The Role of IL-2 and Rheumatoid Factor in Recurrent Spontaneous Abortion

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Abstract: It has been postulated that of repeated pregnancy losses in part may be due to immune causes. This research was carried out as case control study on fifty-six women with three or more RSA history (Group I) and sixty-three healthy women who have had no abortion history (Group II). Sera were examined for the presence of IL-2 and RF. Two out of 56 women in group I had IL-2 in serum. None of the women in group II showed IL-2 in serum. Also, 53.5% women in group I and 6.4% women in group II were positive for RF in different titers (P=0.002). Our finding shows that serum IL-2 concentration dose not affects pregnancy outcome. We recommend that the role of RF in pregnancy outcome should be considered.

Key words: IL-2 • Rheumatoid Factor • RSA

INTRODUCTION

Recurrent spontaneous abortions (RSA) are still a frequent reproductive problem worldwide, with three or more affecting 1% to 2% of women of reproductive age [1]. Despite several well established etiologic factors, the cause of RSA cannot be determined in almost 50% of the cases. It has been postulated that a part of these repeated pregnancy losses may be related to immune causes [2]. The response of T helper (Th) cells following activation is characterized functionally according to the cytokines they produce. Th1 cells secrete mainly interleukin (IL)-2, interferon (IFN)-γ and tumor necrosis factor (TNF)-β [3]. IL-2 figures prominently among cytokines that are particularly determined to the survival of the conceptus. The administration of IL-2 into the pregnant mice causes abortion [4]. Rheumatoid Factors (RF) is antibodies that recognize the Fc portion of IgG molecules as their antigens; RFs can be of any immunoglobulin isotype (IgM, IgG, IgE). Most of the RFs measured clinically are IgM RFs [5]. In the general (health) population, the frequency of RF positive individuals ranges from 1.3-4% in Caucasians to 30% in some tribes of North Americans Indians [6]. The small subset of B cells that express CD5 known as B-1a cells, appear to produce RF [7]. Many studies have illustrated the essential role of T cells in the class switching, where the cytokine production has an important impact on the type of the immunoglobulin produced by the B cells [8]. The aim of this study was to compare the levels of IL-2 (Th1 cytokine) and RF in sera of women having a history RSA and control group.

MATERIALS AND METHOD

This research was carried out as case control study on two different groups referred to Yazd Research and Clinical Centre for Infertility. Group I consisted of fifty-six women with three or more RSA history and group II consisted of sixty-three healthy women who have had no abortion history with at least one successful pregnancy. Aborter samples were normal in karyotype, TORCH negative and had no anatomical or endocrine problems. All cases were primary RSA. Blood samples (5 ml) was collected and as well as information for variables such as age, number of abortions, gestational age at the last abortion for RSA women, also number of pregnancy for control women were provided. The Local Institutional Review Board approved the experimental procedures, and signed informed consent was obtained from each woman. Sera were examined for the presence of IL-2 according to manufacture’s instructions (Bender medsystem GmbH, Vienna, Austria). The sensitivity of IL-2 assay was 3.5Pg ml⁻¹. RF (anti-human immunoglobulin) was determined by latex agglutination test and the presence of agglutination was considered positive.

RESULTS

The mean age of the women in group I was 28.2±4.4 years (range 21-42) and for the ones in group II, it was 26.7±4.8 years (range 18-37). There was no significant difference in the age of women in two groups. Pregnancy
loss numbers varied from 3 to 10 (4.2±1.4). The mean of gestational age in the last abortion was 11.45±2.85 weeks in group I. Two out of 56 women in group I had IL-2 in serum (35Pg ml⁻¹ and 10Pg ml⁻¹). None of the women in group II showed IL-2 in serum. Also, 53.5% women in group I and 6.4% women in group II were positive for RF in different titers (Fig 1). There was significant differences between groups I and II for RF (P=0.002).

**DISCUSSION**

In the present study, we measured IL-2 cytokine in serum of women with history of RSA abortion and reproductive age matched women without any abortion as control. While we were unable to detect IL-2 in the sera of control group, elevated concentrations of IL-2 in normal pregnancy as compared with non-pregnant controls have been reported [9]. Only two out of fifty-six women with history of RSA were positive for IL-2 in serum. In other study, we showed that peripheral blood lymphocytes of women with RSA secrete higher concentrations of certain Th1 cytokines such as IL-2 upon stimulation by mitogen as compared with women with successful pregnancy [10]. However, during pregnancy Th1 cytokine production is down-regulated [11]. Our results could not show similar profile of IL-2 production in studied serum. In the part of this research, RF was measured in two groups. Our results showed that 53.5% of women with history of RSA were positive for RF and its level was significantly higher than control group. It has been reported that some autoantibodies adversely affect the course of pregnancy and fetal growth [12]. For rheumatoid factors, the only report referring to prevalence during pregnancy is that of Ailus [13]. 8.3% of women with RSA history were studied by Iijima et al showed RF in serum [14]. RFs are autoantibodies associated with rheumatoid arthritis. They can be detected in normal individuals, although transiently. Recently, it has been shown B cells that produce RF only do so when activated two signals, one from engagement of the B cell receptor and the other from recognition of a pathogen-associated molecular pattern through a Toll-like receptor. These autoantibodies thus link the innate and acquired immune response [15]. The roles of some infectious agent in recurrent abortions are well known. However maybe, there are correlation between microbial abortion and RF production. We recommended that the role of RF in pregnancy outcome should be considered.

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**REFERENCES**


