Autoimmune Hemolytic Anemia due to Varicella Infection

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Varicella is usually benign exanthematous disease, which primarily affects children. The common complications are bacterial infection of skin eruptions, pneumonia, cerebellar ataxia, hepatitis, thrombocytopenia and arthritis[1]. Autoimmune hemolytic anemia (AIHA) is a rare complication of varicella and only few cases are reported[2-5]. Overall the incidence of AIHA in children is as low as 0.2/100,000 population[3]. We report AIHA due to chickenpox in a child who responded to steroids.

An 11 year old female was brought with fever of one day followed by pleomorphic skin lesions of 8 days and jaundice of 2 days duration. Her urine and stools were normal. She was conscious, temperature was 37.8˚C, HR 160/min, RR 32/min, BP of 90/60 mmHg and SpO2 was 90% in room air. On examination, she had severe pallor and jaundice. There were multiple vesicular and scabbed skin lesions of chicken pox all over the body. There was no evidence of bleeding tendencies, bony tenderness or lymphadenopathy. Abdominal examination revealed 3 cm hepatomegaly and 1 cm splenomegaly. The rest of the examination was unremarkable.

Laboratory investigations: Hb 3.8 g/dL RBC count 1.84×10^6/L, total leucocyte count 12.1×10^9/L (polymorphs 88%, lymphocytes 10%, eosinophils 2%), platelet count 303×10^9/L and reticulocyte count 0.5%. RBC indices (MCV, MCH, MCHC) were normal. Peripheral smear showed normocytic normochromic anemia with clumping of RBCs. The Direct Coombs test using polyspecific anti-IgG and anti-C3b/C3d Complement antihuman globulin reagent was positive. Cold agglutinins were not detected and indirect Coombs Test was negative. Total serum bilirubin was 15.5mg/dL (direct bilirubin 1.3mg/dL), SGOT 30 U/L, SGPT 44 U/L, Alkaline phosphatase 123 U/L, total protien 8.5g/L, serum albumin 4.2g/L and serum LDH was 1580 U/L [Normal 230-460 U/L]. Renal function tests and blood sugar were within normal limits. Urine examination was negative for blood, bile salts, bile pigments and microscopy was normal. Urinary urobilinogen was not increased. Hemoglobin electrophoresis was normal. In view of severe pallor, jaundice, classical chicken pox lesions, positive Direct Coombs test, indirect hyperbilirubenemia and elevated LDH values, a diagnosis of varicella AIHA was made and three units of packed RBCs transfused. On the third day of admission, her vitals were normal, Hb was 12.2 g/dL, and reticulocyte count 1%. On the fourth day she developed pallor, Hb dropped to 7.8 g/dL and reticulocyte count was 1.5%. Other investigations: Serology for IgM varicella, IgM anti HAV, HbsAg, Anti HCV, Anti HEV, HIV were negative. Paul Bunnell, Widal test and Quantitative Buffy coat smear for malarial parasites were also negative. Antibody to double stranded DNA and sickling test were negative. Blood culture was sterile and urine chromatography was normal. On the fifth day, she developed severe pallor and the jaundice was same. Investigations at that time revealed Hb of 3.9g/dL, reticulocyte count 1%, total bilirubin was 5.04mg/dL, LDH 1008/L and liver enzymes were normal. Her serum iron, serum ferritin and total iron Binding capacity levels were normal. Chest x-ray, Computerised Tomography scan of neck, thorax and abdomen were normal. She was given three packed RBC transfusions and was started on oral prednisolone 2mg/kg/day in view of continuous hemolysis. After 2 days of steroids her Hb was 6g/dL. After 6 days of prednisolone there was no pallor, mildly icteric, Hb was 10 g/dL with reticulocyte count of 3%. After 10 days of prednisolone there was no pallor or jaundice, Hb was 10.5 g/dl and she was discharged on oral prednisolone 2 mg/kg/day for 6 weeks. She was followed up once a week and after 6 weeks her Hb was 10.8g/dL. Her serum bilirubin and LDH were normal. Prednisolone was reduced by 10% of the initial dose and was kept at this dose for 2 weeks before it was tapered further. At the end

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of prednisolone therapy Hb reached 14.1g/dL. She was followed up for the next 3 months without any problems.

Chickenpox is one of the most common exanthematous diseases of childhood which can give rise to various complications. AIHA is an uncommon complication of chickenpox [1]. AHIA is characterised by increased erythrocyte destruction due to autoantibodies IgG or IgM directed to red cell antigens[6]. The mortality rate in idiopathic AIHA in children is around 10%[7]. In a series of 865 cases of AIHA only one case was due to chicken pox[8]. In a series of 26 AIHA children, none of them was due to chicken pox[9]. However antivaricella antibodies were not detected in this child. Similar observation during the acute phase of varicella was made by Terada et al[2]. Some authors have made a diagnosis of chicken pox AIHA on clinical criteria without assessing antibody levels[3,6]. In a review of 6 cases of AIHA due to varicella, only 4 were children and all of them developed hemolysis within 2 weeks of the onset of skin eruptions[2]. Our case also presented with hemolysis on 7th day after the onset of skin eruption.

In spite of severe hemolysis in our child, reticulocyte count was low. Similar observation was made by Naithani et al and probably it is due to hemolytic process affecting the reticulocytes also[9]. Even though it is rare in children, cold agglutinins were reported to be positive in some cases of AIHA due to varicella infection[2,4,5]. Cold agglutinins were not seen in our patient. The incidence of AIHA associated with coldagglutinin is higher in adults as a complication of chickenpox than in children[2]. Our child received multiple blood transfusions probably because of continuous destruction of transfused RBCs due to the presence of autoantibodies. Varicella AIHA has been managed conservatively or with the addition of steroids[1,2,3,5]. We started on prednisolone in view of continuous severe hemolysis requiring multiple blood transfusions. Prednisolone was given in the same dose, duration and tapered as described by Naithani et al[7]. At the end of prednisolone therapy Hb reached 14.1g/dL without any complications. The mechanism of action of steroids is probably down regulation of Fc receptors on phagocytes, reduced IL-2 production, suppression of sequestration of opsonized red cells by splenic macrophages and reduction in the binding affinity of autoantibodies for red cells[7]. Even drugs like azathioprine, cyclosporine A, cyclophosphamide and IVIG have been used alone or in combinations in refractory AIHA., these are not consistently effective[9].

Key words: Varicella; Jaundice; Anemia; Autoimmune hemolytic anemia; Steroids

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