
PRESENTATION

Raashid Ali, a 12 year old boy, resident of Gujjar Khan was brought by his parents on 7th Jan, 2009 with complaints of Anuria, Vomiting, and Bilateral Flank pain for 2 days. Vomiting was moderate in amount and not continuous. Past History revealed Swelling of the face 1 month back which was treated. Fever & diarrhea in the past week (after eating 'Pakorray') was also reported. Family History was negative for Diabetes mellitus or any malignancy. Treatment History was negative for any recent surgery. No recent history of burns was reported.

At this stage, we can think of an acute problem. A pre-renal failure due to fluid loss can't be our first thought as the vomiting is not severe, and there is no history of recent surgery or burns. Acute renal or post-renal failure may be a reason.

On examination, Raashid was a co-operative child, well-oriented in time, place & person, & lying comfortably in bed with pulse: 80/min, temperature: 98 F, B.P.: 120/80 mm Hg, marked pallor, without any jaundice and oedema. Skin didn't show any bruises or petechiae. Lymph nodes were not palpable.

Blood pressure is maintained without external support. The problem could be an infective one but he is afebrile. Marked pallor could be due to haematuria or renal failure, but there isn't any history of blood in urine.

Examination of G.I.T. revealed mild tenderness in flanks. Otherwise, examination of C.N.S., Respiration, and C.V.S. was unremarkable.

Findings are pointing towards a renal pathology or an obstruction of urinary tract.

A provisional diagnosis of acute renal failure was made, and a diuretic trial (Inj. Furosemide) was given. He passed urine the very day of treatment!

Possibility of a post-renal cause is far now. Laboratory can help us in revealing underlying pathology.

Table 1.1 Possible causes of acute renal failure due to renal pathology

Acute glomerulonephritis

Acute tubular necrosis

Acute cortical necrosis:

- Severe Ischemia

- DIC

- Snake bite

Acute pyelonephritis

Fig. 1.1 Lab. Results

TLC: 24000/ μ L [4000-11000/ μ L]

A.N.C.: 21000/ μ L [2000-7000/ μ L]

RBC: 2.3×10^6 / μ L [$4-6 \times 10^6$]

Hb: 5 g/dL [13-17 g/dL]

MCV: 75 fL [83-101 fL]

MCH: 24 pg [27-32 pg]

M.C.H.C.: 33 g/dL [31.5-34.5 g/dL]

RDW-SD: 39 fL [39-46fL]

RDW-CV: 15% [11.6-14%]

PLT: 87 000/ μ L [150 000 – 400 000/ μ L]

Anaemia, neutrophil leukocytosis, and thrombocytopenia need a peripheral film morphology to be commentable.

Peripheral Blood Morphology showed RBC fragmentation, Neutrophilia with left shift, a Reticulocyte count of 4.5%. No Malarial parasite was seen. No platelet clumps were seen.

An element of haemolysis, thrombocytopenia and possibility of an underlying infective process has emerged. Neutrophil leukocytosis may be due to stress. Blood culture may be helpful.

Prothrombin time of 22 sec [Control: 14 sec] was noted. Urine R/E showed Albumin 1+, Numerous RBCs, but No crystals or sugar. 24 hr urinary protein was 2.8 g [<0.15 g]. No WBC seen.

Possibility of small renal stones with superadded infection was remote now. Rather a coagulation problem was revealed.

USG abdomen showed Renal parenchymal disease, with Kidney size normal.

Renal stones, renal artery disease, and any abnormal growth were ruled out. Liver morphology appeared normal as well.

ANA [AIHA], Anti-MPO (p-ANCA) [Vasculitides], Anti-proteinase 3 (c-ANCA) [WG], Viral serology for Hepatitis B & C were all negative. Other tests showed Creatinine: 173 micro.mol/L [60 - 156 micro.mol/L], Urea: 20 mmol/L [3.3 - 8.3 mmol/L], S. Potassium: 8.4 mmol/L [3.4 - 5 mmol/L], LDH: 1250 U/L [225 - 450 U/L], Total Bilirubin: 9 micro.mol/L [<17 micro.mol/L], Indirect bilirubin: 4 micro.mol/L [<12 micro.mol/L], ALT: 19 U/L [<41U/L], S. Albumin: 18 g/L [35 - 50 g/L], S. Cholesterol: 3.6 mmol/L [5.7 mmol/L], & S. Triglycerides: 5.6 mmol/L [<1.8 mmol/L].

These tests showed reduced renal function with evidence of haemolysis.

An impression of leukocytosis, thrombocytopenia, and microangiopathic haemolytic anaemia was made.

Differential Diagnosis can include here Haemolytic-Uremic syndrome, Thrombotic thrombocytopenic purpura, Disseminated intravascular coagulation, Renal parenchymal diseases, & Evan's syndrome.⁵

There were not any neurological symptoms & signs,

Final Diagnosis of Haemolytic-Uremic Syndrome was made considering the presentation and laboratory test reports, and he was treated with corticosteroid and RCC transfusion.

Raashid Ali improved and was discharged with a Creatinine level of 90 micro.mol/L (60 – 156 micro.mol/L).

DISCUSSION

Haemolytic–Uremic Syndrome is characterized by Microangiopathic haemolytic anaemia, renal failure, and thrombocytopenia without the features of D.I.C.

It has many types:

-Diarrhea-related:

Exotoxin of E. coli/ S. dysenteriae

-Familial:

Factor H deficiency (Complement regulatory protein)

-Atypical:

Post-partum

Pathogenesis includes a trigger which damages endothelium, resulting in activation of the endothelium & subsequent High levels of Endothelin⁴, vWF multimers⁸ & Low PGI₂ secretion leading to vasoconstriction & platelet aggregation⁴ Verocytotoxin of E. coli can directly activate platelets⁴. Result is a consumptive thrombocytopenia⁶. Ischaemic damage⁶ of renal cortex¹ is a characteristic feature.

Associations:

- E. coli O157: H7 gastroenteritis, S. dysenteriae
- Viral infections
- Drugs⁷:
 - quinine, , ticlopidine, clopidogrel, cyclosporine, & mitomycin C
- Radiation therapy
- Bone marrow transplantation
- Factor H deficiency⁴

Other features include High LDH & Indirect bilirubin. Coagulation abnormalities in HUS are milder from those observed in classic DIC: the PT and aPTT are normal or only slightly prolonged.⁸ No deficiency of vWF-cleaving metalloprotease (ADAMTS13) is found. Low serum C3 level in Factor H deficiency is typical.

Drug treatment:

Diarrhea-related HUS

- In children, self-limited. Conservative Rx of Renal failure^{.1, 5}
- Antimotility drugs are contraindicated.²

-Antibiotics: Sepsis or *S. dysenteriae*.²

-Corticosteroids can be beneficial.⁹

-Dialysis in resistant cases.⁹

Familial & Atypical HUS

In adults, large-volume plasmapheresis with FFP² (upto 80mL/kg) daily until in remission.⁵

Take-home message

1. Undercooked food should be avoided.
2. Diarrhea in children should be investigated for aetiology.
3. Preventable re-exposures (e.g. drugs) should be avoided.
4. Antimotility agents should be avoided in infectious diarrhea.
5. HUS should be in D/D of Renal failure in children.

References:

1: **William's Haematology**, 7th Edition

2: **Postgraduate Hoffbrand**, 5th Edition

3: **Oxford Handbook of Hematology**

4: **Pathologic Basis of Disease**, 7th Edition

5: **Current Medical Diagnosis & Treatment**, 2009 Edition

6: **Haematologica**

7: **Current Opinion in Haematology**

8: **The New England Journal of Medicine**

9: **Treatment of hemolytic uremic syndrome after acute stage** Zhonghua er ke za zhi. Chinese journal of pediatrics 2006;44(3):206-9.