An endocrine problem of obstructive uropathy: pseudohypoaldosteronism

Obstrüktif üropatinin endokrin problemi: Psödohipoaldosteronizm

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Abstract
In the presence of obstructive uropathy, the normal defense mechanisms preventing urinary tract infections (UTI) are compromised, and accordingly, the incidence of pyelonephritis is increased significantly. However, most patients remain without symptoms. Serious electrolyte imbalance is uncommon. Rarely, obstructive uropathy may result in tubular damage or a decrease in nephron number. Tubular damage can result in renal tubular unresponsiveness to aldosterone. This has been called transient pseudohypoaldesteronism (PHA) and clinical manifestations have reported hyponatremia, hyperkalemia and metabolic acidosis. These findings may resemble congenital adrenal hyperplasia (CAH). Therefore, CAH is often an initial presumptive diagnosis, resulting in inappropriate therapy. We report the case of a 29-day-old boy with vesicoureteral reflux and pyelonephritis complicated by pseudohypoaldosteronism leading to excessive salt wasting.

Key Words: **Adrenal hyperplasia, congenital; Hyponatremia; Infant; Pseudohypoaldesteronism; Obstruction, ureteral.**

Özet
Obstrüktif üropatinin varlığında, normal defans mekanizmalarının bozulması pyelonefrit sıklığını belirgin olarak arttırmaktadır. Ancak çoğu hasta semptomsuzdur ve ciddi elektrolit bozukluğu sık değildir. Nadiren obstrüktif üropati tübüler harabiyete ve nefron sayısında azalmaya neden olabilir ve tubulus harabiyeti aldosterona yanıtsızlıkla sonuçlanabilir. Geçici psödohipoaldosteronizm olarak tanımlanan bu klinik tabloda hiponatremi, hiperkalemi ve metabolik asidoz rapor edilmiştir. Bu bulgular konjenital adrenal hiperplaziyi andırabilir ve ilk tanı sıklıkla konjenital adrenal hiperplazi olup uygunsuz tedaviyle sonuçlanabilmektedir. Burada vezikoüreteral reflu ve pyelonefrite bağlı psödohipoaldosteronizm gelişen 29 günlük erkek olgu sunulmuştur.

Anahtar Kelimeler: **Hiponatremi; İnfant; Konjenital adrenal hiperplazi; Psödohipoaldosteronizm; Üreter tıkanıklığı.**

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Introduction

Pseudohypoaldosteronism is a rare syndrome occurring during early infancy, which is mainly characterized by salt-depletion crises. Sodium chloride is lost via the kidneys, resulting in a reduced sodium level and raised potassium level in the serum, leading to life-threatening disturbances of water and acid-base concentration. PHA can be either a hereditary (primary) or acquired (secondary) condition characterized by markedly elevated concentrations of plasma renin activity and aldosterone. The primary type is seen in the recessively inherited defects of aldosterone biosynthesis due to corticosterone methyl oxidase deficiency. This condition may be associated with polyhydramnios. The secondary type has been reported in association with a spectrum of urologic diseases including obstructive uropathy and massive, infected VUR. Secondary pseudohypoaldesteronism can also be acquired as a result of sickle cell disease or amyloidosis (1,2). We report electrolyte imbalance in a male infant with urinary tract malformation.

Case report

A-29 day old male infant was admitted to Gevher Nesibe Hospital with symptoms of poor feeding during the previous 72 h. The boy was born to non-consanguineous healthy parents at term by normal delivery. There was no report of fetal sonography. He was the 2nd child of the family. The other sibling is two years old and healthy. The vital signs on admission were: heart rate 135 beats/min, blood pressure 85/40 mmHg, respiratory rate 52 breaths/min, axillar temperature 36.2 ^{o}C, body weight 3400 g (25-50 centile), height 55 cm (50-75 centile) and head circumference 36 cm (50 centile). Initial evaluation revealed that the child was severely dehydrated. Scrotal hyperpigmentation was noted. He was uncircumcised and he didn't have phimosis. Penile length was 4 cm, testicular volume was 2 ml and other physical findings were within normal limits. Laboratory analysis revealed a hyponatremia 113 mmol/L, a hyperkalemia of 10.2 mmol/L, and metabolic acidosis (Table I). Urinanalysis revealed a significant number of white cells. According to the laboratory results, the primary diagnosis was considered to be CAH. Fluid therapy was initiated with 0.9% NaCl solution at a rate of 20 ml/kg/h. After blood was drawn to evaluate hormonal status, prednisolone and 9-fludrocortisone was administered. The infant was treated intravenously with sodium bicarbonate, glucose, insulin and antibiotics. Serum electrolyte levels and blood gas analysis showed improvement during the treatment period. An abdominal ultrasound examination showed unilateral hydronephrosis. Grade-4vesicoureteral reflux on the left side was detected by voiding cystourethrogram. Renal scintigraphy also demonstrated an obstructive uropathy. Urine cultures obtained at admission yielded candida albicans. Flucanosole was added to antibiotic therapy. Endocrinological studies at admission revealed a greatly increased plasma aldosterone level of > 1161 ng/dL (ref: 90 ng/dL max). Serum levels of ACTH, 17-OH-progesterone were within the normal ranges. High serum cortisol level was considered normal glucocorticoid synthesis. According to these results, CAH could be excluded retrospectively. Considering the anamnestic data and the clinical and laboratory findings, the infant was diagnosed with secondary pseudohypoaldosteronism. The doses of prednisolone and fludrocortison were gradually reduced and discontinued on the 4th day of therapy. Oral sodium supplementation and antibiotic treatment were continued. The patient was referred to another hospital for surgical correction and follow up on the 17th day of therapy. His doctors reported that they had stopped sodium supplementation in the 6th month of life and repeated biochemical analysis showed no electrolyte abnormalities. Surgical correction was performed in the 9th month of life. At one and half year of follow up, his growth and development were normal and serum electrolyte levels were within normal limits.

Discussion

A secondary pseudohypoaldosteronism has been observed in infants secondary to obstructive uropathy, urinary tract infections, and small bowel resection or after kidney transplantation. In these patients, medical or surgical care of the primary disease re-establishes the normal response to aldosterone (1). Rodriguez-Soriano et al. demonstrated the entity of hyponatremia, hyperkalemia, metabolic acidosis and marked elevation of plasma aldosterone associated with obstructive uropathy or VUR in children (3). These data indicate that a hyperkalemic salt-losing state can arise in infants with obstructive uropathy and urinary tract infection as a consequence of tubular unresponsiveness to aldosterone. The underlying mechanism of this condition is still not known. Possible etiological factor is ureteral obstruction leading to profound changes in renal tubular cell function. Therefore, the response of the distal tubule to hormones is impaired. In the course of ureteral obstruction, inflammatory changes in renal parenchymal tissue development, leading to tubular interstitial fibrosis of varying degree and a reduced

number of filtering nephrons (4). Circulating toxic factors may damage aldosterone receptors. Kuhnle et al. (5) found a significant reduction of aldosterone receptors in a male newborn with obstructive uropathy and secondary PHA. Pyelonephritis may be a cause of secondary PHA in patients without obstructive uropathy. It seems that endotoxinemia is probably another factor contributing to hyponatremia. Watanabe et al. (6) demonstrated that infants with acute pyelonephritis exhibit mild hyponatremia and hyperkalemia in the acute phase regardless of the presence or absence of urinary tract anomalies. The risk of secondary PHA seems to be age dependent and the risk increases considerably before 3 months of age in patients. It is considered to be a certain physiological tubular resistance to aldosterone , which is obviously due to renal immaturity.

Melzi et al. (7) investigated 50 infants with pyelonephritis. They were observed in 17 infants < 3 months, accompanied by high plasma aldosterone concentration. All 50 children had severe urinary tract malformation. Our patient was a 29-day-old male infant with obstructive uropathy and VUR. He possessed all risk factors for the development of secondary pseudoaldosteronism. Maruyama et al. (8) reported secondary PHA caused by urinary tract infection in the presence of phimosis without urinary tract malformation. Urinary tract dilatation is increasingly being detected by antenatal ultrasound, with 1:800 pregnancies having an antenatally diagnosed uropathy. Despite improvement in technique, some infants with an abnormal urinary tract still avoid detection, and present during childhood with signs and symptoms of a urinary tract infection. Moreover, some children do not have the opportunity of antenatal ultrasound examination. Our patient had no report of fetal sonography. PHA may resemble CAH. Hyponatremia, hyperkalemia, dehydration, and metabolic acidosis are primary findings, leading to the diagnosis of CAH. Most cases reported in which the diagnosis of CAH was established initially before UTM and UTI were detected (9-11). Early diagnosis is essential since both conditions are potentially fatal and treatment differs significantly. Differential diagnosis may be achieved by urinanalysis and abdominal ultrasound scan. Our patient was initially diagnosed as CAH although the diagnosis was later excluded because bilateral hydronephrosis was detected in abdominal ultrasound. In addition, his blood adrenal precursors, and glucose levels were within normal range, however the aldosterone level was very high. All of these findings supported the diagnosis PHA. In conclusion, we emphasize that ultrasound scan should be performed on every male neonate or infant presenting with hyponatremia, acidosis and hyperkalemia to prevent time-consuming endocrinological studies which may delay the institution of an appropriate therapy. We also emphasize that electrolyte levels should be monitored in infants with obstructive uropathy or UTI in early infancy period. In addition, antenatal sonography is a valuable tool both for detecting obstructive uropathy and the early diagnosis of secondary PHA.

Table I. Laboratory findings in a male infant with urinary tract malformation.

Capillary blood	At Admission	At Discharge
pH	7.14	7.38
pCO_2 (mmHg)	15.3	39.5
pO_2 (mmHg)	47.4	40.2
s-HCO_3 (mmol/L)	5.2	20.6
BE* (mmol/L)	-21.3	-3.4
Hemoglobin (g/dL)	14.9	8.5
White blood cell count (/ mm^3)	52140	7780
Platelet count (/ mm^3)	684000	267000
Sodium (mmol/L)	113	134
Potassium (mmol/L)	10.2	3.5
Chloride (mmol/L)	87	102
Blood urea nitrogen (mg/dL)	136	20
Creatinine (mg/dL)	3.7	1
Aldosteron (ng/dL)	1161	865.7
Cortisol (μg/dL)	156.3	3.3
17 OH progesterone (ng/ml)	78.06	1.48

* Base excess

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