

## Case Report

### **Autoimmune hemolytic anemia: an interesting presentation and review of literature**

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#### **Abstract**

Hemolytic anemia is caused either due to intrinsic red cell defects as in membranopathy/enzymopathy or acquired by extrinsic factors as auto antibodies. We are reporting a 3 year old child case referred to our center as a renal disease, with edema, high BP readings and red colored urine, which on our evaluation turned out to be autoimmune hemolytic anemia. Autoimmune hemolytic anemia, though rare in children, needs to be diagnosed early and followed closely as it may begin with deceptive initial presentation.

**Keywords:** autoimmune hemolytic anemia (AIHA), acquired hemolytic anemia

#### **1. Introduction**

Autoimmune hemolytic anemia (AIHA) represents a group of acquired hemolytic anemia's resulting from the development of auto antibodies against surface antigens of red blood cells<sup>1</sup>. Based on temperatures at which auto antibodies react with red blood cells, AIHA is classified into warm and cold antibody types. Warm antibody AIHA occurs predominantly in children aged 2–12 years. The antibodies belong to IgG class, react at or above 37°C, do not require complement for activity and do not produce agglutination *in vitro*. On the other hand cold antibody AIHA occurs less commonly in children. Antibodies are of IgM classes which react at temperatures 37°C, require complement for activity and produce spontaneous agglutination of red blood cells *in vitro*<sup>2</sup>. Mixed type AIHA is the presence of both warm and cold auto antibodies<sup>3</sup>. Autoimmune hemolytic anemia is an uncommon cause of hemolytic anemia in children with an incidence of approximately 0.2 per 100,000 in 11–20 year's age group<sup>1,2</sup>. We are reporting an interesting presentation of AIHA in a 3 year old child.

#### **2. Case Report**

A 3 year old boy was referred to us with history suggestive of renal edema, red colored urine, high BP measurements and progressive anemia. Our working diagnosis was glomerulonephritis, although the age at presentation was not typical for acute glomerulonephritis (AGN). His repeated BP measurements at different times of the day were between 50<sup>th</sup> and 90<sup>th</sup> centiles for his age and height and needed no treatment. His urine was red colored on gross appearance, no red blood cells (RBC) on microscopy, trace proteinuria and was positive for hemoglobin. His hemoglobin was 6 gm/dL, total bilirubin was 1.8mg/dL, indirect bilirubin was 1.4mg/dL and direct bilirubin was 0.4mg/dL. His peripheral smear showed microspherocytes and fragmented RBC's with a corrected reticulocyte count of 20%. His serum creatinine was 0.4 mg/dL, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and serum electrolytes like sodium, potassium and chlorides were within normal limits. Ultrasonographic examination of abdomen showed normal sized kidneys and no mass lesions or free fluids indicating a normal renal function. His Poly specific Direct Antiglobulin test (DAT) (Coombs test) was positive, but mono specific DAT could

not be done due to lack of facility at our center. The osmotic fragility test and G6PD enzyme levels were within normal limits. With these investigations, an intravascular hemolysis state was considered. Acute infections causing severe anemia like malaria were ruled out in this child. We also considered secondary causes of hemolysis like Mycoplasma infection as a possible cause of hemolysis and treated him with azithromycin for 5 days with no improvement of anemia. Hence we considered primary AIHA as a possible diagnosis and the child was treated with oral prednisolone at a dose of 2mg/kg/day daily. After 4 weeks of steroids his hemoglobin has increased to 12.8gm/dl and urine is clear. His repeat peripheral smear examination showed no evidence of hemolysis. Although there is no recommendation of the duration of prednisolone treatment or any recommendations regarding tapering the dose, we reduced the prednisolone dose to 1mg/kg/day at the end of 4 weeks, which was continued till 12 weeks and stopped. At the last follow up his hemoglobin was 12.4gm/dl and doing well in school.

### 3. Discussion

In children, hemolytic anemia is usually caused by intrinsic defects in red blood cells like in membrane defects, red cell enzyme deficiencies or hemoglobin abnormalities and most of them are inherited in nature. Acquired Hemolytic anemia is usually seen due to extrinsic factors<sup>1</sup>. AIHA belongs to a group of acquired hemolytic anemia's which results from the development of auto antibodies directed against antigens on the surface of patient's own red blood cells. Majority of the cases are mediated by warm reactive auto antibodies while AIHA due to cold reactive antibodies are less common<sup>2</sup>. Diagnosis of AIHA is based on evidence of hemolytic anemia consisting of anemia, jaundice, splenomegaly, reticulocytosis, raised serum bilirubin and a positive DAT (direct agglutination test)<sup>1</sup>. Once AIHA has been identified, differentiation between warm and cold antibodies can be done by monospecific DAT which also identifies responsible mechanisms. If the reaction is positive with anti IgG and negative with anti C3d, it is usually due to warm antibodies which are common in idiopathic or drug associated AIHA. If the reaction is positive with both anti IgG and anti C3d, it also indicates warm auto antibodies and is more common in patients with systemic lupus erythematosus (SLE) and idiopathic AIHA. In cold agglutinin disease (CAD), the reaction is positive with anti C3d but negative with anti IgG<sup>10</sup>. There is also presence of agglutination of red cells at temperatures 37°C in cold type of AIHA<sup>2</sup>. Autoimmune hemolytic anemia is known to be associated with infection, malignancy or other autoimmune diseases but in most cases it is idiopathic<sup>1,2</sup>. Cause of AIHA in children remained obscure in majority of cases labeling them as idiopathic or primary<sup>8,11</sup>. Many medical conditions are associated with AIHA such as viral infections, SLE, Mycoplasma pneumonia, immunization, tuberculosis, diabetes mellitus, Hodgkin's lymphoma, auto immune hepatitis, sepsis with bacterial endocarditis due to Staphylococcus aureus, Guillain-Barre' syndrome and Langerhan cell histiocytosis have been reported<sup>3,6-9,11,12</sup>. Hence long term regular follow ups are needed. In AIHA, only single cell line is affected<sup>1,2</sup> but there are rare reports with a combination of AIHA and immune thrombocytopenia called Evans syndrome<sup>6,11,12</sup>.

Corticosteroid therapy is the mainstay of treatment in warm AIHA. But the duration and the dose of treatment is not clear in literature. The treating physician has to tailor the dose based on clinical response. Transfusion of red cells in AIHA can result in rapid in vivo destruction of transfused cells due to the presence of auto antibodies<sup>12,15</sup>. Transfusions are of transient benefit, but may be required initially in managing severe anemia. Immunosuppressive agents including monoclonal anti-CD20 (Rituximab) may prove useful in refractory cases of warm AIHA. Splenectomy may help in some cases of refractory AIHA<sup>2,16</sup>.

### 4. Conclusion

AIHA has a wide spectrum of presentations varying from subtle to the obvious. As AIHA can be the initial presentation of a more serious condition like Hodgkin's lymphoma, the clinician needs to be cautious and closely follow the patient regularly.

### References

1. De Gruchy GC. The haemolytic anaemias. In: Firkin FC, Chesterman CN, Penington DG, Rush BM, editors. De Gruchy's clinical haematology in medical practice, 5th edn. Edinburgh: Blackwell Science Ltd; 1989. p 172–215.
2. Segel GB. Hemolytic anemias resulting from extracellular factors. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson textbook of pediatrics, 18<sup>th</sup> edn. Philadelphia: Saunders; 2007. p 2042–44.

3. Culic S, Kuljis D, Ivankovic Z, Martinic R, Maglic P, Pavlov N et al. Various triggers for autoimmune haemolytic anemia in childhood. *Paediatr Croat* 1999; 43: 207–10.
4. Sokol RJ, Hewitt S, Stamps BK. Autoimmune haemolysis: an 18- year study of 865 cases referred to regional transfusion centre. *Br Med J (Clin Res Ed)* 1981; 282: 2023–27.
5. Mayer B, Yurek S, Kiesewetter H, Salama A. Mixed- type autoimmune haemolytic anemia: differential diagnosis and a critical review of reported cases. *Transfusion* 2008; 48(10): 2229–2234.
6. Jubinsky PT, Rashid N. Successful treatment of a patient with mixed warm and cold antibody mediated Evans syndrome and glucose intolerance. *Paediatr Blood Cancer* 2005; 45: 347–350.
7. Sheth SS, Karande SC, Nadkarni UB, Lahiri K, Jain MK, Shah MD. Autoimmunehaemolytic anemia: mixed type. *Indian Pediatr* 1991; 28(3): 303–304.
8. Oliveira MC, Oliveira BM, Murao M, Vieira ZM, Gresta LT, Viana MB. Clinical course of autoimmune haemolytic anemia: an observational study. *J Pediatr* 2006; 82 (1):58–62.
9. Wonderjem MJ, Overbeeke M, Som N, Chamuleau M, Jonkhoff AR, Zweegman S. Mixed autoimmune hemolysis in a SLE patient due to aspecific and anti- Jka autoantibodies; case report and review of the literature. *Haematologica* 2006; 91(1):39–41.
10. Lichtin AE. Autoimmunehaemolytic anemia. [www.merckmanuals.com/professional/sec11/ch131/ch131b.html](http://www.merckmanuals.com/professional/sec11/ch131/ch131b.html). Accessed 15 Dec 2009.
11. Gupta V, Shukla J, Bhatia BD. Autoimmunehaemolytic anemia. *Indian J Pediatr* 2008; 75:451–54
12. Park D, Yang C, Kim K. Autoimmunehaemolytic anemia in children. *Yonsei Med J* 1987; 28(4):313–21.
13. Videback A. Auto-immune haemolytic anaemia in systemic lupus erythematosus. *Acta Med Scand* 1962; 171:187–94.
14. Ling R, James B. Classic signs revisited. White-centred retinal haemorrhages (roth spots). *Postgrad Med J* 1998; 74:581–582.
15. Sutaone B, Jain N, Mathur NB, Khalil A. Blood transfusion in autoimmune haemolytic anemia: a practical problem. *Indian Pediatr* 1993; 30:264–266.
16. Laverger G, Bancillon A, Schaison G. Treatment of autoimmune haemolytic anemia in children. *Ann Pediatr* 1989; 36(8):519–523.
17. Win N, Tiwari D, Keevil VL, Needs M, Lakhani A. Mixed-type autoimmune haemolytic anaemia: unusual cases and a case associated with splenic T-cell angioimmunoblastic non-Hodgkin's lymphoma. *Hematology* 2007; 12(2): 159–162