CORRESPONDENCE

Autoimmune Haemolytic Anaemia in a Child Due to Chickenpox

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Dear Editor

Chicken pox is usually a benign and self limiting viral exanthematous infection caused by varicella-zoster virus, which primarily affects children. The complications associated with chickenpox are secondary bacterial infection of skin, thrombocytopenia, bleeding manifestations, encephalitis, cerebellar ataxia, pneumonia, hepatitis, nephritis, nephritic syndrome, hemolytic-uremic syndrome, arthritis, myocarditis, pericarditis, pancreatitis, orchitis, and acute retinal necrosis [1]. Autoimmune hemolytic anemia (AIHA) is a rare complication of varicella and only very few cases are reported in children. We report a case of AIHA due to chickenpox in a child who is successfully treated with steroids.

A 14 year old male was admitted with history of fever of 2 days followed by pleomorphic vesicular skin lesions for 8 days, vomiting and yellowish discoloration of eyes for 3 days. On examination, patient was conscious and oriented, with HR—140/min, RR—36/min, temperature 38° C by axilla, Blood pressure 90/60 mmHg and maintaining 88 % oxygen saturation on room air. Severe pallor, icterus and multiple scabbed skin lesions of chickenpox were noted all over the body. There was no hepato-splenomegaly, lymphadenopathy, petechiae, bruises or bony

tenderness and the rest of examination was unremarkable. There was no past and family history of blood transfusion, jaundice, recurrent abdominal pain and gall stones.

Laboratory findings of patient at the time of admission and during follow-up are summarized in Table 1. Renal function test, hepatic enzymes levels and coagulation profile at the time of admission was as follows—Urea 38.5 mg/dL, Creatinine 0.45 mg/dL, SGPT 48 U/L, SGOT 82 U/L, Alkaline Phosphatase 420 U/L, Albumin 3.77 gm/dL, PT/aPTT/INR 20 s/29 s/1.69, respectively. Peripheral blood smear showed microcytic anemia with neutrophilic leucocytosis. Total red cell counts reduced with polychromasia and anisopoikilocytosis. There were 3 NRBC/100 WBC. Few microspherocytes were seen. Malaria parasite, Widal test, Dengue Ns1Ag/IgM/IgG and HAV IgM were negative. Urine was negative for blood, bile salts, bile pigments and microscopy was within normal limits.

The patient was given supplemental oxygen and supportive treatment with intravenous fluids, antibiotics and acyclovir. Due to auto- agglutination, blood group was in dilemma, and O negative blood was transfused in emergency situation. Later the blood group was re-verified as O positive after repeated saline wash of the cells. Despite three packed red blood cells (PRBC) transfusions Hb was very low (4.7 g/dL). Repeat peripheral blood smear showed predominantly normocytic normochromic erythrocytes with few microcytes, tear drop cells, fragmented RBCs and 18 NRBC/100WBCs. There was neutrophilic leucocytosis with mild shift to left (myelocytes 2 %, metamyelocytes 3 %, neutrophils 72 %, lymphocytes 18 %, monocytes 1 %, and eosinophils 4 %) and platelets were adequate. Smear was suggestive of hemolytic anemia with leucoerythroblastic reaction. Coombs test (Direct Antiglobulin Test) revealed a grade 2+ agglutination

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Table 1 Patient's hematological and biochemical parameters at presentation, during course of treatment and follow-up

Parameters	At time of admission (Day 1)	After 3 packed red cell transfusion, before starting prednisolone (Day 3)	After 5 days of starting Prednisolone	After 2 months of starting Prednisolone
Hemoglobin (g/dL)	3.7	4.7	7.7	11.9
Hematocrit (%)	10.7	12.4	24.4	36.9
RBC count ($10^6/\mu\text{L}$)	1.38	1.38	2.37	4.38
MCV (fL)	77.5	89.9	103	84
MCH (pg)	26.8	34.1	32.5	27.1
MCHC (g/dL)	34.6	37.9	31.6	32.2
WBC Count ($10^3/\mu\text{L}$)	9.75	25.00	4.96	5.5
Platelet Count ($10^3/\mu\text{L}$)	129	167	239	258
Reticulocyte count (%)	4.5			1.2
Serum bilirubin total (mg/dL)	9.68	9.26	1.97	0.62
Serum bilirubin direct (mg/dL)	1.29	1.32	0.94	0.09
Serum LDH (U/L)		890		337
Coombs test (DAT)		Positive		Negative

reaction. Serum LDH level was 890 U/L. Blood culture, HBsAg, HCV IgM, HIV, VDRL and ANA titre were negative. Varicella IgM/IgG (28.52/20.34 respectively; reference value: >11 positive), both were positive. Cold agglutinins were negative. Chest X-ray and ultrasound of neck, thorax and abdomen was normal. Hemoglobin electrophoresis and G6PD level was planned for later, as blood was transfused to the patient. A diagnosis of varicella AIHA was made on the above findings, and after excluding other causes of hemolysis. Oral prednisolone (2 mg/kg/day) was started with two PRBC transfusions. The Hb was 7 g/dL and raised to 7.7 g/dL after 5 days without any further blood transfusion. Patient discharged on prednisolone and kept on regular follow up. After 1 month, Hb increased to 11.1 g/dL and thereafter, prednisolone dose was tapered. Hemoglobin electrophoresis and G6PD activity was normal. Prednisolone tapered further and stopped after complete treatment duration of 3 month. Patient was followed up for the next 3 month without any problems.

AIHA is caused by autoantibodies directed against self red blood cells. It can be idiopathic or secondary to lymphoproliferative syndromes, autoimmune diseases, infections and tumors. AIHA is classified as warm, cold (cold hemagglutinin disease (CAD) and paroxysmal cold hemoglobinuria) or mixed, according to the thermal range of the autoantibody. AIHA is rare in infancy and childhood (0.2 per 10^5 /year), where it is post-infectious in 10 %, immunological in 53 % and primary in 37 % of cases. Mortality is lower in children (4 %), but rises to 10 % if the hemolytic anemia is associated with immune

thrombocytopenia (Evans syndrome) [2]. AIHA after chickenpox is rare and in a series of 865 cases of AIHA only one case was due to chicken pox [3]. In previous studies of AIHA due to chickenpox in children, hemolysis developed within 2 weeks of the onset of skin eruptions. Our case was presented with hemolysis on 8th day after the onset of skin eruption [4, 5]. In some studies anti-varicella antibodies were not detected and some of the other authors have made a clinical diagnosis of chickenpox without assessing antibody levels [4–6]. In our case both IgM and IgG were found positive.

In spite of severe hemolysis in our child, reticulocyte index was low. Similar observation was made by Naithani et al. and Kumar et al. [5, 7], and probably it is due to hemolytic process affecting the reticulocytes also. Cold agglutinins were reported to be positive in some cases of AIHA due to varicella infection, but not seen in our patient [4, 8]. Initial thrombocytopenia that recovered with corticosteroid treatment has most probable an autoimmune basis. Mild thrombocytopenia occurs in 1–2 % of children with varicella and may be associated with transient petechiae [1]. Varicella is also reported to cause Evans syndrome [9]. AIHA secondary to chickenpox has been reported in adults also [10].

Varicella AIHA has been managed conservatively or with the addition of steroids [5]. In our case, prednisolone was started in view of continuous severe hemolysis requiring multiple blood transfusions. Prednisolone started with initial dose of 2 mg/kg/day in divided doses for 4 weeks until hemoglobin levels greater than 10 g/dL is reached, thereafter, gradually and slowly tapered with the

aim of withdrawing the drug. Although one might be tempted to discontinue steroids more rapidly, AIHA patients should be treated for a minimum of three or four months with low doses of prednisone [2].

As AIHA has not been frequently reported with varicella in children, so to outline the prognosis of AIHA in this condition remain anecdotal [2, 4, 5].

Compliance with Ethical Standards

Conflict of interest Author Dr. Mukesh Kumar, Dr. Nirupama Kothari and Dr. BD Gupta declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

References

1. LaRussa PS, Marin M (2016) Varicella–Zoster virus. In: Schor NF, Behrman RE, Kliegman RM, Stanton BF, St Geme JW III (eds) Nelson textbook of paediatrics. Elsevier, Philadelphia, pp 1579–1586
2. Zanella A, Barcellini W (2014) Treatment of autoimmune hemolytic anemias. *Haematologica* 99:1547–1554
3. Sokol RJ, Hewitt S, Stamps BK (1981) Autoimmune haemolysis: an 18-year study of 865 cases referred to a regional transfusion centre. *Br Med J (Clin Res Ed)* 282:2023–2027
4. Terada K, Tanaka H, Mori R, Katoka N, Uchikawa M (1998) Hemolytic anemia associated with cold agglutinin during chickenpox and a review of the literature. *J Pediatr Hematol Oncol* 20:149–151
5. Kumar KJ, Kumar HCK, Manjunath VG, Arun V (2013) Autoimmune hemolytic anemia due to varicella infection. *Iran J Pediatr*. 23:491–492
6. Baran M, Ozgenc F, Berk O, Gokce D, Kavakli K, Yilmaz F (2010) Giant cell hepatitis and autoimmune hemolytic anemia after chickenpox. *Turk J Gastroenterol* 21:448–451
7. Naithani R, Agarwal N, Mahapatra M, Kumar R, Pati HP, Choudhry VP (2007) Autoimmune hemolytic anemia in children. *Pediatr Hematol Oncol* 24:309–315
8. Friedman HD, Dracker RA (1992) Cold agglutinin disease after chicken pox. An uncommon complication of a common disease. *Am J Clin Pathol* 97:92–96
9. Tanaka Y, Masuya M, Katayama N, Miyata E, Sugimoto Y, Shibasaki T et al (2006) Development of mixed-type autoimmune hemolytic anemia and Evans' syndrome following chicken pox infection in a case of low-titre cold agglutinin disease. *Int J Hematol* 84:220–223
10. Ittyachen AM, Jose MB, Abraham V (2013) Autoimmune hemolytic anemia secondary to chicken pox. *Ann Trop Med Publ Health* 6:353–354