

Antiphospholipid Syndrome and Refractory Thrombocytopenia Responding to Mycophenolate Mofetyl and Splenectomy: Case Report

To the Editor: Thrombocytopenia in the context of the antiphospholipid syndrome is a frequent and relevant manifestation, observed in approximately 30% of patients.¹ Anti- β 2-glycoprotein I antibodies have also been described in patients without lupus or anticardiolipin antibodies (antiphospholipid syndrome/cofactor).²

We describe the case of a 19 year old male patient, with a history of deep venous thrombosis complicated with pulmonary thromboembolism 14 months prior to his actual internment, as well as deep venous thrombosis in the left leg 2 months prior to his current problem, characterized by headache, epistaxis, ecchymosis, and petechia of the inferior extremities lasting for 2 weeks. When hospitalized, he had 1000 platelets/ μ L and a longer partial thromboplastin time (TPT) (without coagulation), that was not corrected with the addition of plasma. C protein and S protein as well as antithrombin III, antinuclear antibodies, and anti double stranded DNA antibodies were normal or negative. Anticardiolipin antibodies were reported as follows: IgG, 119.7 U (0-12); IgM, 290.2 U (0-12); and anti- β 2-glycoprotein I IgG, 93.6 U (0-20), integrating the diagnosis of antiphospholipid syndrome. Due to the intense thrombocytopenia and accompanying nasal and lower digestive tract hemorrhage, 1 mg of methylprednisolone every 24 hours for 3 days was started, followed by prednisone 2 mg/kg/day, without response in the platelet count (1000/ μ L), and afterwards, 5 sessions of plasma exchange combined with intravenous and oral cyclophosphamide, also without a response. After the previously described therapies, in the next 28 days sequential and/or combined aspirin, 100 mg/day; danazol, 600 mg/day; dapsons, 100 mg/day; anti-D globulin, 100 μ g/day for 4 days; and thalidomide, 100 mg/day were administered, elevating the platelet count to 9000/ μ L. The decision to start human immunoglobulin 400 mg/kg/day for 4 days was taken. Here was no response. Mycophenolate mofetyl was indicated 1 g/24 h with the intention of carrying out a splenectomy, done after 2 weeks of treatment with a platelet count of 95 000/ μ L and TPT of 26.8 s. The spleen was reported as being of

normal size and histological characteristics. After surgery, the steroid dose was reduced gradually until it was suspended, the patient underwent anticoagulation with coumarin (INR=2) and treatment with mycophenolate mofetyl was continued at 1.5 g/24 h. At 6 months from discharge the patient is asymptomatic, with a prothrombin time of 19.9 s (INR=1.6) and 276 000/ μ L platelets.

Serious thrombocytopenia in patients with APS represents an enormous challenge for the clinician because the patients are confronted both with the risk of thrombosis and the risk of bleeding. Galindo et al³ report that, in a series of patients with APS (primary and associated with lupus erythematosus) and thrombocytopenia under 100 000/ μ L, splenectomy was needed in 20% of patients. In the case of our patient, the use of mycophenolate mofetyl was needed; drug with which the platelets count finally went up, making the splenectomy possible. The use of mycophenolate mofetyl as a successful treatment of refractory thrombocytopenia has been published previously in systemic lupus erythematosus.⁴ We cannot establish if mycophenolate was the sole responsible for the elevation of the platelet count or if the accumulated effect of the previous therapies had a role in this.^{5,6} Splenectomy is an effective therapeutic measure for subjects with antiphospholipid antibodies syndrome and refractory thrombocytopenia, once a safe platelet count has been reached in preparation for surgery.⁷

Mario A. Chávez-López,^a Enrique Ávalos-Romero,^b
Constantino Vela-Rivera,^a and Adán Gallaga-Gutiérrez^a

^aServicio de Reumatología, Hospital de Especialidades Miguel Hidalgo, Aguascalientes, México

^bServicio de Reumatología, Hospital General de Zona I Instituto Mexicano del Seguro Social, Aguascalientes, México

References

1. Cuadrado MJ, Mujic F, Munoz E, Khamashta MA, Hughes GR. Thrombocytopenia in the antiphospholipid syndrome. *Ann Rheum Dis*. 1997;56:194-6.
2. Cabral AR, Amigo MC, Cabiedes J, Alarcon-Segovia D. The antiphospholipid/cofactor syndromes: a primary variant with antibodies to beta 2-glycoprotein-I but no antibodies detectable in standard antiphospholipid assays. *Am J Med*. 1996;101:472-81.
3. Galindo M, Khamashta MA, Hughes GR. Splenectomy for refractory thrombocytopenia in the antiphospholipid syndrome. *Rheumatology (Oxford)*. 1999;38:848-53.
4. Vasoo S, Thumboo J, Fong KY. Refractory immune thrombocytopenia in systemic lupus erythematosus: response to mycophenolate mofetil. *Lupus*. 2003;12:630-2.
5. Alarcon-Segovia D, Sanchez-Guerrero J. Correction of thrombocytopenia with small dose aspirin in the primary antiphospholipid syndrome. *J Rheumatol*. 1989;16:1359-61.
6. Levine JS, Branch DW, Rauch J. The antiphospholipid syndrome. *N Engl J Med*. 2002;346:752-63.
7. Font J, Jiménez S, Cervera R, García-Carrasco M, Ramos-Casals M, Campdelacreu J, et al. Splenectomy for refractory Evans' syndrome associated with antiphospholipid antibodies: report of two cases. *Ann Rheum Dis*. 2000;59:920-3.