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Case Report

Bartter Syndrome

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Abstract

In 1962 Bartter et al. described a new disease entity in two African American who presented with metabolic alkalosis, hyperplasia of juxtaglomerular apparatus, and normotensive hyperaldosteronism. Over the years, several phenotypic and genotypic variants of the original descriptions of Bartters syndrome (BS) have been identified. It is an uncommon inherited renal tubular disorder with hyponatremia, hypokalemia, hypochloremic metabolic alkalosis, hypereninemia with normal blood pressure associated with increased urinary loss of sodium, potassium, calcium and chloride. A history of consanguineous marriage is present in many families. Most cases of BS are present in neonates. Prenatally, neonatal BS can be diagnosed by finding elevated amniotic fluid chloride and aldosterone levels.

Keywords: Bartter Syndrome, Metabolic disorder, Inherited renal tubular disorder.

Introduction

Bartter syndrome is a rare autosomal recessive disorder characterized by-

1. Hypokalemia
2. Metabolic alkalosis
3. Hyperreninemia
4. Hyperaldosteronism
5. Normal blood pressure
6. Urinary wasting of K^+, Na^+,Cl^- and Ca^+
7. Elevated urinary prostaglandin (PGE2) levels.

As the disorder is uncommon, the diagnosis is often missed. Children present in infancy with- Polyuria, Polydipsia, Vomiting, Constipation and Failure to thrive.

In the infantile form, hypercalciuria and nephrocalcinosis are seen. Fetal polyuria may cause polyhydramnios.

Older children may present with-

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Recurrent episodes of dehydration, muscle weakness, muscle cramps, blood pressure is low normal for age.

The molecular basis of Bartter syndrome is an inability to reabsorb chloride and sodium in the thick part of the ascending limb of loop of Henle due to defects in ion transporters.Increased delivery of sodium chloride to distal parts of the nephron leads to salt wasting, hypokalemia, polyuria, volume contraction and stimulation of the renin-angiotensin-aldosterone axis. While urinary sodium is recovered by an increase in aldosterone mediated activity of the epithelial sodium channel, loss of chloride with ammonium or potassium results in hypochloremic metabolic alkalosis and hypokalemia. Hypokalemia, volume contraction and elevated angiotensin increase intrarenal prostaglandin E2 synthesis, which stimulates the renin-angiotensin-aldosterone axis. BS should be suspected in any child with history of failure to thrive and metabolic alkalosis. Early diagnosis and treatment with NSAIDs are lifesaving. To the best of our knowledge our patient is the first reported case of Bartter syndrome in Bangladesh.

Case History

Nusrat (Figure 1) 1year 15 days old, duely immunized, severely underweight child of a non-consanguineous parent, admitted in Diabetic Association Medical College Hospital on 19 July 2018 at 10.30 am with the complaints of recurrent episode of vomiting after each feeding with progressive loss of weight, occasional loose motion for about 3 months. For those complaints she was admitted in Dhaka Medical College Hospital and diagnosed as a case of MAM (Moderate acute malnutrition) with dys-electrolytemia and received treatment. But there was no improvement rather worsening. Then she was admitted in Faridpur Medical College Hospital and diagnosed as SAM (Severe acute malnutrition) and got treatment. Despite the treatment her condition had been worsening day by day. She was admitted in Diabetic Association Medical College Hospital for better management. Her mother also said that she had been suffering from irregular fever for ten days, subsided by taking antipyretic. She was not exclusive breast fed. From four month of age she ate other feeding like solid foods. Her mother said that she usually drinks more

water and micturates large amount of urine. On general examination she looks miserable and irritable, weighs 5.2 kg, WHZ:< -3SD (severely malnourished- SAM), moderately anaemic, temperature 101ºF, BCG mark present. There was no skin rash .Her bowel and bladder habit was normal. Other systemic examination revealed no abnormality.

Investigations findings:

Hemoglobin Total Count	12.8g/dl	Differential Leucocyte Count	
WBC	14.31×10^9/L	Polymorphs	35.9%
RBC	5.35×10^{12}/L	Lymphocytes	52.7%
Platelets Count	216×10^9/L	Monocytes	10.3%
		Eosinophils	0.1%
		Basophils	1.0%

Serum Electrolytes report:

Name of Investigation	Finding according to date						
	1 June 2018	5 June 2018	7 June 2018	9 June 2018	13 June 2018	14 June 2018	19 June 2018
Serum Na^+	125	123	118	118	114	113	123
Serum K^+	1.9	1.8	1.8	1.46	1.9	1.6	1.8
Serum Cl^-	80	82	70	72	83	67	85

Other investigation reports:

Name of Investigation	Finding	Date
Serum $HCO3^-$	33 mmol/l	09-06-18
Serum P^H	8.0	10-06-18
Serum Ca	8.27 mg/dl	10-06-18
Blood for osmolality	236.2 mOsmol/kg	19.6.18
Spot Urine Electrolyte		
● Urine Cl^-	52 mmol/l	10-06-18
● Urinary calcium	130.60 mg/24 hr	11.6.18
USG of whole abdomen	Billateral mild hydronephrosis	19-07-18

We discharged the patient on 21-07-18 with advice to come with report of Serum Renin and Aldosterone level.

Aldosterone/Plasma renin Ratio (CLIA):

Posture	Ref range renin direct micro IU/ml	Ref range aldosterone ng/ml	Interpretation
Upright	4.4-46.1	2.52-39.2	normal
Supine	2.8-39.9	1.76-23.2	normal
Nusrat (patient)	>50000	76.50	

Thus, confirm diagnosis Bartter syndrome.

The case was prescribed IBUPROFEN (syrup) 30mg/kg in daily single dose along with other supportive treatment. She was discharged after 7 days with an advice to come after 1 month (Figure 2).

After 1 month she weighs 6.7kg as compared to 5.2 kg on admission, feeds well tolerated, polydipsia & polyuria almost subsided.

Comparative serum electrolyte reports after given treatment and follow up		
Name of Investigation	Finding according to date	
	20 August 18	14 October 18
Serum Na^+	135.7	136.4
Serum K^+	2.9	3.65
Serum Cl^-	96.1	98.8

Comparative serum bicarbonate reports before and after given treatment		
Name of Investigation	Finding according to date	
	09 June 18	14 October 18
Serum $HCO3^-$	33 mmol/l	21.16 mmol/L

Discussion

It is an uncommon inherited renal tubular disorder with hyponatremia, hypokalemia, hypochloremic metabolic alkalosis, hyperreninemia with normal blood pressure associated with increased urinary loss of sodium, potassium, calcium, and chloride.[1] The primary defect in BS is an impairment in one of the transporters involved in sodium chloride reabsorption in the thick ascending limb of loop of Henle viz., Na-K-2Cl cotransporter (NKCC2) or apical K channel (ROMK) or basolateral chloride channel (ClCNKB).[2] BS is transmitted as an autosomal recessive disorder. The estimated prevalence is approximately 1 per million for BS in the western population. However, the prevalence of heterozygotes may be as high as 1 percent.[3] A history of consanguineous marriage is present in many families. Most cases of BS are present in neonates. Prenatally, neonatal BS can be diagnosed by finding elevated amniotic fluid chloride and aldosterone levels. Only isolated case reports but no case series have been reported so far from Bangladesh.This is the largest series of BS reported so far from this subcontinent.[4-8]

BS should be suspected in any child with history of failure to thrive and metabolic alkalosis. Early diagnosis and treatment with NSAIDs are lifesaving.

To the best of so far our knowledge, it is the first case series to document the clinical profile of BS from Bangladesh. The exact incidence of BS is not known. In Costa Rica, incidence of neonatal Bartter's from live births is estimated

as one per 1.2 million.[9] In Kuwait, it was estimated as 1.7 per million population and in Sweden as 1.2 per million population.[10] The age at admission ranged from 2 to 15 months, with the mean age of 6.45 months which compares with the two published case series.[5-7] In this study, most of the children were male, whereas Abdel-al *et al*.'s series had female predominance and Dillon *et al*.'s series showed equal sex distribution.[5-7] In Abdel-al *et al*.'s study, 11patients (85%) had growth failure, two had nephrocalcinosis (15%), and one had renal failure.[10] The study by Garel *et al*. showed nephrocalcinosis in all the five children by computed tomography scan and ultrasonography.[11]

The study by Abdel-al *et al* also showed hypokalemia, hypochloremia, metabolic alkalosis, and hyperreninemia in all the patients.[10] None of the children in our series were hypertensive despite high renin and aldosterone levels.

Renal biopsy was not performed in our children. The study by Shalev *et al*. revealed mild focal tubulointerstitial fibrosis and minimal mesangial proliferation but no glomerulosclerosis in kidney biopsies from two 7-year-old patients.[12]

Dillon *et al*. used indomethacin in six of ten children for 6 to 24 months.[9] In the study by Abdel-al *et al*., all patients were treated with an aldosterone antagonist (spironolactone) and a prostaglandin synthetase inhibitor (indomethacin or aspirin) sequentially.[10] Growth hormone therapy was not given to our children. But studies have showed that nearly all patients with BS have growth retardation and are given growth hormone therapy along with potassium and indomethacin. A case report showed an association between BS and isolated familial growth hormone deficiency, with growth hormone therapy providing good results.[13]

Abdel *et al*. showed significant catch-up growth in 30.76% and increase in serum potassium value in 61.53%. One baby died (7.69%) of severe pneumonia with respiratory failure from hypokalemic myopathy.[10] The study by Dillon *et al*. showed catch-up growth in all patients treated with indomethacin therapy with remarkable clinical and biochemical improvement.[9] Usually prognosis in many cases is good, with patients being able to lead fairly normal lives.[6]

Genetic studies were not done in this case due to nonavailability of such specialized laboratories in our region. There is no direct correlation between the clinical phenotype and the underlying genotypic abnormality, even with well-characterized defects in a single transporter. However, more severe and earlier clinical manifestations may be seen with mutations leading to defects in Na-K-2Cl cotransporter and the luminal potassium channel.[14]

Figure 1: Nusrat on admission before diagnosis

Figure 2: Nusrat after diagnosis and starting of treatment and during discharge from hospital.

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