Atypical Hemolytic-uremic Syndrome with impending CKD

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CHIEF COMPLAINTS

11 year male child came to casuality with chief complaints of

Fever since 15 days

Vomiting (2-3 episodes) since 10 days

Periorbital edema and abdomen distension since 7 days

Not passed urine since 1 day

HISTORY

- H/o fever since 15 days ,sudden in onset , intermittent, moderate grade ,not associated with chills and rigours,no aggravating factor, fever subsiding on taking medication
- H/o vomiting since 10 days,2-3 episodes per day, non bilious non projectile ,containing mostly of food particles , not associated with loose stools
- H/O **generalized swelling** since 7 days, insidious in onset ,first appearing over periorbital region and face later involving trunk and limbs
- H/O **not passing urine** since 1 day

- No h/o loose stools
- No h/o any drug intake
- No h/o cough , cold ,difficulty in breathing
- No h/o yellowish discoloration of skin
- No h/o any rashes
- No h/o slurring of speech
- No h/o weakness in the limbs
- No h/o convulsions
- No h/o alteration in consciousness

- No h/o reddish or brownish discoloration of urine
- No h/o burning micturition
- No h/o foul smelling urine
- No h/o pain abdomen

- PAST HISTORY – No h/o of similar complaints in the past
  H/o nocturnal enuresis present
  no h/o skin infections
  no h/o gum bleeding and bony pain
  no h/o dysphagia and arthralgia
  no h/o contact with k/c/o tuberculosis

- TREATMENT HISTORY –No h/o intake of any nephrotoxic drugs
- GROWTH AND DEVELOPMENTAL HISTORY – No features suggestive of growth retardation

- FAMILY HISTORY –No h/o similar complaints in family

CLINICAL EXAMINATION

- GENERAL PHYSICAL EXAMITION –

  . child looked irritable but conscious and oriented to time place and person

  .puffiness of face without any dysmorphism

  .eyes were normal

  . generalized edema present (pitting)

  .**pallor present**

  .no evidence of insect bite, rashes

.no neuro cutaneous markers

.no dystrophic nails

.spine was normal

.lymph nodes- not enlarged

- VITALS SIGNS-
  HR- 88 bpm
  RR- 18 breaths/ min
  BP- 136/96 (>99TH CENTILE)
  TEMP- 98.1F (AFEBRILE)
  Pallor(+)
- ANTHROPOMETRY- weight-28 kgs
  height-126 cms
  BMI- 17.7

SYSTEMIC EXAMINATION

- GASTROINTESTNAL SYSTEM-

  INSPECTION- abdomen was distended uniformly

  umbilicus –transversely slit ,normal in position

  all quadrants moving equally with respiration

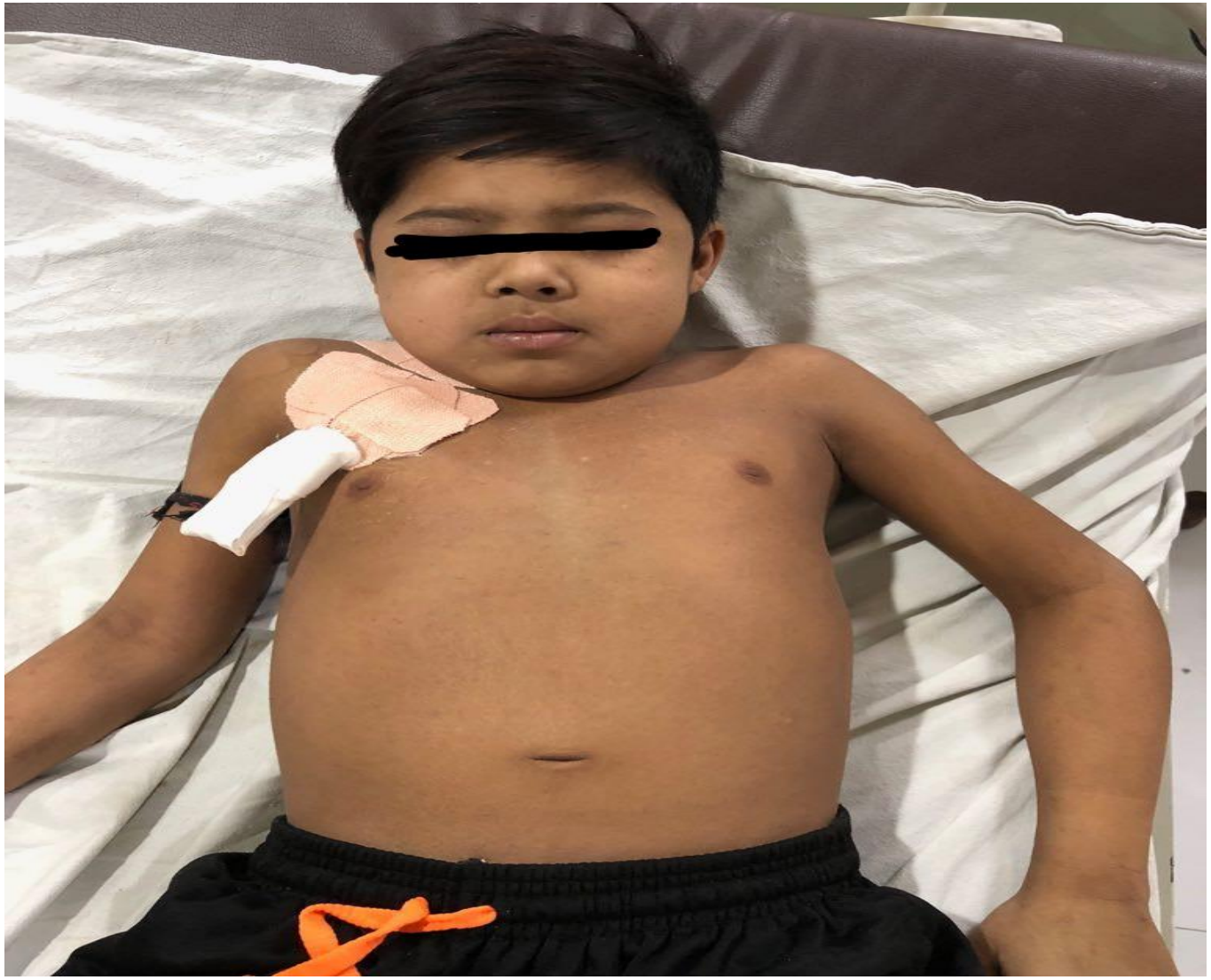
  no visible pulsations or scars or sinuses

  dilated veins seen

  PALPATION- no local rise in temp

  no tenderness,guarding or rigidty

  no organomegaly



- PERCUSSION- fluid thrill present
  shifting dullness present
- AUSCULTATION-bowel sound heard,no bruit
- CENTRAL NERVOUS SYSTEM-
  conscious and oriented , No neurological deficit
  NO flapping tremor
  no signs of peripheral neuropathy

- CARDIO VASCULAR SYSTEM-

  S1 S2 heard, no murmurs

  NO SIGNS OF CONGESTIVE CARDIAC FAILURE

- RESPIRATORY SYSTEM-

  Air entry bilaterally equal

  normal vesicular breath sounds

  no added sounds

INVESTIGATIONS

- 14/2/18- **Hb-6.8 gm%**
  TLC-17800 , DLC-68/28/2/2
  platelet count- 80,000 cells/cu.mm
  retic count- 0.4%
  PBS- EVIDENCE OF MICROANGIOPATHIC HEMOLYSIS PRSENT
  Blood urea-222mg/dl
  Sr creatinine-14.9mg/dl
  sr electrolyte-Na-136mmol/l k-3.6mmol/l
- USG abd and pelvis-
  b/l renal parenchymal disease
  rt kidney-4.9*2.6 Lt kidney-5.3*2.5cms
  raised echogenicity

Lipid profile-

sr triglyceride-147mg%

sr cholesterol-159mg%

HDL – 45mg%

LDL- 97mg%

16/2/18- **C3-58(90-180)**

C4-31(10-40)

17/2/18- PT-18.4sec Aptt-28.4 sec INR-1.6

ASO-Negative

21/2/18- UPCR- 6.73

13/3/18- **LDH – 782U/L**

17/3/18- **ANTI COMPLEMENT FACTOR H ASSAY- 2500 AU/ML**

FINAL DIAGNOSIS

- Atypical HUS due to Factor H deficiency

MANAGEMENT

- SYMPTOMATIC –
  - -Anti-emetics
  - -Anti-pyretics
  - -Antibiotic
- SUPPORTIVE CARE-
  - -Careful monitoring of fluid and electrolyte balance
  - -Control of hypertension
  - -early institution of dialysis
  - -Red cells(washed) transfusions

- PLASMAPHERESIS WITH INFUSION OF FRESH FROZEN PLASMA

  -Plasmapheresis was started on 21/3/18,after confirming the diagnosis of Atypical HUS . Initially it was instituted everyday for the first 6 sessions . Patient responded well to the treatment.Edema decreased ,blood pressure recorded within normal limit . RFT improved drastically (**b.urea-37,sr.cr-3.4**)

  -Later plasmapheresis was given alternate days for 8 more sessions and finally stopped as anti factor H antibody and LDH came down to normal range(**anti factor H-172, LDH-190**) and patient improved clinically

POST PLASMAPHESESIS INVESTIGATIONS-

USG ABDOMEN AND PELVIS-

bilateral renal parenchymal disease

right kidney-4.5*1.4 Lt kidney-5.7*2.4cms

raised echogenicity

PBS- Normocytic normochromic ,

occasional tear drop cells.

DISCUSSION

- Atypical HUS characterized by microangiopathic hemolytic anemia,,thrombocytopenia and renal insufficiency.
- ETIOLOGY-

1.GENETIC- Factor H deficiency,CD46 ABNORMALITIES, complement factor I def,complement factor B mutation,C3 mutations

2.INFECTIONS- STEC-HUS, pneumococcal infections,HIV infection

3.SYSTEMIC DISEASES-Anti phospholipid syndrome,SLE,scleroderma,malignant hypertension,malignancy

4.DRUGS-Mitomycin,quinidine,ticlopidine,clopidogrel,calcineurin inhibitors,oral contraception,gemcitabine

5.metabolic disease- cobalamin c

- PATHOLOGY- Diagnosis usually established by clinical criteria.
  - -thickening of capillary wall
  - -platelet- fibrin thrombi
  - - fibrinoid necrosis of arterial wall
  - -renal cortical necrosis
  - -glomerular sclerosis

- PATHOGENESIS- **Microvascular injury** with **endothelial cell damage** is characteristic of all forms of HUS.

Factor H plays a central role in complement regulation, primarily **arresting amplification and propagation of complement activation.**

Mild endothelial injury which normally resolve instead evolves to an **aggressive microangiopathy**

Endothelial injury leads to localized **thrombosis**,particularly in glomeruli, causing direct decrease in glomerular filtration.Progresive platelet aggregation in areas of injury leads to **consumptive thrombocytopenia**.

Microangiopathic hemolytic anemia results from mechanical damage to the RBCs

- COMPLICATIONS- HUS can be mild or can progress to severe fatal multisystem disease
- Complications include-

1. Renal failure
2. Hyperkalemia
3. Heart failure
4. Seizures and significant encephalopathy
5. Inflammatory Colitis,bowel perforation
6. Intussusception
7. Pancreatitis

- DIAGNOSIS- The diagnosis is made by the combination of microangiopathic hemolytic anemia with schistocytes , thrombocytopenia and renal insufficiency, raised anti factor H antibody

- PROGNOSIS- Atypical HUS has POOR prognosis as compared to diarrhea associated HUS

Frequency- 20-30%

Response to short term plasma therapy- Remission 60%

Rate of death or ESRD- 70-80%(5-10 years after onset)

Outcome of kidney transplantation-Recurrence 80-90%

MANAGEMENT

- SUPPORTIVE CARE-
  - -Careful monitoring of fluid and electrolyte balance
  - -Control of hypertension
  - -early institution of dialysis
  - -Red cells(washed) transfusions
- PLASMAPHERESIS
- ECULIZUMAB- Anti C5 antibody ,inhibits complement activation

THROMBOTIC THROMBOCYTOPENIC PURPURA

- PENTAD-Fever, microangiopathic hemolytic anemia,thrombocytopenia,,abnormal renal function, CNS changes.
- PRESENTATION- Adults, occasionally in adolescents.
- ETIOLOGY-mostly caused by deficiency of metalloproteinase(ADAMTS13), CAN BE CONGENITAL OR AUTOANTIBODY MEDIATED
- C/F- weakness, pain ,emesis, apasia, blindness, seizures
- DIAGNOSIS- microangiopathic hemolytic anemia, thrombocytopenia,raised reticulocytic count,elevated creatinine and blood urea levels
- TREATMENT- Plasmapheresis with fresh frozen plasma infusions