

Anticardiolipin antibodies in women with recurrent abortion

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أضداد مضاد الكارديوليبين في المصابات بالإجهاض المتكرر

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خلاصة: كان هدف هذه الدراسة تحديد ما إذا كان مستوى أضداد مضاد الكارديوليبين لدى المصابات بالإجهاض المتكرر يختلف عنه لدى عامة الناس. وقد استعملت مقايصة الامتصاص المناعي المرتبط بالإنزيم لاكتشاف أضداد مضاد الكارديوليبين في مجموعة مكونة من 26 سيدة عُرفن بأنهن متكررات الإجهاض (عائنين على الأقل ثلاثة إجهاضات تلقائية متوالية)، وفي مجموعة شاهدة مكونة من 26 مريضة وضعت كل منهن على الأقل مولوداً حياً واحداً من دون أي إجهاض. وقد اكتُشف مستوى مرتفع لنشاط أضداد مضاد الكارديوليبين بين 19.23% من متكررات الإجهاض، ولم يلاحظ ذلك في أي مريضة من المجموعة الشاهدة، الأمر الذي يُثبت وجود ترابط بين مستوى أضداد مضاد الكارديوليبين وبين الإجهاض المتكرر.

ABSTRACT The present study sought to determine whether the level of anticardiolipin antibodies in women with recurrent abortion differed from that in the general population. Enzyme-linked immunosorbent assay was used for detection of anticardiolipin antibodies in a group of 26 patients defined as habitual aborters (at least three consecutive spontaneous abortions), and in a control group of 26 patients each of whom had had at least one live birth without pregnancy wastage. A high level of anticardiolipin antibody activity was detected among 19.23% of the habitual aborters but in none of the controls, indicating an association between anticardiolipin antibody level and habitual abortion.

Les anticorps anticardiolipines chez les femmes ayant des avortements à répétition

RESUME Le but de la présente étude était de déterminer si le niveau des anticorps anticardiolipines chez les femmes ayant des avortements à répétition différait de celui de la population générale. L'épreuve immuno-enzymatique a été utilisée pour la détection des anticorps anticardiolipines dans un groupe de 26 patientes définies comme sujettes aux avortements à répétition (au minimum trois avortements spontanés consécutifs), et dans un groupe témoin de 26 patientes ayant eu chacune au moins une naissance vivante sans fausse couche. Un haut niveau d'activité des anticorps anticardiolipines a été détecté chez 19.23 % des personnes sujettes aux avortements à répétition tandis qu'il n'y avait aucune activité chez les témoins, indiquant une association entre le niveau des anticorps anticardiolipines et les avortements à répétition.

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Introduction

Anticardiolipin (aCL) antibodies are circulating autoantibodies (IgG, IgM, IgA) directed essentially against cardiolipin, a negatively charged phospholipid. These antibodies belong to the group of antiphospholipid (aPL) antibodies, which include lupus anticoagulant (LA) and the aspecific antibodies found in syphilis (reagin) detected by the VDRL test [1-4]. These antibodies can be considered a risk factor for thrombotic manifestations. Harris et al. [5] reported the association between aCL and thrombosis and in 1985, Derue et al. [6] reported the association between aCL and fetal loss. These antibodies are associated with antiphospholipid syndrome, which is now recognized as a distinct entity [2-17]. Spontaneous and recurrent abortion and fetal loss are features of this syndrome.

Different enzyme-linked immunosorbent assay (ELISA) methods are commercially available for the detection of aCL antibodies. Screening methods are very cost-effective, providing a one-step (3 immunoglobulin) answer, while isotyping methods allow the differentiation and quantification of the IgG and IgM antibodies. The presence of any one aCL antibody isotype, a combination of two, or indeed all three together may be associated with thrombosis and fetal loss [5,9]. We aimed to assess the level of aCL antibodies in women with recurrent abortion and compare it with aCL levels in women who had not experienced abortion.

Methods

Blood samples from 52 women attending our clinic were assessed for aCL antibodies (IgG, IgM). Half of them had experienced at least three consecutive abortions (Group A: the study group of women with recurrent

abortion) and half had had at least one live birth without pregnancy wastage (Group B: controls). Median age of the women was 30 years (range of 20-40 years).

Results

A raised aCL antibody titre was detected in five (19.23%) patients from Group A (the recurrent abortion group). In the five women, abortion occurred near the end of the first trimester and early second trimester. In only one woman did abortion occur (five times) in the 6-8 weeks after the last menstrual period. High IgG isotype levels (i.e. > 10 GPL units) were detected in five women, while IgM was found to be 8-9 MPL units in three women and negative in two. In the control group (Group B), no cases of raised aCL antibodies were detected.

The difference between aCL antibodies detected in Groups A and B was statistically significant (Fisher exact test = 0.05), indicating an association between raised aCL antibodies and habitual abortion.

Discussion

It has been recognized that women who are positive for aCL antibodies are at increased risk of repeated early miscarriages and second or third trimester fetal death [18]. One potential explanation for this outcome is that the sera of these women contain antibodies reactive with trophoblast cells, which are involved in the establishment of uteroplacental vasculature and maintenance of placental blood fluidity [8]. Another explanation is that aCL antibodies may exert a direct pathogenic effect by interfering with haemostatic processes that take place on the phospholipid membranes of cells such as platelets or endothelium [2,3]. It is also suggested that autoantibod-

ies may cause intravascular coagulation leading to recurrent abortion [9].

Examination of the placenta in individuals with aPL antibodies has shown thrombosis of the placenta and decidual vessel and multiple placental infarcts [19-21]. The extent of placenta infarction alone is usually insufficient to account for fetal death. It is likely therefore that thrombosis is only one of the underlying mechanisms involved in the etiology of pregnancy loss. Nevertheless, according to some authors, autoimmune aPL antibodies associated with thrombosis, thrombocytopenia and recurrent fetal loss tend to be predominantly of the IgG isotype. Furthermore, they tend to be present at higher titres, are persistent and require the presence of a cofactor (serum glycoprotein of 50 kD, also called β 2-glycoprotein) to enhance the anticardiolipin /cardiolipin reaction [22-27]. In contrast, aPL antibodies appearing secondary to drug exposure and infection are usually of the IgM isotype, tend to be at lower titres and transient, and do not require the presence of a cofactor.

A number of studies have found increasingly, an association between raised aCL antibodies and a history of pregnancy loss. In a study carried out by the author in Jordan in 1998, we found that women with a history of two or more miscarriages had a 17.6% prevalence rate of aCL antibodies. Others have found raised aCL antibodies in 19% of women with miscarriage history, compared to 3% in the control group [28]. Maclean et al. found aCL antibodies to be raised in 16.8% of such cases [29].

The prevalence of aCL antibodies in a low-risk obstetric population was studied by Lockwood et al. [30], and found to be 2.2%. A similar prevalence (1.2%) was detected in a low-risk population by Pattison et al. [31]. In a valuable study carried out by Balasch et al. [32], aPL antibody

positivity was found in 0.8% of 125 healthy women who had never been pregnant, but not found in 125 normal healthy parous women with no previous abortion, nor in 52 women in labour after normal pregnancies at term. We can say then that the prevalence of aCL antibodies in a low-risk population is less than 3%.

In the present study, of the 26 women with at least one live birth with no miscarriage (the control group), aCL antibodies were detected in none, while 19.23% of the women with recurrent abortion had raised levels, a highly significant difference. Similar results were obtained by Costa et al. [33], who found that aCL antibodies were raised in 4 (20%) out of 20 habitual aborters.

It is important to mention the study carried out by Takakwa et al. [34] on chromosome analysis, where he found a low incidence of chromosome abnormalities in aborted conceptuses of patients with positive aCL. This suggests that the antibody is strongly implicated in the genesis of recurrent abortions. Rai et al. [35] found first trimester loss of embryonic pregnancy to be the most common type of miscarriage in women with aPL antibodies. This may be a result of defective implantation and subsequent placentation.

It should be stressed that the presence of aCL antibodies does not preclude a successful pregnancy; it merely indicates a higher-risk pregnancy. The relationship between aCL antibodies and miscarriage is not clear. It may be that these antibodies are a result of a non-continuing pregnancy, rather than the cause. It is known that immunological abnormalities are associated in some women with recurrent miscarriages, and the study of other indices may help to establish the relationship between the immune system and miscarriage.

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