drome with membranoproliferative glomerulonephritis had been diagnosed 10 months earlier. At this time, he had normal renal function and a serum cholesterol level of 285 mg/dl. He was treated with a diuretic drug for mild arterial hypertension. His hyperlipidemia was not treated, and his only other apparent risk factor for vascular disease was smoking approximately 15 cigarettes a day. His parents died of nonvascular causes in the fifth and sixth decade, and he had three healthy brothers.

On admission, general examination was unremarkable, with blood pressure of 160/90 mm Hg. Neither xanthomas of the tendons nor xanthelasma or arcus corneus were observed. Neurological examination disclosed an alert appearance, anarxia, left hemiplegia with lower facial weakness, pupil-sparing right third nerve palsy, and left extensor plantar response. Twenty minutes after his arrival at the hospital, he had a generalized seizure and fell into a coma with bilateral Babinski's sign, small pupils with present pupillary light reflex, and left decerebrate posturing in response to noxious stimuli.

Routine laboratory blood and serum determinations were normal except for an erythrocyte sedimentation rate of 94 mm for the first hour, white blood cell count of 13,400/μm³, cholesterol 250 mg/dl, triglycerides 265 mg/dl, high density lipoprotein (HDL) cholesterol 32 mg/dl, low density lipoprotein (LDL) cholesterol 258 mg/dl, total protein 5.1 g/dl, albumin 2.9 g/dl, creatinine 2.8 mg/dl, blood urea nitrogen 79 mg/dl, lactic dehydrogenase 641 units/l, and potassium 2.8 mmol/l. Urinalysis revealed 3+ protein and 3+ hematuria. Apolipoprotein A1 and B levels were normal. Syphilis serology was negative, and the search for anticardiolipin antibodies, antinuclear antibodies, and rheumatoid factor was also negative. Examination of cerebrospinal fluid was normal. Chest roentgenogram, electrocardiogram, and brain computed tomographic scan without contrast were also normal. The following coagulation studies were normal: prothrombin time, partial thromboplastin time; thrombin time; reptilase time; eu- tin time, and fibrinogen were normal. Bone marrow examination showed nonfiling of the left vertebral artery, stenosis of the right vertebral artery, and complete occlusion of the basilar artery.

During the following days, his state did not improve, and on the seventeenth day after admission, the patient deteriorated suddenly and died. Postmortem examination disclosed that the aorta and its branches were markedly involved by atherosclerosis. The circle of Willis also displayed atherosclerosis, particularly the basilar artery, which was occluded by a fibrous plaque and a recent thrombus. There was a 2- or 3-week-old infarction of the brain stem and cerebellum.

Plasma lipid abnormalities are a prominent feature of the nephrotic syndrome. As in our patient, hyperlipidemia is often associated with elevated total and LDL cholesterol levels and normal HDL cholesterol levels. A relation has been found between blood lipids and/or lipoproteins and the extent and severity of cerebrovascular atherosclerosis. Stroke and pathological demonstration of cerebrovascular atherosclerosis have been documented in several cases of nephrotic syndrome, although incomplete data about serum lipids and coagulation have made it difficult to establish their respective pathogenetic relevance. In any case, some authors believe that lipid abnormalities in nephrotic syndrome need not be treated.

It has been established that the nephrotic syndrome is associated with a hypercoagulable state and a risk of cerebral arterial thrombosis and infarction. However, the role of this state, as a pathogenetic factor that leads to the high incidence of thromboembolic complications observed in nephrotic patients, has not been conclusively determined. Extensive coagulation studies in the patient described here revealed no abnormalities.

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. 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.

References

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 dyspnic, and tachyarrhythmic. 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 lact 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...
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patient became comatose with bilateral Babinski's sign and was transferred to the intensive care department. Platelet count fell to 9x10^9/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, the Swedish Ticlopidine Multicentre Study, or in the Studio della Ticlopidina nell'angina Instabile.4 We are aware of only one previous publication of ticlopidine-related TTP.3 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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References

Thrombotic thrombocytopenic purpura associated with ticlopidine.
E Ellie, C Durrieu, P Besse, J Julien and G Gbipki-Benissan

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