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Case Report

CKD-Mineral Bone Disease, A Feature of Delayed Diagnosis of Congenital Anomaly of The Kidney and Urinary Tract in An Eight-Year-Old Nigerian Boy- Case Report

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Abstract

Delay in identifying congenital anomaly of the kidneys and urinary tract (CAKUT) is often encountered in developing countries. This is majorly from poor health seeking behavior and unawareness of the relevance of non-invasive investigation tools that may aid early diagnosis and prompt management of such before progression to chronic kidney disease (CKD) Mineral Bone Disease and End State Renal Disease (ESRD). This is a case report of an 8-year-old boy who presented with difficulty in breathing of one week duration and fever of 12 hours duration. There were no oedema, oliguria, or hematuria. He had a previous medical history of being managed for multiple deformities of the limbs and suspected rickets 6years prior to index presentation but he defaulted. He was noticed to be small for his age, had rachitic rosary, pectus carinatum, double malleoli sign in both ankles and was anemic with packed cell volume of 14.9%, the serum creatinine and urea were elevated (323.3µmol/l and 20.1mmol/l respectively), there was hypocalcemia(1.10mmol/l), elevated alkaline phosphatase (263 IU/l). Abdominopelvic ultrasound showed absent left kidney and right polycystic kidney disease. Sedimented red blood cell was transfused, antibiotic, oral calcium and vitamin D were given, and he was referred for pre-emptive preparation for renal replacement therapy.

Keywords: CKD-mineral bone disease; end stage renal disease; congenital anomaly of the kidneys and the urinary tract; renal replacement therapy

Introduction

CKD-mineral bone disease (MBD) is a term coined by the kidney disease-Improving Global Outcomes (KDIGO) Foundation to describe the wide spectrum of systemic disorder of mineral and bone metabolism due to chronic kidney disease (CKD) [1]. Chronic kidney disease (CKD) is the presence of kidney damage (structural or functional abnormality involving pathological, laboratory, or imaging findings) for > 3 months or a glomerular filtration rate (GFR) < 60 ml/min/1.73 m2 for > 3 months [2].CAKUT contribute to the burden of CKD in the developing world as there is delay in diagnosis and barriers to management such as; late presentation, poor socioeconomic conditions, absence of medical insurance, limited diagnostic facilities and non-availability and affordability of chronic renal replacement therapy (RRT) [3-7]. It is imperative to increase awareness of the relevance of non-invasive investigations

such as ultrasound done in pregnancy and perinatal period as useful tools in identifying children with congenital anomalies in-utero so that prompt interventions, delivery and management can be planned.

Case Report

We present an 8-year-old boy whose admission to our health care facility was premised on the following: Presenting complaints were difficulty with breathing of one week duration and fever of 12 hours prior to presentation. Difficulty with breathing was associated with fast breathing which was insidious in onset, no relieving or aggravating factors and became progressively worse. There was no bluish discoloration of lips or fingers, no history of cough, noisy breathing, body swelling or reduction in urine output. He became febrile 12 hours prior to presentation, fever was on most times and was only temporarily relieved with oral paracetamol.

There was a background history of deformity of the limbs first noticed when he was 2years old, he subsequently presented at a tertiary health care facility where he was investigated for "rickets". He was commenced on tablets vitamin D and vitamin C. However, patients defaulted from clinic visits and discontinued medications 4years ago. Urine volume was noticed to be usually much by the mother; she attributed this to the fact that the child was drinking much water.

There was no history suggestive of hematuria. Mother had antenatal care at a primary health care facility and no abdominopelvic ultrasound was done in pregnancy. He had delay in walking, though he started crawling at 7month, he did not walk until the age of 2years. He was the second of three children in a monogamous family; siblings were alive and apparently well. The parents were petty traders, and their highest level of formal education was secondary school.

a) General physical examination: He was conscious, small for age, in obvious respiratory distress (flaring ala nasi and intercostal recession), febrile (39oC), pale, anicteric, acyanosed, no evidence of dehydration, had mild facial puffiness but no pedal edema.

b) Anthropometry: Weight was 16Kg (62.8% of the expected for his age), Occipitofrontal circumference was 49.8cm, the apparent length was 86cm (67.2% of the expected).

Systemic examination

a) Respiratory: Respiratory rate- 56ycles/minute, pectus carinatum, rachitic rosary bilaterally Trachea was centrally located, chest expansion was equal on both sides. Percussion note was resonant. The breathing sound was vesicular. The SPO2 was 88% in room air, 92% on intranasal oxygen.

b) Cardiovascular- Pulse rate was 110beats/min, regular, full volume. Apex beat was at the 5th left intercostal space mid-clavicular line. Blood pressure was 130/70mmHg. The first and the second heart sound were heard, there was no murmur.

c) Gastrointestinal: Abdomen was full, moved with respiration, there was no area of tenderness. The liver and spleen were not palpably enlarged while the right kidney was bimanually palpable. Bowel sounds were normoactive.

d) Genito-urinary: There was circumcised male external genitalia with two testes palpable par scrotum. The urethra meatus was of normal size.

e) Musculoskeletal: There was posterior deviation of distal ulnar, bilaterally, presence of bilateral tibia sabre and double malleoli sign on the ankles

f) Problems Identified: Breathlessness, tachypnea, anaemia, growth failure, features of rickets, high blood pressure.

Investigations

Abdominopelvic ultrasound- the right kidney was significantly enlarged measuring 15.5cm×8.7 cm and it was completely replaced by multiple cystic lesions with sizes ranging between 3.4-12.5 cm. The cysts have thin walls and contain anaechoic fluid. No normal renal parenchyma tissue was seen. The left kidney was not seen, no evidence of ectopic kidney, urinary bladder was mildly filled with fluid. No cysts demonstrable in other abdominal organs whose dimensions were within normal limits. The final impression was, absent left kidney (renal agenesis) and right polycystic kidney disease.

Results

Blood electrolyte, urea, and creatinine.

Na---137.5mmol/L, K---4.9 mmol/L, CL---112 mmol/L.

HCO3---19mmol/L, Phosphate---0.84mmol/L.

Urea---20.1 mmol/L, Cr---323.3 µmol/L.

Serum Calcium – 1.10 mmol/L.

Hb genotype was AA, retroviral screening was non-reactive.

Full blood count; WBC -9.66x109/L, Lymphocyte – 18.08%.

Neutrophil- 69.32%, Hct – 14.9%, Platelet – 215X109/L.

Urinalysis- pH was 5.0, nil hematuria or proteinuria.

Liver function test (LFT) – Total bilirubin – 7.6mmol/L, Conjugated bilirubin – 4.7mmol/L.

Total serum Protein- 70g/L, Albumin- 41g/L, AST- 16IU/L, ALT-0.6IU/L, ALP- 263IU/L.

Picture and X-ray of the child are as shown below (Figures 1-4).

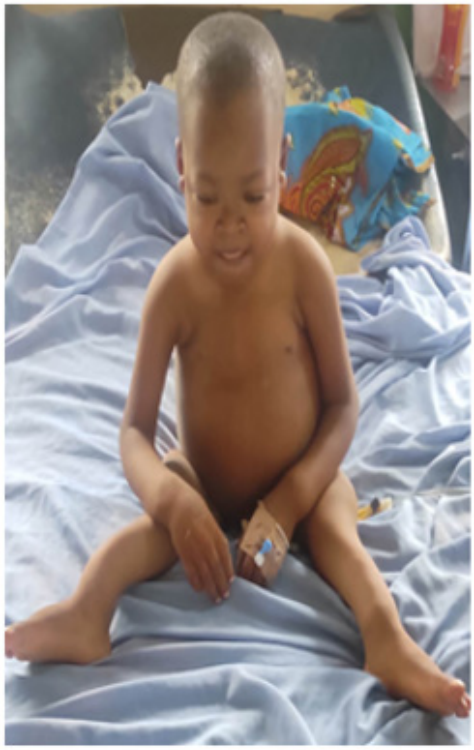

Figure 1: Picture of the 8-year-old boy with CKD-Mineral bone Disease.

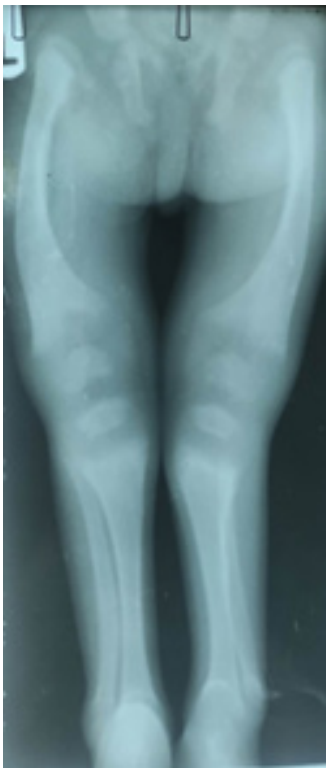

Figure 2: X-ray of femur, tibia and fibula showing features of rickets.

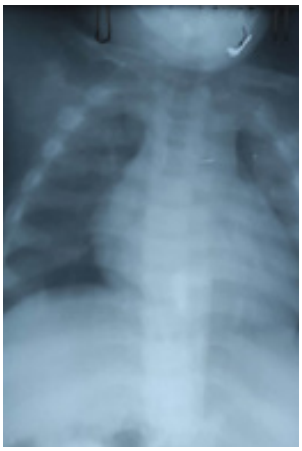

Figure 3: Chest X-ray.

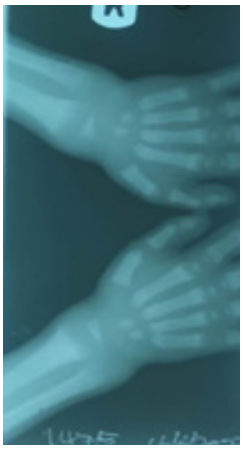

Figure 4: Xray of the wrist joint showing cupping, fraying, and splaying of epiphyseal end of the radius and widening of the wrist joint.

Assessment

a) CKD: mineral bone disease- secondary to right polycystic kidney disease and absent left kidney.

b) Treatment: he was admitted and commenced on intranasal oxygen, antibiotics, and blood transfusion of sedimented red blood cell was given at 15mls/kg, frusemide 1mg/kg, tab calcium lactate 300mg thrice a day and tab vitamin D 400 IU daily. Parents were counseled on the disease entity, need for renal replacement therapy and referral to a tertiary health institution where further investigation and interventions would be made available. The patient was taken away by parents and died at home two days later.

Discussion

Congenital anomalies of the kidney and urinary tract (CAKUT) remain a major cause of chronic kidney disease (CKD) in children3. In index patients, there was delay in diagnosis of the congenital anomaly until he was eight years old when he had features of chronic kidney diseases. The anomaly could have been diagnosed while in-utero with antenatal abdominopelvic ultrasound, subsequently, counseling and planning for renal replacement therapy would have been done earlier. The true burden of CAKUT may not be known in the developing countries because not every pregnancy is registered with appropriate antenatal care [8]. Some of these children may die in infancy and the cause of death may not be unraveled as factors such as cultural/religious belief, fear of disfigurement and emotional stress on parents usually do not favour the conventional postmortem in this society [9]. The ones that survive infancy period may end up presenting with features of CKD as seen in index patient.

The features of short stature and bony deformity were noticed when he started walking. There was a developmental delay as the patient did not walk until the second year of life. This could have been accounted for by the on-going demineralization of the bone due to renal insufficiency. The mineral bone disease of CKD usually

affects the normal bone turnover and mineralization processes, resulting in reduced bone strength, bone pain, fractures, poor final height attainment and subsequent short stature [10-15]. These demineralization processes start in the early stages of CKD and worsen as CKD progresses [16]. The kidneys play major roles in production of the active form of Vitamin D- 1,25 dihydroxyl cholecalciferol (1,25 DHCC). Vitamin D undergoes hydroxylation in the liver to 25-hydroxyl vitamin D, which is a biologically inactive form. There is 1α hydroxylation of 25- hydroxyl Vitamin D in the kidneys to form the active 1,25 DHCC (Calcitriol) which increases intestinal absorption of calcium and phosphates, hereby promoting bone formation [17]. This function is impaired when there is an abnormality in the development of the kidneys. This may explain the hypocalcemia in this patient. The extent of bone mineralization is dependent on calcium availability as well as on the extracellular levels of phosphate and pyrophosphate which is controlled by alkaline phosphatase enzymes [18].

Bone alkaline phosphatase may increase local phosphorus concentrations. The phosphate level is expected to be on the high side but the result from the laboratory showed it to be within normal limit. The rise in alkaline phosphatase in index patient demonstrates high turnover rate in attempt at new bone formation with increase potential for a rise in the serum phosphate. However, it has been noted that biomarkers such as calcium, phosphate and alkaline phosphatase may not correspond well in quantifying bone mineralization in the general population and in disease states such as osteoporosis or CKD. These further buttresses the fact that other factors such as FGF 23 play a key role in bone demineralization as earlier suggested [19]. In CKD stages 2–3, levels of FGF23 rise in order to enhance urinary phosphate excretion. These increased values also suppress renal 1-alpha hydroxylase, resulting in reduced 1,25(OH)_2 vitamin D (calcitriol, 1,25(OH)_2 D) values and, subsequently, increased PTH levels, which also help to reduce blood phosphate levels. In advanced CKD, however, rising PTH levels cause a release of calcium and phosphorus from bone and, when compensatory mechanisms fail, severely impaired glomerular filtration rate (GFR) results in phosphate retention which itself directly suppresses 1α-hydroxylase activity [20]. The parathyroid hormonal assay was not done due to financial constraint. It is expected that there would be secondary hyperparathyroidism from the hypocalcemia as the body fights to keep the calcium level in the normal range.

Features of chronic kidney disease (CKD) such as anaemia were seen in this patient. The haematocrit was 14.9%. The cause of anaemia in CKD is multifaceted; kidneys are responsible majorly for production of erythropoietin that drives new red blood cell formation in the bone marrow. Dysgenesis of the kidney includes aplasia, dysplasia, hypoplasia, and cystic disease. In the patient, there was absence of the right kidney with polycystic left kidney. Unilateral renal agenesis is a congenital anomaly that occurs in 1 in 3000 births [21]. Some individuals are diagnosed as having unilateral renal agenesis based on the finding of an absent kidney on ultrasonography or excretory urography. The coexistence of polycystic kidney (autosomal dominant polycystic kidney disease) and contralateral renal agenesis is rare and occurs in approximately 1 in 1 500 000-3 000 000 individuals [22]. A renal computed tomography would have given detailed images of the renal outline; however, the parents could not afford the high cost of such investigation especially in patients making "out of pocket" payment with financial constraint. The specific genetic abnormality in index patient could not be determined because of the absence of the facility for genetic study in our institution. In spite of these limitations, there is a need to have a high index of suspicion of underlying renal disease in patients with bone deformities. The fact that the child survived for 8 years suggested that he probably had some remnant renal parenchyma that was begging to be helped with renal replacement therapy until this thinned out.

In developing countries with limited resources and dwindling number of personnel due to poor economy and brain drain, prevention is the ultimate weapon. It is imperative to create awareness of the existence of CAKUT in the developing countries and to insist on timely antenatal ultrasound for early diagnosis and planned intervention. The index patient was taken home by the parent and did not go to the tertiary referral hospital. This typifies the fate of most children with chronic illness in the developing countries as parents/guardians may not be able to afford out of pocket payment for the health bill and the health insurance scheme does not have wide coverage. There are more causes of preventable mortality in children that will emerge as advances in diagnostic tools and clinical acumen unfold. Non-nutritional rickets may mirror a chronic kidney disease in children.

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