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Unsuccessful treatment of resistant thrombotic thrombocytopenic purpura with prostacyclin

Prostacyclin has been suggested as a useful agent for patients with thromobotic thrombocytopenic purpura (TTP) refractory to plasma-exchange. We report our unsuccessful experience with iloprost in a patient with TTP resistant to plasma-exchange, vincristine and high dose immunoglobulins.

Sir,

Thrombotic thrombocytopenic purpura (TTP) is a syndrome characterized by thrombocytopenia, microangiopathic hemolytic anemia and, less commonly, fever, fluctuating neurologic abnormalities and renal impairment. The underlying pathology is disseminated thrombotic occlusion of the microcirculation secondary to an abnormal interaction between vascular endothelium and platelets. However, so far, the etiology remains elusive. The primary process might involve endothelial damage with release of ultra large von Willebrand factor vWF (ULvWF multimers),[1] impaired fibrinolytic activity and reduced vascular prostacyclin production.[2] Recently two clinical studies reported the presence of inhibitory antibodies to vWF-cleaving protease.[3,4] Plasma-exchange is the first line treatment of TTP: this treatment works by removing ULvWF, inhibitory antibody and supplying normal protease.[5] The procedure is effective in over 70% of patients.[6,7] For refractory cases there is no standardized treatment. Some reports suggest the effectiveness of vincristine, intravenous γ-globulin (Ig) and splenectomy. Au *et al.* recently reported a favorable outcome with prostacyclin in a patient with TTP diagnosed during immunosuppression with tacrolimus for mismatched liver transplantation.[8] Iloprost, a long-acting PGI_2 analog, inhibits endothelial reactivity and platelet aggregation.[9] We describe our unfavorable experience with iloprost treatment in a patient with TTP resistant to plasma-exchange, vincristine and high-dose IgG.

A 42-year old woman was admitted to our hospital because of asthenia and purpura. Physical examination was negative except for purpura. Laboratories studies revealed severe anemia (Hb: 6.1 g/dL), schistocytes, thrombocytopenia (platelets: 5×10^9/L), high LDH (3,286) and bilirubin levels (3 mg/dL). A diagnosis of TTP was made. Underlying neoplastic disease, autoimmune disorders and immunodeficiency syndrome were excluded.

We immediately started plasma-exchange with cryosupernatant combined with 6-methyl-prednisone 100 mg/day and acetylsalicylic acid. On the third day there was a sudden clinical worsening with seizures, hemiparesis, confusion, coma and renal failure. Immunosuppression therapy was intensified with pulses of vincristine 1 mg/m^2 every 5 days for 8 cycles, and then with intravenous immunoglobulin 400 mg/kg/day for 5 days. Dipyridamole was added to acetylsalicylic acid. A complete clinical remission was obtained but any attempt to discontinue plasma-exchange was followed by relapse.

After 37 plasmapheresis procedures, we started on therapy with iloprost instead of the association of acetylsalicylic and dipyridamole. Following the experience of Au *et al.*,[8] iloprost was given as an eight-hour continuous infusion at the dosage of 50 μg/day for ten days. Stable, complete remission was not achieved and plasma-exchange procedures, repeated at least every other day, were necessary in order to control disease activity.

Other authors report controversial results with prostanoids.[10] So far the role of prostanoids is

still uncertain and the best treatment for refractory TTP remains an unsolved question.

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Key words

Thrombotic thrombocytopenic purpura, refractory, prostacyclin.

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