PSEUDOHYPOALDOSTERONISM

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Abstract — Pseudohypoaldosteronism (PHA) is referred to a state of endorgan unresponsiveness to aldosterone. In this article a 12 day - old male newborn is presented with hyponatremia, hyperkalemia and metabolic acidosis. Aldosterone level and plasma renin activity were high. Mineralocorticoids had no therapeutic effect, but normal saline infusion improved electrolyte imbalance. Salt-rich diet was successful in controlling his state, but he died because of incompliance.
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Key words: Pseudohypoaldosteronism; hyponatremia; hyperkalemia; renin; aldosterone.

INTRODUCTION

Pseudohypoaldosteronism (PHA), a mineralocorticoid unresponsiveness of endorgan, is a heterogenous disease with variable degree of aldosterone insensitivity. Determination of mineralocorticoid receptors affinity and capacity in human mononuclear lymphocytes in these patients has revealed no decrease in this respect (1,2). Its gene is located on chromosome 4 at q31.2 (3).

CASE REPORT

The case was a 12 day-old male neonate who was referred to our hospital because of poor feeding and electrolyte imbalance. He was the sixth child of related parents. There was a case of stillbirth and two neonatal deaths in the family. The latter two infants had poor feeding, hyponatremia and hyperkalemia (Fig. 1). In both of them sepsis was ruled out. Deoxycorticosterone administration had no therapeutic effect. Electrolyte imbalance was resistant to any treatment. They died from hyperkalemia. Our patient was delivered by cesarean section because of abnormal intrauterine posture. Birth weight was 3.3 kg. The newborn was well until 11 days, then he became hypoactive and lost interest in feeding. He had no fever and no focus of infection. He was dehydrated. All neonatal reflexes were decreased. Genitalia was normal. WBC 30000/cmm, PMN 53%, Lymph 33%; Mono 7.2%; Eos 1.3%; LUC 5.5%; Hb 15.4 mg/dl; HCt 47.5%; Na 121 mEq/L; K 9 mEq/L; Cl 100 mEq/L; BUN 20 mdl, Creat 0.75 mg/dl.

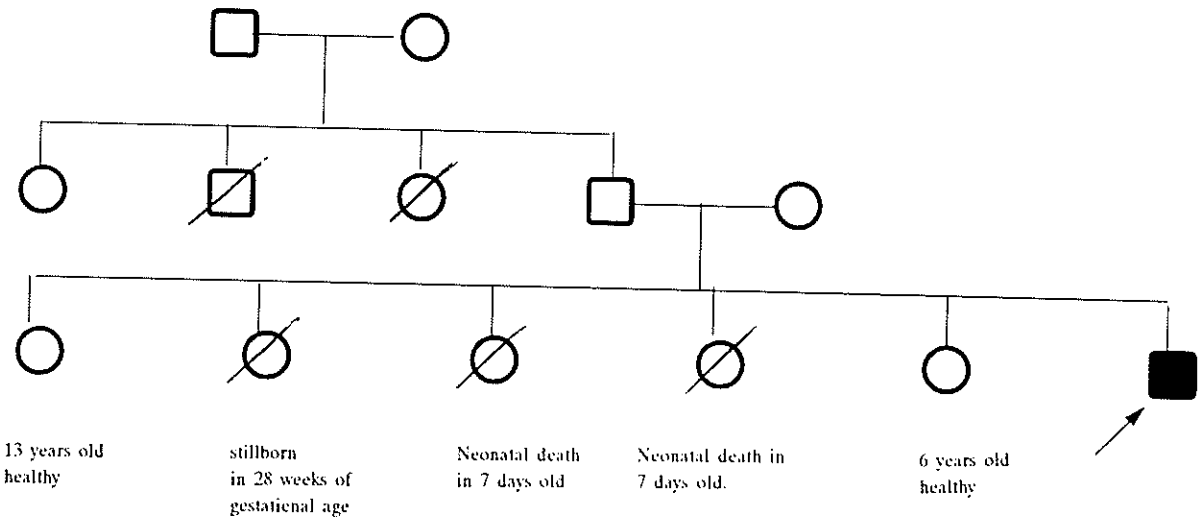

Fig. 1. Pedigree of our Patient

Blood sugar, calcium, uric acid and liver function tests were normal. Blood gas analysis: pH = 7.46; PCO_2 = 12.7 mm Hg; HCO_3 = 8.9 mEq/L; PO_2 146; Serum anion gap = 21.

Urinalysis: specific gravity 1038, pH 5. Cultures of cerebrospinal fluid, blood and urine were negative. Stool exam and culture, ultrasonography of abdomen, liver, spleen, kindneys and adrenals were normal.

Administration of calcium gluconate, sodium bicarbonate, glucose and insulin infusion to treat hyperkalemia were not helpfull. Hyperkalemia increased to over 9.9 mEq/L. Peritoneal dialysis was initiated and caused an increase in serum sodium and decrease in serum potassium. Administration of fluid led to correction of the high anion gap which probably was produced by dehydration. peritoneal dialysis was not effective in maintaining normal potassium level. With regard to existing hyponatremia, hyperkalemia and salt losing (Urine Na^+ 180 mEq/L, K^+ 7.2 mEq/L, fractional excretion of sodium 3.4%. Fludrocortisone (0.06 mg/kg/day) and DOCA (5 mg/kg/day) was begun. Unresponsiveness to these mineralocorticoids induced the impression of pseudohypoaldosteronism. Treatment with normal saline infusion was effective in electrolyte correction. The infant was discharged in good general condition. It was recommended to feed him with salt-enriched fluids in addition to breast milk. The results of hormone assay and electrolyte determination in body fluids were as following:

Plasma 17OH-Progesterone 3.2 ng/ml (N 0.1-0.5 ng/ml)
Plasma Dihydroepiandrosterone sulfate 839 ng/ml (N 8-414 ng/ml)
Plasma Cortisol 57.1 μg/dl (N 8-28 μg/dl),
Plasma testosterone 1.3 ng/ml (N 0.57-2.8 ng/ml),
Plasma androstendione 3.5 ng/ml (N 0.57-2.8 ng/ml),
Plasma aldosterone (supine) 1000 pg/ml (N 7.5-150 pg/ml),
Plasma Renin (supine) 41.3 ng/ml (N 0.2-2.8 ng/ml),
Saliva: Na^+ 40 mEq/L, K^+ 6 mEq/L,
Sweat: Na^+ 180 mEq/L, Cl^- 181 mEq/L (Sweat weight 326 mg)
Stool: Na^+ 143 mEq/L, K^+ 73 mEq/L

The patient had frequent admissions to the hospital with the same electrolyte imbalance for intercurrent infections. Treatment with hydrocortisone, indomethacin and kayexalate was unsuccessful and he was further on high salt intake and kayexolate. He died at home with hypovolemic shock.

DISCUSSION

PHA has two types: primary PHA type A or classic PHA. This is an inherited disease with salt wasting, hyperkalemia, metabolic acidosis, high renin plasma activity and plasma aldosterone. There are two types with distinct clinical and genetical features (4,5). In type I only kidney is involved, in type II multiple organs are invovled. Secondary PHA type B is a rare disorder caused by relative insensitivity of renal tubules to aldosterone in patients with unilateral renal vein thrombosis, juvenile nephronophtisis, neonatal medullary necrosis and urinary tract infection (6,7,8,9). Also cycolosporin A is suggested to be a cause of the disorder (10).

Type B PHA (Chloride shunt): This is a familial syndrome consisting of arterial hypertension, metabolic acidosis, hyperkalemia and decreased plasma renin activity inspite of normal glomerular filtration rate (6,11). In primary disorder there is an increase of NaCl reabsorption in tubules. A defect in voltage channels impairs co-transport of proton and potassium, so reabsorption of NaCl causes intravascular volume expansion and suppression of renin and aldosterone secretion (6,12,13).

With regard to laboratory findings our patient had a primary PHA type I with multiple organ involvement.

Treatment of renal type consists of sodium chloride infusion (3-6 g/day) which causes clinical recovery and correction of electrolyte imbalance (14). Repair of intravascular volume increases tubular flow and sodium reabsorption in distal tubules where there is a gradient for potassium secretion inspite of mineralocorticoid unresponsiveness (6). Although it is a permanent defect, partial recovery may be achieved after 1-2 years because of completion of transport system in proximal tubules, salt craving behavior and increase in tubular responsiveness to mineralocorticoids. In multiple organ involvement, kidney (97%), colon (75%) salivary and sweat glands (75% and 30% respectively) are unresponsive to aldosterone (4). Parents are usually asymptomatic with normal plasma aldosterone.

Patients have poor prognosis because of severe salt losing that begins soon after birth and may succumb in neonatal period. Treatment with NaCl alone is not enough and enema with kayexalate and potassium restriction are necessary. Recovery with increasing age is less probable than in renal type.

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