Case Report

Partially Reversible Acute Diffuse Renal Cortical Necrosis: A rare complication of a HUS in a young children

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Abstract

Renal cortical necrosis is a rare cause of acute kidney injury (AKI). It is rare in children. Diffuse renal cortical necrosis often leads to end-stage kidney disease. However, the outcome of patchy renal cortical necrosis is variable. Here, we reviewed the case of diffuse RCN in a 7-year girl caused by a HUS. She presented with acute abdominal pain, vomiting, and fever. Later she developed absolute anuria and anasarca. On examination, she had hypertension (154/80 mm Hg) and pallor. Laboratory findings were: White Blood Cell 19,930/mm^3, Hemoglobin 6.8 g/dL, Platelets 62,000/mm^3, Blood Urea 221 mg/dl, Sr. Creatinine 11 mg/dL, SGPT 192 IU, SGOT 141 IU, LDH 2482 U/l, Corrected reticulocyte counts 5.7 %, low C3, Anti factor H titer 1270 AU/ml, and CFHR deletion. Renal histopathology revealed diffuse renal cortical necrosis. Thus, diffuse RCN caused by aHUS was the final diagnosis. She was managed with intravenous cyclophosphamide followed by Mycophenolate Mofetil along with oral steroid. Her urine output and renal function improved and became dialysis independent. Thus, early diagnosis and aggressive management of underlying illness may lead to better renal outcomes even in patients with diffuse RCN.

Keywords: aHUS; Children; Partially; Reversible; Renal Cortical Necrosis.

Introduction

Renal cortical necrosis (RCN) is patchy or diffuse ischemic destruction of all the elements of the renal cortex caused by significantly diminished renal arterial perfusion due to vascular spasm and micro vascular injury[1]. Renal cortical necrosis (RCN) is a kidney disease that carries very grave adverse outcomes. Renal cortical necrosis (RCN) is a very rare entity, especially in pediatrics patients; in children, only a few cases have been reported[2, 3, 4]. RCN in pediatric patients is caused by perinatal complications and hemolytic uremic syndrome[3, 4]. It is a rare cause of acute kidney injury (AKI). It is less common in developed countries than the developing country (2% Vs 6%-7% of all causes of AKI). [5, 6] RCN is an irreversible lesion, often leads to end-stage kidney disease in diffuse cortical necrosis. Renal histology is the gold standard method for the diagnosis of RCN. Here, we are reporting a case of diffuse RCN caused by atypical hemolytic syndrome (aHUS) in 7 years young girl presented with AKI.

Case Report

Seven years young female was first presented in the pediatrics surgery clinic for pain abdomen associated with vomiting. Later, she was shifted to the nephrology ward for a sudden decline in renal function. She presented with acute onset generalized, non-colicky, non-radiating, abdominal pain associated with 2-3/day non-projectile, non-bilious vomiting, and low-grade continuous fever for five days. During her illness, she noticed a sudden complete loss of urine output, associated with progressive anasarca which started on the face and involved the whole body over three days. There was no history of the passage of stone or fleshy material in urine, change in urine color, burning micturition, melaena, hematemesis, chest pain, palpitations, orthopnea, sore throat, joint pain, skin rashes, photosensitivity, oral ulcer, and convulsions. He had been a full-term healthy baby at birth, with a gestational age of 40 weeks with a birth weight of around 3,500 g, and had normal developmental milestones. On general examination, she was conscious, oriented and her Blood Pressure was 154/80 mm of Hg in the Right arm supine position, Pulse rate was 94/min, Respiratory Rate- 18/min, body temperature was 100.4F. She had Pallor and anasarca. Systemic examinations were unremarkable. Laboratory findings on first day were as mentioned in Table 1.

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Table 1. Day one Laboratory data.			
TLC	19,930/mm3	**Sr Iron**	19 (58 – 158)
DLC	N85%/L10%	**Sr TIBC**	328 (250- 425)
Platelet	62000/mm3	**TSAT**	5.7 %
Hb	6.8 gm/dl	**Ferritin**	822 (20- 300)
Sr. Creatinine	11 mg/dl	**Lipase/Amylase**	Normal
Blood Urea	215 mg/dl	**HIV/HBsAg/HCV**	Non Reactive
Na^+/k^+	132/ 5.7 mmol/dl	**Para-check**	Negative
Ca^{2+}/P	7.3/ 6.4mg/dl	**PT/aPTT/INR**	14s/27s/1.2
Uric Acid	8.5 mg/dl	**S. fibrinogen**	385 mg/ dl (150- 400mg/dl)
Sr. Bilirubin	0.4 mg/dl	**D-dimer**	**643 ng/ml** (< 500)
SGPT/SGOT	192/141 IU /L	**Direct Coomb Test**	Negative
T. Protein/Albumin	7.4/4.2 gm/dl	**C3 & C4**	57.9 & 26.3 mg/dl
ALP	189 U/L	**ANA/Anti dsDNA Ab/ANCA**	Negative
LDH	2482 U/l (23- 460)	**USG ABD & Renal Doppler**	RK – 9 X 3 cm , CT -10 mm, LK- 8.9 X3.5 , CT -9.9 mm , No renal vessels abnormality
CPK	169 (24- 196)		
RBS	98 mg/dl		

The direct coomb test was negative. Urine examination was not performed as patients had anuria. Ultrasonography of the abdomen revealed ascites, RK 9 X 3 cm, CT -1 cm, LK- 8.9 X3.5 cm, CT -9.9 mm, and CMD accentuated. The Renal Doppler study was normal. Chest x-ray and 2D echocardiogram were normal. Provision diagnosis of acute kidney injury due to atypical hemolytic uremic syndrome was kept. Rapidly progressive glomerulonephritis and sepsis-induced acute tubular necrosis were enlisted in another possible differential diagnosis. She was managed with intravenous antibiotics, antiemetic, antihypertensive, antipyretics, and four units of PRBC transfused. RRT was given in form of hemodialysis (thrice per week). Plasmapheresis was advised but not performed because of financial constrain. On 7th day laboratory findings were as mentioned in Table 2.

Table 2. Day 7 laboratory data.	
TLC	10910/mm3
DLC	N85%/L9%
Platelet	280000/MM3
Hb	8.7 gm/dl
Sr Creatinine	6.3 mg/dl
Blood Urea	111 mg/dl
SGPT/SGOT	28.4/ 31.7 IU/L
LDH	868 U/L
Anti CFH antibody titer	1270 AU/ml (threshold of 150 for Indian control)
CFHR Deletion	Detected.

Despite improvement in leucocytosis, platelet count, and LDH level with one week of antibiotic treatment; she was still anuric (Day 10). Till then no other cause of anuria was established. A kidney biopsy was done and empirical intravenous pulse methylprednisolone (500mgay) was given for 3 days followed by oral prednisolone (1mg/kg/day). Renal histopathology revealed a total of 19 glomeruli, 17 (90%) had global tuft necrosis along with necrosis of adjacent tubules and vasculature (cortical necrosis). The remaining two glomeruli had severe ischemic changes. The necrotic process involved about 80-90% of the sampled cortical area (diffuse renal cortical necrosis). Immunofluorescence microscopy was unremarkable.(Figure 1A, B & C)

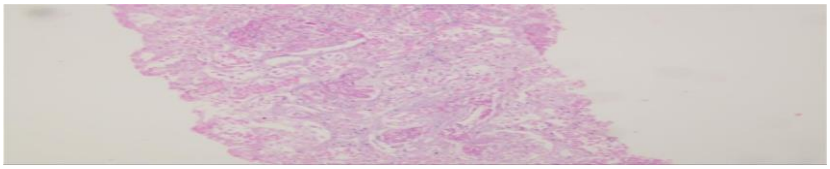

Figure 1A: Diffuse area of cortical coagulative necrosis of glomeruli and tubules.(H&E;10X)

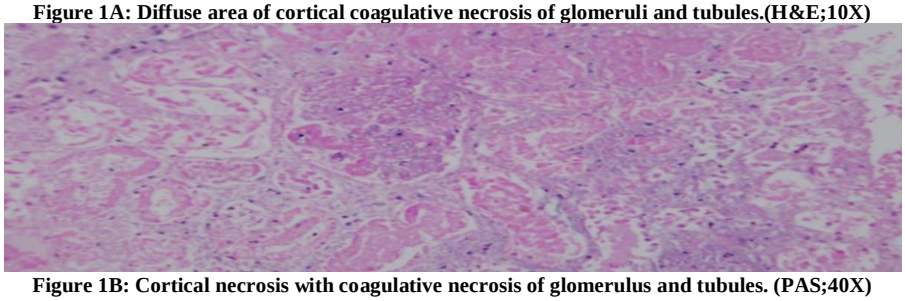

Figure 1B: Cortical necrosis with coagulative necrosis of glomerulus and tubules. (PAS;40X)

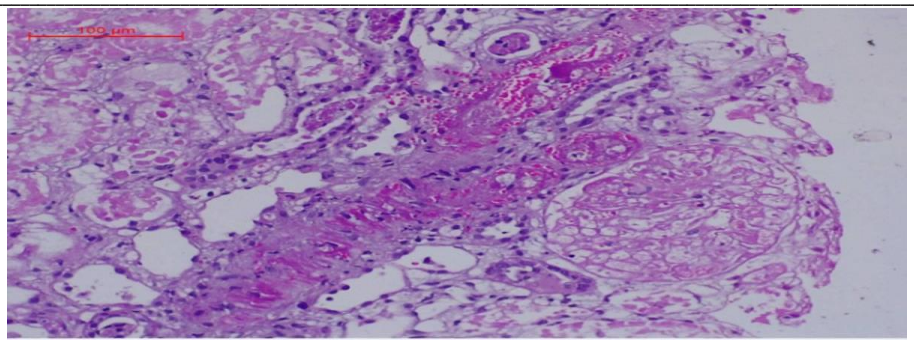

Figure 1C: Cortical necrosis with frank tubular necrosis with ghost-like outline of cells without discernible nuclei as well as pyknotic nuclei and karyorrhexis, characteristic of coagulative necrosis. (PAS;100X)

The cause of renal cortical necrosis was clinically unexplained, further investigation for atypical Haemolytic Uremic Syndrome (aHUS) with complement panel and genetic analysis was advised. She was treated with supportive medication and hemodialysis continued. Complement factor and genetic analysis revealed the presence of **Anti factor H titer 1270 AU/ml (threshold of 150 for Indian control) and CFHR deletion.** Thus, final diagnosis AKI, Diffuse renal cortical necrosis caused by Atypical Haemolytic Uremic Syndrome (aHUS) was made. Six doses of monthly intravenous cyclophosphamide (500 mg) were given along with oral steroid (1mg/kg OD for 4 weeks followed by 1mg/kg A/D for next 4 weeks then tapered down accordingly). After six doses of cyclophosphamide, shifted to Mycophenolate Mofetil for two months and since then she is on Azathioprine 75 mg BD with oral steroid 20 mg alternate day. After starting the intravenous cyclophosphamide, her urine output begins to improve, and attained normal output (1-2 L/day) by 8-10 weeks. Serum creatinine also improved from 11 mg/dl to 1.2 mg/dl and she becomes dialysis independent at 12 weeks. At present, she is continuing her immunosuppressant, dialysis independent, and having a stable renal function. Although, she has landed into Chronic Kidney Disease.

Discussion

Renal cortical necrosis (RCN) was first described in 1883 by Friedlander. It is an extremely rare cause of acute kidney injury and is usually irreversible[7]. We experienced a rare case of diffuse RCN caused by anti CFH antibody-mediated aHUS. Clinically we could not find any specific cause for the abrupt decrease in renal function, we did the kidney biopsy and pulse steroid therapy was started. Further evaluation revealed diffuse cortical necrosis caused by anti CFH antibody-mediated aHUS. Intravenous cyclophosphamide with oral steroid leads to sufficient recovery of renal function and she becomes dialysis independent. Thus, our work revealed the importance of early suspicion and the specific management of underlying cause may provide recovery even in diffuse RCN. RCN contributes less than 2% of cases of all causes of acute kidney injury (AKI) in a developed country[1]. It is very rare in pediatric patients. RCN in childhood is usually secondary to HUS or severe volume depletion. The age of children with HUS was eight months to 12 years[8]. In childhood, RCN equally affects both sexes. Abruptio placentae are the commonest cause of RCN in developed countries[9]; while, septic abortion is a common cause of RCN in developing countries[10,11]. Non-obstetrical causes of RCN are extensive burns, snake bite, sepsis, pancreatitis, HUS, infancy and childhood dehydration, malaria, and drugs and toxin[8,9,12,13]. In infancy and childhood: severe dehydration, congenital heart disease, fetomaternal transfusion, perinatal asphyxia, severe hemolytic disease, and sepsis are the main contributors of RCN[8]. Among non-obstetric causes, HUS was the most common cause 18/25 (72%) of cortical necrosis and RCN has been described in both D+ HUS and D-HUS. (9) In our case RCN is caused by anti CFH antibody-mediated aHUS. Toxin-mediated endothelial injury and vasospasm of small vessels seem to be initiating events in the process of cortical necrosis[14,15]. However, significantly diminished renal arterial perfusion is the final common pathway resulting in ischemic necrosis of the renal cortex. In our case dys-regulated alternative complement pathway activation by CFH inhibitory antibody leads to aHUS and finally diffuse renal cortical necrosis. Absolute anuria or anuria is the usual presenting symptom of acute RCN. The illness-causing RCN is systemic, thus the lesion is usually bilateral. Prolonged anuria (> 4 wk) usually suggests the clinical diagnosis of RCN. Our patients had anuria for 8-10 weeks. RCN can be diagnosed by non-invasive or invasive (kidney biopsy) methods. A kidney biopsy is a gold standard to confirm the diagnosis of RCN. It is the only measure for early (within week) diagnosis of RCN. In our case, there were global tuft necrosis in 17(90%) glomeruli along with necrosis of adjacent tubules and vasculature (cortical necrosis). The necrotic process involved about 80-90% of the sampled cortical area. The remaining two glomeruli had severe ischemic changes. (Figure-1) RCN has variable clinical course and outcomes and it depends on the extent of cortical necrosis. Patchy RCN carries a better outcome and has a chance of renal recovery because surviving nephron carry the function of the remaining kidney and survival without dialysis is possible. While, diffuse cortical necrosis is irreversible, carries poor renal outcomes, and often has a chance of progression into End-Stage Renal Disease. In a subset of patients with RCN, there may be a slow rise in creatinine clearance and a gradual gain in renal function over time, and glomerular filtration rate may reach a final plateau level of approximately 20-24 mL/min[1]. It is assumed that juxtamedullary glomeruli (which comprise 15%-20% of total) are spared in destruction, even in the complete cortical necrosis and that early functional return is due to the recovery of these nephron segments. In our patients too, improvement in renal function occurred after specific management of aHUS with an immunosuppressant, and now she is dialysis independent and has stable chronic kidney disease.

Thus, to summarise we report a 7-year young girl with diffuse RCN caused by aHUS, who showed recovery of renal function after specific management of aHUS. A high index of suspicion is important. Early diagnosis and aggressive management of underlying illness should be undertaken for better renal outcome and prognosis of the patient.

Conclusion

Renal cortical necrosis is an infrequent cause of acute kidney injury especially in children and has a poor prognosis. Thus, early diagnosis and aggressive specific management of underlying cause may change the prognosis of RCN even in diffuse variety of the disease.

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Conflict of interest

None

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