Hiroshima Journal of Medical Sciences
Vol. 32, No. 1, March, 1983
HIJM 32-13

Idiopathic Thrombocytopenic Purpura Treated with High Doses of Intravenous Gammaglobulin and Prednisolone; A Case Report*)

Takashi HAMASAKI[1)], Takashi SAKANO[1)], Yoshito TANAKA[1)], Kohji FUJISAWA[2)], Junichi AKATSUKA[2)] and Tomofusa USUI[1)]

1) *Department of Pediatrics, Hiroshima University School of Medicine, Hiroshima 734, Japan*
2) *Department of Pediatrics, Jikei University School of Medicine, Tokyo 105, Japan*

(Received December 4, 1982)

Key words: *Idiopathic thrombocytopenic purpnra, High-dose intravenous gammaglobulin, platelet-associated IgG*

ABSTRACT

We describe a 13-year-old girl with chronic idiopathic thrombocytopenic purpura who showed a response to a high-dose intravenous gammaglobulin combined with prednisolone, without any response to a high-dose intravenous gammaglobulin therapy alone. This observation suggests the additive or multiplicative effects of these two drugs. Platelet-associated IgG level showed an inverse correlation with the number of platelets.

INTRODUCTION

Idiopathic thrombocytopenic purpura (ITP) in children is usually a self-limited disease with a good prognosis, but in a few cases thrombocytopenia is refractory to steroid therapy, immunosuppressive agents, and splenectomy. It is very embarrassing to treat such patients. Of late, a high-dose intravenous gammaglobulin has been reported to be effective in a certain number of patients with ITP refractory to the conventional therapies[2)]. The present paper describes a 13-year-old girl with chronic ITP who showed a response to the combined therapy of a high-dose intravenous gammaglobulin and prednisolone.

CASE REPORT

A 13-year-old girl with chronic ITP, who had been diagnosed as having ITP two years previously, was admitted with vaginal bleeding, purpura, and pallor. On admission, hematological values were, hemoglobin, 7.0 g/dl; hematocrit, 21.5%; white blood cell count, 7,150/mm^3; 86% neutrophils, 11% lymphocytes, 3% monocytes; platelet count, 1,000/mm^3. Direct and indirect Coombs' tests were negative. Serum anti-platelet antibody was also negative. Examination of bone marrow showed normal granulocytic and erythrocytic series, and many megakaryocytes. After admission she was treated with prednisolone 2 mg/kg/day for 22 days, then splenectomy followed by 6-mercaptopurine 1.5 mg/kg/day for 29 days, but there was no improvement. A high-dose intravenous gammaglobulin treatment was attempted according to the therapy of Imbach et al.[2)] First she received, on 5 consecutive days, 0.4 g/kg/day of gammaglobulin (Venoglobulin-I®) intravenously. This preparation contains a concentrated IgG with intact Fc portion, obtained by treatment with polyethylene glycol. Its in vivo biological half-life is similar to that of the normal serum IgG. The platelet count rose from 2.3×10^4/mm^3 to a maximum of 4.9×10^4/mm^3 in 5 days, but soon returned to 1.0×10^4/mm^3 (Fig.). The second course had no effect. Then, prednisolone 1 mg/kg/day had been given for 19 days orally before the third 5-day course was begun. The platelet count increased from 1.4×10^4/mm^3 to a maximum of 51.9×10^4/mm^3 7 days after the start of the course but returned 1.6×10^4/mm^3 during the next 12 days. A single injection of 0.4 g/kg of the gammaglobulin increased the platelet count from 1.6×10^4/mm^3 to 8.8×10^4/mm^3.

Platelet-associated IgG was measured simultaneously by the Fab-anti-Fab method[5)]. As

*) 濱崎 隆, 坂野 堯, 田中義人, 藤沢康司, 赤塚順一, 臼井朋包：免疫グロブリン大量静注とプレドニソロンとの併用療法を試みた特発性血小板減少性紫斑病の一例

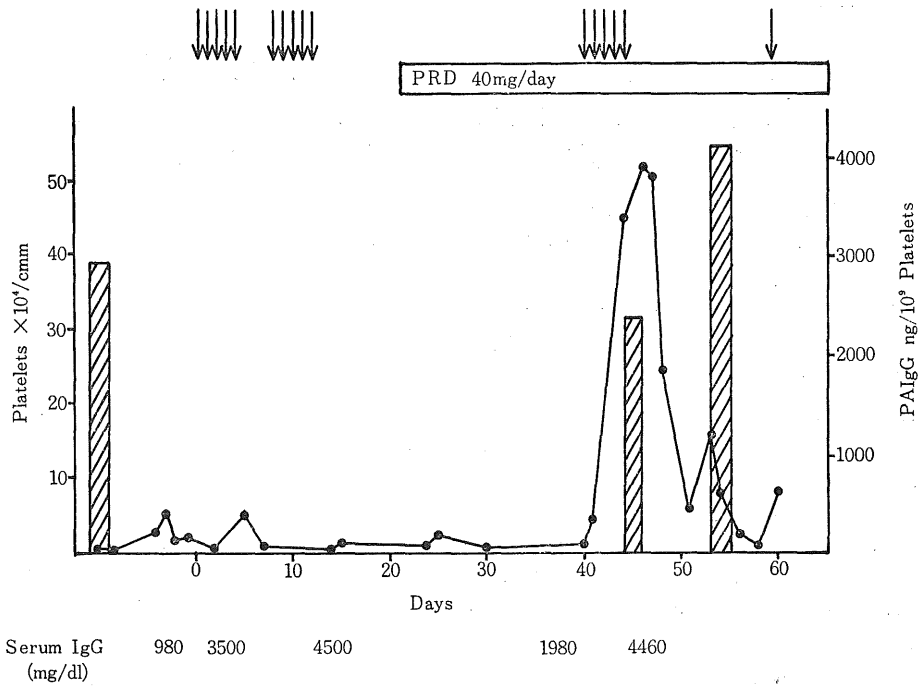

Figure. Clinical course of the patient.
Serial platelet values are represented by the solid line, and serial platelet-associated IgG (PAIgG) values by the hatched bars. An arrow indicates an intravenous injection of gammaglobulin 0.4 g/kg. PRD: prednisolone.

shown in the Figure, the platelet-associated IgG level expressed in ng/10^9 platelets was 2910 before the first 5 consecutive days therapy, 2377 when the platelet count increased during the combined therapy, and 4124 after the platelet count decreased. Serum IgG levels increased according to the amount of gammaglobulin given intravenously.

DISCUSSION

Since 1951, when Harrington et al.[3] demonstrated the presence of thrombocytopenic factor in the serum of patients with ITP, many immunological, experimental, and clinical studies have been reported[1,3,4,6,9]. Antiplatelet antibody is now thought to play an important role of thrombocytopenia in ITP. Antiplatelet antibody is produced in the reticuloendothelial system, mainly in the spleen[3,4] and attach to platelets. These antibody-coated platelets are then caught and destroyed in the spleen, the liver, and other reticuloendothelial system cells leading to thrombocytopenia[1,6,7,9].

The mechanism of high-dose intravenous gammaglobulin has been hypothesized by Imbach et al.[1] as below. Large doses of IgG could overload and block the reticuloendothelial system by IgG catabolism. Immediate effects could be caused by reaction with and inactivation of a circulating antiplatelet factor or interference with platelet-bound IgG and/or C_3. Late effects could be due to activation of T cells and suppression of B cells.

In contrast to Imbach's cases, our patient was resistant to a high-dose intravenous gammaglobulin therapy, and prednisolone treatment alone was also ineffective. However, when given in combination the platelet count greatly increased, although the effect was transient.

Steroid hormone is known to have many effects on the immune systems including phagocytosis and antibody production[8]. There is an indirect evidence that steroid hormone inhibits binding of autoimmune antibody to platelets[3]. The platelet-associated IgG level decreased when the platelet count increased after a high-dose intravenous gammaglobulin combined with prednisolone, and their combination seemed to suppress antibody production and/or binding of antiplatelet antibody to plate-

lets.

These observations suggest that an increased platelet count is due to the additive or multiplicative effects of a high-dose intravenous gammaglobulin and prednisolone. The alterations of platelet-associated IgG before and after the combined therapy appear to reflect the co-operative action of these two drugs.

ACKNOWLEDGEMENT

This work was supported in part by a grant-in-aid from the Japan Medical Research Foundation and by Scientific Research Grants (project No. 57770632) from the Ministry of Education, Science and Culture of Japan.

We are grateful to Dr. Alice S. Cary for assistance in preparing this manuscript.

REFERENCES

1. **Aster, R. H. and keene, W. R.** 1969. Site of platelet destruction in idiopathic thrombocytopenic purpura. Br. J. Haematol. **16** : 61-73.
2. **Imbach, P., Barandun, S., d'Apuzzo, V., Baumgartner, C., Rossi, E., Schöni, M., Vest, M. and Wargner, H. P.** 1981. High-dose intravenous gammaglobulin for idiopathic thrombocytopenic purpura in children. Lancet **1** : 1228-1230.
3. **Karpatkin, S.** 1980. Autoimmune thrombocytopenic purpura. Blood **56** : 329-343.
4. **Karpatkin, S., Strick, N. and Siskind, G. W.** 1972. Detection of splenic antibody systhesis in idiopathic autoimmune thrombocytopenic purpura. Br. J. Haematol. **23** : 167-176.
5. **Lightsey, A. L. J., Koenig, H. M. and McMillan, R.** 1979. Platelet-associated immunoglobulin G in childhood idiopathic thrombocytopenic purpura. J. Pediatr. **94** : 201-204.
6. **McMillan, R., Longmire, R. L. and Tavassoli, M.** 1974. In vitro platelet phagocytosis by splenic leucocytes in idiopathic thrombocytopenic purpura. N. Engl. J. Med. **290** : 249-251.
7. **McMillan, R.** 1977. The pathogenesis of immune thrombocytopenic purpura. CRC. Crit. Rev. Lab. Sci. **8** : 303-332.
8. **McMillan, R., Longmire, R. and Yelenosky, R.** 1976. The effect of corticosteroids on human IgG synthesis. J. Immunol. **116** : 1592-1595.
9. **Stossel, T. P.** 1974. Phagocytosis. N. Engl. J. Med. **290** : 717-723.