The role of platelets in cerebral ischemic pathology,\textsuperscript{1,2} the frequency of thrombotic manifestations in myeloproliferative syndromes\textsuperscript{3} and the frequent neurological complications of essential thrombocythemia\textsuperscript{4} are all known. We report the case of a cerebellar infarction including the detailed study of platelet anomalies which are discussed in relation to published data and the efficacy of antiaggregant treatment is stressed.

**SUMMARY**  A patient suffering from essential thrombocythemia presented manifestations of digital thromboses and two cerebral ischemic strokes. Anomalies of platelet function are discussed in relation to published data and the efficacy of antiaggregant treatment is stressed.

**Primary Thrombocythemia In A Patient With Cerebellar Infarction**

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**Clinical Observation**

Jean Jacques V . . ., a stevedore, was born on April 7, 1950, and was splenectomized in 1978 during a caudal pancreatectomy for a pancreatic pseudocyst. The platelet count became normal during the fourth post-operative month, at which time excessive tobacco and alcohol consumption had been stopped. In 1981, he developed painful peripheral vascular disease of the hands and feet, with subungual cyanosis. On May 4, 1982, he was hospitalized 3 hours after the sudden onset of head pain, vomiting and paresthesias of the four extremities. Examination revealed a moderate impairment of gait and station, hypermetria and asynmetria of the right arm, as well as a paresis of lateral gaze to the right. A right superior cerebellar ischemia was observed: a hypodense area on the CT scan without contrast enhancement and also a fixation image of $^{57}$Co labeled bleomycin radionuclide scan. Arterial pressure was 140/80 in both arms and there was no vascular murmur. Bilateral brachial arteriography, cardiac function tests (ECG, echography, holter) and routine laboratory tests were normal. The VDRL reaction and TPHA were negative and there was no inflammatory syndrome or cryoglobulinemia. The only pathologic signs encountered were a granulocytic leucocytosis (16,1 giga/1) and a thrombocytosis at 839 giga/1 with disturbances in platelet function (long bleeding time; defective aggregation induced by adenosine diphosphate, collagen and arachidonic acid). Spontaneous platelet aggregation could not be detected. An antiaggregant treatment was begun (1000 mg of acetylsalicylate, 450 mg of Dipyridamole per day). Response peripheral vascular syndrome to treatment was spectacular; the neurological signs regressed within two weeks. The platelet count was always high (1105 giga/1) and no malondialdehyde (MDA) production was obtained after platelet stimulation. Therapy was suspended 11 months later, followed by a recurrence of the vascular syndrome and the appearance of a central scotoma in the left eye in spite of chronic heparin therapy (5,000 IU per 8 hours). Thrombocytosis (1015 giga/1) and leucocytosis (12,1 giga/1) persisted. Study of platelets function revealed abnormal spontaneous aggregation (patient 80%, normal 10%), defective epinephrine and adenosine diphosphate induced aggregation, increased factor 3 activity and MDA formation. Factor VIII-von Willebrand factor (VIII-vWF) and antithrombin III, alpha 2 antiplasmin, plasminogen and basic fibrinolytic activity with the von Kaula method\textsuperscript{5} were always normal. All the other examinations were normal (myelogram, bone marrow biopsy, blood and marrow karyotype, hemoglobin electrophoresis, leukocyte alkaline phosphatases), with the exception of the bone marrow culture. The latter was judged to be pathologic as a result of the growth of the erythroblast progenitor line (CFU-E) in the absence of erythropoietin. Hydroxyurea treatment (1500 then 500 mg) led to...
a return of the platelet count to normal levels. A family antecedent of polycythemia vera was noted. The clinical state remained stable for two years on this treatment.

Methods
Aggregation was studied with platelet-rich plasma at 300 giga/1 with the photometric method of Born, using a Labintec apparatus in the presence of buffer or aggregating substances at the concentrations indicated: ADP (Diagnostica Stago, 2.5, 5, 10, 25, 50 μmol), collagen (Dade, 200 mg/ml), arachidonic acid (Sigma, 200 mg/ml), adrenalin (Stago, 5 μmol). Factor 3 activity was assayed with a chromogenic substrate with the modified method of Sandberg, using substrate S 2238 and the preconativ plasma (AB KIABI, Sweden). Platelet malondialdehyde (MDA) was assayed with the modified method of Stuart.

Comments
Cerebellar ischemia associated with a regressive disorder of the brain stem occurred in a young adult, followed several months later by a left monocural involvement in the absence of embolicgenic cardiopathy or an arterial lesion. This appeared to be related to the observed thrombocythemia and hemostasis anomalies. The thrombocythemia was not the result of splenectomy, since the platelet number was initially brought to normal values. These hemostasis anomalies are very different from those observed after ischemic vascular stroke, where an excessive response to aggregating substances is seen, and perhaps induced by the ischemia. An excess of circulating platelet aggregates (method of Wu and Hoak) or a spontaneous pathologic aggregation of platelets (Born method) have also been observed after transitory or constituted ischemic stroke, in the absence of a perfect correlation with responses to aggregating substances. These anomalies are also transitory. In long-term studies after the incident, the only persistent features are a decreased fibrinolytic activity and an increased antigenic activity related to VIII-vWF. This latter lesion would be the reflection of atheromatous arterial lesions and is observed only in cases of ischemia of this origin, not being encountered in cardiac embolisms.

In the present case, the disorders are quite different. At the onset there was a clearcut and long-lasting decrease in the response to aggregating substances, without spontaneous platelet aggregation. Spontaneous aggregation became important secondarily, while factor VIII-vWF was normal. These anomalies are encountered in myeloproliferative syndromes. In our patient, we are dealing with a primary thrombocythemia whose apparent arguments are found in the bone marrow culture, apparently specific for myeloproliferative syndromes, and the hereditary factor in the form of a polycythemia vera in the patient’s father. The thrombotic tendency, expressed clinically by the peripheral vascular syndrome of the fingers and biologically by the elevated factor 3 activity, was strikingly corrected by the acetyl salicylate/dipyridamole combination. These symptoms reappeared when treatment was stopped and disappeared when it was begun again. Platelet malondialdehyde decreased during the treatment period. These manifestations of peripheral thrombocythemia and the efficacy of acetyl salicylate at variable doses (300 to 1800 mg) is a constant feature. Platelet number, however, was not modified by this treatment, proving the essential role of the qualitative deficiency in platelets. Hydroxyurea quantitatively reduced the thrombocytosis.

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