**Introduction:**

Thrombotic thrombocytopenic purpura is a rare thrombotic microangiopathy. It is a life threatening multisystem disease characterized by intravascular platelet aggregation which leads to profound thrombocytopenia (usually < 2000/ul), mechanical hemolytic anemia, fever, and tissue ischemia, commonly affecting the brain and kidneys (thrombosis of the small vessels) (1). It is often fatal in the absence of treatment (mainly based on plasmapheresis). The cause is generally unknown. A drug-related cause is very rarely sought, and a causal link with a drug is difficult to establish. Ticlopidine is the drug most often involved. Recent reports involve clopidogrel. Other drugs, such as cytotoxic and immunosuppressive compounds have also been mentioned (2).

Ticlopidine and clopidogrel are specific and potent inhibitors of platelet aggregation. The two drugs are structurally related derivatives of thienopyridine, differing only by one carboxymethyl group. Ticlopidine has been associated with the development of thrombotic thrombocytopenic purpura, with an estimated incidence of 1 case per 1600 to 5000 patients treated (3, 4).

Clopidogrel is a new antiplatelet drug that has achieved widespread clinical acceptance because it has a more favorable safety profile than ticlopidine (5).

We describe a case of TTP occurred in a patient 20 days after the start of clopidogrel treatment.

**Case Report:**

Our patient is a 71 year – old woman who had an anterior myocardial infarction in April 2004. After percutaneous transluminal angioplasty and stent placement, she was given PLAVIX* (clopidogrel), MONICOR* (5-isosorbid mononitrate), TENORMIN* (Atenolol), ASPEGIC*(Acetyl salicylic acid) and TAGAMET* (cimetidin). Six days after the start of medication, she has developed a stomach pain. A few days later, she has presented an epistaxis, purpura with renal insufficiency and anemia. Platelet counts were 38000/mm3, hemoglobin value was 10,8g/ml. Serum creatinine level was 328umol/l. The patient has also developed an acute liver injury, with marked elevation of serum aminotransferase levels and ASAT/ALAT= 1000/950 µI/l free bilirubin (38 umol/l). The prothrombin level (TP) was very low (19%). The abdominal echography has showed a steatosis. So, the patient underwent a plasma transfusion with withdrawal of all the therapy. The evolution was marked by resolution of symptoms and laboratory abnormalities five days after stopping the drugs. The rechallenge of the therapy with the exception of clopidogrel has not led to recurrence of symptoms.

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**Summary:**

Clopidogrel has replaced ticlopidine (in the united states but not worldwide). Clopidogrel can either be used independently or in combination with other antiplatelet agents. Clopidogrel has a lower frequency of associated thrombotic thrombocytopenic purpura than ticlopidine, a lower rate of neutropenia, and better gastrointestinal tolerance. We describe a case of thrombotic thrombocytopenic purpura in a patient 20 days after the start of clopidogrel treatment. All symptoms are reversed with cessation of clopidogrel. Clinicians should be alert to this adverse effect of clopidogrel and monitor platelet counts in patients receiving it.

**Key-words:** Clopidogrel - thrombotic thrombocytopenic purpura.
Discussion:

An inquiry of pharmacovigilance has been realized according to frensh imputation method. It has allowed to suspect strongly the responsibility of clopidogrel. The score of imputability has been evaluated at (C2 S2) I2 B3 “plausible”. Since clopidogrel was approved by the FDA in early 1998, more than 3 million people have received the drug, and eleven cases of thrombotic thrombocytopenic purpura that occurred after clopidogrel use have been reported until 2000 (6).

Naraw and al in 2001 (7) describe a case of TTP associated with the use of clopidogrel. Discontinuation of the drug and transfusion of 17 units of cryodepleted plasma resulted in resolution of the hematological abnormalities. The eleven reports of TTP were analyzed using the bayesian Adverse Reaction Diagnostic Instrument to calculate the posterior probability that clopidogrel caused the TTP based on epidemiological and clinical trials data (expressed as prior adds) and the clinical characteristics of each case (expressed as likelihood ratios). The result show that clopidogrel was implicated as the causative factor of the TTP (PsP > 0,75) in only five of the 11 cases (8).

It has been demonstrated that TTP plasmas contain heterogeneous platelet aggregating factors and that TTP plasmas induce the opoptosis of microvascular endothelial cell. Fibrinolysis has been shown decreased. Von Willebrand factor (VWF) under high shear stress is unfolded and becomes adshesive to platelets to induce platelet aggregation. Recently it is found that VWF protease is deficient in hereditary TTP, intermittent relapsing TTP, and ticlopidine-induced TTP (9,10,11).

Reference: