Case Report

Liddle's Syndrome Presenting with Periodic Paralysis

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Abstract

Liddle's syndrome is a rare cause of secondary hypertension. Identification of this disorder is important as treatment differs from other forms of hypertension. We report a case of a 53 year old gentleman who presented with periodic paralysis and was subsequently found to have hypertension, hypokalemia and metabolic alkalosis. He was further evaluated and found to have hyporeninemic hypoaldosteronism and was diagnosed to have Liddle's syndrome.

Introduction

One of the indications for screening a hypertensive patient for secondary causes is associated hypokalemia.[1] There are a few conditions associated with this syndrome of hypertension and hypokalemia. We describe an interesting case of a patient with a rare syndrome of hypertension, hypokalemia and periodic paralysis.

Case Report

A 53 year old gentleman presented with history of two episodes, three months apart, of sudden onset, rapidly progressive quadriparesis which began in the lower limbs. He visited a local physician who treated him with intravenous injections and fluids. His weakness gradually resolved within three days (details of the treatment given to the patient at that point of time were not available). Three months after the second episode of quadriparesis, he came to our hospital for further evaluation. He was detected to have hypertension one and half years back but had not been on any treatment for the same. He was also a known case of bipolar affective disorder for nearly twenty years with multiple episodes of depression and one episode of severe mania requiring inpatient treatment five years back. He had been on treatment with sodium valproate controlled release 300 mg in the morning and 500 mg at night for the last five years. There was no family history of hypertension or episodes of limb weakness.

On evaluation, he was found to have hypertension (170/100 mm of Hg). The rest of his physical examination was unremarkable. His investigations revealed hypokalemia (2.2 mmol/L) and metabolic alkalosis (venous bicarbonate of 30 mmol/L). The arterial blood gas revealed a pH of 7.547 and acid base excess of 4.1. His serum creatinine (1.3 mg %) and sodium (137 mmol/L) were within normal limits. His serum cortisol levels were within normal limits (8 am and 4 pm cortisol values were 11.4 and 8.96 microgram/dL respectively). His serum aldosterone level was <10 pg/ml and plasma renin was < 0.01 ng/ml/hr. Computed tomography (CT) of the abdomen was negative for adrenal enlargement or adenoma.

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In a patient with hypertension and hypokalemia, one would consider possibilities of hyperaldosteronism, diuretic therapy and less common causes like Cushing's syndrome, licorice ingestion, some forms of congenital adrenal hyperplasia, Liddle's syndrome and rare renin secreting tumors.[2] In the setting of hypokalemia, the other possibility considered in this patient was one of a proximal renal tubular acidosis secondary to prolonged use of sodium valproate, though the presence of metabolic alkalosis in this patient effectively ruled this out. The patient described here had no history of diuretic therapy or licorice ingestion. His serum cortisol levels were normal ruling out the possibility of Cushing's syndrome. One would not consider congenital adrenal hyperplasia at this age. His CT abdomen was negative for adrenal enlargement or masses and he had low renin and aldosterone levels. Hence, in the setting of hypokalemia, metabolic alkalosis and hypertension with hyporeninemic hypoaldosteronism, a diagnosis of Liddle's syndrome was made. The episodes of quadriparesis were probably due to periodic paralysis secondary to severe hypokalemia. It was decided to treat the patient with amiloride. However, amiloride and triamterene were available only in combination with thiazide diuretics or furosemide which can worsen hypokalemia. Hence he was started on spironolactone 25 mg twice daily. During one year follow up, his serum potassium improved to about 4.5 mmol/L but his blood pressure was not under good control and his blood pressure during his last visit was 150/100 mm of Hg. He did not have any further episodes of limb weakness.

Discussion

Liddle's syndrome is a rare autosomal dominant condition characterized by primary increase in collecting tubule sodium reabsorption and secretion of potassium in majority of the cases.[2] Liddle et al described a familial syndrome of severe hypertension, hypokalemia, and metabolic alkalosis mimicking hyperaldosteronism.[3] However these patients have low renin and aldosterone levels and there is conservation of sodium and excretion of potassium in the absence of mineralocorticoid excess.[2] Genetic studies have revealed that mutations affecting cytosolic tail of the ß subunit of the epithelial sodium channel (ENaC) could lead to this disorder.[3] These mutations apparently cause constitutive activation of the epithelial sodium channel of the luminal membrane of the collecting tubule and result in excessive absorption of sodium leading to volume expansion. This in turn causes hypertension, leading to inhibition of renin and aldosterone secretion. A lack of down-regulation of the

epithelial sodium channels despite persistent volume expansion is the basis behind the pathogenesis of this syndrome. A similar lack of down-regulation of the activity of the epithelial sodium channels may underlie more common forms of low-renin hypertension.[3]

Patients with Liddle's syndrome present with hypertension, often hypokalemia (in most cases) and metabolic alkalosis, similar to that seen in mineralocorticoid excess.[3] Patients mostly present at a young age though occasionally cases may not be detected until well into adulthood. However presentation in the 6th decade of life or later has been reported very rarely.[4,5] Periodic paralysis as a presenting symptom has not been reported in patients with Liddle's syndrome. However muscle weakness associated with hypokalemia (especially in lower limbs) has been described, though rarely, in elderly patients with Liddle's syndrome.[6] It is important to screen for this condition in patients with hypertension, hypokalemia and metabolic alkalosis, as the treatment of Liddle's syndrome differs from other forms of essential or secondary hypertension.[2] Potassium-sparing diuretics like amiloride and triamterene which directly close the sodium channels are effective in Liddle's syndrome whereas mineralocorticoid antagonist spironolactone is ineffective since the increase in sodium channel activity is not mediated by aldosterone in this disorder.[2]

References

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OBITUARY

Dr. K. Ramamoorthy

A Great Pillar of Medical Fraternity

In the death of Dr. K. Ramamoorthy we have lost one of the great conscience keepers of the much maligned noble Medical Profession. It is often said that the, knowledge of medicine is a 'Science' and the practice of it an 'Art', and very rarely both of them are present in significant measure in a doctor. Dr. K. Ramamoorthy had the privilege of being able to combine these two in an intricate manner for the benefit of his patients, combining as it were all the virtuous qualities of a human being with thorough professional excellence. His entire life was dedicated to serving human suffering and in his life span he exhibited all the qualities of a true karma yogi namely simplicity, humility, honesty, uprighteousness, unpretentiousness and sincerity. In our profession we do come across cases which are tricky and difficult to diagnose despite best efforts and in such situations, Dr Ramamoorthy's help was sought, and his contribution was always significant.

Dr. K. Ramamoorthy was equally involved in academics and his contribution in this field was remarkable. He had also participated on various API forums as a speaker. He had made extensive contribution to JAPI and API Text Book of Medicine.

It will not be incorrect to say that in his death the medical profession has lost a person of immeasurable qualities of heart and mind. Such men, seldom come often.

May his soul rest in peace.

Dr. S. Jayaram
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