

# Gestation in patients with high levels of anticardiolipin antibodies, a history of deep venous thrombosis and miscarriages

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## Abstract

The aim is to stress the importance of prophylaxis against deep venous thrombosis in gravidas with high levels of anticardiolipin antibodies with or without a history of repetitive miscarriages.

The evolutions of two gravidas who were treated in pre-natal and vascular surgery outpatients' clinics and who suffered from deep venous thrombosis, miscarriages and high anticardiolipin antibody levels are reported. The gestations terminated at full term after prophylaxis for miscarriages was applied.

The report suggests that patients with deep venous thrombosis and high anticardiolipin antibody levels may present with miscarriages and, therefore, prophylactic treatment is recommended.

**Key words:** anticardiolipin antibodies; miscarriage; gestation; deep venous thrombosis.

## Introduction

Antiphospholipid antibody syndrome is associated with a laboratory criterion, i.e. the presence of antiphospholipid antibodies; and with clinical criteria, which may be either arterial or venous thromboembolic events or repetitive miscarriages (Table I) [1, 2].

This syndrome consists of a heterogeneous group of circulating autoantibodies against anionic phospholipids, among which the most studied are the anticardiolipin antibody and lupus anticoagulant [1, 3]. During pregnancy thromboembolic events are among the main causes of maternal death [4-6]. An association with thrombophilias increases the risk of

**Table I.** Sapporo criteria for the diagnosis of APS [2]

Clinical criteria	Laboratory criteria IgG/IgM ACA-LA
arterial thrombosis	moderate to high titre
venous thrombosis	moderate to high titre
recurrent spontaneous abortions	moderate to high titre

*Persistence is defined as a positive result of the second evaluation performed  $\geq 8$  weeks after the first evaluation.*

pulmonary thromboembolic disease, in which events are more common in the puerperium than during gestation [4, 5]. The treatment of acute thrombotic events is effected using anticoagulation with heparin and chronic prophylaxis with warfarin [7-9].

The characteristics of antiphospholipid antibody syndrome during gestation include a miscarriage within the first three months, repetitive miscarriages in the later two thirds of pregnancy, placental arterial thrombosis and maternal thrombocytopaenia [8]. Some reports have linked deep venous thrombosis to high antiphospholipid antibody levels in gravidas [10]. The aim of this study is to report on the association of these antibodies in pregnant women with deep venous thrombosis and miscarriages.

### Case report 1

A 28-year-old patient who was taking oral contraceptives developed deep venous thrombosis of the left femoral iliac artery. The patient evolved satisfactorily with clinical treatment using warfarin over a 6-month period. One year later she became pregnant for the second time, but suffered a miscarriage during the seventh week. The level of anticardiolipin antibodies was measured and found to be high, with IgG at 19.06 GPL and IgM at 1.8 MPL (Milenia® Anti-Cardiolipin). A test for lupus anticoagulant was negative. After 10 months the patient became pregnant again, but this time prophylactic treatment using 5000 IU SC heparin every 12 hours and ASA at 100 mg daily was administered starting in the third gestational month. An event-free pregnancy terminated with the birth of a child in the 40th week.

### Case report 2

A 23-year-old patient suffered an incomplete miscarriage without any apparent causes. Sixteen days afterwards she presented with pain and a sudden oedema of the lower right limb and deep venous thrombosis was diagnosed. The anticardiolipin antibody levels were investigated and found to be within normal limits. Nine months later the antibody levels were again measured and this time they were high, with IgG at 15.0 GPL and IgM at 8.82 MPL (Milenia® Anti-Cardiolipin). A test for lupus anticoagulant was negative. The patient became pregnant and prophylaxis was initiated using 10,000 IU SC of heparin at 12-hour intervals starting in the third gestational month. The patient suffered from premature contractions in the 33rd week, but the delivery was successful.

### Discussion

In repetitive miscarriage patients with high anticardiolipin antibody levels, prophylaxis using low doses (5000 IU) of heparin every 12 hours is

indicated to prevent further miscarriages. This may be associated with aspirin or not. However, in cases of thrombotic events during or immediately before pregnancy, a full dose of heparin must be used. In this study, one patient with a history of deep venous thrombosis and a single miscarriage was not undergoing anticoagulation therapy when she became pregnant again. In this case, there was no consensus as to whether any type of prophylaxis should be performed, as treatment for deep venous thrombosis had already been concluded and there was no history of repetitive miscarriages. However, she had presented with one miscarriage associated with high anticardiolipin antibody levels. No publications stressing this aspect were found. Nevertheless prophylactic anticoagulation against miscarriages was chosen and the pregnancy evolved well.

The second patient, who presented with a history of miscarriages and a thrombotic event, received prophylaxis against miscarriages and successfully completed the gestation. Both patients suffered from the primary anticardiolipin antibody syndrome. There is no consensus on the proper conduct for embolic events associated with this syndrome. However, after the first thrombotic event anticoagulation for six months is generally performed and on relapse anticoagulation for an indefinite period is suggested, taking into consideration the risks and benefits of each phase of life.

Miscarriages are related to placental thrombotic events and must, therefore, be considered as cases of thrombosis. Thus, in this case the patient suffered two thrombotic events and any following pregnancy is associated with a greater risk of venous thromboembolism. We must question the necessity of this patient to receive prophylaxis to prevent new thrombotic events.

The report suggests that patients with deep venous thrombosis and high anticardiolipin antibody levels may present with miscarriages and, therefore, prophylactic treatment is recommended.

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