LUPUS ANTI-COAGULANT AND UNEXPLAINED PREGNANCY LOSS

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SUMMARY

Out of 60 pregnant patients with unexplained recurrent fetal losses and without clinical systemic lupus erythematosus (S.L.E.) 4 (6.6%) had positive lupus anticoagulant (LAC). These 4 patients and one patient of S.L.E. with +ve LAC, had 6 pregnancies studied. Three pregnancies resulted in abortion 1 at start of treatment and 2 before treatment, while high dose costicosteroid and low dose aspirin therapy in the other 3 pregnancies resulted in favourable pregnancy outcome. Unexplained fetal losses can be due to the lupus anti-coagulant, and early aggressive treatment is necessary for permitting pregnancy to proceed favourably towards term.

INTRODUCTION

Unexplained fetal loss is an obstetric problem which has stimulated much research. Recognition of a subset of women with a high rate of fetal wastage among those with serological evidence of connective tissue disease has pointed towards an antibody : lupus anticoagulant (LAC) as a probable cause (Lubbe et al 1983). It is an immunoglobulin, usually, IgG, a monoclonal antibody reactive with phospholipid from platelet membrane. Approximately 25-70% of individuals with LAC develop thrombosis, and only 40% have systemic lupus erythematosus (SLE), (Schleider et al 1976). In pregnancy, it causes placental thrombosis and infarction which in turn leads to a spectrum of complications such as repeated abortions, intra-uterine growth retardation and intra-uterine deaths. Cortico-steroid and low-dose aspirin therapy normalises the coagulation tests and ameliorates placental abnormalities (Nilsson et al 1975). This research was conducted at the All

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India Institute of Medical Sciences to study the possible link between circulating LAC and fetal loss, especially in non-SLE patients and to study the usefulness of low dose aspirin and high dose prednisolone for improving fetal outcome.

MATERIAL AND METHODS

Sixty patients without clinical SLE, with unexplained fetal losses attending the high risk pregnancy clinic at AIIMS were tested for lupus anticoagulant by the activated partial thromboplastin time and the kaolin clotting time (KCT). One pregnant patient with SLE was found to have LAC. She was referred to the high risk pregnancy clinic for intensive fetal monitoring and delivery.

All patients had history of recurrent first, second or third trimester fetal losses. In all but one case there was no history of thrombotic events, and the serologic syphilitic test was negative in all the cases. If LAC was found positive (+ve) the patient was started on 60 mgm prednisolone per day and then reduced to 40 mgm after 1 week, and continued till KCT returned to normal. The dose of prednisolone was then further reduced, sufficient to maintain KCT at the lower limit of normal. Low dose aspirin (75 mgm/day) was also added.

RESULTS & OBSERVATIONS

Out of 60 non-SLE cases studied, 4 (6.6%) had a +ve LAC. One case of SLE with +ve LAC was also managed. These 5 patients of +ve LAC, with 6 pregnancies had 3 pregnancies resulting in abortion before treatment could be started. Other 3 pregnancies treated aggressively resulted in good outcome.

(1) The first case S.K., 25 yrs. G4PO+3 had a history of previous 3 mid-trimester abortions, but unfortunately before treatment could be started she aborted spontaneously at 14 weeks.

(2) The second case PL, 34 yrs. G4P2+1 with 2 living issues complained of bluish spots for last 4-5 mths and amenorrhoea 10 wks. Missed abortion and was diagnosed at booking and LAC was +ve.

(3) The thrid case SB, 26 yrs. G3PO+2 with previous 2 second trimester missed abortions had platelet count 1,60,000.

KCT 160 "/73"

Partial thromboplasin time with Kaolin (sec) 60/43. At 23 weeks she was started on prednisolone 60 mgm for 1 week and reduced to 40 mgm/day, alongwith 75 mgm aspirin. There was no hypertension or any other complication. At 34 weeks the patient went into spontaneous preterm labour. LSCS was done for fetal distress and a healthy female baby 1.85 kg. was delivered. Placenta weighed 400 gms. There was no infarction. After 2 weeks, LAC levels had decreased and prednisolone was reduced to 10 mgm daily. At 6 weeks the baby was 3.2 kg. in weight and healthy.

(4) The fourth case K.K., 28 yrs. G3PO+2 had a history of previous two 1st trimester abortions. During her third pregnancy she was diagnosed to have LAC +ve, she was started on prednisolone 60 mg for 1 week from 12th week and then reduced to 40 mg/day. It was then reduced to 10 mg/day when KCT returned to normal. Low dose aspirin was also added in the second trimester. She had

spontaneous vaginal delivery at 38 wks, 2.2. kg female baby.

(5) The fifth case K.D., PO+3, prev. 3 mid-trimester abortions, with SLE. 4th preg: Prednisolone 15 mgm started as soon as the patient was booked at 23 weeks, but patient aborted spontaneously after 1 week. 5th preg: At 11 weeks prednisolone 60 mgm/day for 1 week and thereafter 40 mgm/day, and aspirin 75 mgm/day was given. The pregnancy continued uneventfully till 34 weeks, when the patient had premature rupture of membranes and went into labour. L.S.C.S. was done for fetal distress and a healthy 2.1 kg baby was born.

Dose of prednisolone was then reduced to a maintenance of 10 mgm/day within 1 week.

DISCUSSION

Absence of any identifiable disorder apart from recurrent fetal losses or thrombotic episodes may be the only evidence of lupus anticoagulant and may be associated with thrombocytopenia, biologically false positive tests for syphilis or anticardiolipin antibody.

Nilsson et al (1975) suggested an association between LAC and recurrent intra-uterine death, while Firkin et al (1980) described 14 fetal losses in 4 women with +ve LAC. Carreras et al (1981) found LAC in 2/24 women with unexplained repeated fetal losses or IUGR.

Without any treatment, 94% pregnancies result in pregnancy loss (Lubbe and Liggins 1985). Various treatment protocols have been used for the management of this perplexing problem : subcutaneous heparin with aspirin (Christiansen et al 1988), low dose aspirin (Elder et al 1988), low dose prednisolone (Prentice et al 1984), low dose prednisolone with azathioprine (Gregorini et al 1986), low dose steroids with plasma exchange (Frampton et al 1987).

Low dose aspirin and high dose prednisolone were tried by (Orh et al 1989). Lubbe et al (1984) treated 10/12 women with +ve LAC and previous 36 unsuccessful pregnancies with high dose prednisolone and low dose aspirin and successfully managed 8 of them.

Treatment is aimed at suppression of LAC activity by adrenocorticotrophic hormones and normalisation of the coagulation tests. This is accompained by amelioration of placental abnormality, (Nilsson et al 1975). The use of low-dose aspirin (75 mgm/day) selectively inhibits thromboxane synthesis reducing threat of thrombosis in small vessels, thereby permitting pregnancy to proceed further towards term.

Thus, unexplained fetal losses can be due to the lupus anticoagulant and early aggressive treatment and intensive fetal monitoring is necessary to prevent treatment failures for optimal fetal outcome.

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