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ATYPICAL HEMOLYTIC UREMIC SYNDROME – A RARE CASE REPORT

General Medicine

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ABSTRACT

Atypical hemolytic uremic syndrome (aHUS), a rare variant of thrombotic microangiopathy, is characterized by microangiopathic hemolytic anemia, thrombocytopenia, and renal impairment. The condition is associated with poor clinical outcomes with high morbidity and mortality. Atypical HUS predominantly affects the kidneys but has the potential to cause multi-organ system dysfunction. This uncommon disorder is caused by a genetic abnormality in the complement alternative pathway resulting in over-activation of the complement system and formation of microvascular thrombi. Abnormalities of the complement pathway may be in the form of mutations in key complement genes or autoantibodies against specific complement factors. We discuss , clinical manifestations, diagnosis, complications, and management of aHUS.

KEYWORDS

Diacylglycerol Kinase E(dgke), Atypical Hus, Anticomplement Factor H Antibody.

INTRODUCTION:

Atypical Hemolytic uremic syndrome is associated with rapid progression to end stage renal disease. In undiagnosed cases of aHUS, post transplant recurrence is nightmare. Thus pretransplant diagnosis of aHUS should be sought in suspected cases.

Aypical HUS is due to dysregulation of alternative complement pathway and mutations of the gene, diacylglycerol kinase ε(DGKE)(1). Genetic or acquired dysregulation of the complement alternative pathway is detected in 40–60% of patients with aHUS suggesting a genetic predisposition (8). This dysregulation is caused by mutations in genes that encode complement regulatory , Factor H (FH), Factor I (FI), membrane cofactor protein (MCP), complement 3 (C3), Factor B (FB) or thrombomodulin, or presence of anti-FH antibody resulting in activation of the complement system(1). The complement abnormality that is associated with aHUS is very rare with only roughly 1000 reported cases(2,8-15).

The incidence of aHUS is estimated to be 0.23–0.42 cases per million; children (<18-year of age) constitute 0.10–0.11 cases per million(16,17,18). The disease has been triggered by pregnancy, viral illness, and sepsis among other causes; approximately 30% of aHUS results from unknown mechanisms(2). Atypical HUS has a mortality rate of 25% and about 50% of patients may show end stage renal disease (ESRD)(4-7).

Case Summary:

38year old male admitted on 11/07/22 to GMCH Aurangabad with chief complaint of swelling over bilateral lower limb since 1 year, fever since 5-6 days, blood in urine since 5-6 days, yellowish discoloration of eyes since 5-6 days. On examination he is concious, alert, BP 150/90 mmHg, Bipedal edema, pitting type , mild icterus +, periorbital edema +

Investigations-

Hb 11.2 mg/dl TLC 4200 % platelets 37000/ul

Urea- 127 Creatinine -2.4

Bilirubin - 3.2 SGOT 95 SGPT 46

On peripheral smear - Schistocytes++

Urine routine and microscopy - protein ++ RBC 10-12/hpf

24 hr urinary protein-1. 08gm/day

Complement c3- 0.48g/L c4- 0.05g/L

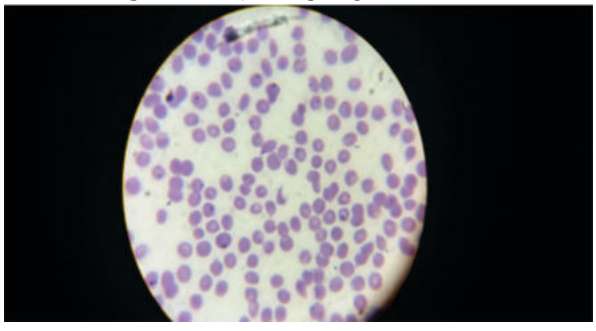
Direct and indirect coombs test - Negative,

Reticulocyte count 1%

ANA (antinuclear antibodies) blot Negative

Anti Complement Factor H - 181.5 AU/mL

Patient underwent 5 cycles of Plasmapharesis with alternate Haemodialysis. Patient was not responding well to this treatment hence he was planned for Inj Rituximab (monoclonal anti-cd20) 375mg/m2 every once in a week for 5 doses . Patient was clinically improved and also labs were improved. Then he was started on maintenance therapy with Mycophenolate mofetil and low dose corticosteroid (prednisolone) with tapering dose for 6 months.



Peripheral smear showing schistocytes :-

Gross hematuria:

DISCUSSION:

Atypical hemolytic syndrome is a rare presentation in adults and is associated with rapid progression to end stage renal disease. It can be familial, sporadic ,pregnancy associated,post bone marrow transplant

and drug induced . It can occur at any age but most commonly seen in young age group. Most common cause is complement factor H mutation.Genetic and sporadic causes leads to dysfunction in complement cascade leading to complement deposition in endothelial cells causing endothelial damage and trapping of platelets which eventually leads to thrombocytopenia,microcirculatory hemolysis and renal dysfunction. Patient presents with hemolytic anemia, thrombocytopenia,renal dysfunction and hypertension. Autoantibodies to complement factor H is seen in 4-14% cases of atypical Hus (in India the incidence is 50-60%) . Hence immunosuppression is recommended for anti-CFH antibody mediated hemolytic HUS. Most of the treatment guidelines advocate use of Plasmapharesis and eculizumab for treatment of ATYPICAL HUS which may not be necessary for antibody mediated HUS. In Indian consensus guideline, anti-CFH antibody mediated HUS requires immunosuppression with cyclophosphamide or rituximab and patient then maintained on immunosuppression using azathioprine or Mycophenolate mofetil.

CONCLUSION:

A strong clinical suspicion of aHUS and complement related glomerulopathy is necessary for young hypertensive patient with anemia and renal dysfunction. Renal transplant in anticomplement factor H antibody-positive aHUS cases can be considered after due explanation of recurrence with the use of pretransplant plasma exchange and rituximab after documenting normal Anticomplement factor H levels.

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