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Case Report

Paediatrics Section

A Case of Neonatal Hypertension with Chronic Kidney Disease Presenting as Anasarca, Hypoalbuminemia and Pulmonary Bleed

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ABSTRACT

Incidence of hypertension is reported to be around 0.2% in healthy term newborns and up to 3% in the infants in Neonatal Intensive Care Units (NICUs). Neonatal Chronic Kidney Disease (CKD) is defined as a decrease in kidney function which manifests in the neonatal period. Neonatal CKD has an estimated incidence of 1 in 10,000 live births. The diagnosis of CKD in the neonatal period is typically made after a renal ultrasonogram, first performed in the prenatal period and repeated soon after birth. This case report is about a 22-days-old male neonate that presented with abdominal distension, generalised pitting oedema and hypertension. On day 33 of life, the baby developed pulmonary haemorrhage. A diagnosis of CKD was made, based on renal ultrasonogram along with urine microscopy and urine protein creatinine findings. Renal Doppler was not suggestive of renal artery stenosis or renal vein thrombosis. A 2D echo was not suggestive of coarctation of aorta or interrupted aortic arch. Ultrasonography of abdomen did not reveal any mass. Plasma renin levels were normal. Hypertension finally normalised on oral amlodipine. Baby has been normotensive on oral amlodipine during follow-up over the last six months. This is a rare case of hypertension with CKD presenting in the neonatal period.

Keywords: End stage renal disease, Kidney, Newborn

CASE REPORT

A 22-days-old male neonate presented with complaints of fever and abdominal distension since three days. The baby was born to a 23-year-old primigravida mother, at 40 weeks gestation. The mother was registered antenatally at a government hospital. She did not had any medical or obstetrical illness. Antenatal period was uneventful and obstetric scans were normal. Delivery was by elective cesarean section in view of premature rupture of membranes and severe oligohydramnios. Baby cried immediately after birth and no resuscitation was required. Birth weight was 2.5 kg, length 51.5 cm and infant was born small for gestational age. The baby was on exclusive breastfeed.

At presentation, abdomen was tender with hepatomegaly. Generalised pitting oedema was present, more on the abdominal wall, lower limb and palms. Systemic examination and examination of external genitalia was normal. Urine output was adequate. Initial Non Invasive Blood Pressure (NIBP) measured by oscillometric method soon after admission was Systolic/Diastolic/Mean Arterial blood Pressure (MAP) → 101/73 (82) between 50-90th percentile. Fever was low grade, present since three days and not associated with cough, rhinorrhea or ear discharge.

Initial sodium levels were 118 mEq/litre with urine specific gravity of 1.044. Serum potassium and chloride levels were normal. Initial creatinine levels were 0.8 mg/dL. Glomerular Filtration Rate (GFR) was calculated to be 26.1 ml/min/1.73 m^2, which was moderately reduced (>1 to <2 SD below the mean).

Urine microscopy showed 15-30 pus cells on day 24 of life. Subsequent urine microscopy showed 16-17 RBCs on day 28. Urine microscopy was normal on day 39. Urine culture was sterile. During this time, baby was admitted and on antibiotics for late-onset sepsis. Urine microscopic findings were suggestive of glomerular and tubular pathology. Urine protein creatinine ratio was 1.57 (high).

Serum albumin level was 1.5 mg/dL. Sepsis screen was positive. Cerebrospinal Fluid (CSF) study was normal. Blood culture was sterile. Serum Thyroid Stimulating Hormone (TSH) levels were normal. Provisional diagnosis at this stage was septic ileus with hypertension due to renal vein thrombosis, renal artery

stenosis, neuroblastoma, Wilm's tumour, coarctation of aorta or interrupted aortic arch.

Ultrasound abdomen was suggestive of mild ascites. On ultrasonography, size of right kidney was 3.1x1.2 cm and left kidney 2.8x1.7 cm. Kidneys were of a smaller size for gestational age and there was increased renal cortical echogenicity and poor visibility of the renal pyramids and the renal sinus. Ultrasonography of abdomen did not reveal any mass. Renal Doppler was not suggestive of renal artery stenosis or renal vein thrombosis. A 2D echo was not suggestive of coarctation of aorta or interrupted aortic arch. Plasma renin levels were normal.

The baby was started on antibiotics-piperacillin tazobactam, amikacin and metronidazole on admission that were continued for seven days. Two doses of intravenous albumin were given and repeat laboratory value of albumin improved to 3.3 mg/dL on day 30 of life. Sodium correction was done followed by fluid restriction in view of suspected Syndrome of Inappropriate Anti Diuretic Hormone Secretion (SIADH) with dilutional hyponatremia. Sodium levels normalised after three days. Full fluids were given after 26 days of life. Abdominal signs and symptoms resolved after seven days.

On day 33 of life, the baby developed pulmonary haemorrhage due to hypervolemia leading to pulmonary oedema and required mechanical ventilation for two hours followed by extubation to non invasive modality of respiratory support for three days. Coagulogram and platelet count at the time of the pulmonary bleed were normal. Creatinine levels stayed within normal limits throughout the course of the disease. Subsequently, BP increased with peak of 135/81(99) which was more than 99th percentile. He was started on intravenous furosemide at 1 mg/kg/day for three days. NIBP remained between 95-99th centile. Medications were switched to oral lasilactone initially at 1 mg/kg/day which was gradually upscaled to 3 mg/kg/day. In view of persisting hypertension, oral amlodipine was added, initially at dose of 0.2 mg/kg/day which was gradually hiked to 0.6 mg /kg/day. Finally, BP normalised between 50-90th centile and the infant was discharged home on oral amlodipine at a dose of 0.5 mg/kg/day. The baby has been normotensive on oral amlodipine during follow-up over the last six months and dose has now been gradually tapered to 0.4 mg/kg/day.

A diagnosis of CKD was made based on sonography findings along with urine microscopy and urine protein creatinine findings. Renal artery stenosis, renal vein thrombosis, coarctation of aorta and interrupted aortic arch were ruled out. Ultrasonography of abdomen did not reveal any mass thereby ruling out neuroblastoma or nephroblastoma. In the present case, ultrasonography did not show evidence of any external compression, dissection or calcification of the left renal artery. In addition, the patient had no history of umbilical arterial catheterisation and had no blood coagulation abnormality.

DISCUSSION

Incidence of hypertension is around 0.2% in healthy term newborns and 3% in infants in NICUs [1]. Incidence is more in high-risk neonates with umbilical arterial catheters, bronchopulmonary dysplasia, intraventricular bleeds, renal failure, and congenital anomalies of kidneys and urinary tract. Hypertension is diagnosed in a newborn if systolic and/or diastolic BP recordings are at or above the 95th percentile for postconceptional age on three occasions [2,3]. Severe hypertension, defined as BP greater than the 99th percentile for postconceptional age , should be managed with pharmaceutical agents [4]. Preterm and small for gestational age infants are predisposed to chronic kidney disease and hypertension due to reduced nephron numbers. Neonatal chronic kidney disease (CKD) is defined as a decrease in kidney function which manifests in the neonatal period [5].

Incidence of neonatal CKD has been estimated to be 1 in 10,000 live births, whereas the incidence of neonatal End-Stage Renal Disease (ESRD) is about 7.1 per million age-related population [5]. Diagnosis of neonatal CKD is based on renal ultrasound in the prenatal period which is repeated soon after birth. Normal GFR in the newborn period is less than 60 mL/min/1.73 m^2. It increases due to increase in renal perfusion by increased mean arterial pressure with a decrease in renal vascular resistance. Neonatal kidney function can be classified as normal, moderately reduced, or severely reduced based on the age-adjusted GFR [Table/Fig-1] [6].

Neonatal CKD classification	GFR
Normal GFR	GFR ≤1 SD below the mean
Moderately reduced GFR	GFR >1 SD to ≤2 SD below the mean
Severely reduced GFR	GFR >2 SD below the mean

[Table/Fig-1]: KDIGO* classification schemata for CKD for ages less than two years [6].
KDIGO: Kidney disease improving global outcomes

The NIBP measurements are important in infants admitted to NICU, because they are at a higher risk for hypertension. Most patients do not exhibit the usual symptoms of hypertension like older children do, and symptoms and signs are difficult to differentiate from those of concurrent medical conditions, such as cardiorespiratory failure, feeding difficulties, irritability, and gastrointestinal symptoms. Nephronogenesis continues postnatally in preterm infants until 36 weeks estimated gestational age and injury to developing nephrons secondary to any insult, whether hypoxia, hypotension or nephrotoxin exposure, leads to more significant and chronic sequelae. In neonatal CKD, renal sonogram reveals disorganised renal architecture or a significant urologic abnormality accompanied by abnormal kidney function [7].

There is limited data for incidence of CKD in neonates. Carey WA et al., estimated the incidence of ESRD in neonates as 0.045 cases per million population per year, or 0.32 cases per 100,000 live births based on the dialysis registry of the North American Pediatric Renal Trials and Collaborative Studies (NAPTRCS). [8]. The most common renal disorders were congenital renal hypoplasia or dysplasia and obstructive uropathy.

Von Schnakenburg C et al., described a four-day-old full-term neonate with severe congestive heart failure and metabolic acidosis and poor systolic function whose continuous monitoring of blood pressure revealed severe arterial hypertension (30-40 mmHg above the 95th percentile). Ultrasonography showed an echogenic left kidney with a raised peripheral renin activity, thrombocytopenia, raised d-dimers, a microhematuria and mild proteinuria. Angiotensin Converting Enzyme (ACE) inhibitor was used to treat hypertension. Later, Mercapto Acetyl tri Glycine (MAG3) renal scan showed complete absence of renal function on the left side. Baby was discharged on captopril therapy. In the present case, the baby had normal peripheral renin activity and was discharged on amlodipine [9].

Barbed Ferrández SM et al., described a term newborn female, with arterial hypertension and congestive heart failure, caused by unilateral renal artery stenosis, with functional abolition and atrophy of the affected kidney. The baby required antihypertensive support during her first days of life with significant clinical improvement, subsequently. This is similar to the index case except that this baby had normal renal Doppler [10].

Kiessling SG et al., described a 2-day-old neonate with feed intolerance and hypertension with renal doppler suggestive of unilateral renal venous thrombosis. Despite aggressive antihypertensive therapy, hypertension was sustained with progressive worsening leading to hypertensive encephalopathy and cardiac dysfunction. Later, renal angiography showed complete thrombotic occlusion of right renal artery and MAG3 imaging showed minimal function of the affected kidney. The infant required nephrectomy in view of medically uncontrollable hypertension and worsening cardiac dysfunction [11]. In the index case, renal doppler was normal and there were no signs of encephalopathy or cardiac dysfunction.

CONCLUSION(S)

In the reported case, hypertension was caused by neonatal CKD most probably due to hypoplastic kidneys. Neonatal CKD presenting with hypertension, anasarca and hypoalbuminemia is rare.

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