

A Pediatric Case of Autoimmune Hemolytic Anemia followed by Excessive Thrombocytosis and Leukocytosis

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Autoimmune hemolytic anemia (AIHA) is characterized by the production of antibodies directed against red blood cells (RBCs). It is usually accompanied by normal white blood cell (WBC) and platelet counts. Severe leukocytosis and thrombocytosis in AIHA are rare. Here, we report a 3-year-old female child who showed AIHA by warm antibody testing with both leukocytosis and thrombocytosis. The patient was treated with oral steroids for 5 days. During treatment, the leukocytosis was noted on hospital day 3 and was up to $60.87 \times 10^9/L$. In addition, the thrombocytosis persisted at up to $725 \times 10^9/L$. After day 7, the WBC and platelet counts returned to the normal range. The clinical condition and vital signs improved. The patient was discharged on day 12. This case demonstrated that patients with primary AIHA, may also have leukocytosis and thrombocytosis. (*Korean J Hematol* 2007;42:288-291.)

Key Words: Autoimmune hemolytic anemia, Leukocytosis, Thrombocytosis

INTRODUCTION

Autoimmune hemolytic anemia (AIHA) is rare in children and is estimated to occur in 0.2 per 1,000,000 individuals under 20 years old.¹⁾ Immune mediated hemolytic anemia is the clinical condition in which IgG and/or IgM antibodies bind to red blood cell (RBC) surface antigens and initiate RBC destruction via the complement system and the reticuloendothelial system.²⁾ Usually the platelets and white blood cell (WBC) counts are normal, unless hemolysis is associated with leukocytosis in lymphoproliferative diseases or thrombocytopenia in Evans syndrome.³⁾ However, AIHA could accompany leukocytosis and thrombo-

cytosis, even though it is extremely rare. There is a previous report of severe hemolytic anemia with excessive leukocytosis in mycoplasma pneumonia.⁴⁾ Here, we report a child who presented AIHA with warm antibodies with excessive leukocytosis and thrombocytosis, without lymphoproliferative or any other malignant disease. Thus, this patient is a rare pediatric case with AIHA by warm antibody and who exhibited both excessive leukocytosis and thrombocytosis.

CASE REPORT

A 3-year-old female patient was admitted to our hospital with the chief complaints of severe abdominal pain, vomiting and anorexia for 2 days.

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She had no past medical, traumatic, or known family disease history. She had pale conjunctiva, icteric sclera, and dried lips. Heart beats were increased but regular and without murmur. Diffuse abdominal tenderness was seen, but without rebound tenderness. Organomegaly was not seen. Laboratory investigations revealed the following values: hemoglobin of 5.3g/dL (reference range : 11.5~15.5g/dL), hematocrit of 13.4% (reference range: 35~45%), RBC count of $2.0 \times 10^9/\text{L}$ (reference range: $3.9 \sim 5.3 \times 10^9/\text{L}$), WBC count of $19.64 \times 10^9/\text{L}$ (reference range: $6.0 \times 10^9/\text{L} \sim 17.5 \times 10^9/\text{L}$), platelet count of $682 \times 10^9/\text{L}$ (reference range: $150 \sim 400 \times 10^9/\text{L}$), mean corpuscular volume of 72.2fl (reference range: 77~95fl), and mean corpuscular hemoglobin of 28.4 pg (reference range: 24~30pg), haptoglobin of 0.058g/L (reference range: 0.22~1.64g/L), and plasma hemoglobin of 1.31umol/L (reference range: <0.47

umol/L). Peripheral blood smear examination revealed polychromasia, anisocytosis, poikilocytosis, neutrophil and shift to left of granulocyte. The direct Coomb's test was positive. Liver enzyme assays were mildly elevated (AST 100U/L, ALT 9U/L, reference range: 15~55U/L, 5~45U/L) and total bilirubin was 71.4umol/L (reference range: 2~14umol/L). Lactate dehydrogenase (LDH) was 4,339U/L (reference range: 150~500U/L). The serum level of C-reactive protein was 63,800ug/L (reference range: <1,800ug/L).

We treated the patient with oral steroids (6mg/kg/day for 2 days, 3mg/kg/day for 2 days and 1.5 mg/kg/day for 1 day) from day 2 to day 6. Since the mainstay therapy for patients with warm-type AIHA is oral steroids, we used oral prednisolone for five days. We did not treat the thrombocytosis because unless additional risk factors were present, children who had thrombocytosis were not at

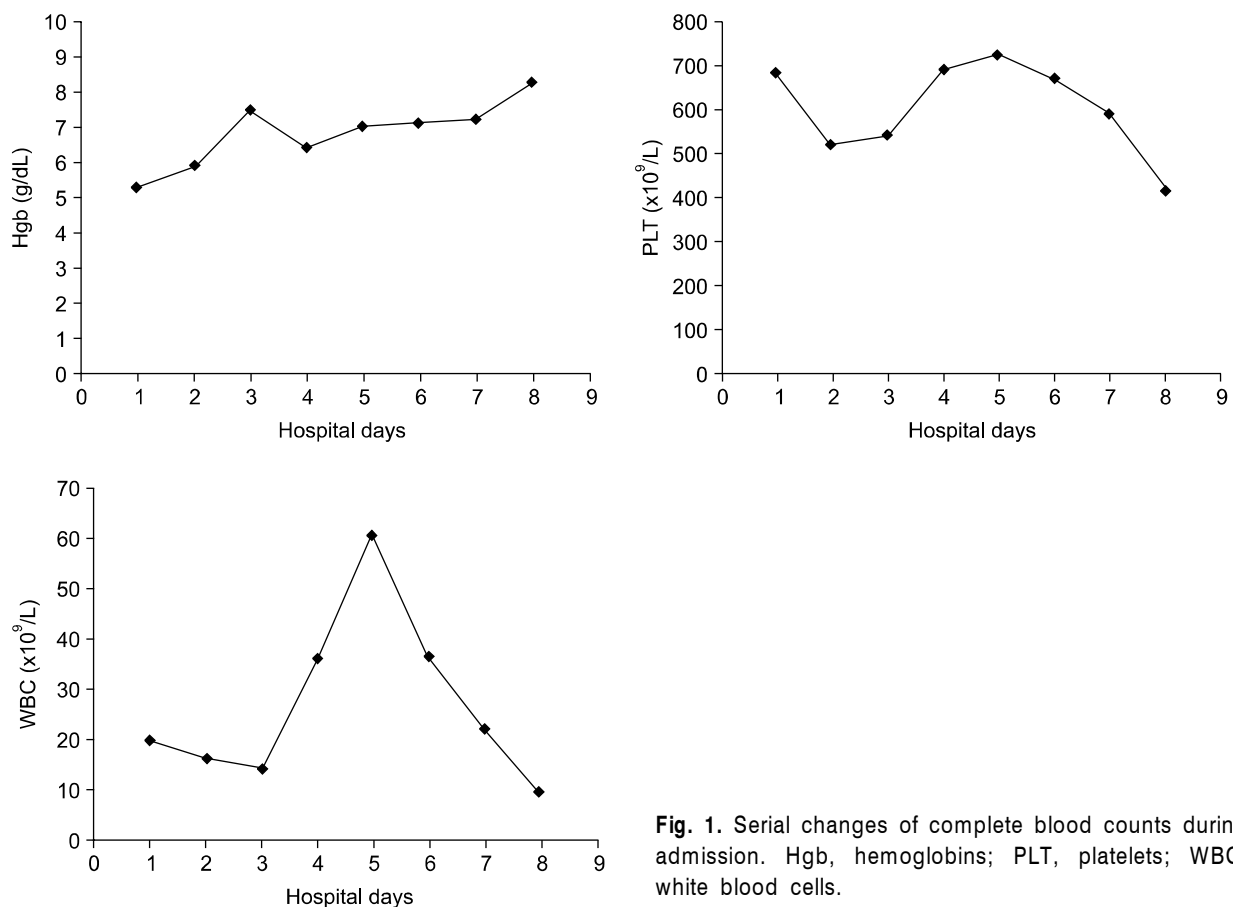


Fig. 1. Serial changes of complete blood counts during admission. Hgb, hemoglobins; PLT, platelets; WBC, white blood cells.

significant risk for thrombosis. During treatment, reticulocyte was increased unexpectedly up to 9.5% (hospital day 1: 2.1%) until hospital day 5. Leukocytosis was seen on hospital day 3 and WBC count was raised up to $60.87 \times 10^9/L$. Also, thrombocytosis continued and platelet count was increased to $725 \times 10^9/L$. After 7 days, WBC and platelet counts declined toward normal range (Fig. 1). Her clinical condition and vital signs improved. The patient was discharged after 12 days of hospitalization.

DISCUSSION

AIHA can be broadly classified into primary or secondary. Primary AIHA is typically idiopathic. Secondary AIHA includes hemolysis secondary to lymphoproliferative disorders (ie, chronic lymphocytic leukemia, Hodgkin's disease, and non-Hodgkin's lymphoma), systemic autoimmune diseases (ie, systemic lupus erythematosus, scleroderma and rheumatoid arthritis), infection, malignancy, and exposure to certain drugs or chemicals (ie, quinine, aspirin, chlorpromazine, antibiotics, naphthalene).^{2,4)} In general, in AIHA platelet and WBC counts are in normal range unless hemolysis is associated with leukocytosis in lymphoproliferative diseases or thrombocytopenia in Evans syndrome.³⁾ There are few cases of AIHA that demonstrate leukocytosis and/or thrombocytosis. Furthermore, AIHA is idiopathic and has no associated diseases.

Although we do not know the mechanism of thrombocytosis and excessive leukocytosis, we may propose that erythropoietin (EPO) levels were increased by severe anemia,⁵⁾ and due to a synergistic effect, thrombopoietin (TPO) activity was also increased, thus causing thrombocytosis. Many studies have been done on the synergistic effect of thrombopoietin and erythropoietin.⁶⁻⁸⁾ Several groups have shown that EPO augments the effects of plasma TPO on megakaryocyte formation in vitro.⁹⁻¹¹⁾ Another study showed the amino acid sequence homology of thrombopoietin

and erythropoietin in thrombocytosis in IDA patients.¹²⁾ In addition, there are studies that may help explain the unexpected leukocytosis seen in our case. One study showed how TPO directly enhanced the formation of multilineage colonies containing granulocytes, macrophages, erythrocytes and megakaryocytes.¹³⁾ The other showed lymphocyte activation and cytokine production in AIHA.¹⁴⁾ However, the exact mechanism and relationships remain to be studied.

To our knowledge, AIHA combined with thrombocytosis and/or leukocytosis is very rare. Here, we experienced that in patients with primary AIHA, leukocytosis and thrombocytosis could be seen simultaneously.

요 약

자가면역성용혈성빈혈은 선행 원인이 불분명한 일차성 또는 특발성일 경우 백혈구나 혈소판의 변화는 없는 경우가 대부분이지만 드물게 백혈구 또는 혈소판의 동반 증감을 경험하기도 한다. 하지만 백혈구 및 혈소판 양쪽 모두의 과도한 증가를 보인 경우는 국내외 보고가 아직 없다. 저자들은 3세 여아에서 온향체 양성의 자가면역성용혈성빈혈과 과도한 백혈구 및 혈소판의 동시 증가가 관찰되었던 1예를 경험하였기에 이를 보고하는 바이다.

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