ADAMTS13 Mutational Analysis in Chinese Patients with Chronic Relapsing Thrombotic Thrombocytopenic Purpura

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Abstract
Mutational analysis of ADAMTS13 gene was performed on three Chinese children with chronic relapsing thrombotic thrombocytopenic purpura, who all showed severe deficiency (<5% activity) of von Willebrand factor-cleaving protease (vWF-CP) and lack of inhibitors. In two patients, three new mutations, namely G194V, R349C and G1181R, were identified along with a fourth mutation A596V recently described in a French patient. No significant ADAMTS13 gene defect was detected in one patient, in whom the presence of low titer or non-neutralizing antibodies to vWF-CP was not excluded. The prevalence of G194V and G1181R mutations was 1.5% and 5.8% among normal Chinese subjects. They may constitute genetic susceptibility factors for thrombosis in the population.

Key words ADAMTS13; Mutation; Thrombotic thrombocytopenic purpura; vWF-cleaving protease

Introduction
Thrombotic thrombocytopenic purpura (TTP) is a life-threatening clinical disorder characterised by the pentad of microangiopathic haemolytic anaemia, thrombocytopenia, fever, renal failure and neurological dysfunction. Major recent advances in understanding the pathophysiology of TTP indicates that this disorder is etiologically linked to deficiency of a specific von Willebrand factor cleaving protease (vWF-CP), which normally cleaves the Tyr-Met bond at A2 domain of the vWF molecule and limits the propagation of platelet thrombus (reviewed in 1). The vWF-CP has been purified by chromatographic methods and shown to belong to the ADAMTS family of metalloproteases. Based on this information, the cDNA and gene structure of the ADAMTS13 gene encoding for vWF-CP is quickly determined. Similar conclusions are obtained independently through positional cloning of familial TTP cases.1 The vWF-CP deficiency that leads to microvascular platelet thrombus formation is due either to autoantibody inhibition of vWF-CP activity in sporadic acquired TTP, or constitutive...