World Journal of Medical Sciences 2 (2): 105-107, 2007
ISSN 1817-3055

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

[1]Hossein Hadinedoushan, [2]Abass Aflatounian and [3]Morteza Anvari

[1]Department of Immunology,
[2]Department of Gynecology and Obstetrics,
[3]Department of Anatomy, Research and Clinical Centre for Infertility, Yazd, Iran

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]. Rhumatoid 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, Austeria). The sensivity 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

Corresponding Author: Dr. Hossein Hadinedoushan, Research and Clinical Centre for Infertility, Yazd, Iran

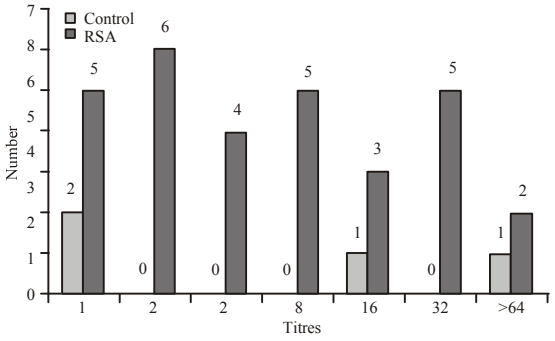

Fig. 1: The frequency of RF titers in RSA and control groups

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 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, althought 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.

ACKNOWLEDGMENT

Shahid Sadoughi University of Medical Sciences supported this work. The authors are grateful to Mr Hossein Fazli for technical assistance.

REFERENCES

1. Regan, L., 1998. Overview of recurrent miscarriage. Gynaecology Forum., 3: 3-7.
2. Laird, S.M., E.M. Tuckerman, B.A. Cork, S. Linjawi, A.I. Blakemore and T.C. Li, 2003. A review of immune cells and molecules in women with recurrent miscarriage. Hum Reprod Update, 9(2): 163-174.
3. Mosmann, T.R. and S. Sad, 1996. The expanding universe of T-cell subsets: Th1, Th2 and more. Immunol. Today, 3: 138-146.
4. Chaouat, G., M. Menu, D.A. Clark, M. Dy, M. Minkowski and T.G. Wegmann, 1990. Control of fetal survival in CBA × DBA/2 mice by lymphokine therapy. J. Reprod. Fertil., 89(2): 447-457.
5. Nielen, M.M.J., D. Van Schaardenburg, H.W. Reesink, R.J. Van de Stadt, I.E. Van der Horst-bruinsma, M.H. De Koning, *et al*. 2004. Specific autoantibodies precede the symptoms of rheumatoid arthritis. Arthritis Rheum, 50: 380-386.
6. Jansen, A.L., I. van der Horst-Bruinsma, D. van Schaardenburg, R.J. van de Stadt, M.H. de Koning and B.A. Dijkmans, 2002. Rheumatoid factor and antibodies to cyclic citrullinated peptide differentiate rheumatoid arthritis from undifferentiated polyarthritis in patients with early arthritis. J. Rheumatol., 29(10): 2034-2040.
7. Mantovani, L., R.L. Wilder and P. Casali, 1993. Human rheumatoid B-1a (CD5+ B) cells make somatically hypermutated high affinity IgM rheumatoid factors. J. Immunol., 151(1): 473-488.
8. Stavnezer, J., 1996. Immunoglobulin class switching. Curr Opin Immunol., 8: 199-205.
9. Favier, R., P. Edelman, J.Y. Mary, G. Sadoul and L. Douay, 1990. Presence of elevated serum interleukin-2 levels in pregnant women. N. Engl. J. Med., 322(4): 270.

10. Hossein, H., M. Mahroo, A. Abbas, A. Firouzeh and H. Nadia, 2004. Cytokine production by peripheral blood mononuclear cells in recurrent miscarriage. Cytokine, 28(2): 83-86.
11. Rezaei, A. and A. Dabbagh, 2002. T-helper (1) cytokines increase during early pregnancy in women with a history of recurrent spontaneous abortion. Med. Sci. Monit., 8(8): 607-10.
12. Kotlan, B., A. Padanyi, J. Batorfi, V. Fulop, I. Szigetvari, K. Rajczy, *et al.* 2006. Alloimmune and autoimmune background in recurrent pregnancy loss-successful immunotherapy by intravenous immunoglobulin. Am. J. Reprod. Immunol., 55(5): 331-40.
13. Ailus, K.T., 1994. A follow-up study of immunoglobulin levels and autoantibodies in an unselected pregnant population. Am. J. Reprod. Immunol., 31(4): 189-196.
14. Iijima, T., H. Tada, Y. Hidaka, N. Mitsuda, Y. Murata and N. Amino, 1997. Effects of autoantibodies on the course of pregnancy and fetal growth. Obstet Gynecol., 90(3): 364-369.
15. Chaiamnuay, S. and S.L. Bridges, 2005. Jr: The role of B cells and autoantibodies in rheumatoid arthritis: Pathophysiology, 12(3): 203-216.