected by patients and the long-term therapy was tolerated with difficulty. When sometimes families do not add salt to the diet of patients, the serum sodium is found near hyponatremia levels.

Polyhydramnios is one of the prenatal signs of pseudohypoaldosteronism (5, 7, 8). Fetal polyuria is the probable cause of hydramnios. The finding of hydramnios in our case 2 is consistent with prenatal signs of PHA. We had no opportunity to ascertain whether case 1 had hydramnios or not. He had not been examined by ultrasound during the pregnancy period. Pseudohypoaldosteronism should be included in the differential diagnosis of hydramnios.

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