Diagnosis and therapy of antiphospholipid syndrome

To the Editor We read with attention the article by Pengo et al[1] about the diagnosis and therapy of antiphospholipid syndrome (APS). We have some comments regarding catastrophic APS. A small group of patients with APS may develop extensive thrombotic disease with visceral damage, referred to as catastrophic APS.[2] Early diagnosis and aggressive therapy are essential to the management of catastrophic APS because mortality rates remain high (approximately 30%).[3] Treatment usually focuses on addressing thrombotic events and suppressing the cytokine cascade. As described by Pengo et al,[1] this typically involves a combination of anticoagulants, systemic glucocorticoids, plasma exchange, and intravenous immunoglobulin (IVIG).[4] However, the use of IVIG in catastrophic APS is still debatable. There is no evidence that IVIG on its own improves survival.[5] On the other hand, IVIG can be removed by plasmapheresis; therefore, it is important to remember that if it is used, it must be administered after the last day of plasma exchange to prevent its removal.

We would like to briefly present a case of catastrophic APS treated at our department. A patient with previously diagnosed APS was admitted because of dyspnea, exhaustion, and chest pain. Two days after admission, the patient developed respiratory failure. He was intubated and put on mechanical ventilatory support. The clinical status and laboratory findings suggested catastrophic APS. Anticoagulation, a 3-day course of pulse steroid, and plasmapheresis were applied. However, IVIG was not administered during the treatment because it could be removed by plasmapheresis. When plasmapheresis was stopped, the clinical status and laboratory results were satisfactory, and, in our opinion, the patient did not require IVIG. During the follow-up period, the patient received cyclophosphamide.

Author names and affiliations Erol Arslan, Şeref Demirbaş, Musa B. Aykan, Gökhan Özgür, Kenan Sağlam (EA, SD, MBA, KS: Department of Internal Medicine, Gülhane Military Medical Academy, Ankara, Turkey; GÖ: Department of Hematology, Gülhane Military Medical Academy, Ankara, Turkey)

Corresponding author Dr. Erol Arslan, Gülhane Military Medical Academy, Department of Internal Medicine, Ic Hastaliklari Bilim Dali, 06010, Kecioren, Ankara, Turkey, phone: +90 312 3044031, fax: +90 312 3044000, e-mail: earslan89@yahoo.com

Conflict of interest The authors declare no conflict of interest.

REFERENCES

1 Pengo V, Denas G, Padayattil SJ, et al. Diagnosis and therapy of antiphospholipid syndrome. Pol Arch Med Wewn. 2015; 125: 672-676.

2 Erkan D, Cervera R, Asherson RA. Catastrophic antiphospholipid syndrome: where do we stand? Arthritis Rheum. 2003; 48: 3320-3327.

3 Bucciarelli S, Espinosa G, Cervera R, et al. Mortality in the catastrophic antiphospholipid syndrome: causes of death and prognostic factors in a series of 250 patients. Arthritis Rheum. 2006; 54: 2568-2576.

4 Cervera R, Rodríguez-Pintó I, Colafrancesco S, et al. 14th International Congress on Antiphospholipid Antibodies Task Force Report on Catastrophic Antiphospholipid Syndrome. Autoimmun Rev. 2014; 13: 699-707.

5 Cervera R, Rodríguez-Pintó I, Espinosa G; Task Force on Catastrophic Antiphospholipid Syndrome. Catastrophic antiphospholipid syndrome: task force report summary. Lupus. 2014; 23: 1283-1285.

Authors' reply We would like to thank Dr. Arslan and colleagues for their interest in our article.[1] We agree that the use of intravenous immunoglobulins (IVIGs) may not improve survival in patients with catastrophic antiphospholipid syndrome (APS). However, if IVIGs are used, they must be administered after the last day of plasmapheresis to avoid their removal. According to recent literature,[2] a treatment that significantly reduces mortality in patients with catastrophic APS is a multiple therapy combining anticoagulation, glucocorticoids, and therapeutic plasma-exchange (TPE) with or without IVIGs. It is important to administer these drugs in a specific order. In our center, we use the following strategy: anticoagulation therapy with intravenous or low-molecular-weight heparin along with TPE, 1 session per day for 3 days, and 1 pulse of methylprednisolone (0.5–1 g) administered immediately after each TPE session. On the day after the last TPE procedure, IVIG therapy is started at a dose

of 0.4 mg/kg/d for 5 days. Simultaneously, the dose of glucocorticoids is reduced to 1 mg/kg and tapered off depending on the clinical condition. It has been demonstrated that immunosuppressants, including cyclophosphamide, do not significantly affect mortality.[2] Therefore, we prefer to avoid the use of these drugs, also considering their heavy side effects.

We would like to stress the fact that we use human albumin solution (4%) as replacement fluid in TPE.[3,4] By evaluating the pathophysiology of the underlying disease, it was possible to choose different types of replacement fluid, including albumin solution (4%) and fresh frozen plasma. We observed that the temporary reduction of coagulation parameters after albumin infusion benefited thrombophilic patients with APS.[4] To recover the decrease caused by plasmapheresis in natural anticoagulants, 1000 IU of antithrombin III was administered at the end of the TPE session if the pretreatment values of antithrombin III were lower than 90% (reference range, 80%–120%).

Since 2009, 5 patients with catastrophic APS have been consecutively treated at our center, using the above strategy. All patients recovered quickly, and no relapse was observed in any of the cases.

Author names and affiliations Vittorio Pengo, Ariela Hoxha, Amelia Ruffatti (VP: Clinical Cardiology, Thrombosis Center, Department of Cardiac Thoracic and Vascular Sciences, University of Padua, Padua, Italy; AH, AR: Rheumatology Unit, Department of Medicine, University of Padua, Padua, Italy)

Corresponding author Vittorio Pengo, MD, Clinical Cardiology, Thrombosis Center, Via Giustiniani 2, 35128 Padua, Italy, phone/fax: +39 49 8215658, e-mail: vittorio.pengo@unipd.it

Conflict of interest The authors declare no conflict of interest.

REFERENCES

1 Pengo V, Denas G, Padayattil SJ, et al. Diagnosis and therapy of antiphospholipid syndrome. Pol Arch Med Wewn. 2015; 125: 672-677.

2 Cervera R, Rodrìgues-Pintó I, Colafrancesco S, et al. 14th International Congress on Antiphospholipid Antibodies Task Force Report on Catastrophic Antiphospholipid Syndrome. Autoimmun Rev. 2014; 13: 699-707.

3 Bortolati M, Marson P, Fabris F, et al. Recovery from catastrophic antiphospholipid syndrome by plasma exchange procedure: report of four cases and review of the literature. Autoimmun Rev. 2009; 8: 297-301.

4 Marson P, Bagatella P, Bortolati M, et al. Plasma exchange for the management of the catastrophic antiphospholipid syndrome: importance of the type of fluid replacement. J Int Med. 2008; 264: 201-203.