ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN — POLONIA
VOL. LV, 3 SECTIO D 2000

[1] Department of Medical Microbiology, University School of Medicine, Lublin
Katedra i Zakład Mikrobiologii Lekarkiej Akademii Medycznej w Lublinie

[2] Department of Medical Genetics, University School of Medicine, Lublin
Zakład Genetyki Medycznej Akademii Medycznej w Lublinie

[3] II Department of Gynaecological Surgery, University School of Medicine, Lublin
Klinika Ginekologii Operacyjnej II Katedry Położnictwa i Chorób Kobiecych
Akademii Medycznej w Lublinie

[4] I Department of Gynaecological Surgery, University School of Medicine, Lublin
Klinika Ginekologii Operacyjnej I Katedry Położnictwa i Chorób Kobiecych
Akademii Medycznej w Lublinie

GRZEGORZ POLAK[1], MARIA KOZIOŁ-MONTEWKA[1],
RAFAŁ TARKOWSKI[2], MAREK GOGACZ[3], JAN KOTARSKI[4]

Concentration of interleukin-10 in peritoneal fluid of women with endometriosis

Stężenie interleukiny-10 w płynie otrzewnowym kobiet z endometriozą

Endometriosis is a common disease, characterised by the presence of endometrial tissue in abnormal locations. In spite of intensive investigations and the fact that endometriosis is one of the most common causes of reproductive failures, the pathophysiology of the disease still remains enigmatic. Accumulated data suggest that a deficient immune response to endometrial implants may be involved in the pathogenesis of the disease [5].

Interleukin-10 (IL-10) is a cytokine produced mainly by Th2 cells. IL-10 modulates the functions of many immunocompetent cells, including the inhibition of proinflammatory cytokines (IL-1α, IL-6, IL-8, TNFα) production. Interleukin-10 also inhibits nitric oxide and reactive oxygen species synthesis of activated monocytes/macrophages [2]. Because IL-10 is involved in the suppression of the inflammatory response, elevated peritoneal fluid (PF) levels of this cytokine may play a role in the pathophysiology of endometriosis.

In 1996 Rana et al. [8] reported that both basal and LPS stimulated production of IL-10 by the peritoneal macrophages was significantly elevated in women with endometriosis. This observation was confirmed by Wu et al. [10] study. However endometriosis had no effect on the basal or stimulated synthesis of IL-10 by peripheral blood monocytes [1]. Several authors found elevated levels of IL-10 in PF of women

with endometriosis [3, 7], however some investigator did not observe such difference [4, 6].

The aim of this study was to estimate the peritoneal fluid interleukin-10 concentration in patients with endometriosis.

MATERIALS AND METHODS

Twenty women of reproductive age were enrolled in the study. The study groups consisted of 10 patients with mild or moderate endometriosis and 10 women with benign, noninflamatory ovarian tumours. The endometriosis was staged according to the revised American Fertility Society classification [9]. In the group with ovarian tumours histologic examination confirmed the presence of functional, follicle cysts. All surgery was performed in the follicular phase of the menstrual cycle.

All peritoneal fluid was aspirated during laparoscopy from the anterior and posterior cul-de-sacs. The aspirated fluid was immediately transferred to the laboratory for further processing. PF was centrifuged at 500 x g for 10 minutes, and the supernatant was frozen at –75°C until analysis.

Peritoneal fluid interleukin-10 concentration was measured by an enzyme-linked immunoasorbent assay according to the manufacturer's instruction (Pharmingen).

Because interleukin-10 concentrations were not normally distributed, they were analyzed using Mann–Whitney U test. The values are presented as mean ± SEM. P value less than 0.05 was considered statistically significant.

RESULTS

IL-10 levels were detectable in PF of all women from both endometriotic and the reference group. Mean (± SEM) peritoneal fluid IL-10 concentrations were 14.36 ± 3.89 pg/ml in patients with endometriosis (Min. 4.71; Max. 37.92 pg/ml) and 12.56 ± 3.9 pg/ml in women without the disease (Min. 1.6; Max. 39.47 pg/ml). No statistically significant difference between the study groups was noted ($p = 0.62$).

The results are presented in Figure 1.

DISCUSSION

In our present study we have found no significant difference in peritoneal fluid interleukin-10 level between patients with endometriosis and women suffering from benign, noninflamatory ovarian tumours. Similar observations were noted by McLaren et al. [6] and Hsu et al. [4], who demonstrated that there was no significant difference in the PF IL-10 levels between women with and without endometriosis. Ho et al. [3] reported that the level of interleukin-10 is increased in PF of women with endometriosis, but their results were obtained in the group of women with the early stage of the disease.

Peritoneal macrophages obtained from patients with endometriosis have been shown to secrete more IL-10 under both basal and LPS stimulated conditions [8, 10].

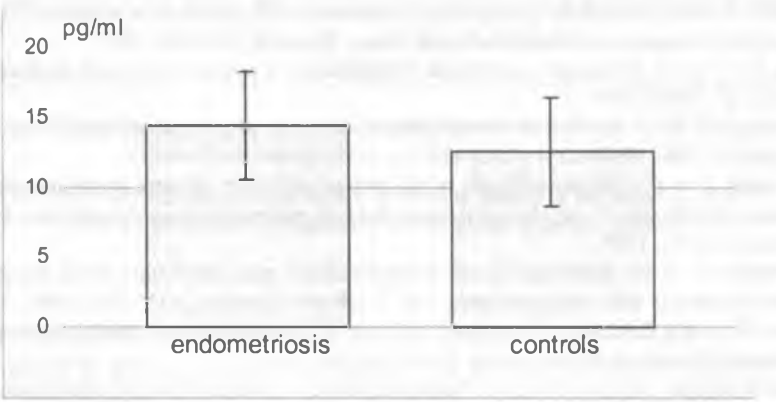

Figure 1. Mean (±SEM) peritoneal fluid interleukin-10 concentration in women with and without endometriosis

Therefore, increased peritoneal fluid levels of this cytokine should be observed in patients with endometriosis. In light of this hypothesis, our results are difficult to explain, but may reflect the increased interleukin-10 metabolism.

In the literature we have not found any data about IL-10 binding to the receptor during the retrograde menstruation, so we can only hypothetize that the retrograde menstrual flow might involve increased binding to IL-10 receptors in order to limit the inflammatory reaction. This hypothesis might be an explanation for our results. This situation may lead to the suppression of macrophage activation, and therefore may be partially responsible for the disturbed immune regulation, observed in women with endometriosis.

In summary, we failed to demonstrate that elevated PF interleukin-10 concentration plays a role in the pathogenesis of the disease. Because of its immunosuppressive properties higher concentration of IL-10 could be one of the factors responsible for the immonologic dysfunction, that have been proposed to explain the pathophysiology of endometriosis.

CONCLUSIONS

Peritoneal fluid interleukin-10 concentration does not appear to be affected by the presence of endometriosis.

REFERENCES

1. *Braun D. P. et al.*: Spontaneus and induced synthesis of cytokines by peripheral blood monocytes in patients with endometriosis. Fertil. Steril., 65, 1125, 1996.
2. *Curfs J. H. A. et al.*: A primer on cytokines: sources, receptors, effects, and inducers. Clin. Microbiol. Rev., 10, 742, 1997.

3. *Ho H. N. et al.*: Peritoneal interleukin-10 increases with decrease in activated CD4+ lymphocytes in women with endometriosis. Hum. Reprod., 12, 2328, 1997.
4. *Hsu C. C. et al.*: Enhanced interleukin-4 expression in patients with endometriosis. Fertil. Steril., 67, 1059, 1997.
5. *Koninckx P. R. et al.*: Endometriotic disease: the role of peritoneal fluid. Hum. Reprod. Update, 4, 741, 1998.
6. *McLaren J. et al.*: Decreased levels of the potent regulator of monocyte/macrophage activation, interleukin-13, in the peritoneal fluid of patients with endometriosis. Hum. Reprod., 12, 1307, 1997.
7. *Punnonen J. et al.*: Increased levels of interleukin-6 and interleukin-10 in the peritoneal fluid of patients with endometriosis. Am. J. Obstet. Gynecol., 174, 1522, 1996.
8. *Rana N. et al.*: Basal and stimulated secretion of cytokines by peritoneal macrophages in women with endometriosis. Fertil. Steril., 65, 925, 1996.
9. The American Fertility Society.: Revised American Fertility Society classification of endometriosis: 1985. Fertil. Steril., 43, 351, 1985.
10. *Wu M. Y. et al.*: Increase in the production of interleukin-6, interleukin-10, and interleukin-12 by lipopolysaccharide- stimulated peritoneal macrophages from women with endometriosis. Am. J. Reprod. Immunol., 41, 106, 1999.

STRESZCZENIE

Pomimo znacznej częstości występowania endometriozy oraz licznych badań etiopatogeneza schorzenia nie została ostatecznie wyjaśniona. Wiele doniesień wskazuje na udział zmian w układzie immunologicznym płynu otrzewnowego w rozwoju choroby. Celem niniejszej pracy była ocena stężenia interleukiny-10 w płynie otrzewnowym pacjentek z endometriozą w porównaniu do kobiet operowanych z powodu niezapalnych, łagodnych torbieli jajników. Średnie (± SEM) stężenie IL-10 w płynie otrzewnowym pacjentek z endometriozą wynosiło 14.36 ± 3.89 pg/ml, zaś w grupie referencyjnej 12.56 ± 3.9 pg/ml. Nie stwierdzono istotnych statystycznie różnic w koncentracji IL-10 w płynie otrzewnowym pomiędzy badanymi grupami ($p = 0.62$).