

Liddle Syndrome in a Six-Year-Old Girl: A Case Report

Sumera Akram¹, Abdul Rehman², Muhammad Ahmed Khan³

¹Assistant Professor, Department of Pediatrics, Bacha Khan Medical College, Mardan KPK, Pakistan

²Associate Professor, Department of Pediatrics, Bahawal Victoria Hospital, Bahawalpur Punjab, Pakistan

³Assistant Professor, Department of ENT, National University of Medical Sciences, Rawalpindi Pakistan

ABSTRACT

Liddle syndrome is a cause of hypertension among children due to mutation in the epithelial sodium channels (ENaC) located in the kidneys. It typically presents with hypertension, hypokalemia, metabolic alkalosis with low renin and aldosterone levels. Although, most cases are children, but adults also present with this disorder owing to late diagnosis. Amiloride and triamterene efficiently improve the condition. Here we present the case of a 6-year-old girl admitted with history of hypertension, diarrhea, vomiting, weakness and palpitations on and off for the last four years. Laboratory investigations revealed metabolic alkalosis, decreased renin and aldosterone levels, hypokalemia and an inverted T wave, U wave and prolonged QT interval on ECG. Any pediatric case presenting with hypertension and electrolyte imbalance should promptly raise suspicion of Liddle syndrome. Timely diagnosis and management play a key role in reducing morbidity and mortality.

Key Words: Electrolyte imbalance, Hypertension, Hypokalemia, Liddle syndrome

Correspondence:

Muhammad Ahmed Khan
Email: akawan79@gmail.com

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Introduction

Liddle syndrome, a rare cause of early hypertension was first described by Liddle and coworkers in 1963.¹ This rare syndrome has an autosomal dominant inheritance and typically comprises of hypertension, hypokalemia and metabolic alkalosis.² Although the affected individuals have high blood pressure since childhood, early diagnosis is missed in some cases.³ Hypokalemia, associated with this disorder causes muscle weakness, fatigue, pain and palpitations.⁴ Liddle syndrome is often termed as “pseudoaldosteronism” because of typical features of hyperaldosteronism (i.e. hypertension, hypokalemia and metabolic alkalosis) in the absence of raised aldosterone levels.⁵ The syndrome is

caused by mutation in genes responsible for making protein complex called epithelial sodium channel (ENaC).⁶ These channels are present in many parts of the body including kidneys, where they transport sodium into cells. Gene mutations cause alteration in sodium channel structure, its subunit proteins are not degraded resulting in abnormally high sodium and water reabsorption, leading to hypertension.⁶ Liddle syndrome is treated effectively with amiloride or triamterene (potassium sparing diuretic) and ENaC inhibitor combined with low sodium diet.⁷ The affected cases can present with complications like hypertensive encephalopathy, myocardial

infarction, cerebrovascular ischemia, nephrocalcinosis and retinopathy, etc.

Case Report

A 6-year-old girl was admitted in Pediatric ICU of Bahawal Victoria Hospital Bahawalpur, Pakistan with history of hypertension, diarrhea, vomiting, weakness and palpitations on and off for 4 years. She had generalized body weakness more marked in lower limbs and neck muscles. Her birth history, feeding history, vaccination and developmental history were unremarkable except for growth retardation. Her height, weight and occipitofrontal circumference were below the 5th centile. Her family history revealed sudden death of one younger male sibling at two years of age due to similar complaints of diarrhea, vomiting and weakness. On examination, her BP was 200/110 mmHg. Her blood pressure was same in all four limbs. She had abnormal facies with prominent ears and a triangular face. Laboratory investigations revealed hypokalemia with serum potassium <2 mEq/L. Renal function tests, serum calcium levels and echocardiography were normal. Electrocardiogram (ECG) revealed signs of hypokalemia with an inverted T wave, U wave and prolonged QT interval. Potassium replacement was initiated and blood pressure was controlled with sodium nitroprusside and sublingual captopril. Her serum potassium levels and blood pressure improved gradually. ABGs showed metabolic alkalosis with raised serum HCO₃ levels (44 mmol/L) and pH (7.92) and decreased serum chloride (53 mmol/L) (Table I). Hypokalemia, metabolic alkalosis and hypertension raised suspicion of Liddle syndrome in this child. Next renin and aldosterone levels were checked for confirmation of our diagnosis. Both levels were markedly decreased (Renin 0.3 ng/mL/h, Aldosterone 0.5 ng/dL) (Table I). She was put on tablet amiloride (5mg, twice daily), to which she responded and hypertension gradually improved.

She was discharged after a week and advised regular follow-up every four weeks.

Discussion

In pediatric cases with hypertension, clinicians should suspect renal, vascular, cardiac (coarctation, etc.) or endocrine disorders (hyperthyroidism or pheochromocytoma). However, children presenting with hypertension along with electrolyte imbalance should raise suspicion of monogenic causes of hypertension, which include Liddle syndrome, Gordon syndrome and familial hyperaldosteronism.⁸ These disorders are called monogenic because they are caused by single gene mutations, which are inherited in Mendelian pattern.^{8,9} To investigate further, serum renin and aldosterone should be checked. Serum renin level is decreased uniformly in all these diseases; however, serum aldosterone is decreased in Liddle syndrome in contrast to others.^{8,9}

Literature search revealed that only one case of Liddle syndrome has been reported in Pakistan by Aziz et al. in 2016 in a 10-month-old female.³ Another research carried out by Gilani et al. in Rawalpindi, Pakistan reported 80 cases of young hypertensives with renin-angiotensin-aldosterone disorders, but they did not find any case of Liddle syndrome in their cohort.¹⁰ Teoh et al. reported three cases of Liddle from Department of Pediatrics, University of Louisville, Kentucky USA with almost similar age group and clinical pictures as our case.⁸ Patel and Kuriacose reported a case of Liddle syndrome from Johnson City, Tennessee USA, but the age of the patient was 48 years.² Tetti et al. reported a case of Liddle in a 13-year-old Caucasian boy with history of sudden death of a sibling, just like in our case.¹¹

Table I: Detailed laboratory investigations of the patient

Laboratory Test	Patient result	Normal Range
Hemoglobin	10.3 mg/dL	12-18 mg/dL
Total leucocyte count	7.7 x 10 ³ / mm ³	4-11 x 10 ³ / mm ³
Platelet count	193 x 10 ³ / mm ³	150-400 x 10 ³ / mm ³
Serum bilirubin	14 mg/dL	1-17.1 mg/dL
Serum alanine transaminase	38 U/L	<40 U/L
Serum alkaline phosphatase	163 G/dL	<279 G/dL
Serum urea	42 mg/dL	10-50 mg/dL
Serum creatinine	0.9 mg/dL	0.6-1.1 mg/dL
Serum magnesium (Mg)	0.94 mmol/L	0.85-1.10 mmol/L
Serum sodium (Na)	142mmol/L	136-146 mmol/L
Serum potassium (K)	<2mmol/L	3.5-5.1 mmol/L
Serum chloride level	53 mmol/L	98-108 mmol/L
Serum bicarbonate	44 mmol/L	20-31 mmol/L
Serum aldosterone level (Recumbent position)	0.5 ng/dl	3-90 ng/dl
Plasma renin level	0.3 uIU/L	8-35 uIU/L
Blood sugar random	126mg/dL	<140mg/dL
Urine chloride	64 mmol/L	140-250 mmol/L
17-hydroxyprogesterone	6 nmol/L	<10nmol/L (females)
Serum calcium	2.3 mmol/L	2.2-2.7 mmol/L

Conclusion

Any pediatric case presenting with hypertension and electrolyte imbalance should promptly raise suspicion of Liddle syndrome. Timely diagnosis and management can reduce morbidity and mortality. Since, it is an autosomal dominant disorder, other family members and siblings should also be screened for a definitive diagnosis of this rare illness.

References

- Liddle GW, Bledsoe T, Coppage WSJ. A familial renal disorder simulating primary aldosteronism but with negligible aldosterone secretion. *Trans Assoc Am Phys.* 1963; 76: 199-213.
- Patel P, Kuriacose R. Liddles syndrome: A case report. *Saudi J Kidney Transpl.* 2015; 26(4): 769-72. Doi: 10.4103/1319-2442.160211.
- Aziz DA, Memon F, Rahman A, Ali M. Liddle's syndrome. *J Ayub Med Coll Abbottabad* 2016; 28(4): 809-11.
- Bogdanovic R, Kuburovic V, Stajic N, Mughal SS, Hilger A, Ninic S, et al. Liddle syndrome in a Serbian family and literature review of underlying mutations. *Eur J Pediatr.* 2012; 171(3): 471-8. Doi: 10.1007/s00431-011-1581-8.
- Yang KQ, Xiao Y, Tian T, Gao LG, Zhou XL. Molecular genetics of Liddle syndrome. *Clin Chim Acta.* 2014; 436: 202-6. Doi: 10.1016/j.cca.2014.05.015.
- Hanssen JH, Nelson-Williams C, Suzuki H, Schild L, Schimkets R, Lu Y et al. Hypertension caused by a truncated epithelial sodium channel gamma subunit: genetic heterogeneity of liddle syndrome. *Nat Genet.* 1995; 11(1): 76-82. Doi: 10.1038/ng0995-76.
- Yamaguchi E, Yoshikawa K, Nakaya I, Kato K, Miyasato Y, Nakagawa T, et al. Liddle's-like syndrome associated with nephrotic syndrome secondary to membranous nephropathy: the first case report. *BMC Nephrol.* 2018; 19(1): 122. Doi: 10.1186/s12882-018-0916-3.
- Teoh Z, Shah S. A case report of three children with secondary hypertension caused by Liddle syndrome. *Clin Nephrol Case Stud.* 2020; 8: 37-40. Doi: 10.5414/CNCS109972.

9. Vehaskari VM. Heritable forms of hypertension. *Pediatr Nephrol.* 2009; 24: 1929-37. Doi: 10.1007/s00467-007-0537-8.
10. Gilani M, Asif N, Akram A, Gilani M, Ijaz A, Malik SS. Spectrum of rennin angiotensin aldosterone system disorders in young hypertensives. *J Pak Med Assoc.* 2018; 68(8): 1179-82. PMID: 30108382.
11. Tetti M, Monticone S, Burrelo J, Matarrazo P, Veglio F, Pasisi B, et al. Liddle syndrome: Review of literature and description of a new case. *Int J Mol Sci.* 2018; 19(3): 812. Doi: 10.3390/ijms190300812.