Acute Transient Variety of Autoimmune Hemolytic Anemia Following Varicella Infection

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Abstract:-

We are reporting a case of an 11 year female presenting with Acute Transient variety of Autoimmune hemolytic anemia following chickenpox, the patient was treated with blood transfusion and prednisolone and discharged with successful rise in hemoglobin.

Key words- auto immune hemolytic anemia, varicella

Case history

An 11 year female child presented with complains of easy fatigability and severe pallor since 10 days. The patient had history of chicken pox 15 days before these symptoms. The parents noted pallor of the whole body which increased in severity gradually over time, requiring admission at Civil Hospital Ahmedabad.

There was no history of bleeding from any site, or any history of jaundice, or blood transfusion. There was no history of blood disorder in the family. Patient had normal growth and development. Menarche was not achieved yet.

On examination, the patient was fairly nourished. There was tachycardia and tachypnea, with normal blood pressure. Rest of the systemic examination was normal.

On investigations, Hemoglobin was found to be 4.1 g/dl with total WBC being 23,700/mm3 (increased) with differential count of PMN-25%, L-65%, M-8%, E-2% and platelets were 2,89,000/mm^3(normal), RDW was 22.2 and peripheral smear showed normocytic normochromic RBCs with anisopoikilocytosis. Reticulocytes were 1.67% ESR was 130 mm/hr (high), serum iron was 240µg/dl, and vitamin B_{12} was 1253pg/ml.

HIV, HBSAg and HCV were non-reactive and urea, creatinine, electrolytes and liver enzymes were within normal range. There was slight elevation of S.Bilirubin (3 mg/dl). PT, APTT were normal and urine routine was non-specific, and there was no evidence of hemoglobinuria. Serum LDH levels were 1741.9u/dl (increased). Direct Coomb's test was grade IV positive with Indirect Coomb's test grade I positive. Antibody screen was pan positive with initial difficulty in determining the blood group.

After admission, patient was started on acyclovir and prednisolone (2mg/kg/day) and transfused with Packed RBCs (grade IV incompatible) Multi-vitamin and folate supplementation was given. With ongoing hemolysis, patient required multiple (7) PCV transfusions, but as it was not responding to oral steroids, pulse of iv methyl prednisolone

with 3 days of oral cyclophosphamide was given. After 17 days of admission, Hb was maintained at 11 g/dl hence patient was discharged on oral cyclophosphamide and methylprednisolone at 1mg/kg/day, to be followed up for repeat Hb levels at 1 week after discharge.

On follow up at 1 week, patient was clinically better, with no pallor and Hb level had risen to 13g/dl and the peripheral smear showed no evidence of hemolysis.

Discussion-

Varicella zoster virus (VZV) is a neurotropic human herpes virus with double-stranded DNA genome. AIHA is an uncommon complication of chickenpox[1].   AIHA   is characterized by hemolysis and anemia caused by auto-antibodies to red cell antigens. The hallmark of the disease is positive direct Coomb's test in as many as 98% cases where polyclonal antisera is used to detect both IgG and IgM antibodies.[1] Our patient also showed hemolysis with positive Coomb's test. The mortality rate in idiopathic AIHA in children is around 10%[1]. In a series of 865 cases of AIHA only one case was due to chicken pox[2].In a review of 6 cases of AIHA due to varicella, only 4 were children and all of[1] them developed hemolysis within 2 weeks of the onset of skin eruptions[4]

AIHA can be classified on the basis of type of antibody—AIHA associated with 'warm' antibodies, and AIHA associated with 'cold' antibodies. It can also be classified according to etiology as 'Primary AIHA' and 'Secondary AIHA'[4]

Primary AIHA
• Warm reactive antibody (mainly IgG)
• Cold agglutinin disease (mainly IgM and complements)
• Paroxysmal Cold Hemoglobinuria (mainly IgG and complements)
Secondary AIHA
• Underlying autoimmune disorders e.g. SLE, Evan's syndrome
• Drug induced e.g. penicillin
• Immunodeficency e.g. HIV, Primary immunodeficiency Specific infections e.g. mycoplasma
• Malignancies e.g. Lymphomas, leukemia

Autoimmune Hemolytic Anemias Associated With "Warm" Antibodies—the auto antibodies are an inappropriate immune response to an RBC antigen. It manifests clinically in two variants-- **Acute transient** type lasting 3-6 months and occurring predominantly in ages 2-12 yr, accounts for 70-80% of patients. It is frequently preceded by an infection. There is good response to glucocorticoid therapy, a low mortality rate, and full recovery. Our patient presented with this variety. **Chronic type,** frequent in infants and in children >12 yr old. Hemolysis may continue for many months or years. The mortality rate is approximately 10%.

Laboratory Findings are – Profound anemia, with hemoglobin levels <6 g/dl is seen, and the peripheral smear shows spherocytosis, nucleated RBCs and polychromasia (reflecting the reticulocyte response). Leukocytosis is common. The platelet count is usually normal.

Other markers of Hemolysis-High serum LDH levels, indirect bilirubin and hemoglobinuria may be seen. As seen in our patient, Direct antiglobulin test are strongly positive. These antibodies are active at 35-40 C ("warm" antibodies) and most often belong to the IgG class.

In the treatment of anemia transfusions may be lifesaving but, In general, all tested units for transfusion are serologically incompatible. Patients with mild disease and compensated hemolysis may not require any treatment. Glucocorticoids decrease the rate of hemolysis by blocking macrophage function and decreasing the production of the autoantibody, Prednisone is given at a dose of 2-6 mg/kg/day. Treatment should be continued until the hemolysis decreases. IV immunoglobulin, Plasmapheresis and Rituximab have been used in chronic cases refractory to therapy. Splenectomy may be beneficial but risk of infection with encapsulated organisms is there, hence prophylaxis is indicated with appropriate vaccines. Other modalities of treatment are; high dose dexamethasone, vincristine, cyclophosphamide, azathioprine, Dnazol and cyclosporine.

AIHA Associated with "Cold" Antibodies[4]-- "Cold" antibodies agglutinate RBCs at temperatures <37 C. They are primarily IgM**.** They may occur in primary or idiopathic cold agglutinin disease, secondary to infections such as those from *Mycoplasma pneumoniae* and Epstein-Barr virus, or secondary to lymphoproliferative disorders. Severe hemolysis may occur and may be heightened on exposure to cold. It is less common in children. Treatment includes immunosuppression and plasmapheresis or Rituximab. Splenectomy is not useful in cold agglutinin disease.

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