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Thrombotic Parameters in Recurrent Fetal Loss

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Summary

One hundred & forty five patients with fetal loss were evaluated for presence of Lupus Anticoagulant (LAC). In 43 of these with recurrent fetal loss APC resistance was evaluated. The occurence of LAC positivity was higher in patients with underlying SLE (31.5%) in contrast to those with no underlying disease (2.38%). LAC was found positive in 8 of the 82 (9.7%) patients with recurrent fetal loss in contrast to one of the 63 (1.6%) patients with lesser abortions. A similar trend was seen in the SLE and non-SLE group patients. None of the controls showed LAC positivity. APC resistance was found in one (2.3%) patient with recurrent fetal loss and in 1 (2.3%) control. It is thus suggested that whereas APC-R has no role in Indian patients with recurrent fetal loss, LAC should be requisitioned in patients fulfilling the criteria of unexplained recurrent fetal loss or those with underlying connective tissue disorder.

Introduction

Placental thrombosis has been implicated in the causation of recurrent abortions in a large number of patients (Greer, 1994). This may be secondary to underlying lupus anticoagulant (LAC) or activated protein (APC) resistance. The latter has recently been implicated in recurrent abortions in the Western population (Hellgren et al 1995, Rai et al 1996, Benjamin et al 1997). Presence of underlying LAC in recurrent fetal loss has been widely reported in western and Indian literature (Infante Rivard et al 1991, Das et al 1991, Parazzini et al 1991). However, the guidelines of patient criteria meriting LAC testing are not yet clear and need to be defined in order to prevent the indiscriminate requisitioning of this test. This is especially relevant in laboratories with financial and manpower constraints. With this in mind, we evaluated patients with abortions for LAC and APC resistance.

Material and Methods

The study group consisted of 145 women, aged 20-37 years presenting for evaluation of abortions without any known underlying cause. The patients were divided into two groups based on presence or absence of recurrent fetal loss. Recurrent fetal loss was defined as presence of at least 3 successive first trimester or 2 successive second trimester abortions or 1 intrauterine fetal death (IUFD) with 1 or 2 abortions. TORCH infections, diabetes mellitus, renal disease, pregnancy induced hypertension and mechanical pathological causes of fetal loss were excluded in all patients. The patients were investigated for presence of systemic lupus erythematosus (SLE) and / or antiphospholipid syndrome (APS) by ds DNA, RF and ANA tests. Age and ethnically matched women (n=125) with at least 2 normal deliveries and no history of abortion or thrombosis served as controls.

The lupus anticoagulant (LAC) was determined in all patients by mixing tests of kaolin clotting time (KCT) with normal plasma (1:1) (Exner et al 1978) and diluted Russel Viper Venom time (DRVVT) test with and without phospholipid (inosithin) (Thiagarajan et al 1986). Absence of correction of prolonged KCT by normal plasma and its correction by inosithin was considered diagnostic of lupus anticoagulant (Saxena et al 1993).

The APC resistance tests were performed in 43 women with normal APTT, at least 3 months after the last pregnancy. Briefly, activated partial thromboplastin time (APTT) was performed in all samples, with and without 16 nm of APC (obtained from Diagnostica stago, Asnieres France) using Asolectin (Associates concentrates New York, USA) and Kaolin (Sigma). The APC resistance was expressed as normalized APC sensitivity ratio (nAPCSR) (Dahlback & Carlsson 1993).

The n APC SR was calculated according to the formula.

$$\text{Normalised APC Sensitivity ratio} = \frac{\text{APC SR of test plasma}}{\text{APC SR of control plasma}}$$

$$\text{Sensitivity ratio of APC (APC SR)} = \frac{\text{APTT with APC}}{\text{APTT without APC.}}$$

The normal range of nAPC SR has found to be 0.76-1.2 (in controls). The modified APC resistance test using factor V deficient plasma (Trossaent et al 1994) was performed in borderline cases (nAPCSR<0.80). Patients with nAPCSR<0.79 by modified test were considered to have APC resistance, its normal range in our laboratory being 0.79-1.02.

Results

One hundred & fifty five patients with abortions were evaluated and LAC was positive in 9 cases (6.1%) with 8/82 (9.75%) being in cases with recurrent fetal loss and 1/63 (1.6%) being in cases having fewer number of fetal losses. Nineteen patients were detected to have SLE whereas no underlying disease was identified in others. The results are given in Table I.

Amongst the SLE group, 6/19 (31.5%) showed LAC. One of the 12 (8,3%) patients without recurrent abortions and 5 of the 7 patients with recurrent abortions were detected to have LAC. Amongst the 126 patients with no underlying disorder, 3 (2.3%) had LAC positivity. None of the patients with fewer fetal losses and 3 (4%) of the 75 patients with recurrent abortions were detected to have LAC. None of the controls showed LAC positivity.

Amongst 43 patients with normal APTT in whom APC Resistance test was performed, 1 patient (2.3%) showed APC-R positivity. One of the controls showed presence of APC-R positivity.

Discussion

Placental thrombosis leading to fetal ischaemia resulting in increased fetal loss has been well documented (Hellgren et al 1995). It is attributed to increased level of procoagulant factors or presence of underlying APC resistance or antiphopholipid syndrome. In the present study, LAC and APC-R have been evaluated. APC-R observed in 2.3% of our patients is comparable to its prevalence of 2.3% in the controls and also to that observed in normal Indian Population (Grewal et al 1997). It therefore, has limited significance in recurrent abortions amongst Indians.

The presence of LAC in 9.75% of patients with recurrent fetal loss is comparable to that reported in literature (Infante Rivard et al 1991, Das et al 1991, Parazzini et al 1991). This is in contrast to the 1.6% LAC positivity in those with lower number of fetal losses. Moreover, the LAC positivity was significantly higher in patients with SLE (31.1%) in contrast to those with no underlying disorder (2.38%). This is similar to earlier findings in all cases of SLE (Saxena et al 1994). Amongst the SLE group itself, the percentage of patients with LAC positivity was higher in recurrent abortions in contrast to those with lesser fetal losses. A similar trend was seen in patients with no underlying disease where no patient with low fetal losses was observed to have LAC. It is thus suggested that LAC test should be requisitioned in patients with recurrent fetal losses with no underlying

Table I
Lupus anticoagulant in 145 cases with abortions

		SLE cases (n=19)			Non SLE Cases (n=1226)		
	n	No. of Cases	LAC+ve n	Cases (%)	No. of Cases	LAC+ve n	Cases (%)
Recurrent fetal loss	82	7	5	(71.4%)	75	3	(4%)
Non recurrent fetal loss	63	12	1	(8.3%)	51	0	(0%)
Total	145	19	6	(31.5%)	126	3	(2.38%)

disease or in patients with underlying connective tissue disorder with any number of abortions. This would minimize the indiscriminate requisitioning of LAC test.

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