44 Management of Antiphospholipid Syndrome in Pregnancy

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Introduction

Antiphospholipid syndrome (APS) predominantly affects young women and there has been a growing awareness of this condition amongst obstetricians and gynecologists over the last 15 years. In this chapter we discuss the association between APS and adverse pregnancy outcome and present some of the dilemmas in the management of on-going pregnancies in women with APS. Although clinicians are becoming increasingly familiar with these management options, knowledge of the pathogenesis of poor pregnancy outcome in APS remains incomplete, and in the last part of this chapter we outline some of the areas of research in this rapidly evolving field.

Making the Diagnosis of APS

The criteria for the classification of APS are well described [1] and it is critical that these are applied strictly to avoid inappropriate management of patients [2]. Similarly, even in those with a robust diagnosis, all adverse pregnancy outcomes should not be entirely attributed to the syndrome as there are numerous other associations with poor outcome that may be causative or contributory, for example, cervical incompetence, "unexplained" intrauterine death. It is therefore essential to apply good clinical judgment in each individual case to avoid interventions that may be unnecessary or even harmful.

The Effect of Pregnancy on APS

Pregnancy is a hypercoagulable state and women with APS are at increased risk of thrombosis unless thromboprophylaxis or anticoagulation is adequate. Some studies have demonstrated that a significant proportion of pregnant patients still have thrombotic episodes despite thromboprophylaxis [3, 4]. These patients need long-term anticoagulation with warfarin aiming for an international normalized ratio (INR) of at least 2.0–2.9 [5]. Pregnancy can also exacerbate pre-existing

thrombocytopenia, and this may be further compounded by medication because aspirin and heparin administered during pregnancy may cause thrombocytopenia. Thromboprophylaxis, full anticoagulation, and the management of thrombocytopenia in pregnant women with APS are discussed in more detail below.

The Effect of APS on Pregnancy

APS and Early Pregnancy Complications

Many cases of APS are diagnosed following investigation of recurrent miscarriage. The association between APS and recurrent miscarriage is well known [6–9], with second trimester loss being particularly common [10]. The prospective fetal loss rate in primary APS is reported to be 50% to 75% [11, 12]. In patients with systemic lupus erythematosus (SLE) and secondary APS some studies suggest this may be as high as 90% [13, 14], although this is likely to be an overestimate. It has been suggested that the risk of fetal loss is directly related to the antibody titer [15, 16], but this is certainly not true of all cases. Some studies have shown maternal IgG aCL to be a particularly reliable predictor of miscarriage [17, 18]. Although this makes theoretical sense as this subfraction of antibodies can cross into the fetoplacental circulation [19], many women with recurrent miscarriage have IgM aCL antibodies only. It is impossible to predict which women will develop complications in pregnancy, and some women with persistently elevated aPL titers and a history of thromboses and/or thrombocytopenia will have no obstetric complications at all. Previous poor pregnancy outcome remains the most important predictor of future risk [20–22].

APS and Late Pregnancy Complications

In pregnancies that do not end in miscarriage or fetal loss, there is a high incidence of early onset pre-eclampsia (PET) [23–26] and intrauterine growth restriction (IUGR) [20, 27], placental abruption [28], and premature delivery [29, 30]. Because patients with APS form a heterogeneous group, the incidence of these complications varies between units. Indeed it is now clear that the substantial differences in APS patient populations in studies of pregnancy inevitably results in large differences in reported adverse pregnancy outcomes, and whilst attempts are being made to define management in certain subgroups, many recommendations are not strictly evidence based [31, 32]. Those units which manage women with systemic manifestations of APS have a higher incidence of complications in pregnancy [33], whilst those which recruit women predominantly from recurrent miscarriage clinics have a lower incidence of these complications [34, 35]. It is essential to appreciate these differences in order to critically appraise the literature, advise women appropriately, and rationalize therapy [36]. In a recent study from our own unit, 35 pregnancies in women with primary APS resulted in a live birth in 32 cases (91%) with a mean gestation of 38.4 (27.5–42) weeks and a mean birth weight of 2895 ± 165 g. Complications included miscarriage in 3 cases (9%), fetal growth restriction in 4 cases (12%), placental abruption in 1 case (3%), pre-eclampsia in 2 cases (6%), preterm delivery in 8 cases (24%), and maternal thrombotic events in 5 cases (14%). Labor was induced in 8 (25%) cases and delivery was by Caesarean section in 19