

# Autoimmune Hemolytic Anemia

## Otoimmün Hemolitik Anemi

### Şinasi Özsoylu

Retired Prof of Pediatrics, Hematology, Hepatology, Ankara, Turkey  
Honorary fellow of American Academy of Pediatrics  
Honorary member of American Pediatric Society

#### To the Editor,

I would like to make few comments on the Sarper and her colleagues' article entitled "Management of autoimmune hemolytic anemia in children and adolescents: a single center experience" published in the recent issue of the Journal (2011;28:198-205) [1].

First of all, Coombs test was negative two out of 13 patients with hemolytic anemia (patients 3 and 10). Although Coombs positivity may not correspond to hemolysis, because of low titer, reversals may not be expected.

As recently brought to the attention once more, the disease may differ despite of similar pathogenesis [2]. Therefore, Evans syndrome (ES) should be presented separately then autoimmune hemolytic anemia (AIHA) as of Wiskott-Aldrich syndrome (WAS) in which Coombs positivity may develop as of alloimmune reaction.

In addition "Patients with ES have sequential or spontaneous" thrombocytopenia, but it is not called ITP [3].

Although corticosteroids are the main drugs for the treatment of AIHA, it should not be used in divided doses as substitution treatment as of surrenal insufficiency; which has been applied previously; Rather it should be given at once around 6 a.m preferentially as Megadose methylprednisolone (MDMP) [4] intravenously or orally as described by us which was used in partially one of the authors' patient (30 mg/kg/day, for 3 days).

May I also remind that blood group changes may occur in autoimmune diseases, which should be correlated with the parents blood groups.

Since the patients retrospectively reviewed, was ethic comimette approval required?

#### References

1. Nazan S, Suar ÇK, Emine Z, Sema Aylan G. Management of autoimmune hemolytic anemia in children and adolescents: a single center experience. Turk J Hemato 2011;28:198-205
2. Fere W, Gregory, Guttmacher AC. Genomics and the multifactorial nature of human autoimmune disease. NEJM 2011;365:1612-23
3. Özsoylu Ş. Is every immune thrombocytopenia. Idiopathic thrombocytopenic purpura. Acta Paediatrica 2004;93: 1129-1130
4. Özsoylu Ş, İrken G, Karabent A. High-dose intravenous methylprednisolone for acute childhood idiopathic thrombocytopenic purpura. Eur J Hematol 1989;42: 431-435

#### Reply,

In discussion we reported that false negative direct Coombs test may be found in 2-4% of patients with autoimmune hemolytic anemia (AIHA) due to low titers of antibodies or low sensitivity of the test. We have already referred, reference 7 and 8 on the subject in our study [1,2]. Our patients with negative Coombs test were responsive to steroids. Özsoylu et al says that false positive Coombs test may be observed but false negative can not be observed in OIHA. He might not have such an experience.

**Address for Correspondence: Şinasi ÖZSOYLU, M.D.,**  
Beysukent Altınşehir Sitesi No:30, Ankara, Turkey  
Phone: +90 312 235 41 88 E-mail: sinasiozsoylu@hotmail.com

Received/Geliş tarihi : November 21, 2011  
Accepted/Kabul tarihi : November 21, 2011

The aim of presenting cases with Evans syndrome and W.Aldrich syndrome in the same article was to attract attention to these cases presenting with hemolytic anemia and underlying immunodeficiency. In the last paragraphs of the abstract and discussion we said that hemolytic reactions of these cases may require other immunosuppressive agents and each case must be considered individually before splenectomy. In the recent literature Evans syndrome is presented under the title of autoimmune hemolytic anemia [3]. In Wiscott-Aldrich syndrome autoimmune hemolytic anemia develops as many other autoimmune and inflammatory complications [4], but Özsoylu says that it is an alloimmune reaction.

Özsoylu says that "Patients with ES have sequential or spontaneous thrombocytopenia, but it is not called ITP<sup>2</sup>". I think he wants to say "simultaneous" instead of "spontaneous". In the study we already reported that thrombocytopenic and hemolytic anemia attack may be sequential even second cytopenia may emerge over the course of ten years. When the first attack is thrombocytopenia you have to diagnose it as immune thrombocytopenic purpura because at that moment you do not know that this patient will also develop an autoimmune hemolytic anemia attack. In the recent literature Evans syndrome is described as follows [5]: "Evans syndrome (ES) is characterized by the coexistence of an autoimmune hemolytic anemia (AIHA) and **immune thrombocytopenic purpura (ITP)**".

Özsoylu says that corticosteroids should not be used in divided doses as substitution treatment as of surrenal insufficiency; which has been applied previously. Rather it should be given at once around 6 a.m preferentially as megadose methylprednisolone (MDMP)<sup>3</sup>. In text book "Williams Hematology" " it is written that, in adults oral methylprednisolone should be used at an initial daily dose of 60-100 mg. Critically ill patients with rapid hemolysis may receive **100-200 mg in divided dose** over the first 24 hr." [6]. If hemoglobin level is already stabilized at a reasonable level, I do not think megadose methylprednisolone is required. Özsoylu may prefer such high doses. In Manual of Pediatric Hematology and Oncology by Philip Lanzkowsky also, 2-6 mg/kg/day prednisolone or methyl

prednisolone is recommended [7]. I do not think divided doses of corticosteroids are used always as substitution treatment of surrenal insufficiency. Divided doses are also used in leukemia.

Özsoylu says that, blood group changes rarely occurs in autoimmune diseases. So we want to attract attention to rare cases. Patient 2 was referred to us from another center after some transfusions and corticosteroid replacement and still ongoing hemolysis. We observed that blood group typing was false and transfusion with incompatible packed red cells also contributed to hemolysis.

As a conclusion, I could not find any scientific error in our article regarding Özsoylu's comments.

**Nazan SARPER**

*Kocaeli University, School of Medicine,  
Department of Pediatric Hematology, Kocaeli, Turkey*

### References

1. Agarwal B. Autoimmune hemolytic anemia. 1998; 65: 663-668
2. Collins PW, Newland AC. Treatment modalities of autoimmune blood disorders. 1992; 29: 64-74
3. Baek SW, Lee MW, Ryu HW, Lee KS, Song IC, Lee HJ, Yun HJ, Kim S, Jo DY. Clinical features and outcomes of autoimmune hemolytic anemia: A retrospective analysis of 32 cases. Korean J Hematol 2011; 46: 111-117
4. Dupuis-Girod S, Medioni J, Haddad E, Quartier P, Cavazzana-Calvo M, Le Deist F, de Saint Basile G, Delaunay J, Schwarz K, Casanova JL, Blanche S, Fischer A. Autoimmunity in Wiskott-Aldrich syndrome: Risk factors, clinical features and outcome in a single-center cohort of 55 patients. Pediatrics 2003; 111: 622-627
5. Eddou H, Helissey C, Konopacki J, Souleau B, de Revel T, Malfuson JV. Evans syndrome: Be careful of over-diagnosis. Rev Med Interne 2012; 33 (3): 155-158
6. Beutler E, Lichtman MA, Coller BS, Kipps TJ, Seligsohn U. Williams Hematology. Sixth edition 2001, McGraw-Hill Companies, New York
7. Philip Lanzkowsky. Manual of Pediatric Hematology and Oncology, Fifth edition, 2011 Academic Press, London