CASE REPORT

Pseudohypoaldosteronism, Hypothyroidism and Hypoparathyroidism in a Two-Year-Old Boy

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ABSTRACT

A two-year-old boy, found to have a persistent hyperkalemia, hyponatraemia with metabolic acidosis in addition to repeated episodes of apnoeic attacks secondary to low serum calcium. Except for failure to thrive, his physical examination was within normal. Laboratory values confirmed the unusual combination of pseudohypoaldestronism, hypoparathyroidism and congenital hypothyroidism. Renal function was normal. Hormonal evaluation revealed normal cortisol, as well as 17- hydroxyl progesterone which were done to exclude the possibility of congenital adrenal hyperplasia as the cause of electrolyte disturbance. In the absence of aldosterone deficiency or renal dysfunction, it was assumed that this infant had primary renal resistance to aldosterone, known as pseudohypoaldestronism. We attempted to report an unusual combination of persistent yet 3 endocrinopathies in closely related parents.

Key words: Aldosterone, thyroid, hypocalcaemia, hypoparathyroidism.

INTRODUCTION

Pseudohypoaldosteronism (PHA) is a rare condition of salt wasting in infancy with renal tubular resistance to the actions of aldosterone. The disease is divided into 2 forms: primary and secondary (transient) PHA. The primary form is further divided into type 1 and type 2. Type 1 is subdivided into renal type 1 (also known as Cheek and Perry syndrome), Multiple Target Organ Defect type 1 (MTOD) and Early Childhood Hyperkalemia. Type 2 is subdivided into Gordon Syndrome (also known as Chloride Shunt syndrome), and adolescent hyperkalemic syndrome. The underlying pathology differs according to the types and subtypes of PHA, which is due either to a defect in the quantity and functions of aldosterone receptors, the epithelial sodium channels or the sodium-chloride co-transporters.

The first case of primary PHA was reported in 1958 by Cheek and Perry[1]. Signs and symptoms vary according to the types of PHA. It is a state of hyponatermic, hyperkalemic metabolic acidosis, which might occur at early infancy but can also be present in utero; (polyurea leading to polyhydramnios, which was presented in our case or during adolescence (hypertension). Anorexia and vomiting usually develop after birth with signs of dehydration and failure to thrive. Short stature is seen in children as they get older. Blood pressure varies according to type. Furthermore, there is a higher incidence of lower respiratory tract infections in children with MTOD. Death may occur from cardiac arrhythmia due to severe hyperkalemia. Investigations usually reveal a hyponatremic, hyperkalemic metabolic acidosis. Aldosterone levels maybe low, normal or high, according to the type of PHA and volume status. Plasma renin levels are usually high. Cortisol levels

and renal function should be normal. Renal ultrasound is usually indicated to rule out any urinary tract malformations, urinalysis and urine culture should be done to rule out urinary tract infection. Management includes rehydration, correction of acidosis and hyperkalemia with alkalinizing agents (sodium bicarbonate). Potassium binding resins (sodium resonium) are usually prescribed to control hyperkalemia. High sodium and low potassium diets are advised, in addition to the supplementation of sodium (sodium chloride). The use of exogenous mineralocorticoids has no role in correcting the abnormalities of this disorder. During outpatient care serum electrolytes, height, weight and blood pressure should be closely monitored. We present a case illustrating the unusual association of pseudohypoaldosteronism, hypothyroidism and hypoparathyroidism in a two-year-old boy.

CASE REPORT

A two-year-old male patient, product of 34 weeks of gestation, with a birth weight of 1.8 kg presented to the emergency room of King Abdul-Aziz University Hospital, Jeddah, Saudi Arabia, a few days after birth. He had a two-day history of frequent attacks of apnea, associated with bluish discolouration of his lips (each lasted for a few seconds), poor activity, reduced oral intake and poor weight gain since birth. His vital signs were stable except for an oxygen saturation of 88% on room air. He was lethargic and irritable, in addition to being underweight for his age but with no dysmorphic features.

Regarding family history; his parents were first degree cousins, and his brother died during infancy at the age of 3 months in another hospital secondary to hypocalcemic convulsions and electrolyte imbalance. There was no medical record of the brother's case. During his first admission, the laboratory investigations revealed severe hyponatraemia of 125 mmol/L (136-145), hyperkalemia of 6.4 mmol/L (3.5-5.1) and moderate metabolic acidosis pH: 7.22 (7.37-7.45), a serum bicarbonate level of 18.5 mmol/L (21-26). A hormonal study was done showing a normal serum cortisol level of 170.6 nmol/L (138-636), normal levels of 17- hydroxyprogesterone of 3.2 ng/ml (0.6-7), normal ACTH level of 18.76 pmol/L (9-52), and a normal aldosterone level of 129 ng/dl (5-132).

During hyponatremia, (a sample was taken when sodium levels were low) and we found a high serum rennin level of 104 pg/ml (6-80). Renal ultrasound revealed no urinary tract malformations, urinalysis and culture revealed no urinary tract infection. Based on the previous findings the diagnosis of pseudohypoaldosteronism was established. Regarding the investigations of the repeated attacks of hypocalcemia, patient total serum calcium was 1.32 mmol/L (2.12 - 2.5), his serum phosphate levels were high, 2.5 mmol/L (0.81-1.58), with a normal serum alkaline phosphatase level of 231 U/L (136 - 325). The diagnosis of hypoparathyroidism was made because of low parathyroid hormone level of 0.35 Pmol/L (1.6 - 6.9) during the hypocalcaemic attacks. Also, low levels of free T4 11.7 Pmol/L (12 - 22), and a high TSH level of 8.7 IU/L (0.27 - 4.2) with the diagnosis of hypothyroidism were reported as well. Series of investigations were done during the repeated attacks and admissions that showed similar values. No genetic analysis has been done due to unavailability of genetic testing. The patient has been following up in the pediatric endocrinology clinic till now. Currently, the patient is on oral medications that include sodium bicarbonate, potassium binding resins (sodium resonium), one-alpha drops, calcium carbonate, sodium chloride solution and L-thyroxine. The patient's last visit was at the age of 3 years and it showed TSH level of 3.1 IU/L, T4 14.6 Pmol/L, PTH 0.41 Pmol/L, serum calcium 2.1 mmol/L, potassium 3.6 mmol/L and sodium 136 mmol/L. Our patient's maintenance therapy improved his electrolyte disturbances and thyroid function; however, due to his permanent endocrinopathies his hormone levels did not improve.

DISCUSSION

A thorough literature review regarding the topic at hand (pseudohypoaldosteronism, hypothyroidism and hypoparathyroidism) that extended to the past decade revealed no reported cases with similar associations. The cases we found were of transient pseudohypoaldosteronism with urinary tract malformations, i.e. vesicoureteral reflux[2]

obstructive uropathy and posterior urethral valve[3]. There were reported cases of pseudohypoaldosteronism with pustular miliaria rubra[4] and a case associated with right renal duplication anomaly with poorly functioning upper pole moiety which was resolved due to surgical intervention.

Many studies were conducted on the association of hypothyroidism[5] and hypoparathyroidism[6] with thalassemia major due to iron overload. Such studies focused on the means of prevention through good chelation therapy. There were reported cases of hypothyroidism in ANA positive Juvenile Rheumatoid Arthritis and Systemic Lupus Erythematosus which showed a connection between thyroid disease and autoimmune diseases[7]. One such case reported the onset of neonatal hypothyroidism after trophoblastic disease during pregnancy in a hyperthyroid mother[8]. Other cases revealed the association of autoimmune hypothyroidism with Down syndrome and Celiac disease. Hypothyroidism was also seen in those patients with William's syndrome.

Several cases of transient neonatal hypoparathyroidism born to hyperparathyroid mothers were reported[9]. There was one case of hypoparathyroidism associated with Pallister-Hall Syndrome[10]. Our literature review revealed no similar cases that could be linked to ours. We believe this is the first reported case that reveals the association between pseudohypoaldosteronism, hypothyroidism and hypoparathyroidism.

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