ARC Journal of Hematology
Volume 5, Issue 1, 2020, PP 15-19
www.arcjournals.org

Anti-Phospholipid Antibody Syndrome During Heart Disease The Aristide Le Dantec Hospital In Dakar

Ocko Gokaba LT[1,5*], Sall A[1], Seck M[2], Sene A[1], Faye BF[2], Fall S[3], Simo Louokdom J[5],Ndiaye FSD[3], Dieye TN[4], Diop S[2], Toure AO[1]

[1]*Laboratoire d'hématologie, Hôpital Aristide Le Dantec, Sénégal*

[2]*Centre National de Transfusion Sanguine, Sénégal*

[3]*Service de médecine interne, Hôpital Aristide Le Dantec, Sénégal*

[4]*Laboratoire d'immunologie, Hôpital Aristide Le Dantec, Sénégal*

[5]*Faculté des Sciences de la Santé, Université Marien Ngouabi, Congo*

Corresponding Author: *Ocko Gokaba LT, *Laboratoire d'hématologie, Hôpital Aristide Le Dantec, Sénégal Faculté des Sciences de la Santé, Université Marien Ngouabi, Congo*

Abstract

Introduction: *Anti-phospholipids (aPLs) are a very heterogeneous family of antibodies that induce various clinical manifestations, including thrombotic, obstetrical and cardiac. The purpose of this study on anti-phospholipid syndrome (APLS) is to analyze anti-phospholipid antibodies during cardiac events.*

Patients and Methods: *Nine month analytical cross-sectional study conducted at the Aristide Le Dantec Hospital in all patients with heart disease. The search for antiphospholipids was done using the STA compact™ and by enzyme immunoassay. The diagnosis of APLS was based on the persistence of antiphospholipids for three months. The variables studied were epidemiological (age, sex, survival), clinical (valvular disease, ischemic heart disease, dilated cardiomyopathy) and biological (lupus anticoagulant, antiβ2Glycoprotein I, anticardiolipid).*

Results : *Fifty-five patients were collated, with 34.54% of APLS cases. Patients with APLS were not different (p>0.05) from those without APLS in terms of age and sex. APLS was found more often (p=0.01) in valvulopathies (51.5% vs. 48.5%). In the other cardiopathies the difference (p 0.05) was not significant: ischaemic cardiopathies (42.1% vs 52.9%) and dilated cardiomyopathies (60% vs 40%). Lupus anticoagulant and anticardiolipid IgG were found in 92% and 8% of cases respectively. The mean normalized ratio of LA positive was 1.24 0.6. Cumulative survival in the presence and absence of antiphospholipids was 67% and 90%, respectively.*

Conclusion: *The frequency of APLS is high during cardiac damage. These are dominated by valvulopathies, and the antiphospholipids found are lupus anticoagulan and anticardiolipids.*

Keywords: *lupus anticoagulant, anticardiolipids, antiβ2GPI, APLS, cardiopathies*

1. INTRODUCTION

Anti-phospholipids (aPLs) are a very heterogeneous family of antibodies directed against anionic phospholipids and/or proteins. They can persist for 12 weeks, defining the Anti-Phospholipid Syndrome (APLS) and induce a variety of clinical manifestations including thrombotic, obstetrical, cutaneous and cardiac [1].

The occurrence of cardiac disease is multifactorial with two new risk factors, homocysteine and aPL [2, 3]. The cardiovascular system is one of the target organs of the aPLs. Indeed, aPLs are responsible for 40% of cases of coronary heart disease, valvular disease, intracavitary thrombosis, and 4-6% of cases of severe morbidity [2]. Among aPLs, anticardiolipids (aCLs) are an independent risk factor for myocardial infarction or cardiac arrest. Nevertheless, these cardiac events remain outside the criteria for defining APLS, which were updated in 2006 [1].

In Senegal, the 2006 lupus heart disease study showed a positive correlation between lupus anticoagulant and tricuspid insufficiency [4]. Thus, the objective of the present APLS study is to analyse antiphospholipid antibodies during cardiac injury at the Aristide Le Dantec Hospital in Dakar.

2. PATIENTS AND METHODS

This was an analytical cross-sectional study conducted from 1 March to 30 November 2015 in the Cardiology Department and the Haematology and Immunology Laboratories of the Aristide Le Dantec Hospital in Dakar. Patients were recruited from among those hospitalised for valvular insufficiency and/or narrowing and/or valvular disease; ischaemic heart disease (unstable or stable angina, chronic ischaemic cardiomyopathy, myocardial infarction), and non-hypertensive dilated cardiomyopathy. This recruitment was based on clinical diagnosis. Electrocardiogram, cardiac ultrasound and angio-scan were used to confirm cardiac damage. Participants who were 70 years of age or older, or who had a severe infectious syndrome less than 3 months previously, or who had been treated with quinine, quinidine, beta-blockers, benzodiazepines, phenobarbital, or anticoagulants were not included. The variables studied were epidemiological (age, sex, survival); clinical (valvular disease, ischemic heart disease, dilated cardiomyopathy), and biological (LA, aCLs and antiβ2GPI IgM and IgG isotypes).

For each patient, 5 ml of venous blood was drawn into three (03) tubes containing 0.109 M trisodium citrate at a ratio of one volume of citrate to nine volumes of blood. These samples were double centrifuged at 3000 rpm for 15 minutes to obtain a platelet-poor plasma. The plasmas were stored at -80°C until the aPL assay. The LA was determined by Diluted Russell's Viper Venom Time (DRVVT) using the STA compact™ with screening and confirmatory tests. When the ratio 1 (patient clotting time to calculated pool clotting time) obtained in DRVVT-Screen® was greater than 1.2; the ratio 2 (patient clotting time to calculated pool time) in DRVVT-Confirm® was then determined. Thus, any normalized ratio (ratio1/ratio2) greater than or equal to 1.2 reflected the presence of LA. The aCls and antiβ2GPI IgM and IgG isotypes were determined by enzyme-linked immunosorbent assay with the asserachrom kits from Diagnostica Stago laboratories. The reference values of the aCLs were less than 10 GLP units/ml for IgG and 10 MPL/ml for IgM and those of the anti-β2GPI, less than 1 GAU unit/ml for IgG and 9 MAU units/ml for IgM.

The data were analyzed using SPSS v22 software. The Fisher and Kruskal-wallis tests were used to compare the variables of interest. Cumulative survival was assessed using the Kaplan Meier method and the Log-rank test was used to compare survival curves. The significance level was set at $p < 0.05$.

3. RESULTS

Fifty-five patients were collated, including 19 cases of APLS, being 34.54% of cases. Patients with APLS were not different (p>0.05) from those without it in terms of age and sex. APLS was found more often (p=0.01) in valvulopathies (51.5% vs. 48.5%). In the other cardiopathies the difference (p 0.05) was not significant: ischaemic cardiopathies (42.1% vs 52.9%) and dilated cardiomyopathies (60% vs 40%) [Table I].

Table1: *distribution of patients according to epidemiological and clinical characteristics*

	APLS		p-value	OR [IC 95%]
	Present	Absent		
	n (%)	n (%)		
Sex				
Male	15 (51.7)	14 (48.3)	0,03	4 [1.07-15.06]
Female	4 (21.1)	15 (78.9)		
Clinical				
Valvulopathies	17 (51.5)	16 (48.5)	0.01	6.9 [1.3-35.5]
Mitral	10 (40)	15 (60)	0.30	-
Aortic	7(53.8)	6 (46.2)	0.23	2.6 [0.5-13.0]
Tricuspid	5 (33.3)	10 (66.7)	0,27	0.4 [0.08-2.06]
Pulmonary	3 (50)	3(50)	0.66	1.5 [0.23-9.38]
Ischaemicheartdisease	9 (42.1)	11 (57.9)	0.77	1.19 [0.36-3.87]
Dilated cardiomyopathies	9 (60)	6 (40)	0.05	3.45 [0.96-12.31]

Median age : 43 years [29 ; 55] vs 41[32 ; 53] (p=0.86)

APLS: Anti-phospholipid antibody syndrome

LA and IgG isotype aCLs at 40 GPL/ml were found in 92% and 8% of cases respectively. The mean normalized ratio of positive LA was 1.24 0.6. The ratio of DRVVT in valvular disease, ischemic heart disease and dilated cardiomyopathy was 1.27 vs 1.11; 1.24 vs 1.10 and 1.27 vs 1.17, respectively (Figure 1).

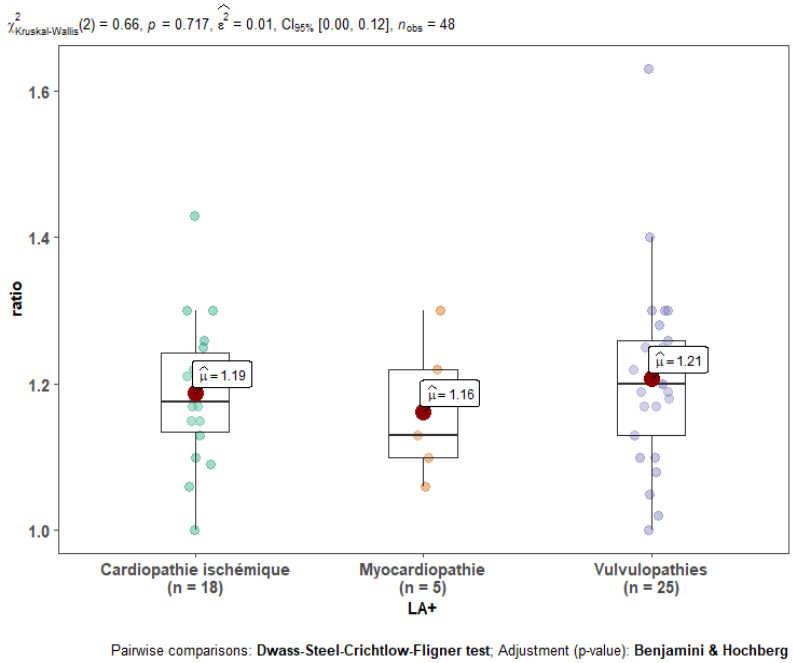
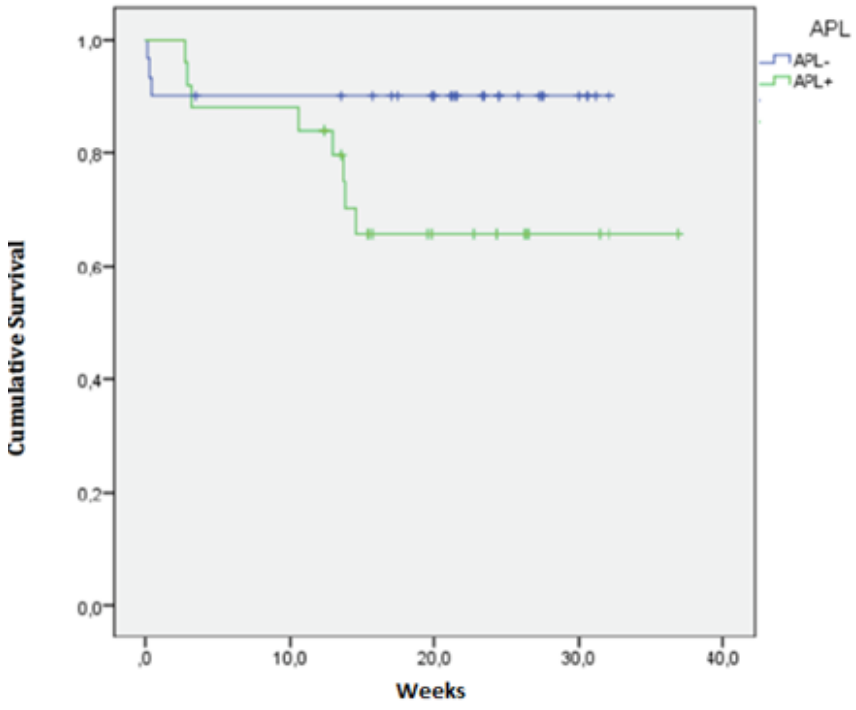


Figure1: *distribution of Heart Disease by Ratio of Russell's Viper Venom Time Diluted.*

The mean duration of follow-up was 19.5 ± 9.23 weeks with extremes of 0.14 and 36.8 weeks. The incidence of death was higher in patients with aPLs (72.7% vs. 27.3% cases; p= 0.04). Cumulative survival during and in the absence of aPLs was 67% and 90%, respectively (Figure 2).



Log-Rank test = 0.05

Figure2: *patient survival curves in the presence and absence of antiphospholipids*

4. DISCUSSION

Anti-phospholipid syndrome (APLS) is an evolving concept and much work has focused on its role in cardiac disease [5, 6, and 7]. This study investigated antiphospholipid antibodies /anti-phospholipid syndrome (APLS) in cardiac disease. In the absence of standardization of the enzyme immunoassay methods used for the detection of anticardiolipids and anti-beta2glycoproteins I, the determination of these antibodies was done with the same kit, in the same laboratory, and the definition of APLS cases according to criteria updated in 2006 [1]. Thus, in our study the frequency of APLS is

34.54% of cases. The median age (43 years [29; 55]) of our patients who presented with APLS is within the range of mean ages reported in the Canadian and European literature [8, 9, 10, 11]. Indeed, it varies according to the studies because patients are included either systematically, some of whom are over 70 years old, or by having the status of APLS beforehand. However, other authors state that the relevance of testing for lupus anticoagulant is low in subjects who are advanced in age, because age is a significant risk factor in the development of cardiovascular manifestations in patients with anti-phospholipid antibodies [8, 12]. Valvular impairment, which is significantly higher in APLS (p=0.01), has nevertheless been described in American and European studies [8, 13, 14]. It is thought to be due to the role of lupus anticoagulant and anticardiolipids in the pathogenesis of cardiac valve disease [15]. Khamasha et al, in a lupus anticoagulant and anticardiolipid patient population, reported higher frequencies of mitral vegetations (16%) and mitral regurgitation (38%) compared to 1.2% and 12% respectively in patients without anti-phospholipids [16]. Cardiomyopathies during antiphospholipid syndrome are poorly described and poorly known [12]. The high proportion (60% of cases) in our study, mostly hypokinetic dilated cardiomyopathies, is in agreement with the observations of Tektonidou et al who reported a higher prevalence of right heart diastolic dysfunction during primary antiphospholipid syndrome compared to secondary antiphospholipid syndrome, with or without anticardiolipids [17, 18].

Concerning APLS in ischemic heart disease, its frequency (42.1% of cases) in our patients is much higher than that (5 to 15%) described in the literature during myocardial infarction [12]. It should be noted that, under the term ischaemic heart disease, we have included both acute coronary syndromes (myocardial infarction and unstable angina) and chronic ischaemic cardiomyopathies (after-effects of infarction and stable angina).

At the end of a mean follow-up period of 19.5+ /- 9.3 weeks, mortality was significantly (p=0.04) higher in the presence of anti-phospholipid antibodies, both of which were aCLs at 40GPL/ml. Our observations are consistent with those of other studies conducted in Canada, France, and China; among them, Moc et al, in a population of 679 patients, reported 20% mortality in patients with aPLs versus 9% in patients without aPLs (p=0.02) [9, 19]. Indeed, it is recognized that a high level of aCLs is a risk factor for myocardial infarction or cardiac arrest. [2]. the difficulty is all the more marked as the dilatation and systolic dysfunction of the left ventricle constitute the ultimate stage of various myocardial attacks, whether hypertensive, ischaemic or post-myocardial. In addition, Neville et al have shown that aPLs are not only associated with but also predictive of death [9]. However, Bulckean et al in France did not observe a positive correlation although mortality is common in the group of patients with anti-phospholipids (32% vs 23%) [10]. The difference could be explained by the low potency of his sample, the inclusion of patients operated for valve diseases, and those at high risk of thrombosis.

Cumulative survival was higher (90%) without significant difference in patients without aPLs from the first two weeks of hospitalization compared to patients with aPLs, where it decreased from the second week to the 20th week with a value of 67% (Figure 2). Our observations were nearly similar to those of Neville et al. who reported cumulative survival of 90% and 72% respectively in the groups of patients with and without antiphospholipids [9].

5. Conclusion

Anti-phospholipid syndrome (APLS), which occurs with high frequency during heart disease, is diagnosed in young patients with poor survival. Valvulopathies are cardiac conditions found in association with lupus anticoagulant and anticardiolipids.

References

[1] Miyakis S, Lockshin M D, Atsumi T, Branch D W, Brey R L, Cavera R and al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost. 2006; 4:295-306.

[2] Cervera R. Coronary and valvular syndromes and antiphospholipid antibodies. Thrombosis Research. 2004; 114:501-07.

[3] Gentian D, Seema P J, Alessia B, Giacomo Z, Vittorio P. Antiphospholipid syndrome and the heart: A case series and literature review. Autoimmunity Review. 2015; 14:214-22.

[4] Touré A. O, Doupa D, Diop S, Kane A, Ka MM, Dieye T et al. Relation lupus – antiphospholipides et cardiopathie lupique. Ann Biol Clin. 2006; 64(3): 231-5.

[5] Levesque H, Dérumeau G, Le normand C, Borg J, Tron F, Letac B et courtois H. Atteinte

cardiaque et anticoagulant circulant : intérêt de l'échographie doppler Trans-œsophagienne. A propos de 26 observations dont 10 avec un syndrome des anticorps anti phospholipides primitif. La Revue de Médecine Interne. 1991; 12(3): S74.

[6] Leraki R, Bletry O, Horellou MH, de Zuttere D, Weill B, Dormond D et al. Corrélation entre anticorps anti phospholipides (APL) et lésions neurologiques centrales ou cardiaques. La Revue de Médecine Interne. 1990; 11(3): S2 85.

[7] Erdozain J.G, Ruiz-Irastorza G, Segura M.I, Amigo M.C, Espinosa G, Pomar J.L et al. Cardiac valve remplacement in patients with antiphospholipid syndrome. Arthritis care Research. 2012; 64(8): 1256-60.

[8] Djokovic A, Stojanovich L, Kontic M, Stanisavljevic N, Radovanovic et Marisavljevic D. Association between cardiac manifestations and antiphospholipid antibody type and level in a cohort of serbian patients with primary and secondairy antiphospholipid syndrome. IMJ. 20 14; 16:162-7.

[9] Neville C, Rauch J, Kassis J, Solymoss S, Joseph L, Belisle P et al. Antiphospholipid antibodies predict imminent vascular events independently from other risk factors in a prospective cohort. Thromb haemost. 2009; 10 1(1): 100-7.

[10] Bulckaen H, G. Puisieux F.L, Bulckaen E. D, Di Pompeo C, Bouillane O. M, Watel A. A et al. Antiphospholipid and the risk of thromboembolic events in valvular heart disease. Mayo Clin Proc. 2003; 78 :294-98.

[11] Bouillanne O, Millaire A, de Groote P, Puisieux F, Cesbron J Y, Jude B et al. Prevalence and clinical significance of antiphospholipid antibodies in heart valve disease: A case-control study. American Heart Journal. 1996; 132:790-95.

[12] Geri G et Cacoub P. Atteinte cardiaque au cours du syndrome des anti phospholipides. Press med. 2011; 40:758-64.

[13] Cieśla M, Wypase k et Undas A. IgA Antiphospholipid antibodies and anti-domain1 of beta2glycoprotein1 antibodies are associeted with livedo reticularis and heart valve disease in antiphospholipid syndrome. Adv Clin Exp Med. 2014; 23(5): 729-33.

[14] Roldan C.A. Valvular and coronary heart disease in heart systemic inflammatory diseases: systemic disorders in heart disease. Heart. 2008; 96:1089-101.

[15] Kampolis C, Tektonidou M, Moyssakis I, Tzelepis G.E, Moutsopoulos H et Vlachoyiannopoulos P.G. Evolution of cardiac dysfunction in patients with antiphospholipid antibodies and / or antiphospholipid syndrome: A 10 year follow-up study. Seminars in Arthritis and Rheumatism. 2014; 43:558-65.

[16] Pardos –Gea J, Ordis J, Cortès–Hermandez J, Balada E, Evangelista A et al. Echography at diagnostic of antiphospholipid syndrome provives prognostic information on valvular disease evolution and identifies two subtypes of patients. Lupus. 2010; 19:575-82.

[17] Tektonidou MG, Loannidis JP, Moyssakis I, Boki KA, Vassiliou V, Vlachoyinnopoulos PG et al. Right ventricular diastolic dysfunction in patients with anticardiolipin antibodies and antiphoslipid syndrome. Ann Rheum Dis. 2001; 60(1): 43-8.

[18] Paran D, Caspi D, Levartovsky D, Elkayam O, Kaufman I, Litinsky I et al. Cardiac dysfunction in patients with systemic lupus erythematosus and antiphospholipid syndrome. Ann Rheum Dis. 2007; 66(4): 506-10.

[19] Mok CC, To chan P, Ho L Y, Yu K L and To C H. Prevalence of the antiphospholipid syndrome and its effects on survical in 679 chinese patients with systemic lupus erythematosus. Medicine. 2013; 92:217-22.

Citation: *Ocko Gokaba LT, Sall A et.al, Anti-Phospholipid Antibody Syndrome During Heart Disease The Aristide Le Dantec Hospital In Dakar. ARC Journal of Hematology. 2020; 5(1):15-18.*