16 Catastrophic Antiphospholipid Syndrome

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Introduction

The syndrome of multiple vascular occlusions associated with high titer antiphospholipid antibodies (aPL) is known as catastrophic antiphospholipid syndrome (CAPS). Although antiphospholipid syndrome (APS) is typically characterized by thrombotic events that either occur singly or, when recurrent, are seen many months or even years apart, some patients with this syndrome may develop widespread, non-inflammatory vascular occlusions.

The first reports of patients with multiple non-inflammatory vascular occlusions appeared in 1974, by Dosekun [1], and in 1987, by Ingram [2]. However, it was not until Greisman reported in 1991 on two patients with *"acute, catastrophic, widespread non-inflammatory visceral vascular occlusions associated with high titer antiphospholipid antibodies"* that the full spectrum of clinical features associated with aPL became appreciated [3]. This spectrum was outlined in an editorial by Harris and Bos [4] that accompanied the Greissman report [3]. The authors described two additional patients with "acute disseminated coagulopathy–vasculopathy associated with antiphospholipid syndrome" and identified three cohorts of patients with these antibodies. They recognized that aPL may be "asymptomatic" and observed in patients free of thrombosis or associated with one or two episodes of thrombosis typically involving only one artery or vein at a time with long periods (months to years) free of occlusive events. Alternatively, aPL may confer a risk for an ominous disorder characterized by multiple, typically three or more, wide-spread thrombotic occlusions often with marked ischemic changes in the extremities, livido reticularis, as well as renal, cerebral, myocardial, pulmonary, and other visceral organ thrombotic vasculopathy. Asherson, describing 10 such patients in an article published in 1992, first proposed the term *catastrophic APS* [5].

Over the past 12 years, several reviews of CAPS have been published [6–9]. It is estimated that CAPS comprises 1% of cases of APS syndrome. To date, approximately 250 cases are described in the literature. In 2000, an international registry of patients with CAPS was created by the European Forum on Antiphospholipid Antibodies and can be referenced via the internet at http://www.med.ub.es/MIMMUN/FORUM/CAPS.HTM, consisting of 220 patients as of August 1, 2004 [10]. Additionally, a set of classification criteria for CAPS was presented at the 10th International Congress on Antiphospholipid Antibodies in 2002 at Taormina, Sicily (Table 16.1) [11–13].This chapter will describe the clinical, therapeutic, and pathogenic aspects of this condition.

Table 16.1. Criteria for the classification of catastrophic antiphospholipid antibody syndrome.

Criteria for the classification of catastrophic antiphospholipid antibody syndrome:
1. Evidence of involvement of three or more organs, systems, or tissues.
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.[†]
4. Laboratory confirmation of the presence of aPL (lupus anticoagulant or aCL).
Definite catastrophic antiphospholipid antibody syndrome
All four criteria.
Probable catastrophic antiphospholipid antibody syndrome
All four criteria, except only two organs, systems, or tissues are involved.
All four criteria, except for the absence of laboratory confirmation at least 6 weeks apart because of the early death of a patient never previously tested for aPL before the catastrophic event.
Criteria 1, 2, and 4 antiphospholipid.
Criteria 1, 3, and 4, and the development of a third event in more than a week, but less than a month, despite anticoagulation.

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 (greater than 190/110 mm Hg), or proteinuria (greater than 500 mg/24 hours).

[†]For histopathologic confirmation, significant evidence of thrombosis must be present, although vasculitis may coexist occasionally. If the patient has not been previously diagnosed as having APS, the laboratory confirmation requires that the presence of aPL 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 clinical criteria for the classification of definite APS.

Clinical Aspects

Patients with catastrophic APS can be broadly categorized into those with systemic lupus erythematosus (SLE), "lupus-like" illness satisfying two to three of the modified ACR criteria, primary APS, or secondary to an another autoimmune, connective tissue disease such as rheumatoid arthritis, scleroderma, dermatomyositis, polychondritis, primary, systemic necrotizing vasculitis, inflammatory bowel disease, or Behcet's syndrome [14–21].

Demographic Characteristics

Amongst 220 patients with catastrophic APS in the registry, 156 (70%) are females and 64 (30%) males (2.5:1 female:male ratio) with an age range of 9 to 74 years and an average of 36 years. Thirteen (6%) patients developed the clinical picture before the age of 16 and 19 (9%) after the age of 60. Ninety-one (41%) patients who developed acute, multi-organ involvement suffered from primary APS, 79 (36%) from SLE, 12 (5%) from "lupus-like" illness, and 9 (4%) from other connective tissue disease.

Preceding Thrombotic History

A slight majority (112/220, 50%) of the patients had a prior history of thrombophilia and thrombotic event. A total of 42 (19%) of the 220 patients had a history of venothromboembolic phenomena, including deep venous thrombophlebitis