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Letter to the Editor

Acute renal failure in the emergency – Should we think beyond classical Hemolytic Uremic syndrome?

Hemolytic uremic Syndrome is the first diagnosis considered in any young child presenting with acute renal failure to the pediatric emergency. It is most commonly associated with diarrhea producing strains of enterohemorrhagic E.coli (0157:H7) as well as Shigella dysenteriae type 1 infection, classically producing D+ HUS (80 – 90%).(1) Here we present three children with acute renal failure treated in our hospital in the last month.

Case 1

A 10 month old developmentally normal child presented to the emergency with history of vomiting, loose stools, respiratory distress, decreased urine output and multiple episodes of convulsions of 2 days duration. He was born to a third degree consanguineous marriage and his sibling had also developed renal failure and died at the age of 10 months. The exact cause of renal failure in the sibling was not known. On examination, child was drowsy and dehydrated with acidotic breathing. Investigations revealed deranged renal parameters (Serum creatinine: 2.2) and microangiopathic hemolytic anemia (MAHA) (Hb – 5.6 g/dl). In view of anuria and persistent metabolic acidosis, peritoneal dialysis was instituted. Stool analysis for shiga toxin (stx) gene was negative. Considering the family history and the absence of stx gene in the stools, a diagnosis of hereditary HUS was considered and four units of fresh frozen plasma were transfused over the next two days. But the child developed refractory seizures on day 4 and ultimately succumbed to the illness. The blood samples of the child were sent for complement factor H antibodies which was found to be positive in the child.

Case 2

A 10 month old male child presented to the pediatric emergency with decreased urine output and respiratory distress of 10 days duration and vomiting for 2 days. There was no history of diarrhea or fever. He was born to a non consanguineous marriage and there was no significant past or family history. On examination, he was irritable with severe pallor and edema. Hypertension (158/100 mm Hg) was present with features of congestive cardiac failure for which he was managed with fluid restriction, diuretics and sodium nitroprusside infusion. Investigations revealed MAHA and altered renal parameters (Serum creatinine: 2.0 mg/dl). Serum lactate dehydrogenase (LDH) was 1023 IU/L and C3 and C4 was normal. There was no evidence of any long standing hypertension (normal ocular fundus, ECG and ECO heart) and abdominal ultrasound revealed normal sized kidneys with increased echogenicity. Peritoneal dialysis was started in view of oliguria and rising renal parameters. Stool cultures and tests for Shiga toxin were negative. Renal functions gradually improved over 5 days. He still needs antihypertensives to maintain normal blood pressure. Assays for complement factor H have been sent and are awaited.

Case 3

A 4 year old female child was admitted with chief complaints of fever, edema and increasing pallor for 10 days. There was no significant past or family history and no history of diarrhea. On examination, she had pallor, edema of the limbs with hypertension. Renal parameters were deranged (serum creatinine: 2.7mg/dl), hemoglobin was 7 g/dl with features of MAHA on peripheral smear. Serum

LDH was high (759 IU/l) and C3, C4 was normal. USG abdomen revealed normal sized kidneys bilaterally. Since she had normal urine output, she was managed conservatively with anti hypertensives and diuretics. Stool cultures were sterile. Work up for complement factor H and I is awaited.

In all the three children few clinical features were atypical: absence of diarrhea in case 2 &3, positive family history (case 1), insidious onset of symptoms (case 2&3), prominent extra renal manifestations (case 1&2) and persistent hypertension (case 2&3). Presence of these atypical features raised the suspicion of an alternate diagnosis. Testing of stool for shiga toxin assays helps to differentiate D+ HUS from atypical HUS and should be carried out as part of routine work up. The current recommendations are to screen all patients diagnosed with non infectious HUS for complement factors and ADAMTS13 deficiencies.(2) The management of atypical HUS rests on daily plasmapheresis (50 – 100ml/kg/day) or plasma infusions(10 – 20 ml/kg) to be initiated empirically for replacement of the deficient factors and clearing autoantibodies if present against the complement factors(3). The only exception being Pneumococcal infection induced HUS which will be exacerbated with plasma transfusions (due to presence of anti TF IgM antibodies in plasma). Rituximab(anti CD20 antibody) and Eculizumab(by blocking cleavage of C5a in alternate pathway) offer a new hope in the management of relapses of atypical HUS(3,4). Since the prognosis of atypical HUS is poor (25% mortality,50% ESRD) (5), rapid diagnosis and early initiation of treatment are the keys to favourable outcome.

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