3. Griffin JH, Mosher DF, Zimmerman TS, Kleiss AJ: Protein C, an antithrombotic protein, is reduced in hospitalized patients with intravascular coagulation. Blood 60:261–264, 1982.

Ineffectiveness of High-Dose Intravenous Gammaglobulin Infusion in Thrombotic Thrombocytopenic Purpura

To the Editor: Thrombotic thrombocytopenic purpura is a rare disorder characterized by fluctuating neurological abnormalities, fever, renal disease, and hematological features, including microangiopathic hemolytic anaemia and thrombocytopenia [1]. Improvement is achieved most frequently with a combination of glucocorticoids, platelets inhibitors, and therapeutic plasma exchange. The pathogenesis is unknown; it has been proposed that deficiency of an IgG that inhibits the platelets aggregating factor present in normal plasma is responsible for inappropriate and excessive platelet activation in some cases of the disease [2]. There have been several anecdotal case reports suggesting that IV gammaglobulin injection may be beneficial in thrombotic thrombocytopenic purpura [3–11]. Our experience did not support these results.

Three patients with severe thrombotic thrombocytopenic purpura, i.e., platelet count $<20{,}000/mm^3$, hemoglobin <6 g/dl, lactic dehydrogenase >1,200 mU/l, and neurologic manifestations were treated with high-dose intravenous gammaglobulin 1–3 weeks after multimodality treatment with plasmapheresis, acetylsalicylic acid, dipyridamole, and prostacyclin infusion failed to achieve lasting remission. After the infusion of gammaglobulin (Veinoglobulin, Merieux, France) in a dose of 500 mg/kg/day for 5 days, the patients' results were unchanged. All three patients have subsequently required further therapy. In two of them, the administration of vincristine, 1 or 2 mg once per week for 5 weeks, was followed by prompt and durable remission (total dose 8 mg). The third patient succumbed to his disease despite aggressive plasma exchange with cryosupernatant, corticosteroids, and splenectomy.

Case reports have not demonstrated that IV gammaglobulin is effective in thrombotic microangiopaty. Unfortunately, the rarity of thrombotic thrombocytopenic purpura and its often fulminant course make a randomized study to determine the best initial approach or the assessment of new pharmacological agents difficult to perform. Based on our experience, we conclude that high-dose IV gammaglobulin infusion is not an effective therapy for severe thrombotic thrombocytopenic purpura.

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References

1. Kwaan HC: Clinicopathologic features of thrombotic thrombocytopenic purpura. Semin Hematol 24:71–81, 1987.
2. Lian ECY, Min PTK, Siddigin FA, Chin AYY, Chin LLS: Properties and identification of a plasma factor which inhibits the platelet aggregation induced by thrombotic thrombocytopenic purpura plasma. Thromb Haemost 50:101, 1983.
3. Gilcher RO: Refractory thrombotic thrombocytopenic purpura responding to intravenous gamma globulin. Blood 64[suppl]:1237a, 1985.
4. Krishnamurthy M, Bellevue R, Lian ECY, et al.: Intravenous immunoglobulin in thrombotic thrombocytopenic purpura. A new mode of treatment. Blood 66[suppl]:291a, 1985.
5. Messmore HL, Yeshwant C, Remilinger K, et al.: Intravenous gamma globulin in refractory thrombotic thrombocytopenic purpura. Thromb Haemost 54:127, 1985 (abstract).
6. Viero P, Cortelazzo S, Bueill M, et al.: Thrombotic thrombocytopenic purpura and high dose immunoglobulin treatment. Ann Intern Med 104:282, 1986 (letter).
7. Wong P, Itoh K, Yoshida S: Treatment of thrombotic thrombocytopenic purpura with intravenous gamma globulin. N Engl J Med 314:385–386, 1986.
8. Finn NG, Wang JC, Hong KJ: High-dose intravenous immunoglobulin infusion in the treatment of thrombotic thrombocytopenic purpura. Arch Intern Med 147:2165–2167, 1987.
9. Staszewski H, Colbourn D, Donovan D, Ludman H: Thrombotic thrombocytopenic purpura: Report of a case with a possible response to high-dose intravenous gamma globulin. Acta Haematol 82:201–204, 1989.
10. Heyman MR, Sweet T: Thrombotic thrombocytopenic purpura with high-dose intravenous gamma globulin. South Med J 83:1471–1474, 1990.
11. Sheth KJ, Gill JC, Leichter HE: High-dose intravenous gamma globulin infusions in haemolytic-uremic syndrome: A preliminary report. Am J Dis Child 144:268–270, 1990.

Low β_2-Glycoprotein I Levels in Patients With Disseminated Intravascular Coagulation

To the Editor: β_2-Glycoprotein I (GPI) (apolipoprotein H) was first reported by Schultze et al. [1], and its amino acid sequence was subsequently determined by Lozier et al. [2]. However, its function and clinical significance are still not clarified fully. Nimpf et al. [3] and Schousboe [4] have recently reported that GPI blocks activation of the intrinsic blood coagulation cascade and inhibits platelet aggregation. Furthermore, Galli et al. [5] and McNeil et al. [6] have confirmed that GPI is the cofactor of anticardiolipin antibody (aCL). Hence a possible mechanism causing the thrombosis frequently observed in patients with aCL would be inhibition of the antithrombotic properties of GPI by such autoantibodies. We postulated that GPI levels would decrease in patients with disseminated intravascular coagulation (DIC) due to consumption and conducted this study to test our hypothesis.

Blood was collected from nine patients (seven with acute myeloid leukemia [AML] and two with abdominal aortic aneurysm) at the time of the initial diagnosis of DIC. Samples were also collected serially from six patients during the course of DIC.

IgG fraction was purified from the rabbit immunized with purified GPI in our laboratory [4,7] and was used to measure GPI levels by the single radial immunodiffusion technique. The significance of differences between groups was assessed using Student's t test.

The GPI level of one patient (patient G) was normal, but the mean level (±SD) for all the DIC patients (156 ± 35 μg/ml) was significantly lower than in the 77 controls (193 ± 30 μg/ml) ($P < 0.01$) (Fig. 1). During the course of DIC, the GPI level fell further in patient 6 and remained low in another five patients despite extensive treatment for DIC.

It is well known that many blood coagulation/fibrinolysis factors are consumed during the process of DIC. Under these circumstances, the GPI levels might also be reduced due to consumption. Schousboe [4] previously proposed this hypothesis, but precise data have not been published before now.

In this study, we found that the GPI level was significantly low in eight of nine DIC patients. It is well known that DIC causes multiorgan failure and often produces liver damage. Liver damage might then cause a reduction in GPI production. However, this seems unlikely in that liver function showed only mild to moderate abnormalities in our patients.

Another possibility for the diminution in GPI could be accelerated consumption during the course of DIC. It is still unclear how far GPI contrib-