Short Communication

Psychosocial Factors Regulating Natural-Killer Cell Activity in Recurrent Spontaneous Abortions

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PROBLEM: The preconceptional natural-killer cell (NK) activity predicts subsequent miscarriage among women with unexplained recurrent spontaneous abortion (RSA). Psycho-neuro-immuno-endocrine network has recently been proposed as a mechanism for abortions. We therefore examined which psychosocial factors influenced the NK activity among women with RSA.

METHOD OF STUDY: We measured the preconceptional NK activity of 61 women with a history two consecutive unexplained first-trimester miscarriages and no live births. We also administered semi-structured interviews and a battery of self-report questionnaires to assess their social support, personality, self-esteem and psychiatric symptoms.

RESULTS: The preconceptional NK activity was negatively correlated with the women's neuroticism personality trait ($r = -0.32$, $P = 0.01$) and current depressive symptoms ($r = -0.26$, $P = 0.05$), and positively correlated with their self-esteem ($r = 0.34$, $P = 0.01$).

CONCLUSIONS: In addition to several substances such as transforming-growth-factor beta and granulocyte-macrophase colony-stimulating factor, we found that low neuroticism, low depression scale score and high self-esteem contributed to high NK activity among women with RSA.

Key words:
Depression, natural-killer cell, personality, recurrent spontaneous abortion, self-esteem, social support

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INTRODUCTION

Spontaneous abortion is a common complication of pregnancy. An estimated 5–15% of women will lose at least one pregnancy in the form of a clinically detectable miscarriage[1,2]; and some 2% will have recurrent spontaneous abortions (RSA).[3] No credible cause is currently available for more than half of these cases with RSA.[4]

We have previously reported that the preconceptional natural-killer cell (NK) activity predicts subsequent miscarriage among women with unexplained RSA.[5] Immunologic function is known to be under influence of various psychological factors,[6] and psycho-neuro-immuno-endocrine network has recently been proposed as a mechanism for abortions and for prevention of abortions.[7]

The present short communication, therefore, examined psychosocial factors influencing preconceptional NK activity among women with RSA.

SUBJECTS AND METHODS

Subjects were 61 women with a history of two consecutive first-trimester miscarriages and no live births. None of the women had any identifiable causes for RSA, such as uterine anomalies, endocrine abnormalities including luteal-phase defects, polycystic ovary syndrome, chromosomal abnormalities in either partner, autoimmune abnormalities including evidence of antiphospholipid antibodies, or metabolic disorders. All women and their husbands gave written informed consent.

Blood samples for NK activity assessment were taken from these women at least 3 months after their second spontaneous abortion and before they had conceived again. NK activity was measured by a chromium-51 release cytotoxicity assay,[8] with K562 human myeloid leukemia cells as targets. 3.7×10^3 Bq ^{51}Cr-labelled target cells (1×10^4 per well) were seeded with 2×10^5 per well effector cells (fresh peripheral blood mononuclear cells) in triplicate in U-bottomed 96-well plates. After 4 hr incubation at 37°C, activity in the supernatant from each well was measured in an autogamma-scintillation counter. The % cytotoxicity was calculated as: ([test cpm − spontaneous cpm]/ [maximum cpm − spontaneous cpm]) × 100, where cpm = counts per minute and % cytotoxicity was taken to represent NK activity.

Semi-structured interviews with tape-recording were also conducted at the same time for each couple in separate rooms of the hospital. Interviews probed about the household environment, educational and occupational history, and emotional impacts of the first and second abortions as well as coping styles and social support that the women received on each occasion. Each interview lasted approximately 1–2 hr.

The subjects were also asked to complete a self-report questionnaire battery including the NEO Five Factor Index (NEO FFI), Rosenberg's Self-Esteem Scale (SES), Intimate Bond Measure (IBM), and Symptom Checklist-90 Revised (SCL-90-R). The NEO-FFI[9] assesses the subject's personality according to the five-factor model, which is gaining increasingly wider acceptance in recent years. The so-called Big Five factors refer to neuroticism, extraversion, openness to experience, agreeableness and conscientiousness. The past decade has in fact witnessed a rapid convergence of views regarding the structure of personality traits, because these five factors have repeatedly been found to account for a large amount of variance in the data, irrespective of sampling procedures, instruments used, modes of rating and techniques of factor analysis.[10]

Self-esteem refers to positive feelings towards oneself. The well-adjusted person has some appreciation of his own self-worth and feels accepted by those around him. This positive appreciation about oneself was measured by Rosenberg's SES,[11] one of the most widely used scales in social psychology.

The IBM is a reliable and valid measure of care and control experienced with one's marital partner.[12] It provides a simple and efficient measure of two central constructs underlying intimate relationships.

Finally, the SCL-90-R is an inventory designed primarily to reflect the psychological symptom patterns of psychiatric and medical patients. On factor analysis, the following nine dimensions have been identified: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. Its reliability and validity have been well-documented.[13] It is widely used and well-accepted, and is considered to be the best of its kind, especially because it covers all aspects of psychopathology.[14]

RESULTS

The average age of the women was 29.5 (SD = 3.6).

The preconceptional NK activity did not show any significant correlation with the women's perceived social support or marital quality. It was negatively correlated with the women's neuroticism personality trait ($r = -0.32$, $P = 0.01$) and current depressive symptoms ($r = -0.26$, $P = 0.05$), and positively correlated with their self-esteem ($r = 0.34$, $P = 0.01$).

In order to search for the strongest predictor for the NK activity, we entered these three variables into stepwise multiple regression and found self-esteem to be the only significant predictor ($\beta = 0.34$, $P = 0.01$).

DISCUSSION

In normal pregnancies, NK activity seems to be downregulated. Women with a raised preconceptual level of NK activity were 3.5 times more likely to lose the next pregnancy than those with normal levels of NK activity.[5] On the other hand, successful pregnancies were achieved in recurrent spontaneous aborters whose NK activity decreased after allogeneic leucocyte immunotherapy.[8,15] Several substances such as prostaglandin E2, transforming-growth-factor beta, and granulocyte-macrophase colony-stimulating factor seem to play a part in the immunoendocrine network in pregnancy maintenance.[16,17]

The present authors further found that low neuroticism, low depression scale score and high self-esteem contributed to high NK activity. Briefly, neuroticism is the predisposition to experience psychological distress in the form of anxiety, anger, depression, and other negative affects. These findings may, therefore, appear somewhat counter-intuitive, because they suggest that emotionally stable women with high self-esteem show raised NK activity and thus may have smaller chances of successful pregnancies. However, if we postulate that high self-esteem is linked to survival of individuals rather than to survival of species, the observed association may appear more plausible. Or it

may also be possible that individuals who are able to ventilate out their negative emotions are more likely to have lower NK activity and succeed in the next pregnancies. Some psychoimmunological studies have documented negative association between NK activity and neuroticism[18] or depression[19] and that negative self-evaluation can lower NK cell activity,[20] although there are conflicting reports as well.[21,22] For example, Laudenslager[23] reported out that depression, comorbid with PTSD, was associated with increased natural cytotoxicity. Many psychological factors may therefore interact and bear on NK activity. This seems to complicate immuno-psychological relationships.

We are currently following up this cohort throughout their third pregnancies and will examine how the psycho-neuro-immunological network interacts in the causation of RSA.

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