Artigo Original

TH1 AND TH2 IMMUNE RESPONSES RELATED TO PELVIC ENDOMETRIOSIS

Sergio Podgaec[1*], João Antonio Dias Junior[2], Charles Chapron[3], Ricardo Manoel de Oliveira[4], Edmund Chada Baracat[5], Maurício Simões Abrão[6]
Trabalho realizado no Departamento de Obstetrícia e Ginecologia da Faculdade de Medicina da Universidade de São Paulo

SUMMARY

Objective. This study analyzed the relationship between clinical characteristics of endometriosis and Th1/Th2 immune response patterns.

Methods. A prospective study was performed with 65 patients with endometriosis (Group A) and 33 without the disease (Group B). Measurement of IL 2, 4 and 10, TNF-alpha and IFN-gamma was carried out in peripheral blood and peritoneal fluid.

Results. Serum TNF-alpha was higher in patients with endometriosis who had deep dyspareunia compared to controls (mean 4.5 pg/ml and 2.3 pg/ml, $p<0.05$). Among these patients ($n=32$), 65.5% had deep endometriosis. Patients with endometriosis and infertility had higher IL-2 concentrations in peritoneal fluid than controls (mean 5.9 pg/ml and 0.2 pg/ml, $p<0.05$). Among these patients ($n=22$), 63.5% ($n=14$) had deep endometriosis. A higher concentration of IL-10 was also observed in patients with ovarian endometriosis when compared to those without this type of disease, as well as when compared to control group patients (mean 50pg/ml, 18.7pg/ml and 25.7pg/ml, $p<0.05$).

Conclusions. These results suggest that when specific clinical data are associated with a higher production of certain cytokines, there is a Th1 response pattern that may be related to deep infiltrating endometriosis.

Correspondência:
Rua João Moura 627, cj
23 - Jardim América
São Paulo - SP
CEP: 05412-911

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Introduction

Endometriosis is characterized by the presence of endometrial glands and/or stroma in extrauterine sites, principally in ovaries and uterosacral ligaments, and affects around 10-15% of women during menacme[1]. Deep endometriosis is the more aggressive form of this disease and it infiltrates the retrocervical area, posterior vaginal wall, rectosigmoid regions, ureters and bladder to a depth of more than 5 mm and may even involve pelvic lymph nodes[2,3].

Various investigators have studied the role of the immunological system in endometriosis, and several abnormalities have been detected[4]. The principal line of current reasoning provides an update on the menstrual reflux theory[5] by hypothesizing that the endometrial cells penetrating the peritoneal cavity should normally be swept out by the organism defense system since these cells do not belong to this site. However, in women with endometriosis, this mechanism could suffer a bias and the process of adequate cell removal would fail to occur, permitting implantation and development of these cells in the peritoneal cavity, leading to formation of the initial endometriotic foci[6].

The Th1/Th2 imbalance hypothesis is based upon the concept that T helper lymphocytes are involved with two different patterns of cytokine secretion[7]. Th1 cells stimulate production of IL-2 and IFN-gamma, cytokines that promote the action of NK cells and macrophages and Th2 cells stimulate the production of IL-4 and IL-10, cytokines involved with B cells. When Th1 immune response pattern is magnified, it could be associated to rheumatoid arthritis, multiple sclerosis and type 1 diabetes and

1. Doutor em Ginecologia pela Faculdade de Medicina da Universidade de São Paulo – USP e Médico Assistente da Clínica Ginecológica do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo – HCFMUSP, São Paulo, SP
2. Pós-graduando pela Faculdade de Medicina da Universidade de São Paulo – FMUSP, São Paulo, SP
3. Professor Department de Gynécologie CHU Cochin- Sant Vincent de Paul, Université Descartes Paris V, Paris France, Paris, France
4. Patologista Clínico e Médico Chefe da RDO Diagnósticos, São Paulo, SP
5. Professor Titular da Disciplina de Ginecologia da Faculdade de Medicina da Universidade de São Paulo – FMUSP, São Paulo, SP
6. Professor Livre Docente pelo Departamento de Obstetrícia e Ginecologia da Faculdade de Medicina da Universidade de São Paulo – FMUSP, São Paulo, SP

a Th2 overstated pattern is present in allergic diseases[8].

In several clinical situations, depending on the characteristics of each disease, such as AIDS[9], cardiac[10] and neurological disorders[11] and in human reproduction[12], a certain type of Th1/Th2 immune response pattern is predominant. Our previous results showed that endometriosis is a complex disease with co-existence of both responses since we observed an increase in Interferon-gamma and IL-10 in patients with endometriosis when compared to a control group of patients without the disease[13].

In deeply infiltrating endometriosis, the characteristics of cell immunity appear to predominate, with the action of cells, enzymes and cytokines provoking adhesion, infiltration and maintenance of the foci of ectopic endometrial tissue. In view of these findings, the present study brings the theory of Th1/Th2 balance to endometriosis by proposing to evaluate the predominant pattern of Th1 over Th2 immune response in accordance with characteristics of the disease such as clinical status, staging and sites affected by endometriosis.

Methods

Ninety-eight patients were consecutively included in a prospective study between January 2004 and November 2005 at the Endometriosis Clinic, Department of Gynecology at the Teaching Hospital of the University Of São Paulo School Of Medicine. The institution's internal review board approved the study (Approval # 601/03), and all participants read and signed the informed consent form.

Clinical suspicion of endometriosis was based upon patient symptoms and included dismenorrhea, deep dyspareunia, chronic pelvic pain, infertility and cyclical alterations in bowel and urinary habits occurring only during menstruation. After physical exam, patients were submitted to transvaginal ultrasound and MRI. According to the suspicion of presence of ovarian endometrioma, deep infiltrating lesions or if the patient had persistent pain or infertility, a surgical laparoscopic procedure was indicated. Laparoscopy was performed by the same surgeons (SP, MSA), all endometriotic tissue was resected for histological confirmation of the disease.

Once the surgical indication had been defined, 5 ml of peripheral blood were collected prior to initiating anesthesia procedures. Immediately after the lens was passed through the infraumbilical catheter, 2-10 ml of peritoneal fluid were collected from the anterior and/or posterior cul-de-sac. There was no peritoneal fluid in twelve patients during laparoscopy, peritoneal flushing was not used to obtain fluid samples and there was no gross blood contamination. The material was frozen at -80ºC and was only thawed for cytokine measurement after all data had been collected.

Patients were then divided into two groups: those with endometriosis (group A) and those without the disease (group B). Inclusion criteria for Group A were: 18-40 years of age, histologically confirmed endometriosis, absence of autoimmune disease, eumenorrheic patients with menstrual cycles of 26-32 days and non-use of hormone therapy in the three months preceding surgical procedure. Inclusion criteria for Group B were identical to those for Group A except for absence of endometriosis, which was confirmed during surgery.

During the surgical procedure, patients with endometriosis had their disease classified in stages I to IV in accordance with the criteria of the American Society for Reproductive Medicine (Revised ASRM, 1996). However, for the purposes of statistical analysis, stages I and II were grouped together and referred to as initial stages, while stages III and IV were grouped together and referred to as advanced stages of the disease. Sites affected by the disease were defined according to the following criteria: for the disease to be considered peritoneal, foci had to be exclusively peritoneal without presence of the deep disease (retrocervical, posterior vaginal wall and rectosigmoid regions, ureters and bladder) or ovarian disease. Ovarian endometriosis was defined as the absence of deep disease irrespective of peritoneal foci, whereas in the definition of deep endometriosis no restrictions were made with respect to the presence of peritoneal or ovarian disease.

Cytokine measurement

The cytokines analyzed in this study, tumor necrosis factor-alpha, interferon-gamma, interleukin-2, interleukin-4 and interleukin-10, were measured using a flow cytometer (BD FACS-Calibur, Franklin Lakes, New Jersey, USA). The kit used for measuring cytokines was the BD Cytometric Bead Array (CBA), catalogue 551809, manufactured by Pharmingen, Becton Dickinson & Co. (San Diego, California, USA). All tests were carried out in accordance with the manufacturer's instructions.

Statistical analysis

Categorical variables were analyzed using the Chi-square test and continuous quantitative variables were compared using the non-parametric Mann-Whitney test. Patients with endometriosis were classified according to stage and site affected, and non-parametric analysis was carried out using the Kruskal-Wallis test. All statistical calculations were performed with the SPSS software program (SPSS Inc., USA) and the level of significance established was 5%.

Results

Ninety-eight women were analyzed, 65 with endometriosis (Group A) and 33 without the disease (Group B). Mean age of patients in Group A was 32.1 ± 5.4 years, not significantly different from that of patients in Group B, 32.9 ± 5.1 years.

Concerning clinical data, there was a statistical difference between the two groups: 64.6% and 49.2% of patients with endometriosis presented, respectively, dysmenorrhea and cyclic bowel symptoms, while 27.3% and 6.1% of patients without the disease presented these complaints. Among patients with endometriosis who complained of deep dyspareunia (n=32), 65.5% had DIE, while among those who did not have this symptom (n=33), 30.3% had deep endometriosis.

Table 1 compares median values of serum concentrations of cytokines in group A and B patients according to the symptoms referred. An increase in TNF-alpha was found in patients of Group A with deep dyspareunia compared to patients of Group B. Comparison of the median serum concentrations of cytokines in relation to characteristics of patients in Groups A and B disclosed no difference with respect to staging (ASRM, 1996) and affected sites (Table 2).

Table 1 - Comparison of median (range) serum cytokine concentrations (pg/ml) between groups of patients with (A) and without endometriosis (B) according to clinical status.

	TNF-alpha	IFN-gamma	IL-2	IL-4	IL-10
Dysmenorrheaa					
Group A (n=42)	2.6 (0-9.1)	1.7(0-5.6)	7.2(0-26)	2.0(0-6.3)	3.3(0-12.9)
Group B (n=9)	4.4(1.3-9.8)	2.4(1.3-3.5)	9.3(2.5-9.7)	3.0(0-4.1)	4.9(1.2-6.9)
Dyspareunia					
Group A (n=32)	4.5*(0-9.6)	1.6(0-4.1)	7.6(0-23.3)	1.8(0-6.1)	3.0(0-6.1)
Group B (n=12)	2.3(1.3-3.5)	2 (0-6.6)	8.0(0-26)	2.9(1.2-3.5)	3.6(0-4.5)
Chronic pelvic pain					
Group A (n=39)	2.0(0-8.1)	0.9(0-11.7)	6.1(0-34.1)	1.7(0.6-4)	3.2(0-12.1)
Group B (n=13)	3.5(2.1-10.4)	2.1(1.8-6.5)	9.7(2.8-9.9)	2.6(1.5-2.9)	3.0(1.2-3.9)
Infertility					
Group A (n=22)	2.2(0-5.5)	1.7(1.1-5.2)	5.9(2.5-8)	1.7(0-6.1)	2.5(0-4.5)
Group B (n=8)	4.2(1.8-10.4)	1.8(1.3-6.5)	2.7(0-11)	2.0(1.2-4.1)	3.1(0-5.9)
Cyclical alterations in bowel habits					
Group A (n=32)	2.3(1.1-9.5)	1.4(0-11.7)	6.1(1.3-8.2)	1.5(0.8-6.3)	3.6(0-12.5)
Group B (n=1)	6.2	2.8	8.1	2.2	2.6
Cyclical alterations in urinary habits					
Group A (n=1)	2.3	0.8	4.6	1.4	2.8
Group B (n=0)	-	-	-	-	-

* p<0.05

Table 2- Comparison of median (range) serum cytokine concentrations (pg/ml) between groups of patients with (A) and without (B) endometriosis according to staging (ASRM, 1996) and site affected by endometriosis.

	TNF-alpha	IFN-gamma	IL-2	IL-4	IL-10
Staging					
Initial (n=28)	3.8(0-9.4)	2.0(0-5.6)	8.1(0-18.1)	2.1(0-6.3)	2.8(0-10.5)
Advanced (n=37)	2.3(0-9.6)	1.5(0-11.7)	6(0-34.1)	1.7(0-6.3)	3.7(0-12.9)
Group B (n=33)	3.7 (0-10.4)	2.1 (0-6.6)	8.3 (0-26)	2.0 (0-4.1)	3.1 (0-7.5)
Site affected					
With peritoneal disease (n=12)	2.3(0.4-9.1)	1.8(0-2.1)	3.4(0.5-9.8)	2.1(0-4.7)	3.3(0-9.1)
Absence of peritoneal disease (n=53)	2.4(0-8.3)	1.5(0-3.2)	8.8(1-30.1)	1.7(0-5.4)	3.2(0-8.8)
Group B (n=33)	3.7 (0-10.4)	2.1 (0-6.6)	8.3 (0-26)	2.0 (0-4.1)	3.1 (0-7.5)
With ovarian disease (n=19)	2.7(0-4.5)	1.6(0-3.5)	8. 9(0-28.2)	1.9(0.5-6.1)	3.4(0.5-11)
Absence of ovarian disease (n=46)	2.3(0.8-8.1)	2.0(0.5-4)	4.5(0-8.7)	1.9(0-3.8)	2.5(0.9-3)
Group B (n=33)	3.7 (0-10.4)	2.1 (0-6.6)	8.3 (0-26)	2.0 (0-4.1)	3.1 (0-7.5)
With deep disease (n=34)	2.0(0-9.6)	1.6(0-11.7)	8.3(0-34.1)	1.7(0-6.3)	3.4(0-12.9)
Absence of deep disease (n=31)	3.8(0.7-7.1)	1.9(0.9-2.1)	7.8(0-21.1)	2.1(0.8-6.2)	3.0(0-6.2)
Group B (n=33)	3.7 (0-10.4)	2.1 (0-6.6)	8.3 (0-26)	2.0 (0-4.1)	3.1 (0-7.5)

Table 3 - Comparison of median (range) cytokine concentrations measured in peritoneal fluid (pg/ml) between groups of patients with (A) and without endometriosis (B) according to clinical status.

	TNF-alpha	IFN-gamma	IL-2	IL-4	IL-10
Dysmenorrhea					
Group A (n=42)	1.5(0-9.5)	1.1(0.5-4.9)	2.4(0-4.5)	4.5(0-8.5)	4.5(0-8.3)
Group B (n=9)	4.4(1.9-12.4)	0.3(0-3.4)	1.0(0-6.2)	8.1(0-66.3)	8.4(3.9-10.5)
Dyspareunia					
Group A (n=32)	3.4(0-7.4)	0.5(0-1.7)	0.8(0-7.1)	2.4(0-4.5)	7.4(0-12.9)
Group B (n=12)	4.0(2.1-20.7)	0.4(0-2.7)	0.8(0-2.5)	1.8(1.1-7.4)	10.8(5.4-92.7)
Chronic pelvic pain					
Group A (n=39)	4.5 (2.5-11.5)	1.5(0-4.8)	1.5(0.8-7.1)	1.5(1-29.8)	6.4(3.5-11)
Group B (n=13)	2.9 (2.4-20.7)	2.3(0.2-1.5)	0.9(0-5.6)	1.9(0-9.8)	10.7(4.5-11.5)
Infertility					
Group A (n=22)	2.8 (1.7-8.4)	1.2(0.5-1.5)	**5.9***(0.7-7)	2.1(0.5-5.7)	5.7(1.5-772.5)
Group B (n=8)	3.5 (2.0-14.5)	0.5(0-3.4)	1.8(1.1-6.2)	1.5(1.1-4.4)	10.1(8-45.6)
Cyclical bowel symptoms					
Group A (n=32)	0.8(0-30.3)	0.4(0-4.8)	1.8(0-6.4)	3.4(0-121.3)	4.4(1-12.5)
Group B (n=2)	3.1(2.4-19.5)	0.2(0-3.1)	0.9(0.8-5)	2.2(0-3.5)	10.7(4.9-11.5)
Cyclical urinary symptoms					
Group A (n=2)	1.4	0.8	1.2	2	4.3
Group B (n=0)	-	-	-	-	-

* $p<0.05$

Comparison of median cytokine concentrations measured in peritoneal fluid of patients evaluated, is shown in Table 3. Patients with endometriosis, who had infertility, had higher IL-2 levels than controls. Among all patients with infertility and endometriosis (n=22), 63.5% (n=14) were found to have DIE.

Comparing the characteristics of the disease between cases and controls in relation to cytokine measurements in peritoneal fluid, higher IL-10 levels were found in cases of ovarian endometriosis in absence of deep disease, irrespective of the presence of peritoneal foci (Table 4).

Discussion

Endometriosis is a disease with different facets. It probably starts from endometrial reflux or cell metaplasia and provokes pelvic pain and infertility or may cause no clinical symptoms[14]. Participation of the immunological system in some of steps in this process is logical and agrees with current literature[4]. The humoral immune response may explain endometriosis in general terms, in accordance with the characteristics of an autoimmune disease[15]. Particularly, in more aggressive, infiltrating forms of the disease, there appears to be a predominant action of cell immunity, with cells, enzymes and cytokines provoking adhesion, infiltration and maintenance of the foci of ectopic endometrial tissue.

Deeply infiltrating endometriosis is a major issue in several studies related to this disease, including etiopathogenesis, clinical data, imaging methods and an intense clinical and surgical treatment debate [16,17,18,19,20,21] . There are still some topics that have no consensus, such as the best imaging method for diagnosis of deep lesions (mainly bowel endometriosis)[18,19] and the best option for treatment of these lesions, due to the complication risk related to the more advanced surgical procedures[20,21]. It is however known that deep lesions have a distinctive feature when compared to peritoneal superficial lesions, mainly when endometriotic nodules infiltrate the bowel, the bladder or the vagina. In these cases, patients usually refer to symptoms related to the

Table 4 - Comparison of the median (range) cytokine concentrations measured in peritoneal fluid (pg/ml) between groups of patients with (A) and without endometriosis (B) according to staging (ASRM, 1996) and site affected by endometriosis

	TNF-alpha	IFN-gamma	IL-2	IL-4	IL-10
Staging					
Initial (n=28)	3.3(0-13.2)	0.4(0-2.1)	1.5(0-7.1)	1.2(0-21.4)	18.7(0-78.1)
Advanced (n=37)	2.9(0-30.3)	0.6(0-4.9)	1.4(0-4.3)	2.1(0-121.3)	46.1(0-772.5)
Group B (n=33)	1.4 (0-20.7)	0 (0-3.4)	0 (0-6.2)	0 (0-66.3)	25.7 (3.2 -92.7)
Site affected					
Peritoneal disease (n=12)	2.8(0-11.3)	1.1((0.5-2.9)	0.8(0-1.2)	2.0(0-121.3)	27.1(0-34.1)
Absence of peritoneal disease (n=36)	3.4(1.2-21.1)	0.9(0-1.2)	0.8(0.5-1.1)	1.6(0-12.1)	30.9(3.1-55.2)
Group B (n=33)	1.4 (0-20.7)	0 (0-3.4)	0 (0-6.2)	0 (0-66.3)	25.7 (3.2 -92.7)
Ovarian disease (n=19)	2.4(0-3.9)	2.2(0.5-1.8)	2.1(1.1-4.5)	1.7(0.5-4.3)	50*(5.4-772.5)
Absence of ovarian disease (n=24)	3.8(0.5-9.2)	0.7(0-4.9)	0.7(0-7.1)	2.0(0.9-11)	18.7(0-32.7)
Group B (n=33)	1.4 (0-20.7)	0 (0-3.4)	0 (0-6.2)	0 (0-66.3)	25.7 (3.2 -92.7)
Deep disease (n=34)	3.2(1.5-30.3)	2.9(0-4.9)	0.8(0-3.2)	2.0(1.1-23)	30.9(0-98.4)
Absence of deep disease (n=31)	2.4(0-7.1)	1.5(0.8-4.1)	1.4(0-1.9)	0.6(0-9.8)	25.5(2.2-57.3)
Group B (n=33)	1.4 (0-20.7)	0 (0-3.4)	0 (0-6.2)	0 (0-66.3)	25.7 (3.2 -92.7)

* $p<0.05$

site affected by the disease, such as intestinal and urinary cyclic alterations and deep dyspareunia, respectively[22]. Further, Chapron et al. (2009) evaluated 500 patients with deep endometriosis and observed that presence of ovarian endometrioma can be a marker for severity of deeply infiltrating endometriosis and when the patient has severe dysmenorrhea, pain is probably due to deep lesions, mainly rectal infiltration, and not to the ovarian cyst[23,24].

In this study, we have endeavored to identify the cytokine profile associated with Th1 and Th2 response that may predominate in patients with endometriosis, and which would confirm participation of immunological alterations and encourage further research leading to new therapeutic modalities for the disease. The design of this study has its own limitations due to the variability of cytokine concentrations as seen in the wide range of these measures and in the use of median values for statistical analysis of data. In addition, the different volume of peritoneal fluid obtained from each patient is a factor that has to be considered as in 12 patients there was no fluid in the peritoneal cavity. We did not propose a peritoneal flush because mechanical infusion of any liquid and action involved in washing the peritoneal cavity could provoke local stress, "unbinding" molecules not spontaneously present in the peritoneal fluid, as well as leading to a quick inflammatory response with alterations in the microenvironment under evaluation. These points could affect true results of cytokine concentration.

Our previous report analyzed this cytokine profile and showed that IFN-gamma and IL-10 increased significantly in the peritoneal fluid of patients with endometriosis compared to those without endometriosis. However, there was a significant alteration of Th2:Th1 ratios in peritoneal fluid of patients with endometriosis, with a predominance of IL-4 and IL-10, reflecting a shift towards Th2 immune response despite increased IFN-gamma concentrations. These results allowed us to conclude that endometriosis is an inflammatory disease involving a possible shift towards a Th2 immune response component[13].

Analysis of the clinical status of groups in this study revealed a statistically significant difference with respect to patients with endometriosis, a higher percentage of those with dysmenorrhea and cyclical alterations in bowel habits compared to women without the disease. This agrees with the clinical profiles of the disease evaluated in Brazil[25] and in other countries[26,27], where almost 90% of patients with endometriosis complained of dysmenorrhea and 40% reported cyclical alterations in bowel habits.

Comparison was made between the intensity of symptoms reported by patients and severity of the disease as diagnosed during surgical procedures. A direct correlation was observed, the more intense the symptoms, the more severe the disease. One example of this finding is that 65.5% of patients with endometriosis who reported deep dyspareunia had a deeply

infiltrating form of the disease, and of those who did not report this symptom, only 30.3% had deep endometriosis. Fauconnier & Chapron (2005) reached similar conclusions and showed that, in cases of deep endometriosis, symptoms had some specificity with the site affected by the lesion[28].

In cases of greater extension of the disease, with adherences and significant anatomical distortion, the explanation for the symptomatology reported by patients has been credited to the inflammatory process that installs itself in the pelvis, with an increase in production of prostaglandins and lysosomal enzymes inducing fibrosis[29]. Alterations observed in this study are in accordance with these data, since in patients with deep dyspareunia, there is an increased concentration of TNF-alpha, a cytokine that may be a marker of Th1 response, but may also be produced by other cell types in a non-specific inflammatory response. Regardless of its origin, TNF-alpha is directly involved in the action of NK cells, cytotoxic T lymphocytes, VEGF secretion and metalloproteinase matrix enzymes, and also plays an important role in the apoptosis observed in sites of acute or chronic inflammation.

Patients in Group A reporting infertility had higher concentrations of IL-2 in peritoneal fluid compared to patients in Group B. Analysis of patients in whom this increase occurred revealed that in 63.6% of the cases, deep endometriosis was detected. This type of disease generally impairs fertility more often than superficial endometriosis due to fibrotic processes that may affect the uterine tubes, essential organs in the process of spontaneous fertilization[30]. The elevation of a pro-inflammatory citokyne such as IL-2 in patients with deep endometriosis could be involved in the pathogenesis of infertility, but clearly further studies have to be made to confirm this hypothesis.

A single study involving IL-10 in cases of advanced disease showed an increase of this cytokine in the peritoneal fluid of patients with this specific type of endometriosis[31]. In the present analysis, IL-10 was higher in the peritoneal fluid of patients with ovarian endometriosis but not in those with the deep disease, irrespective of the presence of peritoneal lesions. Our previous results showed that IFN-gamma was higher in the peritoneal fluid of patients with endometriosis compared to patients without the disease, and when analysis was made of these cases, it was found that 9 out of 13 patients (69.2%) who had increased levels of IFN-gamma had deep endometriosis[13].

Regarding staging of endometriosis, no statistically significant differences were found in our study about cytokine measurement and Th1 and Th2 response patterns. Increased concentrations of TNF-alpha have already been described in relation to advanced stages[32], initial stages[33] and in cases where no relation could be perceived with the stage of endometriosis[34]. Concerning deep endometriosis, statistical analysis showed no significant difference in cytokine concentrations. Nevertheless, according to our findings, there appears to be a trend towards stronger participation of Th1 response in these cases.

Results achieved in this study are coherent with those previously published that allowed us to stress that endometriosis is a complex disease with an inflammatory behavior and a Th2 immune response component. IFN-gamma concentrations in the peritoneal fluid were increased in patients with the disease[13]. In the present study, TNF-alpha and IL-2 had higher concentrations in endometriosis patients with dyspareunia and infertility when compared to patients without the disease. These cytokines, mainly IFN-gamma and IL-2, are related to Th1 immune response and almost 70% of patients that presented these results had DIE lesions

In conclusion, although there were no differences concerning Th1/Th2 immune response patterns in relation to the site of endometriotic lesions, information presented here suggests that, when specific clinical data are associated with a greater production of specific cytokines, there is a Th1 response pattern that may be associated with deeply infiltrating endometriosis.

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Resumo

Resposta imunológica Th1 e Th2 relacionada à endometriose pélvica

Objetivo. Este estudo analisa a relação entre as características clínicas da endometriose e os padrões da resposta imune Th1/Th2.

Métodos. Estudo prospectivo realizado com 65 pacientes com endometriose (Grupo A) e 33 pacientes sem a doença (Grupo B). Foram realizadas avaliação no fluido peritoneal e sangue periférico de IL 2, 4 e 10, TNF-alfa e IFN-gama. A significância foi estabelecida em $p < 0,05$.

Resultados. TNF-alfa encontrava-se elevado em pacientes com endometriose que apresentavam dispareunia de profundidade comparado com controle (média 4,5 pg/ml e 2,3 pg/ml, $p< 0,05$). Dentre essas pacientes ($n=32$), 65,5% apresentavam endometriose profunda. Pacientes com endometriose e infertilidade apresentavam concentrações maiores de IL-2 no fluido peritoneal quando comparadas com controle (média 5,9 pg/ml e 0,2 pg/ml, $p< 0,05$), sendo que neste grupo, 63,5% ($n=14$) apresentavam endometriose profunda. Foi observada também maior concentração de IL-10 nas pacientes que apresentavam endometriose ovariana quando comparadas às sem esse tipo de endometriose, assim como quando comparadas às pacientes do grupo controle (média 50pg/ml, 18,7pg/ml e 25,7pg/ml, $p<0,05$).

Conclusão. Estes resultados sugerem que quando dados clínicos específicos associam-se a uma produção elevada de certas citocinas, ocorre um padrão de resposta Th1 que pode estar associado à endometriose profunda. [Rev Assoc Med Bras 2010; 56(1): 92-8]

Unitermos: Endometriose. Alergia e Imunologia.Citocinas.Células Th1.Células Th2.

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