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RESEARCH ARTICLE

A CASE OF ADULT ONSET BARTTERS SYNDROME.

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Abstract

Bartter syndrome is a rare inherited disorder which usually presents in childhood and is characterized by hypokalemia, metabolic alkalosis with normal blood pressure and hyperreninemia. Bartter syndrome is an autosomal recessive renal tubular disorder, with an inherited defect in the thick ascending limb of the loop of Henle and distal convulated tubules. Bartter syndrome is classified into two types : Neonatal and Classic type. Neonatal type present usually at 24 to 30 weeks of gestation with polyhydroaminos. Classic type present during first two years of life or later. We report a case of 27 year old male who presented with quadriparesis and episodes of carpal spasm and investigations were suggestive of Bartters syndrome, which presented as hypokalemic paralysis. Patient was treated with potassium supplementation after which weakness improved completely. We report this case because adult onset Bartters syndrome is rare.

Introduction:-

Bartter syndrome is an autosomal recessive renal tubular disorder, with an inherited defect in the thick ascending limb of the loop of Henle and distal convulated tubules. It is characterized by hypokalemia, hypochloremia, metabolic alkalosis, and normal blood pressure with hyperreninemia[1].

Bartter syndrome has traditionally been classified into two main clinical variants, as follows:

1. Neonatal (or antenatal) Bartter syndrome
2. Classic Bartter syndrome

A widely used system classifies Bartter syndrome on the basis of the underlying genetics, as follows[2] :
Type 1:- Antenatal Bartter syndrome: Results from mutations in SLC12A1, the sodium-chloride-potassium cotransporter gene
Type 2 :- Antenatal/neonatal Bartter syndrome: Results from mutations in the ROMK gene
Type 3:- Classic Bartter syndrome: caused by mutations of the chloride voltage-gated channel Kb gene (CLCNKB), which encodes the ClC-Kb chloride channel involved in NaCl reabsorption in the renal tubule[3]
Type 4:- Bartter syndrome with sensorineural deafness: Results from the loss-of-function mutations in BSND[4,5,6], which encodes an essential beta subunit for CLC chloride channels
Type 5:- Gitelman syndrome: Results from mutations SLC12A3, the sodium-chloride cotransporter

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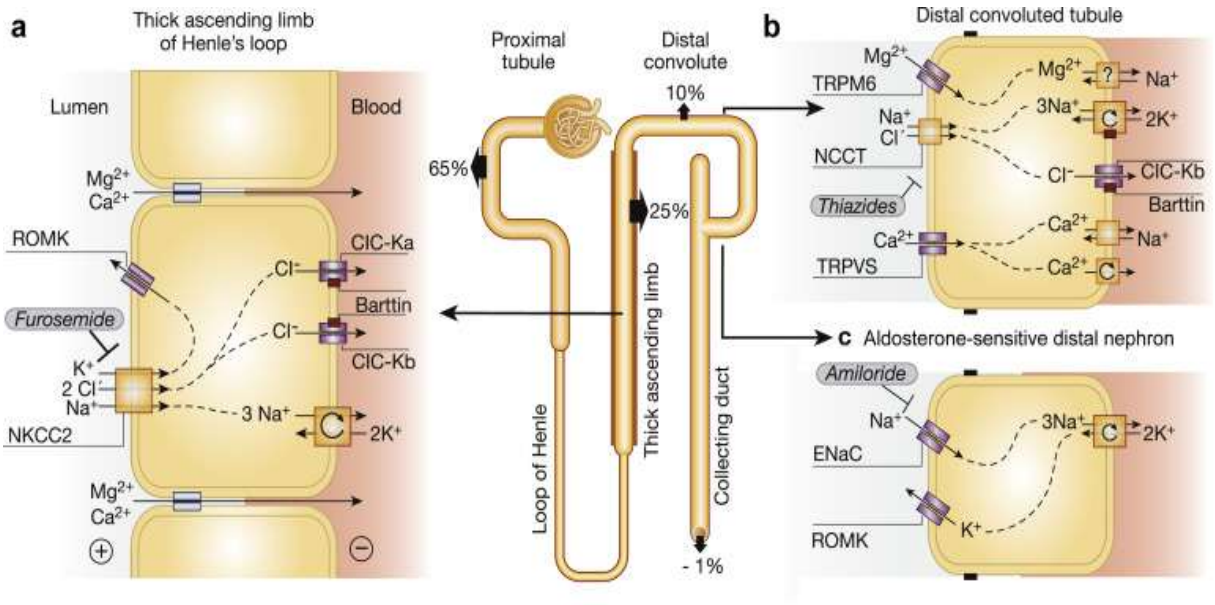

Case report:-

A 27 year old male presented with a history of sudden onset weakness of all four limbs which evolved over a period of 24 hours and bilateral symmetrical. Weakness was more in proximal muscle groups as compared to distal. Patient also had 2 episodes of carpal spasm in 24 hours. Patient also had complaint of polyuria and polydipsia since last 3 years

On examination

Temp: normal, pulse: 68/min, bp: 122/80 mmhg

CNS examination: higher functions : normal, no cranial nerves involved, tone was normal in all four limbs, power was grade 3 in proximal muscles of upper limb grade 4+ in distal muscles of upper limb , power was grade 2 in proximal muscles of lower limb and grade 4+ in distal muscles of lower limb.

Sensory system examination was normal and reflexes in all four limbs normal with planters flexors.

Investigations:-

Serum potassium: 2mEq/L, serum bicarbonate: 32.7mEq/L, 86.1 mmHg PaO2: 96.1 mmHg, PaCO2: 38.4mmHg, pH of arterial blood: 7.5 and that of urine 7.0, thus metabolic alkalosis with hypokalemia was present. Serum sodium: 134 mEq/L, chloride: 98 mEq/L, total calcium: 4 mEq/L, ionized calcium 1.8 mEq/L, magnesium: 1.6 mEq/L, uric acid: 4.8 mg/dl, serum osmolality: 289 mosl/kg, blood urea nitrogen: 44.0 mg/dl, serum creatinine 1.7 mg/dl and creatinine clearance 35 ml/min.

There were no proteinuria, hematuria and abnormality of the urinary sediment. Urine creatinine level was 35mg/dl, urine calcium: 11 mg/dl with urine calcium to urine creatinine ratio of 0.3. urine potassium: 41mEq/L.

Hemoglobin level, hematocrit value, white blood cell count, total protein, albumin, alkaline phosphatase and transaminase levels were within normal range. Twenty four-hour urinary excretion of sodium: 183 mEq, potassium: 67 mEq, chloride 247 mEq, calcium:120 mg, protein: 150 mg, glucose: 30 mg and urine amounts:2,300ml, urinary specific gravity :1.010 and osmolality 310 mosm/kg. The plasma renin activity was 48.2 ng/ml/hr and aldosterone level 34.4 ng/dl. FENa was 2.6%, FECl, 5.7%, FEK 55%, and FEUric acid 8.2%. Electrocardiography revealed ST segment depression, T wave inversion in chest leads with prominent U waves. Audiometry examination of ear revealed bilateral mild to moderate sensorineural hearing loss.

Ultrasound examination revealed bilateral normal sized kidney with slightly increased echotexture with cortico-medullary differentiation maintained.

The patient was initially treated with parenteral potassium chloride 40 mEq, given slowly, after which patient's weakness improved completely within 24hours. Also calcium supplements were given to relieve carpal spasms. Patient was then started with oral potassium supplements, potassium rich diet and was discharged on spironolactone 50 mg two times a day, enalapril, 2.5 mg a day and indomethacin, 25 mg three times a day. The administration of medications led to an increase in serum potassium to 4mEq/L and the patient did well for the following three months

Discussion:-

Defects in either the sodium chloride/potassium chloride cotransporter or the potassium channel affect the transport of sodium, potassium, and chloride in the thick ascending limb of the loop of Henle (TALH). The result is the delivery of large volumes of urine with a high content of these ions to the distal segments of the renal tubule, where only some sodium is reabsorbed and potassium is secreted.

Familial and sporadic forms of Bartter and Gitelman syndromes exist. When inherited, these syndromes are passed on as autosomal recessive conditions. Chloride is passively absorbed along most of the proximal tubule but is actively transported in the TALH and the distal convoluted tubule (DCT).

Failure to reabsorb chloride results in a failure to reabsorb sodium and leads to excessive sodium and chloride delivery to the distal tubules, leading to excessive salt and water loss from the body.The renin-angiotensin-aldosterone system (RAAS) is a feedback system activated with volume depletion. Long-term stimulation may lead to hyperplasia of the juxtaglomerular complex. Angiotensin II (ANG II) is directly vasoconstrictive, increasing systemic and renal arteriolar constriction, which helps to prevent systemic hypotension. It directly increases proximal tubular sodium reabsorption. ANG II–induced renal vasoconstriction, along with potassium deficiency, produces a counterregulatory rise in vasodilating prostaglandin E (PGE) levels. High PGE levels are associated with growth inhibition in children. High levels of aldosterone also enhance potassium and hydrogen exchange for sodium. Excessive intracellular hydrogen ion accumulation is associated with hypokalemia and intracellular renal tubule potassium depletion. This is because hydrogen is exchanged for potassium to maintain electrical neutrality. It may lead to intracellular citrate depletion, because the alkali salt is used to buffer the intracellular acid and then lowers urinary citrate excretion. Hypocitraturia is an independent risk factor for renal stone formation. Excessive distal sodium delivery increases distal tubular sodium reabsorption and exchange with the electrically equivalent potassium or hydrogen ion. This, in turn, promotes hypokalemia, while lack of chloride reabsorption promotes inadequate exchange of bicarbonate for chloride, and the combined hypokalemia and excessive bicarbonate retention lead to metabolic alkalosis. Persons with Bartter syndrome often have hypercalciuria. Normally, reabsorption of the negative chloride ions promotes a lumen-positive voltage, driving paracellular positive calcium and magnesium absorption. Continued reabsorption and secretion of the positive potassium ions into the lumen of the TALH also promotes reabsorption of the positive calcium ions through paracellular tight junctions. Dysfunction of the TALH chloride transporters prevents urine calcium reabsorption in the TALH. Excessive urine calcium excretion may be one factor in the nephrocalcinosis observed in these patients. Calcium is usually reabsorbed in the DCT. Theoretically, chloride is reabsorbed through the thiazide-sensitive sodium chloride cotransporter and transported from the cell through a basolateral chloride channel, reducing intracellular chloride concentration. The net effect is increased activity of the voltage-dependent calcium channels and enhanced electrical gradient for calcium reabsorption from the lumen. The ClC-Kb channel is found in the basolateral membrane of the TALH, while the barttin subunits of ClC-Ka and ClC-Kb are found in the basolateral membrane of the marginal cells of the cochlear stria vascularis. In the inner ear, an Na-K-2Cl pump, called NKCC1, on the basolateral membrane increases intracellular levels of sodium, potassium, and chloride. Potassium excretion across the apical membrane against a concentration gradient produces the driving force for the depolarizing influx of potassium through the ion channels of the sensory hair cells required for hearing. The sodium ion is excreted across the basolateral membrane by the Na-K-adenosine triphosphatase (ATPase) pump, and the ClC-K channels allow the chloride ion to exit to maintain electroneutrality. Sensorineural deafness associated with type IV Bartter syndrome, a neonatal form of the disease, is due to defects in the barttin subunit of the ClC-Ka and CIC-Kb channels[7,8]. Mutations in only the ClC-Kb subunit, as occurs in type III Bartter syndrome, do not result in sensorineural deafness.

Common presenting symptoms include Polyuria, Polydipsia, Vomiting, Constipation, Salt craving, Tendency for volume depletion, Failure to thrive, Linear growth retardation. Other symptoms, which appear during late childhood, include fatigue, muscle weakness, cramps, and recurrent carpopedal spasms. Patients may have a history of maternal polyhydramnios and premature delivery.

Treatment usually includes: Sodium and potassium supplements for the electrolyte imbalances. Aldosterone antagonists and diuretic spironolactone are the mainstay of therapy. Angiotensin-converting enzyme (ACE) inhibitors are used to counteract the effects of angiotensin II (ANG II) and aldosterone. Indomethacin is used to decrease the prostaglandin excretion. Growth hormone (GH) is used to treat short stature in children. Calcium or magnesium supplements may occasionally be given if tetany or muscle spasms are present.

In this case, the patient was diagnosed to be adult-onset Bartter's syndrome due to hypokalemia, relative hypotension, increased renin activity, increased aldosterone level and juxtaglomerular hyperplasia. In appropriate medical therapy, a positive potassium balance and an increase in serum potassium concentration. In association with this improvement in the serum potassium concentration, the patient's muscle strength was rapidly recovered and the patient did well for the following two months. Bokhari SRA, Mansur A. Bartter Syndrome. 2017 Jun.

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