

Thrombotic Thrombocytopenic Purpura: diagnosis, pathogenesis and modern therapy

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Thrombotic thrombocytopenic purpura (TTP) is an uncommon multisystem disorder, sometimes associated with predisposing conditions such as pregnancy, cancer, exposure to certain drugs, bone marrow transplantation and HIV-1 infection. An abnormal interaction between the vascular endothelium and platelets which occurs in certain organs leads to thrombosis, endothelial proliferation, minimal inflammation and microangiopathic hemolysis. Recent studies suggests that endothelial cell perturbation and apoptosis caused by an as yet unknown plasma factor(s) may lead to the release of abnormal Von Willebrand factor which facilitates the deposition of platelet microthrombi. We isolated specific anti-endothelial Ab from four patients with TTP, by incubating their isolated serum IgG fraction with human bone marrow capillary endothelial cells (TrHBMEC), followed by elution of bound antibodies. The affinity-purified F(ab)2 of the anti-EC Ab were found to bind and differentially activate only microvascular EC (TrHBMEC) and not large vessel human umbilical cord EC (HUVEC). The EC activation was mani-

fested by enhanced IL-6 and vWF release and by the expression of adhesion molecules (P-selectin, E-selectin, VCAM-1 and CD36), facilitating increased monocyte adhesion.

A special issue of TTP is its occurrence during pregnancy and women with a history of TTP show a tendency for recurrent TTP in subsequent pregnancies. TTP during pregnancy carries a significant morbidity and mortality both to the mother and the fetus and may require premature termination of the pregnancy.

Exchange transfusions of plasma or plasma-cryosupernatant remain the cornerstone of the treatment of TTP along with corticosteroids, platelet inhibitor drugs, vincristine and splenectomy. In most cases remissions can be attained and cures are now common although approximately one-half of the patients will relapse. While relapses are usually milder, they still carry a significant mortality and preventive therapies are not always effective. The special issue of therapy for pregnancy associated TTP will be also discussed.