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APS ACTION in Brazil

The 13th International Congress on antiphospholipid antibodies (aPL) occurred in Galveston, Texas, in April 2010. The topics discussed were diverse – among them, new pathophysiological mechanisms, [1] other aPL associated with antiphospholipid syndrome (APS),[2] and controversies regarding both clinical and obstetric manifestations.[3] Another important part of the Congress was the creation of six "task forces" to evaluate the quality of information we have on APS, review controversies, and decide what direction research must go.

The "task forces" had the following topics: laboratory criteria; obstetric APS; catastrophic APS; neurological manifestations; management of thrombosis in patients with APS; and clinical research. The latter group was chaired by Doruk Erkan and Michael D. Lockshin, from Hospital for Special Surgery, Cornell University Medical Center, New York, and focused on evaluating the limitations of clinical research on the theme, creating guidelines so that researchers can improve the quality of studies, and formulating ideas to develop a multicenter well-designed clinical trial.

This task force reported that five elements hindered APS clinical trials and the development of evidence-based treatment: 1) the detection of aPL is based on partially standardized or non-standardized tests; clinical and basic studies included patients with heterogeneous aPL profiles and different risks of clinical events; 2) clinical and basic studies on APS included patients from a heterogeneous group with different aPL-related manifestations, of which some were controversial; 3) the quantification and stratification of the risk of thrombosis and/or adverse obstetric events are rarely incorporated into APS clinical research; 4) most APS clinical studies included patients with tests that were positive only on one occasion and/or with low aPL titers measured by ELISA, as well as the fact that most studies were retrospective and not population-based, with few prospective and/or controlled studies; 5) the lack of understanding of particular mechanisms of clinical events mediated by aPL limits the optimal clinical trial design. The conclusion was that there was urgent need for an international collaborative approach to design and conduct prospective, large-scale, and well-designed clinical trials in clinically significant patients with persistent aPL.[4]

The same group met again in November 2010 in Miami, when the APS ACTION – the Antiphospholipid Syndrome Alliance for Clinical Trials and International Networking – was created with the primary objective of facilitating the design of multicenter, prospective multidisciplinary, and high-quality studies on the disease, in addition to the formation of an international database. The APS ACTION will provide guidelines for the creation of studies and will mainly standardize the patients included based on the clinical and laboratory criteria for APS described in 2006.[5] The group has currently 32 members from 19 centers in 10 countries.

The first step, perhaps the most ambitious one, is the database creation. Considering that the clinical manifestation of the disease (thrombosis and/or obstetric complications) is a rare event, the initial proposal is to follow 2,000 patients with persistently positive aPL for 10 years, with regular assessments, as well as data collection in the event of thrombosis. This database will allow us to estimate the risk of recurrence and factors that influence the onset of the thrombotic event, in addition to better study the association with manifestations that were not included in the international criterion of 2006, such as thrombocytopenia and migraine. Another important part is the monitoring of patients with APS who had only obstetric complications (APS-OB), assessing whether the risk of venous or arterial thrombosis is higher than that for the general population.

This question is the justification for the second study proposed by APS ACTION: the use of hydroxychloroquine as the primary prophylaxis for thrombosis in patients with persistently positive aPL. The rationale for use hydroxychloroquine is the decrease in thrombotic events in patients with systemic lupus erythematosus and positive aPL. The patients will be randomized to receive hydroxychloroquine or just for routine follow-up and thrombotic events will be reported should they occur.

In August 2012 the inclusion of participating centers from different parts of the world was concluded, as can be checked on the website apsaction.org. The database has already been approved by the regulatory agencies in New York and Galveston,

in the USA; in Brescia, Italy; in Athens, Greece; and in Rio de Janeiro, Brazil. Approval is awaited in other centers in China, Japan, Israel, Colombia, Jamaica, Canada, England, Holand, Italy, and Brazil. Two papers submitted as ACR abstracts, by the APS ACTION Young Scholars were accepted for presentation: Andreoli L, Banzato A, Chighizola CB, Pons-Estel GJ, Ramires de Jesus G, Lockshin MD, and Erkan D on Behalf of APS ACTION. The Estimated Prevalence of Antiphospholipid Antibodies in General Population Patients with Pregnancy Loss, Stroke, Myocardial Infarction, and Deep Vein Thrombosis. - November 13, 2012, Presentation Time: 3:15 PM - 3:30 (oral); and Chighizola CB, Ramires de Jesus G, Andreoli L, Banzato A, Pons-Estel GJ, Lockshin MD, and Erkan D on Behalf of APS ACTION. The Estimated Prevalence of Antiphospholipid Antibodies in the General Population with Pregnancy Morbidity. - November 13, 2012, 9:00 AM - 6:00 PM (poster).

The possibility of being able to treat patients with APS based on well-designed, multicenter studies with a significant number of patients appears to be very close. We also expect that initial data from APS ACTION and further studies on this disease, a relatively recent one, can be shown at the 14th International Congress on Antiphospholipid Antibodies, which will be held in Rio de Janeiro from 18th–21st of September, 2013 (www.kenes.com/ APLA-LACA).

Roger Abramino Levy, for APS ACTION GROUP

PhD in Biological Sciences, Universidade Federal do Rio de Janeiro – UFRJ;
Adjunct Professor of the Discipline of Rheumatology,
Universidade do Estado do Rio de Janeiro – UERJ.

Guilherme Ribeiro Ramires de Jesús, for APS ACTION GROUP

Gynecologist and Obstetrician, UERJ;
Post-Graduated in Fetal Medicine, Instituto Fernandes Figueira – IFF/Fiocruz

REFERENCES

1. Rand JH, Wu XX, Quinn AS, Taatjes DJ. The annexin A5-mediated pathogenic mechanism in the antiphospholipid syndrome: role in pregnancy losses and thrombosis. Lupus 2010; 19(4):460–9.
2. Atsumi T, Koike T. Antiprothrombin antibody: why do we need more assays? Lupus 2010; 19(4):436–9.
3. Levy RA, Jesus GR, Jesus NR. Obstetric antiphospholipid syndrome: still a challenge. Lupus 2010; 19(4):457–9.
4. Erkan D, Derksen R, Levy R, Machin S, Ortel T, Pierangeli S *et al*. Antiphospholipid Syndrome Clinical Research Task Force report. Lupus 2011; 20(2):219–24.
5. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R *et al*. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006; 4(2):295–306.