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Lessons from the catastrophic antiphospholipid syndrome (CAPS) registry

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Abstract

Although less than 1% of patients with the antiphospholipid syndrome (APS) develop the catastrophic variant, its potentially lethal outcome emphasizes its importance in clinical medicine today. However, the rarity of this variant makes it extraordinarily difficult to study in any systematic way. In order to put together all the published case reports as well as the new diagnosed cases from all over the world, an international registry of patients with catastrophic APS ("CAPS Registry") was created in 2000 by the *European Forum on Antiphospholipid Antibodies*. Currently, it documents the entire clinical, laboratory and therapeutic data of more than 300 patients whose data has been fully registered. This registry can be freely consulted at the Internet (www.med.ub.es/MIMMUN/FORUM/CAPS.HTM) and it is expected that the periodical analysis of these data will allow us to increase our knowledge of this condition.

Keywords: Catastrophic antiphospholipid syndrome; Antiphospholipid antibodies; Anticardiolipin antibodies; Lupus anticoagulant; Antiphospholipid syndrome

Contents

1. Introduction

In the 1980s and early 1990s, isolated case reports appeared in the world literature documenting patients who suffered from an often fatal complication associated with the demonstration of antiphospholipid antibodies

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(aPL). The clinical picture comprised widespread multi-organ thrombosis and consequent organ failure and was referred to by the authors as a "devastating non-inflammatory vasculopathy" [1], "occlusive vasculopathy" [2] or "acute disseminated coagulopathy–vasculopathy" [3] when describing individual cases. In 1992, 10 patients with this unusual condition were first reviewed and, in an attempt to define its acuteness and severity, the adjective "catastrophic" was attached to this variant of the antiphospholipid syndrome (APS) [4].

Although less than 1% of patients with the APS develop this complication [5], its potentially lethal outcome, despite all recommended therapies, emphasizes its importance in clinical medicine today and, although many publications have drawn attention to its existence, it seems clear that many more cases still remain undiagnosed and inadequately treated in hospital settings the world over. The majority of these patients end up in intensive care units (ICU) with multi-organ failure and, unless the condition is considered in the differential diagnosis by the attending physicians, it may be completely missed with a disastrous outcome for the patients [6,7].

2. CAPS Registry

The rarity of the syndrome made it extraordinarily difficult to study in any systematic way. In order to put together all the published case reports as well as the new diagnosed cases from all over the world, an international registry of patients with catastrophic APS ("CAPS Registry") was created in 2000 by the *European Forum on Antiphospholipid Antibodies*, a study group devoted to the development of multicentre projects with large populations of APS patients.

Ricard Cervera, Jean-Charles Piette, Yehuda Shoenfeld, Josep Font, Silvia Bucciarelli and Ronald A. Asherson are the main coordinators of the "CAPS Registry". It documents the entire clinical, laboratory and therapeutic data of all published cases with catastrophic APS as well as of many additional patients whose data has been fully registered. The sources of information are the personal communications of the physicians who treated these patients and the periodically computer-assisted search of the medical literature (Medline, National Library of Medicine, Bethesda, MD) to locate all cases of published reports in English, Spanish, French, German and Italian of patients with catastrophic APS (keywords: catastrophic, antiphospholipid, catastrophic antiphospholipid syndrome).

This registry can be freely consulted through the Internet at: www.med.ub.es/MIMMUN/FORUM/CAPS.HTM. Currently, it documents the clinical, laboratory and therapeutic data of more than 300 patients whose data has been fully registered.

3. Main results

The initial results of the project have been already published in several original papers that provide information on the long-term outcome of patients with this syndrome [8], the characteristics of associated thrombotic microangiopathic hemolytic anemia [9], disseminated intravascular coagulation [10], acute respiratory distress syndrome [11], and causes of death and prognostic factors [12].

Additionally, the heterogeneity of the different clinical forms of presentation of the catastrophic APS led to the necessity of developing a consensus criteria for definition and classification of patients with this condition. In September of 2002, a pre-symposium workshop in the "Tenth International Congress on aPL" held in Taormina, Italy, allowed the establishment of preliminary criteria for the classification of catastrophic APS by using the data from the "CAPS Registry" [13] (Table 1). This

Table 1
Preliminary criteria for the classification of catastrophic APS

1. Evidence of involvement of three or more organs, systems and/or tissues[a]
2. Development of manifestations simultaneously or in less than a week
3. Confirmation by histopathology of small vessel occlusion in at least one organ or tissue[b]
4. Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant and/or anticardiolipin antibodies)[c]

Definite catastrophic APS: all four criteria.
Probable catastrophic APS: all four criteria, except for only two organs, systems and/or tissues involvement; all four criteria, except for the absence of laboratory confirmation at least 6 weeks apart due to the early death of a patient never previously tested for aPL prior to the catastrophic APS event; 1, 2 and 4; 1, 3 and 4 and the development of a third event in more than a week but less than a month, despite anticoagulation.

[a] Usually, clinical evidence of vessel occlusions, confirmed by imaging techniques when appropriate. Renal involvement is defined by a 50% rise in serum creatinine, severe systemic hypertension (>180/100 mm Hg) and/or proteinuria (>500 mg/24 h).

[b] For histopathological confirmation, significant evidence of thrombosis must be present, although vasculitis may coexist occasionally.

[c] If the patient had not been previously diagnosed as having an APS, the laboratory confirmation requires that presence of antiphospholipid antibodies must be detected on two or more occasions at least 6 weeks apart (not necessarily at the time of the event), according to the proposed preliminary criteria for the classification of definite APS [9].