Autoimmunity Reviews 13 (2014) 157–162

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev

Review

Pediatric catastrophic antiphospholipid syndrome: Descriptive analysis of 45 patients from the "CAPS Registry"

Horacio Berman [a,1], Ignasi Rodríguez-Pintó [a,1], Ricard Cervera [a], Simone Gregory [b], Ernesto de Meis [b], Carlos Ewerton Maia Rodrigues [c], Nádia Emi Aikawa [c,d], Jozélio Freire de Carvalho [c], Janusz Springer [e], Maciej Niedzwiecki [e], Gerard Espinosa [a,*], on behalf of the Catastrophic Registry Project Group (European Forum on Antiphospholipid Antibodies) [2]

[a] Department of Autoimmune Diseases, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Hospital Clinic, Barcelona, Catalonia, Spain
[b] Department of Hematology, National Cancer Institute, Rio de Janeiro, Brazil
[c] Instituto da Criança, Hospital das Clinicas da Facultade de Medicina da Universidade de Sao Paulo, SP, Brazil
[d] Pediatric Rheumatology Unit, Instituto da Criança, Hospital das Clinicas da Facultade de Medicina da Universidade de Sao Paulo, SP, Brazil
[e] Medical University of Gdansk, Poland

ARTICLE INFO

Article history:
Received 1 October 2013
Accepted 13 October 2013
Available online 19 October 2013

Keywords:
Catastrophic antiphospholipid syndrome
Antiphospholipid syndrome
Pediatric
Infant

ABSTRACT

Given the lack of information about catastrophic antiphospholipid syndrome (APS) in pediatric patients, the objective of the current study was to describe the clinical characteristics, laboratory features, treatment, and outcome of pediatric patients with catastrophic APS and compare them with the adult patients with catastrophic APS.

We identified patients who were under 18 years of age at time of catastrophic APS diagnosis included in the international registry of patients with catastrophic APS (CAPS Registry). Their main demographic and clinical characteristics, laboratory features, treatment, and outcome were described and compared with those of adult patients with catastrophic APS.

From the 446 patients included in the CAPS Registry as of May 2013, 45 (10.3%) patients developed 46 catastrophic events before 18 years of age (one patient presented two episodes). Overall, 32 (71.1%) patients were female and the mean age was 11.5 ± 4.6 years (range, 3 months–18 years). A total of 31 (68.9%) patients suffered from primary APS and 13 (28.9%) from systemic lupus erythematosus (SLE). The main differences between the two groups of patients were the higher prevalence of infections as precipitating factor for catastrophic event in the pediatric population (60.9% versus 26.8% in the adult population, $p < 0.001$) and of peripheral vessel thrombosis (52.2% versus 34.3%, $p = 0.017$). In addition, catastrophic APS was the first manifestation of APS more frequently in pediatric patients (86.6% versus 45.2%, $p < 0.001$). Interestingly, pediatric patients showed a trend of lower mortality, although the difference was not statistically significant (26.1% versus 40.2%; odds ratio, 1.9; 95% confidence interval, 0.96–3.79; $p = 0.063$). No differences were found neither in the laboratory features nor in the isolated or combination treatments between groups.

Catastrophic APS in pediatric patients is a rare disease. There are minimal differences in the clinical and laboratory features, treatment, and outcome of pediatric and adult catastrophic APS patients.

Contents

* Corresponding author at: Servei de Malalties Autoimmunes, Hospital Clínic, Villarroel 170, 08036 Barcelona, Catalonia, Spain.
E-mail address: gespino@clinic.ub.es (G. Espinosa).
[1] These two authors contributed equally to this study.
[2] See complete list of members at the appendix at the end of article.

1568-9972/$ – see front matter
http://dx.doi.org/10.1016/j.autrev.2013.10.004

1. Introduction

The catastrophic antiphospholipid syndrome (APS) is characterized by multi-organ thrombosis developing over a short period of time [1]. This life-threatening variant of the APS that represents less than 1% of all patients with APS, was first described more than 20 years ago [2]. Since then, more than 400 cases have been collected in the catastrophic APS international registry (CAPS Registry). This registry was created by the European Forum on Antiphospholipid Antibodies, a study group devoted to the development of multi-center projects with large populations of APS patients [3]. The analysis of this registry has generated a cluster of knowledge of the main clinical, and laboratory features as well as the outcome of patients with catastrophic APS [4]. In addition, classification criteria and treatment guidelines for its management have been established [1,5,6].

Age at onset might modulate the clinical expression and prognosis of patients with different autoimmune diseases [7]. Particularly for classic APS, a review of 121 patients with pediatric APS, defined as the onset of APS before the patient's 18th birthday, demonstrated some important differences between the pediatric and adult APS patients [8]. In fact, the high female preponderance in adult patients (female/male ratio of 5:1) with classic APS does not occur in the pediatric subset (1.2:1). Deep venous thrombosis in the legs was the most frequent venous thrombotic event both in pediatric and adult APS patients (40% versus 32%, respectively). However, cerebral sinus venous thrombosis and ischemic stroke as a first manifestation of APS were significantly more frequent in the pediatric APS patients. In addition, the presence of lupus anticoagulant (LAC) was also more frequent in patients with pediatric APS [8].

In the present article, we describe the clinical characteristics, laboratory features, and outcomes of patients who presented with catastrophic APS in the pediatric age and compared them with those of adult patients with catastrophic APS.

2. Patients and methods

2.1. Data collection

We identified the patients with catastrophic APS in the pediatric age included in the CAPS Registry, the website-based international registry of patients with catastrophic APS. The sources of information for the CAPS Registry are: a) periodic Medline search of published catastrophic APS reports; and b) personal communication with physicians in charge of catastrophic APS patients for the unpublished cases (physicians fill out a standardized data form collecting demographic, clinical, therapeutic, and outcome information) [3]. The registry documents the clinical, laboratory and therapeutic data of all reported cases of catastrophic APS which can be freely consulted through the website (http://infmed.fcrb.es/en/web/caps).

Patients were considered as having pediatric catastrophic APS if the onset of catastrophic episode occurred before 18 years of age. Data from these patients were summarized in a standardized data-form, including sex, age and diagnosis of the underlying disease, precipitating factors, main thrombotic clinical features, laboratory findings, treatment, disease evolution and final outcome.

2.2. Statistical analysis

Results from continuous variables are presented as mean ± standard deviation (SD) and categorical data as percentages. Comparisons were performed using the Mann–Whitney test for continuous variables, whereas Fisher's exact test was used for categorical variables. Differences were considered significant when $p < 0.05$.

3. Results

3.1. General characteristics

From the 446 patients included in the CAPS Registry since May 2013, 45 (10.3%) patients developed 46 catastrophic events before 18 years of age (one patient presented two episodes). Overall, 32 (71.1%) patients were female and the mean age was 11.5 ± 4.6 years (range, 3 months–18 years) (Table 1). A total of 31 (68.9%) patients suffered from primary APS, 13 (28.9%) from systemic lupus erythematosus (SLE) and one from a lupus-like disease (2.2%).

3.2. Precipitating factors and clinical presentation

Precipitating factors were identified in 35 (76.1%) events. Infection was the most frequent precipitating factor found in 28 (60.9%) of them, followed by neoplasia (8; 17.4%), surgery (3; 6.5%), and SLE flares (2; 4.3%), whereas oral contraceptives and Cesarean section accounted for once case each (2.2%). In the remaining case, the precipitating factor was not specified. In nine events, two concomitant precipitating factors were identified. The catastrophic event appeared as the first manifestation of APS in 86.7% of cases.

The clinical characteristics of patients with pediatric catastrophic APS are summarized in Table 1. Kidney manifestations were present in 29 (63.0%) episodes and mainly consisted of renal failure, arterial hypertension, and proteinuria. Lung involvement appeared in 29 (63.0%) cases in the form of acute respiratory distress syndrome and pulmonary embolism. Cardiac involvement was present in 27 (57.4%) episodes and included cardiac failure, myocardial infarction and heart valve lesions. Cerebral involvement was also frequent, present in 22 (47.8%) cases, and included encephalopathy, cerebrovascular accidents and seizures. Liver involvement and peripheral venous thrombosis appeared in 19 (40.4%) cases each. The skin was involved in 17 (37.0%) episodes presenting as livedo reticularis, skin ulcers, cutaneous necrosis, gangrene, digital ischemia and purpura. Raynaud's phenomenon was not reported. The gastrointestinal tract was involved in 8 (17.4%) episodes, spleen infarcts were described in 7 (15.2%) and adrenal gland involvement was reported in 3 cases (6.5%). Involvement of bone marrow, peripheral nervous system, pancreas, and eye occurred in less than 5% of patients.