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Original Research Paper

Medicine

A RARE CASE OF ADOLESCENT ONSET BARTTER'S SYNDROME

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ABSTRACT Bartter's syndrome is a group of renal tubular disease characterized by impaired salt reabsorption in thick ascending limb of henle's loop and clinically by the association of hypokalemia,metabolic alkalosis,hypercalciuria/nephrocalcinosis,low/normal blood pressure,vascular resistance to angiotensin II.Most of the cases have been noted in pediatric age group and adult onset cases are rare.Here we report a case of 19 year old female patient with adolescent onset of bartter's syndrome who presented with persistent hypokalemia,metabolic alkalosis, normotension, nephrocalcinosis.

KEYWORDS : Bartter's syndrome,Salt wasting renal tubulopathy,Metabolic alkalosis,Hypokalemia,Normotension,Nephrocalcinosis

INTRODUCTION:

Bartter's syndrome ,originally described by Bartter's and colleagues in 1962,represents a set of closely related autosomal recessive renal tubular disorder characterised by hypokalemia,metabolic alkalosis,nephrocalcinosis,low or normal blood pressure and vascular resistence to angiotensin II.Histologically,there is hyperplasia of juxtaglomerular cells.

Prevalence : 1 in 10,00,000.

Classification: (on the basis of underlying genetics)

- Type 1-Antenatal Bartter's syndrome:results from mutation in SLC12A1(sodium-chloride-potassium cotrnsporter gene)
- Typr 2-Antenatal/neonatal Bartter's syndrome:results from mutations in ROMK(renal outer medullary potassium channel) gene
- Type 3-Classic Bartter's syndrome:Late childhood or adolescent onset,caused by mutations of CLCNKB (chloride voltage gated channel kb gene)
- Type 4-Bartter's syndrome with sensorineural deafness:results from loss of function mutations in BSND(Beta subunit of chloride channels)
- Type 5-Gitelman syndrome:results from mutations in SLC12A3(sodium-chloride cotransporter)

CASE REPORT:

A 19 year old female patient was admitted to Civil Hospital, Ahmedabad with complaints of generalised weakness,easy fatigability,nausea and lower abdominal pain for last 1 month.Patient had multiple admissions in last 7-8 months with similar complaints of generalised weakness and bodyache,lower abdominal pain,constipation and easy fatigability.Old reports(table-1) were suggestive of hypokalemia , bilateral multiple renal stones with other normal renal and liver function test and haematological parameters.For that patient was treated symptomatically with medications and D-J stenting for renal stones(removed after 2 months) and then referred to Civil hospital ,Ahmedabad for further evalution of her generalised weakness and fatigability.

Table-1.

Hb	9.9 g/dl	ANA(IF)	Negative
Wbc	10,456 /cmm	ANA PROFILE	Negative
Platelets	278000/cmm	ANTI-CCP	27 u/ml(-ve)
ESR	69 mm/hour	RA FACTOR	<10 iu/ml(-ve)
CRP	98 mg/l	TOTAL PROTIEN	6.37 g/dl
SGPT	14 u/l	S.ALBUMIN	3.57 g/dl
S.CREATINE	0.89 mg/dl	URINE R/M	NAD
S.POTASSIUM	2.9 mEq/l	S.SODIUM	144 mEq/l
USG ABDO-KUB	Left kidney shows stone in middle(5mm) and lower(3 mm) calyx with right kidney shows presence of stone in middle (4mm)and lower(3mm)calyx and mild hydronephrosis with stone (7mm)in right ureter just below PUJ.		

After admission to civil hospital ,routine investigations done which were suggestive of hypokalemia with normal renal function test,liver function test,complete blood counts and usg abdomen-pelvis was suggestive of bilateral multiple small stones in calyx of both kidney and ureters. ABGA was done for further evaluation of persistent hypokalemia and recurrent renal stones which was showing metabolic alkalosis with compensatory respiratory acidosis(pH-7.72, Po_2-92 mmHg,Pco_2-52mmHg, S.HCO_3-42 mmol/l,O_2sat-98%).

So for further evaluation of metabolic alkalosis,hypokalemia and renal stones,urinary potassium was done to rule out extra renal causes of hypokalemia like vomiting,diarrhea, diuretics,steroids use.Other causes of hypokalemia like thyroid disorders,starvation,hypomagnesemia were ruled out.

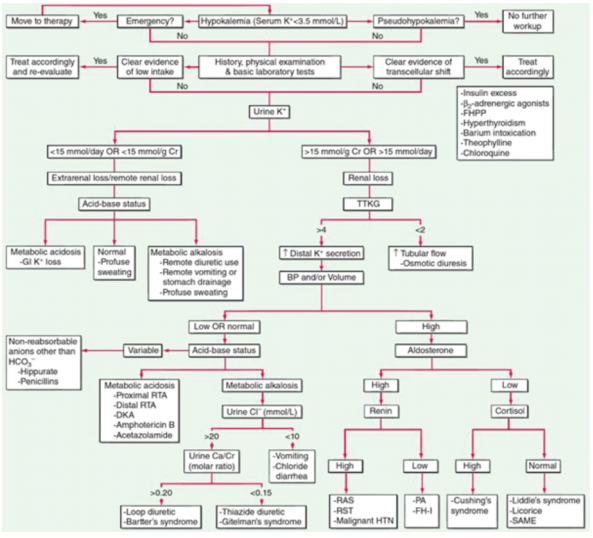
24 hour Urinary potassium was 68.7 mmol/day,spot urinary chloride was 34.2mEq/l with TTKG >4 confirming the renal source of potassium loss.S.aldosteron and S.cortisol were normal which ruled out possibility of liddle's syndrome, Cushing's syndrome,syndrome of apperent mineralocorticoid excess.With above workup salt-losing tubulopathy and channelopathy like bartter's syndrome or Gitelman's syndrome was suspected.So To differentiate between bartter's

syndrome (which is associated with hypercalciuria) and Gitelman's syndrome urinary calcium creatinine ratio and serum calcium were done which was 0.32 and 6.9 mg/dl respectively.So clinical diagnosis of bartter's syndrome was made as she was presented with laboratory investigations suggestive of persistent hypokalemia,metabolic alkalosis,recurrent renal stones,hypercalciuria and low serum calcium level.For confirmation of diagnosis genetic study was planned to find out mutations like BSND,CLCNKA,KCNJ1,SLC12A1,SLC12A3,CLCNKB but could not be done due to economical issues.

Patient was treated with potassium chloride 20 meq 4 times a day ,spironolactone -50 mg twice a day and symptomatic treatment was given .The administration of medication led to increase in serum potassium to 3.7 to 4.3 meq/l.This improvement in serum potassium concentration also led to reversal of ECG changes,improvement in patient's muscle strength with generalised well-being.

DISCUSSION:

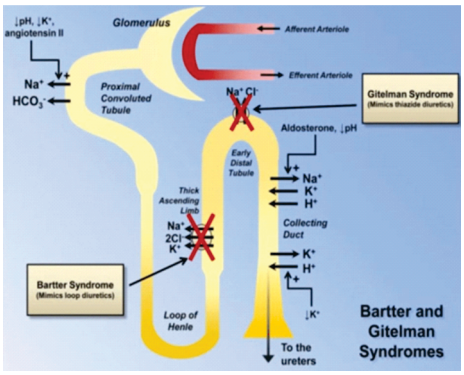
Hypokalemia is a common clinical problem,the cause of which can usually be determined from the history(as with diuretic use,vomiting or diarrhea.)But in some cases,however, the diagnois is not readily apparent.The diagnostic workup of patients with hypokalemia is reviewd here.There are two major components to diagnostic evaluation:assessment of urinary potassium losses from other causes of hypokalemia and assessment of acid-base status,since some causes of hypokalemia are associated with metabolic alkalosis or metabolic acidosis.



The clinical symptoms of Bartter's syndrome are dominated by hypokalemia causing generalised weakness,fatigue, nausea,constipation,anorexia and proxima muscle weakness with cardiac arrythamias in sever cases.

Clinically Bartter's syndrome can be divided in at least two groups:one with early(infancy)and other with late onset of symptoms.Neonatal Bartter's syndrome characterised by intrauterine onset of polyuria,leading to polyhydroamnios between 22nd and 24th weeks of gestation.In adults ,fatigue,nausea,proximal weakness,tetany,renal stones are most common presenting features.

The primary defect in Bartter's syndrome is an impairment in one of the transporters involved in sodium chloride reabsorption in the loop of henle.The combination of secondary hyoeraldosteronism due to impaired sodium chloride reabsorption and volume depletion leads to increased distal flow and sodium delivery enhances potassium and hydrogen secretion at the secretory sites in the connecting tubules and collecting tubules leading to metabolic alkalosis and hypokalemia.



The tubular defects in Bartter's syndrome cannot be corrected thus treatment must be lifelong and is aimed at minimizing the effects of extracellular volume depletion as well as correcting the electrolytes abnormalities.Potassium supplementation, hypomagnesemia correction,NSAIDS, drugs blocking distal sodium-potassium ehchange(spironolactone, eplerenone, amiloride),angiotensin inhibitors(ACEI) are cornerstone of the treatment.Kidney transplantation has been performed in rare patients who developed end-stange renal disease due to coexisting renal disease or the effects of chronic volume depletion,electrolyte abnormalities,drug related side effects and/or nephrocalcinosis.

CONCLUSION:

Bartter's syndrome is rare autosomal recessive genetic disorder whose primary pathogenic mechanism is defective transepithelial chloride reabsorption in thick ascending limb of loop of henle due to defective function of proteins responsible for transporting ions to renal cells. As it is rare disorder it requires extensive workup for diagnosis including genetic study for nonspecific clinical presentation of syndrome. The tubular defects of Bartter's syndrome cannot be corrected, symptomatic treatment with correction of underlying acid-base and electrolyte abnormalities is the rule.

REFERENCES

1. Bartter FC, Pronove P, Gill JR, MacCardle RC (1962). "Hyperplasia of the juxtaglomerular complex with hyperaldosteronism and hypokalemic alkalosis. A new syndrome". Am J Med. 33 (6): 811–28. doi:10.1016/0002-9343(62)90214-0. PMID 13969763. Reproduced in Bartter 2.FC, Pronove P, Gill JR, MacCardle RC (1998). "Hyperplasia of the juxtaglomerular complex with hyperaldosteronism and hypokalemic alkalosis. A new syndrome. 1962". J. Am. Soc. Nephrol. 9 (3): 516–28.
3. Gitelman HJ, Graham JB, Welt LG (1966). "A new familial disorder characterized by hypokalemia and hypomagnesemia". Trans Assoc Am Physicians. 79: 221–35.
4. Fremont OT, Chan JC. Understanding Bartter syndrome and Gitelman syndrome. World J Pediatr. (2012) 8:25–30. 10.1007/s12519-012-0333-9
5. Ji W, Foo JN, O'Roak BJ, Zhao H, Larson MG, Simon DB, et al. Rare independent mutations in renal salt handling genes contribute to blood pressure variation. Nat Genet. (2008) 40:592–9. 10.1038/ng.118
6. Jentsch TJ, Stein V, Weinreich F, Zdebik AA. Molecular structure and physiological function of chloride channels. Physiol Rev. (2002) 82:503–68. 10.1152/physrev.00029.2001
7. Simon DB, Bindra RS, Mansfield TA, Nelson-Williams C, Mendonca E, Stone R, et al. Mutations in the chloride channel gene, CLCKNB, cause Bartter's syndrome type III. Nat Genet. (1997) 17:171–8. 10.1038/ng1097-171
8. Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo S. Harrison's Principles of Internal Medicine, vol. 2. 18th ed. USA: The McGraw Hill Companies; 2012. p. 2360–1.