Open Journal of Obstetrics and Gynecology, 2013, 3, 383-385 **OJOG**
http://dx.doi.org/10.4236/ojog.2013.34071 Published Online June 2013 (http://www.scirp.org/journal/ojog/)

Antiphospholipid antibody syndrome and pregnancy

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Received 27 February 2013; revised 30 March 2013; accepted 6 April 2013

ABSTRACT

Recurrent foetal loss in early and late stages of pregnancy is a common problem of women affected by anti-phospholipid antibody syndrome. The therapeutic scheme consisting of associating aspirin and heparin has shown an improvement of the prognosis for the next pregnancies. We report 3 cases of anti-phospholipid antibody syndrome and pregnancy, and we underline the clinical, therapeutic and prognosis features of this syndrome.

Keywords: Anti-Phospholipid Antibody Syndrome; Pregnancy; Treatment; Prognosis

1. INTRODUCTION

The anti-phospholipid antibody syndrome (APAS) is an acquired autoimmune disorder associating clinical thrombo-embolic and obstetric manifestations, and the presence of antibodies against phospholipids or against protein factors related to phospholipids.

There are two forms of APAS; the first is called primitive or isolated, the second autoimmune pathology.

The diagnosis of APAS should be suggested whenever having obstetric history such as repeated pregnancy arrest, foetal loss without any malformation or foetal death in utero.

2. OBSERVATION

2.1. Observation 1

A 32-year-old nulliparous patient at her fourth pregnancy has had the antecedent of recurrent spontaneous arrest of pregnancy (3 times). The karyotypic study of two products of conception was normal, the syphilitic serology was negative, anti-DNA antibodies were negative. However, the study of anti-cardiolipin antibodies (immunoglobulin G: IgG) was positive. The rest of the assessment was without abnormality. By the diagnosis of the fourth pregnancy, the patient was put under preventive treatment based on a weak dose of both platelet anti-aggregant (aspirin 100 mg/day) and heparin of low molecular weight (HLMW) and corticoid (prednisone 40 mg/day). The follow-up of pregnancy didn't show any abnormality. The aspirin was stopped by the 35th week of amenorrhea. A preventive caesarian section was realized by the 39th week of amenorrhea, this gave birth to a male newborn weighing 3700 g. The follow up was simple, and the patient remained asymptomatic within a recession of 15 months.

2.2. Observation 2

A 30-year-old nulliparous patient at her third pregnancy has had the antecedent of recurrent spontaneous arrest of pregnancy (2 times). The karyotypic study of two products of conception was normal, the syphilitic serology was negative, anti-DNA antibodies were negative. However, the study of anti-cardiolipin antibodies (IgG) was positive. The rest of the assessment of systemic disease was without abnormality.

By the diagnosis of the third pregnancy, the patient was put under preventive treatment based on (aspirin (100 mg/day) and heparin of HLMW and the evolution was favorable. The follow-up of pregnancy didn't show any abnormality. Following an acute fetal suffering, a preventive caesarian section was realized by the 39th week of amenorrhea. This gave birth to a female newborn weighing 3500 g. The follow up was simple.

2.3. Observation 3

A 40-year-old patient nulliparous patient at her fifth pregnancy has had a history of recurrent arrest of pregnancy (3 spontaneous and one stopped pregnancies). The sero-

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logical assessment was normal including the parental karyotypic study; except the study of anti-cardiolipin antibodies (IgG) that was positive. By the diagnosis of the fifth pregnancy, the patient was treated using anticoagulant and corticoids (prednisone 40 mg/day). Considering the antecedents of the patient, a preventive Caesarian section was realized by the 39th week of amenorrhea, this gave birth to a female newborn weighing 3800 g. The follow was simple, and the patient remained asymptomatic within a recession of 24 months.

3. DISCUSSION

The anti-phospholipid antibody syndrome is an autoimmune disorder which associates clinical thrombo-embolic with obstetric manifestations, is associated with the presence of auto-antibodies directed against phospholipids or plasmatic proteins [1]. In obstetrics, it is defined [2] as history of foetal loss consisting of three spontaneous pregnancy arrests or one foetal death in utero without malformation, associated to the presence of anti-phospholipid antibodies such as anti-cardiolipin and/or circulating anticoagulant. Anti-phospholipid antibodies are involved in the genesis of obstetric accidents by a thrombopenia phenomenon [3]. Hence, spontaneous pregnancy arrests are provoked by premature placental thromboses. These thromboses are due to antibodies-proteins 2-GP1 connection and prothrombin. The involvement of circulating anticoagulants in the repeated pregnancy arrest is well established. Nevertheless, the cardiolipin is subject to controversies [4,5]. However, a recent study has shown the presence of anti-cardiolipin antibodies decreasing the rate of survival births by 48% [6].

The diagnosis of APAS is based on clinical and biological manifestations. In obstetrics, the clinical revelations are according to the international symposium of Sapporo [7]: death in utero after the twelfth week of the amenorrhea, premature birth before the thirty-sixth week of the amenorrhea in a context of preeclampsia, uteroplacental deficiency, or three spontaneous arrest of pregnancy before the twelfth week of the amenorrhea.

The biological expression constitutes a diagnostic difficulty considering the heterogeneous tests used. These tests are realized twice at six weeks intervals for eliminating transient positivity that might be due to an inflammatory syndrome, a viral infection or other factors [3]. Circulating anticoagulants are assessed using coagulation test. Anti-cardiolipin antibodies are searched using ELISA test; and the anti β2 glycoprotein is correlated with the risk thrombopenia [1-8]. Contrary to the test ELISA, coagulation tests are rarely positive in obstetric accidents. Actually, another protein annexin V would be responsible for the equilibrium of haemostatic phenomena [8].

In summary, the biological diagnostic should be achieved in the following steps: Firstly, to search for a circulating anticoagulant and anti-cardiolipin especially IgG which constitute a major criteria. Once these tests are negative, a test of β2GP1 antibody has to be performed. Finally, phosphatidyl-ethanolamine or anti-prothrombin and anti-annexin have to be assessed.

At present the therapeutic prevention of obstetric accidents related to APAS saves 70% of survival births compared to 10% without treatment [9]. Several treatments were studied, in particular aspirin, heparin, corticoids, immunoglobulin and plasmapheresis. However, most authors indicate the association of aspirin and heparin at low molecular weight [2-9]. Indeed, this association therapy allows reducing the foetal loss by 54%. At present the therapeutic indications are not consensual. Evermore, the indication according to the rate of antibodies is controversial. Indeed studies defend this therapy for high rates of antibodies, contrary to those indicating it even at weak rates of antibodies. Actually, most studies have shown that the best therapy of APAS is offered by aspirin (60 to 100 mg) and heparin of LMW (an injection a day in preventive dose). This treatment is begun once the pregnancy diagnosed. The aspirin should be stopped by the 35th week of amenorrhea while the heparin is continued during 6 weeks after the childbirth. This treatment seems to be deprived of any maternal or foetal complication. Corticoids are suggested only if there is an extra-obstetrical [9] or inflammatory system disease, this without exceeding 20 mg/day. The treatment by the heparin requires a weekly supervision of platelet especially during first weeks of the treatment [5]. Immunoglobulins generate a solubilisation of the immune complexes. However, a randomized study didn't show any profit of using IgG compared a placebo in patients treated by aspirin and heparin, particularly on the rate of children survival and the prematurity [10]. Plasmapheresis wasn't studied in the treatment of APAS during the pregnancy. Besides these treatments, an obstetric care based on the close observation is essential.

In 2013, Jing Xiao *et al.* [11] presented a study to evaluate the effect of traditional treatment (prednisone and aspirin) and comprehensive treatment (prednisone, aspirin, low molecular weight heparin (LMWH) and IVIg on the pregnancy outcome, obstetric complications and foetal outcome in women with antiphospholipid syndrome (APS). In this present trial, they observed and evaluated 129 women with APS. Eighty-seven patients received traditional treatment and 42 patients received comprehensive treatment. In the traditional treatment group and comprehensive treatment group, the live birth rate was 83%, 91% and 97%, 62%, respectively, and the obstetric morbidity was 22%, 99% and 7%, 14%, respectively. The neonatal weight in the comprehensive treatment group was increased compared with the traditional treatment

group, however, no differences were found in gestational age at delivery or preterm labor. Comprehensive treatment improved the result of gestation and reduced obstetric complications, and is a more effective treatment for APS than the traditional method using prednisone and aspirin. Two our patients were put under preventive treatment based on (aspirin (100 mg/day)) and heparin of HLMW and prednisone and the evolution was favorable also one patient was put under preventive treatment based on aspirin and heparin of HLMW with favorable evolution.

Shrimati Shetty *et al.* [12] reported that low-molecular-weight heparin with low-dose aspirin has been found to be the most effective treatment for women with antiphospholipid antibodies and recurrent foetal loss. Differences in dosage, timing of treatment, inclusion criteria, outcome assessment parameters are some of the factors which have resulted in discrepancies in various reports.

4. CONCLUSION

Actually, it is well established that the anti-phospholipid antibody syndrome engenders obstetrical accidents, particularly pregnancy interruption. Identification of the immunological mechanisms involved in pregnancy loss and the action of different therapeutic reagents is important so that effective therapies can be designed and investigated.

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