Case Reports

Nephrogenic Diabetes Insipidus is a Rare Complication of Chronic Kidney Disease - A Case Report

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Abstract

Nephrogenic Diabetes Insipidus (NDI) may occur as a complication of chronic kidney disease (CKD). The incidence of NDI is very rare. So recognition of this potential complication is very important. In our country, this rare complication is not yet reported. So, to make awareness among the paediatricians, we report a case of NDI as a rare complication of CKD. A 4-year old boy was admitted in the Department of Paediatric Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU) with the complaints of failure to thrive, refusal to feed, nausea and vomiting since 18- months of his age. For the last six months, he had also complaints of polyuria and polydipsia. In addition to this, he developed muscle pain, constipation, bowing of leg and occasional unexplained fever. He was moderately pale with deep sighing respiration and his blood pressure was above 95th centile for age and sex. His creatinine level was high with low TCO_2 and calcium level. His plasma osmolality was very high while urine osmolality was inappropriately low which did not increase after desmopressin (nasal spray) administration. Initial treatment with Indomethacin was ineffective while the combination of hydrochlorothiazide and Indomethacin was effective and well tolerated.

Introduction

Chronic kidney disease (CKD) is defined as evidence of structural or functional kidney abnormalities (abnormal urinalysis, imaging studies or histology) that persists for at least 3 months with or without decrease in glomerular filtration rate (GFR), as defined by a GFR of less than 60 mL/min/1.73 m^2. CKD occurs in 1 of every 5000 people[1]. The prevalence is 1.5 to 3.0 per 1000000 child population[2]. Aetiologically it can occur from glomerulonephritis (GN), recurrent urine infection, obstructive uropathy, hypoplastic or dysplastic kidneys etc. In our continent, GN is reported as the main cause of CKD[2]. These patients have various medical (renal ostedystrophy, anaemia, growth retardation, raised blood pressure) and psychosocial problems. Secondary Nephrogenic Diabetes Insipidus (NDI) may occur as a complication of CKD[3]. The recognition of this potential complication is very important. The incidence of NDI is very rare. The recent estimate of prevalence of NDI in Canada is 8.8: 1000000 in male[4] In our country, CKD patients with rare complication of NDI is yet to report for making awareness among the Paediatricians. So, we are reporting here a child who presented with NDI as a complication of CKD. Initially polyuria, polydipsia were not prominent in this particular patient rather he had history of failure to thrive, vomiting and convulsion.

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Case Report

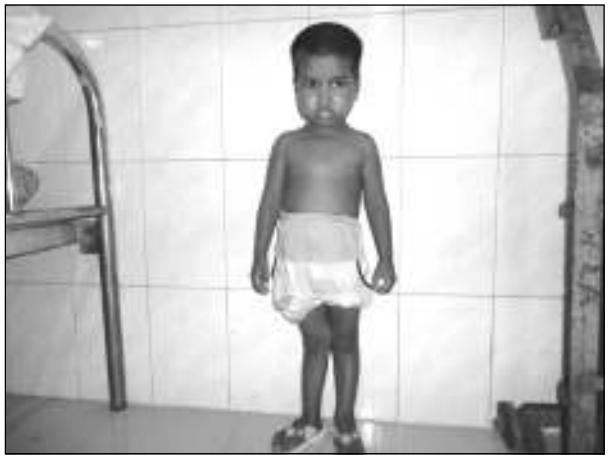
A 4 year old boy was admitted in the department of Paediatric Nephrology of Bangabandhu Sheikh Mujib Medical University (BSMMU) with the complaints of failure to thrive, refusal to feed, nausea and vomiting

since 18 months of his age. For the last six months he had also complaints of polyuria and polydipsia. In addition to this, he developed muscle pain, constipation, bowing of leg and occasional unexplained fever. On enquiry, the attendant also gave history of two episodes of convulsion which was generalized tonic and clonic in nature following a diarrhoeal episode at his 3 years of age and that time he was admitted on Sylhet Osmani Medical College & Hospital. He had no h/o dysuria, hematuria, abdominal pain or narrow stream of urine during voiding. He also had no history of taking any nephrotoxic drugs. (Lithium etc). He was born after an uneventful pregnancy period and delivered at 40 wks of gestation. He is the 4^{th} issue of healthy, unrelated parents. Other sibs are healthy.

On examination, the boy was moderately pale with deep sighing respiration and his respiratory rate was 44 breaths/min. His blood pressure was 110/90 mm Hg which was above 95^{th} centile for his age and sex. His weight was 11.2 kg (weight for age Z score -3.1) and height was 93 cm (height for age Z score -2.1). His 24 hours fluid intake and output were 2200 ml and 2500 ml respectively. His bed side urine for albumin was nill He had bowing of legs with knock knee. Other systemic examinations specially nervous system was normal.

Laboratory investigations revealed microscopic hematuria (RBC – 10 to 15/HPF) and few pus cells (4 to 6/HPF) with absence of proteinuria in urine microscopic examination and no growth on culture of urine. Twenty four hours urine for protein was normal. Urine P^H was 6.5. Hemoglobin level was 8.2 gm/dl, Blood film showed moderate microcytic hypochromic anaemia.Serum iron and serum feritin level were normal. Serum Creatinine was 1.6 mg/dl. Estimated GFR was 31.3 ml/min/1.73m^2. Serum alkaline phosphatase was high (287 U/L), Inorganic phosphate was 6 mg/dl and parathyroid hormone level was high (376 pg/ml). Serum Calcium (7.9 mg/dl) level was decreased. Complement level (C3) was normal and antinuclear antibody and anti double strand DNA were negative. Serum Electrolyte showed hypernatraemia (Na – 158 meq/L) with normal chloride and potassium level and TCo_2 level was decreased (17 mEq/L). As there was evidence of hypernatraemia on electrolyte report, we did some further investigations such as serum and urine osmolality with urine specific gravity. Report showed hyperosmolality of plasma (315 mosm/kg) with inappropriately low urine osmolality (145 mosm/kg) and urine specific gravity was low (<1.001)

Ultrasonography(USG) of kidney, ureter and bladder (KUB) showed bipolar length of both kidneys were decreased (Right kidney – 4.3 cm, Left kidney – 5.1 cm) MCUG excluded vesico ureteric reflux. DMSA Renal Scintigraphy showed both kidneys were ill outlined with poor tracer uptake. Radiographs of pituitary fossa (cone view) was normal. Metaphysial widening at wrists and ankle joints and subperiosteal resorption of sacroiliac joints were present on radiological evaluation. CT scan excluded structural abnormalities of the hypophysis and surrounding area. Water deprivation test was done to exclude NDI from central DI.But there was no response to 1 desamino – 8- D – arginin vasopressine (DDAVP) given by nasal spray. Serum osmolality raised from 315 mosm/kg to 365 mosm/kg after DDAVP but urine osmolality did not change (145 mosm/kg), which was suggestive of tubular defect causing Nephrogenic Diabetes



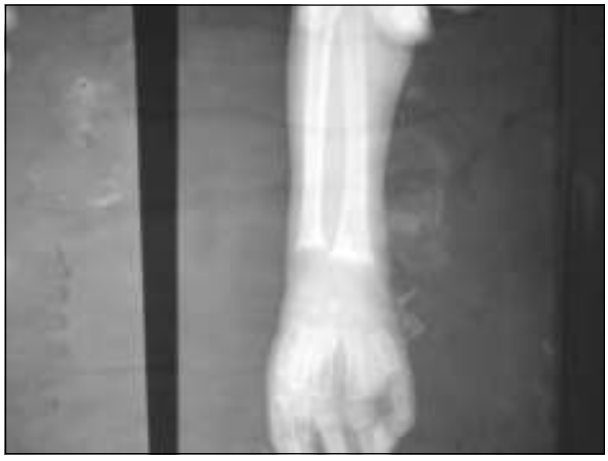


Fig.- 1 & 2 : *Before treatment*

Insipidus. So we come to a conclusion regarding diagnosis is CKD (Stage-3) with NDI with Renal osteodystrophy with failure to thrive.

Treatment was given with the restriction of protein, milk and milk products, fruits and salt. For the correction of anaemia and renal osteodystrophy, haematinics (iron, zinc,folic acid, vitamin B – Complex) Calcium (oral form), Vit. D3 were given. In addition to this, tablet sodibicarbonate and anti hypertensive (Calcium channel Blocker) were given.

For Nephrogenic Diabetes Insipidus, Indomethacin (2mg/kg/day) three times daily after meal together with large intake of fluid and low solute diet was prescribed. But there was no improvement of polyuria and polydipsia as well as serum and urine osmolality. Then hydrochlorothiazide - 3 mg/kg/day– two divided doses was prescribed in combination with indomethacin. After a few days significant improvement was noticed in serum and urine osmolality with improvement of polyuria and polydipsia. Then patient was discharged and advised for regular follow-up. After a couple of weeks of treatment, he had radiological improvement of bony deformity. On his last follow-up at 5 years of age his weight and height were 15 kg (weight for age in 25th centiles) and 96 cm (height for age is 10th centile) respectively. He was normotensive (95 over 70 mm Hg) and respiratory rate was 28 breaths/minute. His Hb level was 10.2 gm/dl and blood film showed normocytic normochromic anaemia and serum creatinine was 0.6mg/dl. Serum calcium was 9.3mg/dl and serum alkaline phosphatase was 105U/L. Serum PTH level was 67pg/ml and plasma osmolality was 285 mosm/kg and urine routine examination showed no abnormality. His coagulation profile (Bleeding Time and Clotting Time) was normal.

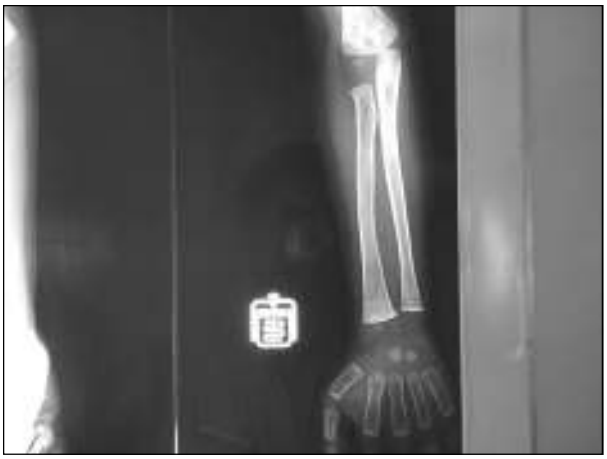


Fig.-3: *After treatment, Radiological correction*

Discussion

Congenital renal anomalies, recurrent urine infection, reflux nephropathy and GN play major role in paediatric CKD[1].

This particular patient had no history of cystitis or recurrent urine infection. From USG of KUB we excluded dysplastic or multicystic kidney and obstructive uropathy (post urethral valve, vesico ureteric reflux) as bladder outline was normal with insignificant amount of post voidal resudue (PVR). This patient had microscopic hematuria with pus cell and he was hypertensive. We could not perform renal biopsy because the size of the both kidney were small. In this case the cause of CKD may be due to congenital small kidney. There was no clinical & lab. evidence of GN. Lupus nephritis was excluded from negative ANA and Anti DS DNA test with normal complement level.

This reported patient had association with NDI, probably as a complication of renal disease. We have excluded other causes of NDI. Though it is a rare disease, it is relatively common in older sick patients with acute or chronic kidney diseases[5,6]. This patient had been suffering since 18 months of his age and that time he had no complain of polyuria and polydipsia. Though in terminal stages of CKD, these complains are not present rather fluid is locked-in there. But for the last six month, this patients had complains of polyuria and polydipsia. So, in our reported case, CKD is attributed to be responsible for NDI (acquired form). It was reported that NDI as a complication of CKD is due to increased solute excretion per functioning nephron and also decreased expression of mRNA for the V_2 asopressin receptor[5,6,7].

In NDI, the actual defect is inability of renal tubule to respond to anti diuretic hormone (ADH). It may be primary (inherited) or secondary (acquired). Acquired form is more common[7]. Inherited NDI usually manifest within first weeks of life. Here main defect is vasopressin receptor. In 90% cases, it is inherited as X – linked disorder[8]. Our presenting case, has another brother with good health.

In acquired form, drugs (lithium, amphotercin B), renal cause (CKD, medullary cystic diseases, Barter's syndrome etc), metabolic diseases, obstructive uropathy and sickle cell disease are included[9]. This particular patient had no history of taking any offending drugs, his serum chloride level was normal with TCo_2

showed mild metabolic acidosis. So, Barter's syndrome was excluded. Medullary cystic disease was excluded from USG of KUB report as there was no cyst.

Polyuria polydipsia, both are more common feature for CKD and NDI. Some times they are not manifested in child with NDI. Non specific sign symptoms such as unexplained fever, convulsion, failure to thrive may be presenting feature[10]. This boy had history of convulsion with unexplained fever which was probably due to dehydration and was aggravated by diarrhoeal episodes.

Water deprivation test was done to exclude NDI from central DI. This is very important to choose the appropriate treatment[11].

In this case initial treatment was started with indomethacin along with conservative management of CKD. As indomethacin has been reported to decrease urinary osmolality by inhibit hydrosmotic effect of anti-diuretic hormone. It can also enhance the ability of ADH to concentrate urine by blocking the action of prostaglandin in renal medullary collecting duct[12] .On initial trial Indomethacin was ineffective in this case. Then combination of hydrochlorothiazide and indomethacin were given. This combination was effective as serum osmolality became normal without any side effect. This combination was better than indomethacin alone. Though there was risk of gastrointestinal, renal, hematological complication. But nothing happened in our case. If such happened combination of hydrochlorothiazide and amiloride could be prescribed[13,14] In this case, we achieved good and quick results with hydrochlorothiazide and indomethacin combination.

In our case, radiological features of renal osteodystrophy and associated biochemical abnormalities showed response with Calcium and vitamin D supplementation within 8 weeks.

In conclusion, this case report illustrates that the early recognition of potential complication is important as it has direct implication for clinical management. This report will also help to create awareness among the pediatricians regarding a rare complication of CKD in children.

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