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A Case of Adult-Onset Bartter's Syndrome

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Bartter's Syndrome is characterized by renal potassium wasting with hypokalemia, metabolic alkalosis, increased renin-angiotensin-aldosterone system, normal blood pressure, resistance to the pressor effects of angiotensin II and juxtaglomerular cell hyperplasia. Most of the cases have been noted in the pediatric age group and adult-onset cases are very rare. We report a case of adult-onset Bartter's syndrome.

Key Words : *Bartter's syndrome, Metabolic alkalosis, Hypokalemia, Increased renin-angiotensin-aldosterone system, Juxtaglomerular cell hyperplasia*

INTRODUCTION

In 1962, Bartter et al.[1] described a clinical syndrome characterized by hypokalemia, metabolic alkalosis, hyperreninemia, hyperaldosteronism and normal blood pressure. Further findings include a resistance to the pressor effects of norepinephrine and angiotensin II. Histologically, there is hyperplasia of the juxtaglomerular cell. It occurs mostly in childhood or adolescence, and initial presentation in patients over 40 years of age was very rare[2]. Bartter's syndrome is a rare cause of chronic hypokalemic alkalosis in adults. Neverthless, Neverthless, the syndrome has aroused great interest in many clinical investigators because it may provide new insights in to renal electrolyte metabolism and the pathophysiology of hypertension[3].

We recently experienced a case of adult-onset Bartter's syndrome who showed hypokalemia, metabolic alkalosis, normotension, hyperreninemia, hyperaldosteronism and juxtaglomerular cell hyperplasia.

CASE REPORT

A 40-year-old woman was admitted to the Chonnam University Hospital, with a three months history of severe generalized weakness and fatigue.

The first episode occurred three years ago and spontaneously remitted from it following bed rest. she denied ingestion of licorice, diuretics, laxative or any other medication, and she had no significant nausea, vomiting or diarrhea.

The patient appeared relatively well and had a height of 154 cm and a weight of 52 kg. The pulse rate was 98/min, the blood pressure 100/70 mmHg, and the respiration rate 18/min. The remainder of her physical examination was within normal limits.

Laboratory findings included persistent hypokalemic alkalosis with 2.4 mEq/L for serum potassium, 32.7mEq/L for serum bicarbonate, 86.1mmHg for PaO_2, 48mmHg for $PaCO_2$ and 32mmol/L for total CO_2 content. The pH of plasma was 7.44 and that of urine 7.0. Electrocardiography revealed PR prolongation and T wave-flattening. Serum sodium averaged 139 mEq/L, chloride 85mEq/L, total calcium 5.1mEq/L, ionized calcium 2.0mEq/L, inorganic phosphorus 4.7mg/dl, magnesium 1.6mEq/L, uric acid 13.4mg/dl and serum osmolality 289mosl/kg. The blood urea nitrogen was 44.0mg/dl, serum creatinine 1.7mg/dl and creatinine clearance 35ml/min. There were no proteinuria, hematuria and abnormality of the urinary sediment. Pertinent studies of the blood and serum revealed a normal hemoglobin level, hematocrit value, white blood cell count, total protein, albumin, alkaline phospha-

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Table 1. Clinical Manifestations Before and After Treatment

	Before treatment	After treatment
Muscle weakness	+	-
Paresis	-	-
Fatigue	++	-
Tetany	-	-
Paraesthesia	-	-
Polyuria	+	-
Polydipsia	++	-
Nocturia	+	-
Enuresis	+	-
Constipation	-	-
Salt craving	+	-
Dehydration	+	-
Orthostatic hypotension	+	-
Failure to thrive	-	-
Delayed growth	-	-
Short stature	-	-
Hypogonadism	-	-
Mental retardation	-	-
Gout	-	-
Chondrocalcinosis	-	-

tase and transaminase levels. Twenty four-hour urinary excretion of sodium was 183mEq, potassium 67mEq, chloride 247mEq, calcium 120mg, protein 150mg, glucose 30mg and urine amounts 2,300cc. The urinary specific gravity was 1.010 and osmolality 310mosm/kg. The plasma renin activity was 48.2ng/ml/hr and aldosterone level 34.4ng/dl. FE_{Na} was 2.6%, FE_{Cl} 5.7%, FE_{K} 55%, and $FE_{Uric\ acid}$ 8.2%. Thiazide and furosemide were not detected in her urine by high-performance liquid chromatography at the Department of Pharmacology, Chonnam University Medical School, Kwangju, Korea.

The renal biopsy was performed without difficulty. The biopsy specimen contained up to 8 glomeruli per section. Some glomeruli revealed focal and segmental glomerulosclerotic changes. Juxtaglomerular hyperplasia of varying degrees and multiple vacuolization of proximal tubule due to chronic hypokalemia were noted (Fig. 1, 2). The tubules, interstitium and blood vessels were entirely normal with no scarring or atrophy. The constellation of hypokalemia, relative hypotension, increased renin activity, increased aldosterone level and juxtaglomerular hyperplasia substantiated the diagnosis of Bartter's syndrome.

Following the renal biopsy, the patient had been treated with potassium chloride, 40mEq twice a day, spironolactone, 50mg three times a day, propranolol, 20mg three times a day, enalapril, 2.5mg a day and indomethacin, 25mg three times a day. The administration of medications led to an increase in serum potassium to 3.5 to 4.5mEg/L.

In association with this improvement in the

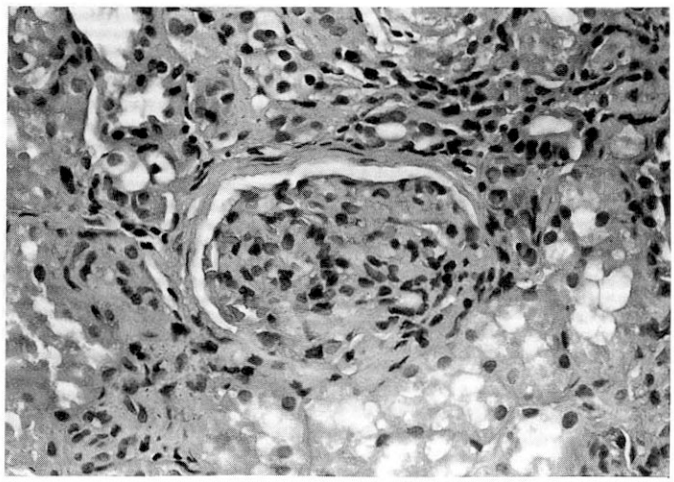

Fig. 1. Increased number of cells lie in the afferent arteriole at the hilum of the glomerulus and multiple vacuoles in the proximal tubules.. Light microscopy. Homatoxylin and eosin stain, origisnal magnification X 200.

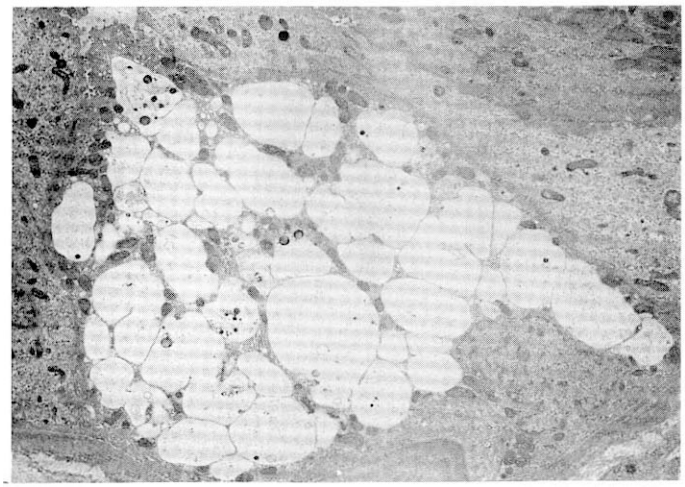

Fig. 2. Varying sized multiple vacuoles in the proximal tuble. Electron microscopy. X 8000.

serum potassium concentration, the patient's muscle strength was rapidly recovered and the patient did well for the following two months (Table 1).

DISCUSSION

Bartter's syndrome consists of hypokalemia due to renal potassium wasting, elevated plasma renin activity and aldosterone secretion, normal blood pressure, hyporesponsiveness of blood pressure to infused angiotensin II and hyperplasia of granular cells of the juxtaglomerular apparatus of the kidney[1]. The clinical symptoms of Bartter's syndrome are dominated by hypokalemia[3]. Proximal muscle weakness may cause incapacity and force families to seek medical help.

Gastrointestinal symptoms include anorexia and constipation due to renal water loss and hypokalemic ileus. Clinically, Bartter's syndrome can be divided into at least two groups : one group with an eary (infancy), and the other with a late onset of symptoms. Neonatal Bartter's syndrome is characterized by the intrauterine onser of polyuria, leading to polyhydroamnios between the 22nd and 24th weeks of gestation. In adults, fatigue, proximal muscle weakness and tetany are the most common presenting features[4].

The primary etiolgy of Bartter's syndrome is still unknown. With the findings of abnormalities in plasma and urinary prostaglandins, many investigators considered a defect in prostaglandin homeostasis as the primary defect[5]. Elevated prostaglandin levels could explain peripheral vasodilatation and a lack of responsiveness to pressors. The inhibition of chloride transport in the loop of Henle by prostaglandins, especially in the face of hyperaldosteronism, would lead to potassium wasting and alkalosis[6]. However, prostaglandin inhibition does not completely cure the defects in Bartter's syndrome. Also, continued use of prostaglandin inhibitors may not result in continuous benefit to patients with Bartter's syndrome[7]. Stein[8] reviewed the published material and the data derived in his laboratory with Bartter's syndrome, and concluded that Bartter's syndrome may have more one underlying etiology.

Bartter[9] and Baehler et al[10] favored primary chloride wasting as the defect of Bartter's syndrome. These hypotheses all consider the resulting potassium deficiency as the cause of the prostaglandin, bradykinin, kallikrein, and vasopressor abnormalities. Sodium, chloride, and potassium losses result in volume depletion, increased aldosterone levels, and metabolic alkalosis. Bartter's syndrome may be mimicked by magnesium deficiency, diuretic use or vomiting. Magnesium depletion causes kaliuresis, diuretics cause potassium and volume depletion and vomiting causes renal potassium wasting and volume depletion.

Treatment is generally focused on the repair of hypokalemia by inhibition of the renin-angiotensin

-aldosterone or the prostaglandin-kinin system. Potassium supplementation, magnesium repletion, propranolol, spironolactone, prostaglandin inhibitors and conventing enzyme inhibitors all have been advocated, but each has met with limited success[8].

In this case, the patient was diagnosed to be adult-onset Bartter's syndrome due to hypokalemia, relative hypotension, increased renin activity, increased aldosterone level and juxtaglomerular hyperplasia. In appropriate medical therapy, a positive potassium balance and an increase in serum potassium concentration. In association with this improvement in the serum potassium concentration, the patient's muscle strength was rapidly recovered and the patient did well for the following two months.

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