ORIGINAL RESEARCH PAPER

Paediatric Medicine

A TYPICAL PRESENTATION OF ATYPICAL HEMOLYTIC UREMIC SYNDROME IN A 5-MONTH-OLD MALE: A CASE REPORT

KEY WORDS: Atypical HUS, thrombocytopenia and Inherited disorder

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ABSTRACT

Background: Atypical Hemolytic Uremic Syndrome (aHUS) can present with diverse symptoms, often complicating timely diagnosis and treatment. This report highlights a case in a young child with atypical clinical features. **Case Presentation:** A 5-month-old male presented with respiratory distress, elevated lactate levels, and significant hemolytic parameters. Despite initial treatment for pneumonia, further investigations led to the diagnosis of aHUS. **Conclusion:** The absence of thrombocytopenia at presentation does not exclude the possibility of aHUS. Genetic evaluation revealed Complement Factor H deficiency, emphasizing the need to consider inherited conditions in pediatric HUS cases.

INTRODUCTION

Hemolytic anemia, thrombocytopenia, and abrupt renal failure due to thrombotic microangiopathy are the hallmarks of the uncommon condition known as atypical hemolytic uremic syndrome (aHUS) (1).The lack of STEC infection sets it apart from normal or Shigatoxin-producing Escherichia coli (STEC) HUS. It has been discovered in recent years that complement alternative pathway dysregulation is linked to aHUS. Mutations in genes encoding complement-regulating proteins have been found in nearly 60% of aHUS patients (2, 3). In addition to abnormalities in these genes, cobalamin C (cblC) illness caused by mutations in the cblC MMACHC gene has also been linked to aHUS (4).

The majority of mutations in complement-regulating proteins are found in factor H (CFH).

The prevalence of aHUS is determined to be 3.3 per million in the population of children under the age of eighteen(5).Up to 50% of patients of 7 aHUS progress to end-stage renal disease (ESRD), and the condition has a bad prognosis with a death rate of 25%(6). Mortality can be prevented with early diagnosis.

Case Report:

Master X 5 month old male child born out of non-consanguineous marriage, no significant birth history presented with complaints of Cough for 2 days, vomiting for 2 days and increased work of breathing for 10 hours with history of difficulty in feeding and reduced oral intake for 2 days. No history of fever, decreased urine output / loose stools and child was treated outside with Prednisolone for 2 days , cefaclor syrup 2 doses , kufril LS drops and Phenergan syrup. h/o nebulisation 2 weeks before on OPD basis in outside clinic with no significant family history or neaontal death. In view of respiratory distress in ER Child was dull looking tachypneic with respiratory rate – 52/min.VBG done revealed Lactate- 11.64, HCO3- 14, Hb- 6.04 mg/dl ,K- 6.27, PH- 6.93 and PCO2-59.5 , connected to 4 L oxygen and shifted to PICU .

In PICU Chest x-ray revealed Cardiomegaly with right middle lobe pneumonia, hence iv antibiotics was started and ECHO done revealed structurally normal heart with LV dysfunction for which dobutamine infiusion was started. Baseline investigation revealed Hb- 5.6 with PCV- 19.1 elevated total counts and platelet – 1.96 , with mild elevation of BUN – 39 , creatinie – 1 and hyperkalemia – 6.8 with HCO3-10 .Further evaluation for hemolysis revealed DCT negative with elevated reticulocyte count of 12.1 , Elevated LDH of 106.82 and peripheral smear showed 8% schistiocytes with normal platelets .

Differential Diagnosis :

1) Posssible HUS (Pneumococcal/Inherited HUS
2) DCT negative Autoimmune hemolytic anemia .

Paedaitric hematologist and oncologoist opinion obtained and hemolytic workup done PNH by flow cytometry , G6PD , Osmotic fragility test , C3, C4 was normal . Considering possibility of primary immunodeficieny , Immunoglubulin level sent and immunoglobulin given .Infective causes of hemolytic anemia with pneumonia respiratory panel sent which was negative for pneumococcal and mycoplasma . In view of worsening distress with acidosis child was electively intubated. Serial Platelets, Hemoglobin, reticulocyte count, platelet and LDH monitoring was done daily showed initial raise in hemoglobin and platelets followed by a fall till Hb- 6.9 and platelets – 89000 where as in contrast creatinine was in decreasing trend

During the course in ICU child developed Hypertension and Acute kidney injury for which child was treated with multiple antihypertensive and Hemodialysis. Evaluation revealed Serum. Renin angiotensin levels and USG abdomen done was normal. Renal biopsy done revealed features suggestive of Thrombotic microangiopathy . Multidisciplinary meet with Paedaitric nephrologist, hematologist and PICU consultant. Plasmapheresis was done for consecutive 4 days, responded by decreasing LDH and schistiocytes count in peripheral smear. Child continued to have systemic hypertension inspite of this measures. Child developed generalised anasarca hence 2 cycles of SCUFF done. Child developed MODS hence vasopressors and ionotropes started and following day child was succumbed to death.

Whole exome sequencing revealed Complement Factor H deficiency (heterozygous variant)

DISCUSSION:

Atypical HUS can be Sporadic or familial ,Caused by dysregulation of the alternative complement pathway

1) Factor H(FH),
2) Factor I (FI)
3) Membrane cofactor protein (MCP),
4) Deletions in FH related proteins
5) Gain-of-function mutations in C3 and FB)

Out of which MCP carries good prognosis (recovers on its own without plasma exchange and anti-complimentary therapy), Among aHUS CFH mutation carries 25 %.FH prevents autolysis of C3 in plasma, and together with FI, prevents Amplification and complement mediated degradation.

Mutations in aHUS are heterozygous. Penetrance of mutations

in familial aHUS is not complete (~50%) and only about half of the individuals that carry an abnormal mutation would develop the clinical manifestations of aHUS.

The Joint Committee of the Japanese Society of Nephrology and the Japan Pediatrics Society (JSN/JPS) (7)has developed diagnostic criteria for aHUS which includes three crucial clinical features. The first feature is thrombocytopenia, which is characterized by a platelet count below 150,000/ L. The second feature is microangiopathic hemolytic anemia, which manifests as low hemoglobin levels (below 10 g/dL), increased lactate dehydrogenase levels, reduced haptoglobin levels, and the presence of fragmented red blood cells observed in the peripheral blood smear. The third feature is acute renal failure, as defined by the KidneyDisease. In our case child initially presented with hemolytic anemia followed by hypertension and at last with renal failure

Treatment of atypical HUS

1) Blood transfusions (Except platelet)
2) Dialysis
3) Plasma exchange. (daily exchange of 1.5 to 2 of plasma volume or daily plasma infusion of 20 to 30 mL/kg of body weight.
4) Blood pressure control

FDA approved 2 drugs

1) Ecluzimab (900mg once weekly X 4 weeks , 1200 mg on alternate weeks)
2) Ravulizumab(long acting c5 inhibitor)

C3 / THBD mutations/anti-FH antibodies are more responsive to plasma therapy.FH or FI mutations are less responsive.

CONCLUSION

1. Absent thrombocytopenia at presentation does not rule out Hemolytic uremic syndrome.
2. HUS in young children - should think of inherited condition.

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