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Original Research Paper

Medicine

ATYPICAL HEMOLYTIC UREMIC SYNDROME- A RARE DISORDER

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ABSTRACT

Atypical Hemolytic uremic syndrome (HUS) is defined by the triad of microangiopathic hemolytic anemia, thrombocytopenia and renal impairment. Atypical HUS is the result of congenital complement dysregulation. The affected patient have low C3 and normal C4 level,.Factor H deficiency, the most common defect, linked to familial with aHUS . Mutations in the genes encoding complement regulatory proteins factor H, membrane cofactor protein (MCP), factor I or thrombomodulin have been demonstrated and mutations in the genes of C3 convertase proteins, C3 and factor B,In additionof patients have anti-factor H antibodies .. The disease should have no association with Shiga toxins, and TTP should also be exclude

33 A year old male patient, came to our emergency department with the chief complaints of decreased urine output and multiple purpuric skin lesions since 2 days and recent history of diarrhoea 15 days back followed by fever 10 days back.

On Investigation s.Creatinine 7.28, s.urea 107.40,Hb:9.96,TC:12,200 and PC:78000 SGPT:29 Direct Billrubin:0.8, Indirect Billrubin:1.9 Total Billrubin:2.7 . Other special investigation were done,:Retic count -0.6, S.LDH- 735IU/L (normal range ,248 IU/L), ANA- Negative, C-ANCA-Negative, P-ANCA-Negative, LA - Negative, CRP- Negative, RA- Negative, ASO- Negative, C3 LEVEL- 0.63 (normal range- 0.9-1.83),C4 LEVEL-0.16 (normal range- 0.1-0.4), CPK TOTAL- 52. patient's 2D ECHO was normal and his ultrasound abdomen pelvis showed raised cortical echogenecity in both kidneys with preserved Cortico medullary differentiation. confirmative diagnosis was made by ANTI FACTOR H ANTIBODY LEVEL which was 76.1 AU/ml (normal range 0-20 AU/ml).Patient treated with plasmapheresis and hemodialysis & other supportive theraphy.

KEYWORDS :

INTRODUCTION

33 A year old male patient, came to our emergency department with the chief complaints of decreased urine output and multiple skin lesions since 2 days and recent history of diarrhoea 15 days back followed by fever 10 days back. No significant past & family history.

ON EXAMINATION

Patient was conscious,oriented to time, place and person.Multiple purperic skin lesion present and pallor present on cojuctiva .Temp:Normal, Pulse:98/min, BP:156/90mmhg.

ON INVESTIGATION

Patient had already been to couple of local hospitals and his initial investigation revealed s.Creatinine :7.28, s.urea:107.40. Hb:9.96. TC: 12,200,PC: 78000 Direct Billrubin:0.8, Indirect Billrubin:1.9 Total Billrubin:2.7 SGPT:29, . Other special investigation were done and came out to be as follows : Retic count -0.6, S.LDH- 735IU/L (normal range ,248 IU/L), S.ANA- Negative, C-ANCA- Negative, P-ANCA-Negative, LUPUS ANTICOAGULANT - Negative, CRP- Negative, RA-Negative, ASO- Negative, C3 LEVEL- 0.63 (normal range- 0.9-1.83),C4 LEVEL- 0.16 (normal range- 0.1-0.4), CPK TOTAL-52.

2D ECHO was normal and USG abdomen pelvis showed raised cortical echogenecity in both kidneys with preserved Cortico medullary differentiation.

Confirmative diagnosis was made by ANTI FACTOR H ANTIBODY LEVEL which was 76.1 AU/ml (normal range 0-20 AU/ml).

MANEGMENT

Patient's treatment modality consisted of Plasmapheresis and hemodialysis as a main line treatment. 4 cycles of plasmapheresis and 4 cycles of hemodialysis were done alternatively which resulted in clinical improvement along with renal function improvement (s. creatinine - 0.94) within 15 days of admission. Other supportive treatment was given to the patient in the form of Antibiotics, IV fluids and skin emmolients for skin lesions

DISCUSSION

Atypical Hemolytic uremic syndrome (HUS) is defined by the triad of microangiopathic hemolytic anemia, thrombocytopenia and renal impairment. Atypical HUS is the result of congenital complement dysregulation. aHUS is caused by changes or mutations to the genes that produce proteins that control part of the body's complement system called the alternative pathway. As part of the body's immune system, this pathway is always turned 'on', ready to attack foreign invaders. During a time of "attack," a healthy complement system has proteins (called regulators) that are able to protect the body's own healthy cells. If one or more of these regulators are defective, the complement attack is also directed against healthy body cells, such as the inner lining of blood vessels.When blood vessels are damaged by this "self-attack," a clotting system is activated in the blood and blood/platelet clots (called thrombi) form. The affected patient have low C3 and normal C4 level, charecteristic of alternative pathway. The incidence of complement-aHUS is not known precisely. Factor H deficiency, the most common defect, linked to familial with Atypical HUS.Factor H competes with factor B to prevent the formation of C3bBb and act as cofactor for factor I,

which poatentially degrades C3b.Deficiency in other complementary-regulatory, such as factor I, factor B,membrane cofactor protein,c3,complement factor H-related protein 1(CFHR1),CFHR3,CFHR5 and thrombomodulin.Mutations in the genes encoding complement regulatory proteins factor H, membrane cofactor protein (MCP), factor I or thrombomodulin have been demonstrated in 20-30%, 5-15%, 4-10% and 3-5% of patients respectively, and mutations in the genes of C3 convertase proteins, C3 and factor B, in 2-10% and 1-4%. In addition, 6-10% of patients have anti-factor H antibodies,an autoimmune variant of aHUS, also known DEAP(deficient for CFHR protein and positive for factor H autoantibody) .A definitive diagnosis of aHUS is made when the triad of microangiopathic hemolytic anemia, thrombocytopenia, and AKI is present. The disease should have no association with Shiga toxins, and TTP should also be exclude. Investigation of the complement system is required (C3, C4, factor H and factor I plasma concentration, MCP expression on leukocytes and anti-factor H antibodies; genetic screening to identify risk factors). Despite the potential for damage to many of the body's organs, most often, aHUS targets the kidneys. The disease is familial in approximately 20% of pedigrees, with an autosomal recessive or dominant mode of transmission.

Plasma exchange/infusion may play role in aHUS by replacing complement-regulatory protein. Eculizumab is a monoclonal antibody to c5 that is approved for use in aHUS ,for which ongoing theraphy may be necessary. Plasma therapy — Plasma therapy was the first-line therapy for patients during the acute episode of atypical HUS before eculizumab was introduced. Although there are no supportive data from clinical trials, most experts in the field advocate plasma exchange (plasmapheresis) rather than plasma infusion as a means to both remove defective mutant proteins and antibodies to CFH, and restore normal functioning complement proteins Initiation of dialysis therapy in patients with symptomatic uremia, azotemia (defined as a blood urea nitrogen >80 mg/dL [29 mmol/L]), severe fluid overload, or electrolyte abnormality refractory to medical that therapy.is

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