

11. Freyburger G, Bilhou-Nabera C, Dief S, et al. Technical and biological conditions influencing the functional APC resistance test. *Thromb Haemost* 1996; 75:460-5.
12. D'Angelo A, Mazzola G, Crippa L, Fermo I, Viganò D'Angelo S. Hyperhomocystenemia and venous thromboembolic disease. *Haematologica* 1997; 82: 211-9.

Atypical microangiopathy in a patient treated with ticlopidine

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Microangiopathies are rare complications during treatments with ticlopidine. We describe an atypical microangiopathy, affecting almost exclusively myocardium, and thrombocytopenia, shortly after onset of ticlopidine. The patient died a few days after. Autopsy showed no bleedings or large thrombi in most organs, but were compatible with microangiopathy in myocardial small vessels.

Ticlopidine is an inhibitor of platelet aggregation frequently being used in stroke prevention and other thromboembolic events. Its probable association with the appearance of microangiopathies, especially thrombotic thrombocytopenic purpura (TTP) has been described by several authors.¹⁻⁵ We present the case of a patient that developed atypical characteristics and deadly evolution microangiopathy in the course of treatment with ticlopidine.

The patient was a male of 46 years, without personal antecedent of interest. Three weeks before admission, he was diagnosed with left eye acute anterior ischemic neuropathy, beginning treatment with ticlopidine at usual doses (250 mg a day). At this time, blood cell count, coagulation tests and routine study of hypercoagulability were normal.

Seven days after beginning treatment, the patient presented skin rash, with pruritus and febricula, being treated with antihistaminic drugs, which improved the symptoms. In the following days, and in a progressive way, the patient complained of general discomfort, nausea and vomiting. Analytical study showed intensive thrombocytopenia (6×10^9 platelets/L) and moderate anemia, so he was referred to our Hospital.

On admission, the patient appeared ill, showing dry mucosae and injuries from scratching. No petechial purpura, evident hemorrhages or neurological abnormalities were found. Spleen and liver were not palpable. No thoracic abnormal murmurs were detected. Laboratory tests confirmed the existence of intensive thrombopenia and anemia (hemoglobin of 8.8 g/dL); leukocytes and formula were normal; schistocytes were not found in blood smears. Biochemical study showed

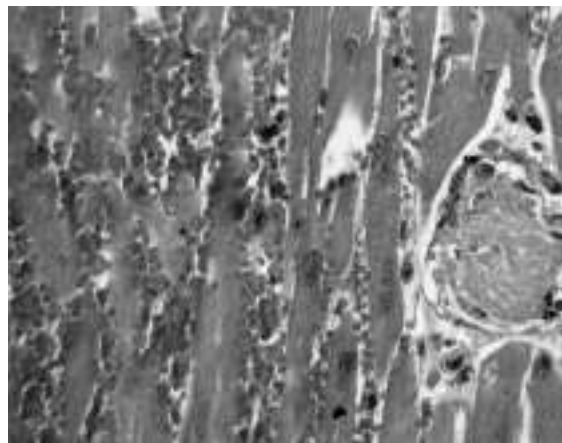


Figure 1. Thrombi and hemorrhages in myocardium.

high levels of lactodehydrogenase (LDH) (3.873 U/L) and creatinine (2 mg/dL). Bilirubin, transaminases, proteinogram, ions, glycemia and coagulation tests were normal. D-Dimers were in low levels (0,5-1 mg/L). Urine was of normal aspect; urinary sediment showed microhematuria (200 erythrocytes/ μ L). Coombs test was negative. Bone marrow aspirate showed megakaryocytic hyperplasia and mild eosinophilia.

After fluid replacement and discontinuation of ticlopidine, treatment with prednisone was administered (1 mg/kg/d). On the first day after admission the general condition improved and the urine was clear. On the second day, LDH and creatinine values were slightly lower (2.454 U/L and 1.2 mg/dL). Anemia and great thrombocytopenia persisted. On the third day, the patient entered into a sudden confusion status; urgent cranial scanner was reported as absence of hemorrhage. Few hours later, he developed intense agitation, and died by cardiorespiratory arrest. Necropsy was performed. Hemorrhagic effusions were found only in myocardium. Macroscopic findings were irrelevant, except the presence of hemorrhages in a stripped pattern in myocardium. The microscopic examination showed the existence of multiple fibrinous thrombi in myocardial small vessels (Figure 1), and in a reduced number of small vessels in adrenal glands, liver, kidneys and pancreas.

The temporal relationship suggests that this microangiopathy was due to ticlopidine treatment.

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Key words

Ticlopidine, microangiopathy, Moskowitz, purpura, thrombosis.

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References

1. Page Y. Thrombotic thrombocytopenic purpura related to ticlopidine. *Lancet* 1991; 337:774-6.
2. Jiménez FJ. Púrpura trombótica trombocitopénica asociada a la ticlopidina. *An Med Interna* 1996; 13:46-7.
3. Franchimont D. Moskowitz syndrome in a patient treated with ticlopidine. *Rev Med Liege* 1996; 51:214-6.
4. Kovacs MJ. Thrombotic thrombocytopenic purpura associated with ticlopidine. *Ann Pharmacother* 1993; 27:1060-1.
5. Falezza G. Thrombotic thrombocytopenic purpura developed during ticlopidine therapy. *Haematologica* 1992; 77:525.

Pulmonary mucosa-associated lymphoid tissue lymphoma and myasthenia gravis.

A case report

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We describe a low-grade, MALT-lymphoma with multiple, unusually large opacities involving both the lungs in a woman suffering from myasthenia gravis. Unlike other autoimmune diseases, myasthenia gravis has never been associated with MALT-lymphoma thus far. After cyclophosphamide treatment, a complete detersion of the pulmonary opacities was obtained.

Although not frequent, pulmonary mucosa-associated lymphoid tissue (MALT) lymphomas are well-recognized.^{1,2} However, the case we describe here presents some aspects that render it noteworthy.

In June 1995, a 55-year-old woman began complaining of great-joint arthritis and erythema nodosum. Her chest radiography showed multiple, large opacities involving both the lungs (Figure 1). Myasthenia gravis had been diagnosed 20 years before and pyridostigmine was continuously taken thereafter, with good control of the neuromuscular symptoms. Laboratory analyses included elevated ESR; monoclonal M- γ -globulin; antiacetylcholine receptor antibodies; absence of serum markers of cancer; normal values for hemochrome and other routine tests. Total CT-scan showed multiple, solid opacities with diameter up to 8 cm within both the lungs; liver, spleen and lymph nodes were normal. Fiberoptic bronchoscopy showed a pervious bronchial tree. Transbronchial biopsy was not diagnostic, whereas a surgical biopsy of the large, apical, right-sided lesion led to the diagnosis of *low-grade pulmonary MALT-lymphoma* according to well-recognized

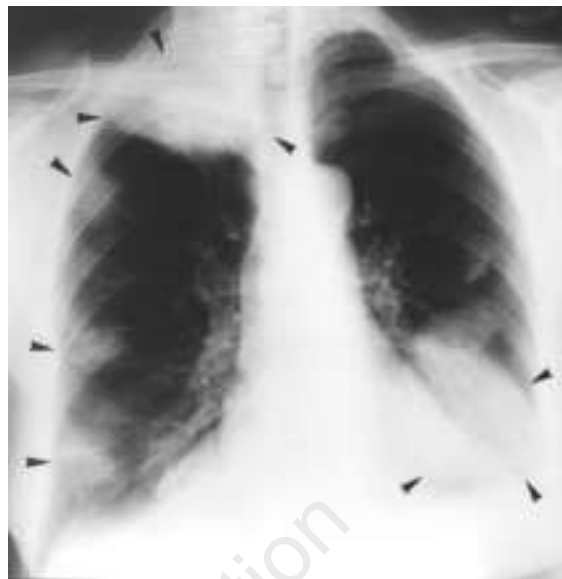


Figure 1. Chest radiography before the treatment. Multiple pulmonary opacities (arrows) are evident in both pulmonary fields. Very large lesions, 8 cm in diameter, are localized in the upper right lobe and in the lower left one.



Figure 2. Chest radiography after cyclophosphamide treatment. Complete detersion of the pulmonary opacities.

histological, immunohistochemical and genetic findings.^{3,4} Finally, a bone marrow biopsy showed normal hematopoiesis, without lymphoma localization.

In September 1995, the patient started oral cyclophosphamide treatment (100 mg/die), initially associated with oral prednisone. Both great-joint arthritis and erythema nodosum resolved within a few days; ESR normalized after a few weeks; and monthly monitoring by chest X-ray showed a progressive