Our young patient had increased lipid levels for several months before his stroke, the only additional risk factors for vascular disease being mild arterial hypertension and possibly smoking. An autopsy study revealed extensive atherosclerosis with basilar artery thrombosis. Pathologically confirmed severe atherosclerosis has been previously reported in patients with nephrotic syndrome of short duration.49 In this patient, accelerated atherosclerosis was most probably due to hypercholesterolemia associated with his nephrotic syndrome. This lends weight to the rule that if the long-term outlook for a patient is otherwise good, attempts should be made to reduce the cholesterol level in nephrotic patients.7

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Thrombotic Thrombocytopenic Purpura Associated With Ticlopidine

To the Editor:

Ticlopidine is a potent inhibitor of platelet aggregation increasingly used in the prophylactic treatment of patients at high risk for thromboembolic events and recently approved by the US Food and Drug Administration for prevention of strokes in patients intolerant of aspirin. We report a case of fatal thrombotic thrombocytopenic purpura (TTP) associated with ticlopidine.

A 69-year-old man was referred with a 2-day history of headache, mental confusion, lumbar pain, and hematuria. Five weeks before, he had suffered an uncomplicated myocardial infarction and had been started on ticlopidine (250 mg twice daily), diltiazem (60 mg daily), and percutaneous nitroglycerine (10 mg daily).

On examination he was feverish (38°C), slightly dyspneic, and drowsy. A computed tomographic (CT) scan of the head was normal. Biological tests were as follows: erythrocyte sedimentation rate 120 mm in the first hour, urea concentration 25.3 mmol/l, creatinine concentration 374 mmol/l, total serum bilirubin 41 μmol/l, serum lactic dehydrogenase 7,450 units/l, hemoglobin concentration 11.4 g/dl, white cell count 9.1×109/l, and platelet count 24×109/l. Prothrombin time, activated partial thromboplastin time, and fibrinogen were normal. Bone marrow examination was normal, and antibodies to platelets (ELISA test) were present in the serum. Ticlopidine was stopped, but by the next day the
Letters to the Editor

923

patient became comatose with bilateral Babinski’s sign and was transferred to the intensive care department. Platelet count fell to $9 \times 10^9/l$ and hemoglobin to 5.6 g/dl within 3 days. Coombs tests were negative. Serum creatinine rose to 901 mmol/l, serum haptoglobin was 12.1 mg/dl, and peripheral blood smears showed numerous fragmented erythrocytes. A diagnosis of TTP was made, and the patient was started on plasmapheresis (50 ml/kg daily), intravenous aspirin (600 mg daily), dipyridamole (600 mg daily), and hemodialysis. Renal function, hemoglobin, and platelet count gradually improved, but the patient remained comatose, with intermittent seizures and left-sided hemiplegia. Ten days after admission, CT scan of the head revealed multiple hypodensities of the white matter. Electroencephalogram showed electrocerebral silence. The patient developed staphylococcemia, then a pneumonia with septic shock caused by *Acinetobacter calcoaceticus*, and finally died 3 weeks after admission. Autopsy disclosed multiple rounded, small cerebral infarctions, sometimes hemorrhagic, in both centrum semiovale, basal ganglia, and brain stem.

Although a fortuitous association cannot be excluded, it is likely that in this case TTP was induced by ticlopidine because other etiologies such as autoimmune disorders, solid tumors, or infections could be discarded, and the patient did not take drugs known to be related to TTP such as heparin, penicillin, contraceptive treatment, antineoplastic or anesthetic agents. Moreover, the TTP therapeutic standards joined to cessation of ticlopidine yielded to expected results before the patient died from a severe nosocomial sepsis. The most commonly reported adverse effects associated with ticlopidine in major clinical trials were gastrointestinal effects, with diarrhea affecting 20% of patients in the Ticlopidine Aspirin Stroke Study (TASS).1 Severe neutropenia was recorded in 1% of patients. TTP has not been reported in the Canadian American Ticlopidine Study and TASS studies,1,2 the Swedish Ticlopidine Multicentre Study,2 or in the Studio della Ticlopidina nell’angina Instabile.4 We are aware of only one previous publication of ticlopidine-related TTP.5 An immunosuppressive mechanism could be involved in our case because antibodies to platelets were found in the patient’s serum. This is in agreement with the study of Claas et al,4 which showed that antibodies to ticlopidine had been detected in the serum of a 71-year-old man after 5 weeks of ticlopidine therapy and had destroyed platelets to which the drug adhered.6

TTP is a rare but potentially severe adverse experience from ticlopidine. A careful monitoring of blood cell and platelet counts is recommended during the first 3 months after the start of ticlopidine, but it is of note that our patient had normal values 1 week before admission.

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