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Atypical haemolytic uremic syndrome in patient of CKD

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Abstract

Atypical HUS is characterised by microangiopathic haemolytic anaemia, thrombocytopenia, and renal insufficiency. Factor H deficiency is one of the main cause of atypical HUS, wherein anti-complement factor H antibody is high leading to deficiency of factor H.

We report a case of atypical HUS due to factor H deficiency in a patient of CKD which presented with fever, vomiting (without loose stools) and generalised Edema. OIE child looked pale, pitting type of Edema present, B.P was raised. Investigations showed evidence of microangiopathic haemolytic anaemia, thrombocytopenia, renal insufficiency. Anti-complement factor H assay was raised. USG confirmed features of CKD. Dialysis was started, FFP was infused with little improvement. Patient responded well to plasmapheresis. Patient improved clinically.

Keywords: Atypical haemolytic, uremic syndrome, patient of CKD

Introduction

HUS is a common cause of community acquired acute kidney injury in young children. It is characterised by the triad of microangiopathic hemolytic anaemia, thrombocytopenia and renal insufficiency. Etiologies are classified into infection induced, genetic, medication induced, and HUS associated with systemic diseases. Genetic forms of HUS (atypical, non-diarrheal) compose the second major category of the disease. The major feature of genetic form of HUS is the absence of diarrheal prodrome. Genetic forms can be indolent and unremitting. Diagnosis is usually established by clinical criteria.

Pathological changes seen in HUS are thickening of capillary wall, formation of platelet fibrin thrombi leading to decrease in blood flow which leads to fibrinoid necrosis of arterial wall, eventually causing renal cortical necrosis.

Micro vascular 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. In the absence of factor H, mild endothelial injury which resolves normally evokes an aggressive microangiopathy.

Diagnosis of atypical HUS due to factor H deficiency is made by the combination of microangiopathic haemolytic anaemia with schistocytes, thrombocytopenia, renal insufficiency, raised anti-factor H antibody.

Atypical HUS has poor prognosis as compared to diarrheal HUS.

The reported case was a child who developed atypical HUS, due to factor H deficiency with signs of impending CKD. His anti-complement factor H assay was found to be very high which subsequently reduced after plasmapheresis and child improved clinically

Case Report

11 year old male child, presented with fever since 15 days, vomiting 2-3 episodes since 10 days, periorbital Edema and abdominal distension since 5 days, not passed urine since 1 day. Fever was sudden in onset, intermittent, moderate grade not associated with chills and rigor, vomiting was non bilious non projectile containing mostly food particles, not associated with loose stools. Swelling was insidious in onset first appearing over periorbital region and face later involving trunk and limbs. There was no history of drug intake, respiratory distress, slurring of speech, convulsions or alteration of consciousness.

No history of similar complaints in the past. No history of skin infections, gum bleed or bony pain. No history of intake of nephrotoxic drugs.

On clinical examination child looked irritable but conscious and oriented to time place and person. There was puffiness of face without facial dimorphism. Generalised Edema was present (pitting type). Child looked very pale. Patient was stable hemodynamically. BP was raised 136/96 mm of Hg (more than 99 centile).

On systemic examination abdomen was distended uniformly, transversely slit umbilicus, all quadrants was moving equally with respiration. On palpation there was no guarding, rigidity or tenderness, no organomegaly present. Fluid thrill and shifting dullness was present on percussion. On auscultation bowel sounds heard. Rest of the systemic examination was normal.

Investigations showed evidence of microangiopathic haemolytic anaemia with thrombocytopenia, and renal insufficiency. Hb was 6.8gm%, Platelet count of 80,000 cells /cumm, retic count of 0.4%. There was evidence of microangiopathic haemolysis on peripheral blood smear. RFT was deranged (Blood Urea: 222mg/dL, S. creat: 14.9gm/dL). LDH was raised (782U/L). Anti-complement factor H assay was 2500 au/mL. USG abdomen and pelvis reported small and contracted kidney with raised echogenicity. Based on the clinical findings and investigations we reached to the diagnosis of Atypical HUS due to factor H deficiency in a known case of CKD.

We started symptomatic treatment and supportive care. Careful monitoring of fluid and electrolyte balance was done. Child was started on anti-hypertensive, dialysis was started along with red cell transfusions. Child showed little improvement.

Plasmapheresis with infusion of Fresh Frozen Plasma was started initially it was instituted every day for the first 6 sessions. Patient responded well to the treatment, edema decreased, BP recorded within normal limit, RFT improved drastically (Blood Urea: 37 mg/dL, S. Creat: 3.4gm/dL). Later plasmapheresis was given on alternate days for 8 more sessions and finally stopped as anti-factor H antibody and LDH level came down drastically. USG abdomen and pelvis was repeated after a month which reported Bilateral renal parenchymal disease, bilateral small and contracted kidney with raised echogenicity.

Discussion

The atypical form of HUS is characterised by microangiopathic haemolytic anaemia, thrombocytopenia, and renal insufficiency^[1]. Atypical HUS is associated with defective complement regulation. The complement system represents an innate immune defence system that eliminates invading microbes. Genetic form of HUS composed the second major category of the disease. Inherited deficiency of either Von Will brand factor – cleaving protease (ADAMTS 13) or Complement factor H, I or B and defects in vitamin B12 metabolism can cause HUS. A specific genetic defect has not been identified in approx. 50% of familial cases transmitted in classic mendelian autosomal dominant or recessive patterns. A major feature characteristic of genetic HUS is the absence of preceding diarrhea prodrome. Genetic forms of HUS can be indolent and unremitting once they become manifest or they have a relapsing pattern precipitated by infectious illness^[2, 3].

HUS Can be superimposed on any disease associated with micro vascular injury, including malignant hypertension, SLE, APLA syndrome^[4].

Kidney biopsies are rarely performed in HUS because the diagnosis is established by clinical criteria. Pathological changes include thickening of the capillary walls causing narrowing of the capillary lumens, platelet-fibrin thrombi are seen in glomerular capillaries thus compromising on blood supply causing fibrinoid necrosis of the arterial wall leading to renal cortical necrosis from vascular occlusion^[1, 4, 5]. Micro vascular injury with endothelial damage is characteristic of HUS. Factor H plays a central role in compliment regulation primarily arresting amplification and propogation of complement activation. In the absence of factor H, mild endothelial injury which resolves normally evokes an aggressive microangiopathy^[6, 7]. Endothelial injury leads to localised thrombosis, particularly in glomeruli, causing direct decrease in glomerular filtration. Progressive platelet aggregation in areas of injury leads to consumptive thrombocytopenia. Microangiopathic hemolytic anemia results from mechanical damage to RBC's as they pass through damaged and thrombotic micro vasculature.

Complications of HUS include renal failure, hyperkalemia, heart failure, seizures and significant encephalopathy, inflammatory colitis, bowel perforation, intussusception, pancreatitis etc.

Diagnosis is made by combination of microangiopathic hemolytic anaemia with schistocytes, thrombocytopenia, renal insufficiency, raised anti-factor H antibody. Prognosis of atypical HUS is poor as compared to diarrheal HUS. Frequency of atypical HUS due to factor H auto antibodies is 20-30%. Remission in response to short term plasma therapy is 60%. Rate of death or ESRD is 70-80% (after 5-10 years of onset). Recurrence after kidney transplantation is 80-90%^[8, 9].

Management includes careful monitoring of fluid and electrolyte balance, control of hypertension, early institution of dialysis, red cells transfusions, plasmapheresis, and drugs like Eculizumab (anti C5 antibody, inhibits complement activation)

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