TRANSIENT PSEUDOHYPOALDOSTERONISM TYPE 1 ASSOCIATED WITH URINARY TRACT INFECTION AND POSTERIOR URETHRAL VALVE: CASE REPORT

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ABSTRACT

Persistent, severe neonatal hyponatremia coexisting with hyperkalemia and metabolic acidosis though not a very common yet is a fatal condition. Among the differential diagnosis of gastrointestinal fluid loss, salt loosing congenital adrenal hyperplasia and type IV renal tubular acidosis, Pseudohypoaldosteronism Type 1 (PHA 1) should also be kept in mind. Here we report a case of 2 months old baby boy with poor feeding, failure to thrive and persistent vomiting. His biochemical profile revealed severe hyponatremia, hyperkalemia, metabolic acidosis and raised Plasma Aldosterone and Plasma Active Renin Mass Concentration (ARC). Child had severe multi drug resistant urinary tract infection by Klebsiella oxytoca complicating obstructive uropathy caused by posterior urethral valve. Subsequently the PHA 1 subsided once the child was treated successfully for urinary tract infection and posterior urethral valve was removed surgically. Thus, highlighting association of urinary tract infection and posterior urethral valve with development of transient PHA type-1.

Key Words: Neonatal hyponatremia, Urinary tract infection, Transient pseudohypoaldosteronism type 1.

This case report can be cited as: Younas A, Ali A, Malik SS, Aamir M, Haroon ZH, Khadim MT. Transient pseudohypoaldosteronism type 1 associated with urinary tract infection and posterior urethral valve: case report. Pak J Pathol. 2019; 30(4): 113-115.

INTRODUCTION

Pseudohypoaldosteronism type 1 (PHA 1) is a rare disorder affecting about one in 47,000-80,000 per live births [1]. This serious condition occurs due to resistance of epithelial Sodium channels (ENac) or ameloride sensitive channels to aldosterone located in principle cells of renal cortical collecting tubules. PHA 1 is further sub divided into primary (i.e. Autosomal dominant PHA 1 (Renal) and Autosomal recessive PHA 1 (multiple target organ defects) and secondary or transient type. Primary PHA Type 1 results due to various mutations of NR3C2 gene encoding mineralocorticoid receptors [2,3]. While secondary PHA Type-1 has found to have association with urinary tract infections and urinary tract anomalies. Physicians if timely advice urinary sodium and plasma active renin concentration and aldosterone levels in scenarios of severe hyponatremia and hyperkalemic metabolic acidosis can easily pick this dangerous but treatable condition

CASE REPORT

A 2 months old baby boy was referred to our institute for workup of poor feeding, failure to thrive, frequent vomiting and irritability with normal genitalia. He was born full term via cesarean section with a low birth weight of 2 kgs. Antenatal ultrasonography had revealed bilateral hydronephrosis. Soon after birth, baby developed difficulty in passage of urine with poor urine stream. Micturating Cystourethrogram revealed irregular trabeculated outline of bladder with two narrow out pouchings suggestive of bladder diverticulae and posterior urethral valve. Cystoscopy was performed, and fulguration was done. Though, initial obstructive urinary symptoms improved but child developed poor feeding and frequent emesis. There was more than 3 percent loss of birth weight. Post fulguration he was admitted to NICU with hyperkalemia (serum potassium level: 7.4 mmol/L), hyponatremia (serum Sodium level:117 mmol/L) and metabolic acidosis (serum bicarbonate levels: 13 mmol/L). Baby was found to be anemic with a hemoglobin level of 8.3 mg/dL and had a raised total leukocyte count (16 $X10^9$/L). He was initially managed with intravenous bicarbonate, calcium gluconate, kaexylate and meropenem. Treating physician initially had suspicion of congenital adrenal hyperplasia. So,17-Hydroxyprogesterone (17-OHP) was advised and fludrocortisone and hydrocortisone were started. His condition improved but hyperkalemia and hyponatremia with acidosis persisted. Urine analysis revealed pyuria with positive nitrite test. Urine culture and sensitivity was done which yielded a growth of multi drug resistant Klebsiella oxytoca >100,000 CFU after 48 hours of incubation at 35^0C. The organism had shown

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Received: ***22 Oct 2017****; Revised:* ***16 Jan 2017****; Accepted:* ***06 Mar 2018***

sensitivity only to Colistin. Patient's urinary sodium level was raised (45 mmol/L) indicating renal loss of Sodium. Plasma ACTH level was within reference interval (13.9 pg/mL) but serum cortisol levels were raised (>1360 nmol/L). Since, initial levels of 17-OHP were mildly raised (16.4 nmol/L), Short Synacthen Test was performed but post ACTH stimulation level of 17-OHP (30 nmol/L) ruled out the congenital adrenal hyperplasia (salt loosing type). Plasma aldosterone level was markedly raised (9124 pmol/L) and so was the Plasma Active Renin Mass Concentration (5940 µIU/mL). These findings were suggestive of resistance of renal tubules to aldosterone action. Baby's UTI was treated with i/v colistin along with sodium chloride and bicarbonate supplements and kayexalate. In the ensuing weeks patient's urine became sterile and his electrolyte disturbance also improved. Presently he is healthy, active one-year old baby with normal weight and good milestones and stable biochemical profile (Table-1).

Table-1: Pre and Post treatment comparison of patient's biochemical and endocrine profile.

Analyte	Pre treatment	Post treatment	Reference Interval
Serum Sodium	117	138	136-149 mmo/l
Serum Potassium	7.4	4.2	3.5-5.0 mmol/l
Spot Urine Sodium	45	20	Normal serum sodium 20 mmo/l Hyponatremia >20 mmo/l Renal Cause <10 mmo/l Extrarenal Cause
Serum Bicarbonate	13	25	22-29 mmol/l
Arterial blood pH	7.19	7.4	7.35 - 7.45
Plasma Aldosterone	9124	800	140-2520 pmol/l
Plasma Active Renin Mas concentration	5940	22	8-35 µIU/l

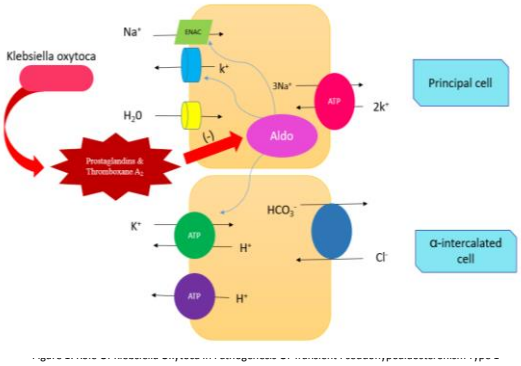

Figure-1: Role of Klebsiella oxytoca in pathogenesis of transient Pseudo Hypoaldosteronism-1

DISCUSSION

Aldosterone, a mineralocorticoid plays pivotal role in salt and water homeostasis by acting on mineralocorticoid receptors located on colon and renal tubules. It acts on epithelial sodium channels in cortical collecting tubules resulting in absorption of sodium followed by passive water flow. Sodium reabsorption causes development of negative intraluminal gradient leading to efflux of potassium ions. Thus, aldosterone deficiency or resistance causes hyponatremia and hyperkalemia induced metabolic acidosis. Congenital adrenal hyperplasia has become part of neonatal screening in many regions [4]. There is dire need of creating awareness among endocrinologists regarding association of urinary tract abnormalities with secondary PHA Type I [5]. Our patient presented with severe hyponatremia, hyperkalemia and metabolic acidosis. He was found to have severe urinary tract infection complicating posterior urethral valve. Endotoxins produced by gram negative Klebsiella oxytoca are associated with renal release of cytokines such as prostaglandins and thromboxane A2. These, inflammatory effects may contribute to renal vasoconstriction, decreased GFR, increased sodium renal loss accompanied by hyperkalemia and metabolic acidosis [6] (Figure-1) These, observation form the basis of strong association between urinary tract infection and anomalies with renal tubular aldosterone resistance especially in babies <1 year of age [7,8]. Early neonatal period itself is associated with unresponsiveness to aldosterone actions as seen in our patient [9]. A very high level of serum cortisol has been observed which is similar to findings of study carried out in Leeds Teaching Hospitals NHS Trust in 2017. These findings are to fact that stressful condition like severe hyponatremia causes increased cortisol secretion [10]

CONCLUSION

Transient Pseudohypoaldosteronism type 1 albeit a rare condition yet should be kept in mind in condition of severe neonatal hyponatremia and hyperkalemic metabolic acidosis. Antenatal hydronephrosis and polyhydramnios call the attention of treating physicians to rule out neonatal urinary tract abnormalities and early intervention. Thus, by keeping a high index of suspicion and timely ordering of urinary sodium, plasma renin and aldosterone levels, we can promptly diagnose and effectively manage a potentially fatal condition.

AUTHORS CONTRIBUTION

Alveena Younas: Principal author, paper writing and results compilation.
Asif Ali: Data collection, literature review.
Saima Shakil Malik: Literature review.
Muhammad Aamir: Overall supervision of project.
Zujaja Hina Haroon: Result compilation.
Muhammad Tahir Khadim: Literature review.

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