The Turkish Journal of Pediatrics
Volume 25, No. 1, January - March 1983

A CASE OF AUTOIMMUNE HEMOLYTIC ANEMIA FOLLOWING THROMBOCYTOPENIA*

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Key words: autoimmune hemolytic anemia, Coombs' positive hemolytic anemia, thrombocytopenia

Evans et al[1] first described a group of patients with acquired hemolytic anemia and primary thrombocytopenic purpura in 1951. Since then this combination has been called Evans' syndrome[1-3]. In this syndrome, thrombocytopenia may occur in association with Coombs' positive hemolytic anemia or be followed by it[3-5].

Recently we have observed a child in whom thrombocytopenia was the first finding, followed by leukopenia 17 days later. In this case Coombs' positive hemolytic anemia developed five months after the diagnosis of thrombocytopenia, when leukocyte and platelet counts had returned to normal. Antibodies responsible for the positivity of the direct antiglobulin test were more prominently related to IgA than IgG. This patients is presented in detail because of his unusual laboratory findings.

Case Report

KU, a 9-year-old boy, was referred to the Hacettepe Pediatric Hematology Unit in September 1981 with the complaints of fatigue and purpura confined to the abdomen and the lower half of the body following an infection of the upper respiratory system.

Physical examination revealed an underdeveloped boy (weight 23 kg, height 120 cm, both below 5th percentile) with a blood pressure of 110/85 mmHg. His general condition was good, but he had a purpuric rash on the abdomen and extremities. The liver and spleen were not palpable.

Laboratory findings revealed thrombocytopenia (hemoglobin 14.70 g/dl, white blood cells 8000/μl, platelets 68,000/μl) and mild lymhpocytosis (64% lymphocytes).

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Coombs' test, LE cell (3 x), Paul-Bunnell and dye tests were all negative, and no pathogenic microorganism was grown from the throat culture. The cellular bone marrow did not show infiltration or megaloblastic changes. Since antiplatelet antibodies were present, the diagnosis of idiopathic thrombocytopenic purpura was made, and he was given oral prednisolone (2 mg/kg). When he was seen 17 days later, in addition to the mild thrombocytopenia, leukopenia with granulocytopenia was also observed (Table I). Corticosteroid was discontinued. He came back 5 months later with complaints of fatigue and paleness. A hemogram revealed anemia (Hb 8.95 g/dl) and reticulocytosis (6.6%) with normal leukocyte and thrombocyte counts; some spherocytes and polychromasia were seen on the peripheral smear. Physical examination of the patient revealed splenomegaly in addition to his paleness. At this time, a direct Coombs' test (using polyspecific antiglobulin serum from Gamma Biological Inc.) was positive using the standard tube technique; antibodies responsible for the positivity of the Coombs' test were related mostly to IgA classes. In order to detect the class of the immunoglobulins on the red cells, specific anti-IgG, anti-IgM, anti-IgA, anti-C_3 and anti-C_4 serums from the Biotest Serum Institute were used.

Cold agglutinins, LE cells, FANA, and anti-DNA antibody were all negative. Thereafter he was given prednisolone (2 mg/kg orally) to which his hemoglobin responded rapidly (Table I), and his hematologic findings became stable with a negative Coombs' test; serum antibody screening studies remained negative.

Discussion

It has been suggested by Fagiolo[6] that autoimmune hemolytic anemia is a complex syndrome in which anti-platelet and anti-leukocyte antibodies might also be present. Leukopenia, in addition to the thrombocytopenia and hemolytic anemia in Evans' syndrome is not infrequently seen in its subacute and chronic forms[3]. Anti-thrombocyte and anti-leukocyte antibodies can be shown if the patients present with thrombocytopenia and leukopenia. The anti-leukocyte antibodies are usually shown to be neutrophil specific. These specific antibodies might appear at different times during the course of the syndrome[6].

In general, hemolytic anemia and thrombocytopenia appear together in Evans' syndrome. But in our patient, Coombs' positive hemolytic anemia developed five months after his initial diagnosis of idiopathic thrombocytopenic purpura (ITP). Among the 32 patients with Coombs' positive hemolytic anemia reported by Fagiolo[6], only two had had thrombocytopenia previously, as had our patient. In this patient, leukopenia with granulocytopenia was also observed on the seventeenth day of his disease, which resolved spontaneously. Anti-leukocyte antibodies were unfortunately not studied in this case; therefore viral infection as a cause of neutropenia with relative lymphocytosis could not be rejected.

TABLE I

Some Hematologic Findings of the Patient

Date	Hb g/dl	White blood cells/μl	Thrombocyte count/μl	Reticulocyte %	Coombs' test	Anti-thrombocyte antibody	Differential count (%)
4.9.1981	14.70	8000	68,000	—	—	Increased	64 lymph, 32 pnl, 4 mono
21.9.1981	15.99	3600	96,000	—	—	Increased	84 lymph, 11 pnl, 1 eo, 1 mono, 3 young
31.3.1982	8.95	930(	400,000	6.2	IgA + + IgG + C_3, C_4 —	Increased	60 pnl, 38 lymph, 1 mono, 9 norm, 1 eo
6.4.1982	11.51	12400	364,000	3.9	IgA + + IgG + C_3, C_4 —		44 pnl, 48 lymph, 6 eo, 2 young
20.4.1982	13.11	9700	—	0.4	IgA — IgG + C_3, C_4 —		68 pnl, 29 lymph, 3 eo
11.5.1982	14.07	5400	304,000	0.4	(—)		48 pnl, 33 lymph, 15 young, 1 mono, 3 eo

Cines et al[7] reported a patient with immune pancytopenia associated with IgG antibodies directed to his own red blood cells, platelets and granulocytes. In our patient platelet-specific IgG antibodies were shown when his Coombs' test was negative at the time of thrombocytopenia and leukopenia. Later he developed antiglobulin test positive hemolytic anemia with normal platelet and leukocyte counts. Other causes of Coombs' positive hemolytic anemia associated with thrombocytopenia, such as systemic lupus erythematosus (SLE), scleroderma, mixed connective tissue disease, Hashimoto thyroiditis, thrombotic thrombocytopenic purpura (TTP), leukemia, chronic active hepatitis and sarcoidosis, were not found in this patient[8-13]. To our knowledge a similar case with thrombocytopenia followed by leukopenia and Coombs' positive hemolytic anemia has not been reported, at least in childhood.

Another rare finding of our patient was his Coombs' positivity, which was more prominently determined by IgA antibodies than by the usual IgG types. In a short period of time IgA-type antibodies disappeared but the IgG class antibodies stayed in his circulation for at least 3 weeks (Table I).

Summary

A 9-year-old boy who first had thrombocytopenia and later developed leukopenia and Coombs' positive hemolytic anemia is presented. In the light of this case, Evans' syndrome is briefly reviewed. To our knowledge this case is unique from the standpoint that the antibodies related to Coombs' positivity in our patient were more prominently related to the IgA class.

Acknowledgement

We wish to thank Dr. Çiğdem Altay for her helpful discussion concerning this patient; Dr. Uğur Dilmen, who performed the anti-platelet antibody determinations; and Dr. Hassan Jama, who helped us in preparing the article.

REFERENCES

1. Evans RS, takahashi K, Duane RT, et al. Primary thrombocytopenic purpura and acquired hemolytic anemia, evidence for common etiology. *AMA Arch Int Med* 87: 48, 1951.
2. Silverstein MN, Aaro LA, Kempers RD. Evans' syndrome and pregnancy. *Amer J Med Sci* 252: 206, 1966.
3. Pui CH, Wilimas J, Wang W. Evans syndrome in childhood. *J Pediatr* 97: 754, 1980.
4. Habibi B, Homberg JC, Schaison G, Salmon C. Autoimmune hemolytic anemia in children. A review of 80 cases. *Am J Med* 56: 61, 1974.

5. Zupańska B, Lawkowicz W, Górska B, et al. Autoimmune haemolytic anaemia in children. *Br J Haematol* 34: 511, 1976.

6. Fagiolo E. Platelet and leukocyte antibodies in autoimmune hemolytic anemia. *Acta Haematol* 56: 97, 1976.

7. Cines DB, August CS, Schreiber AD. IgD mediated immune pancytopenia: A case report. *Clin Res* 27: 290 A, 1979.

8. Favre H, Chatelanat F, Miescher PA. Autoimmune hematologic diseases associated with infraclinical systemic lupus erythematosus in four patients. A human equivalent of the NZB mice. *Am J Med* 66: 91, 1979.

9. Ivey KJ, Hwang YF, Sheets RF. Scleroderma associated with thrombocytopenia and Coombs-positive hemolytic anemia. *Am J Med* 51: 815, 1971.

10. Segond P, Yeni P, Jacquot JM, Massias P. Severe autoimmune anemia and thrombopenia in mixed connective tissue disease (letter). *Arthritis Rheum* 21: 995, 1978.

11. Fagiolo E. Thrombotic thrombocytopenic purpura with autoimmune pancytopenia. *Acta Haematol* 52: 356, 1974.

12. Renoux M, Bernard JF, Vroclans M, et al. Syndrome d'Evans au cours de leucémies aiguës myélomonocytaires. Présentation de deux cas. *Sem Hop Paris* 54: 805, 1978.

13. Semple P. Thrombocytopenia, haemolytic anaemia, and sarcoidosis. *Br Med J* 4: 441, 1975.