

Chronic Endometritis in Patients with Failure of IVF

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Abstract

Background: Chronic endometritis (CE) is highly prevalent in patients with unexplained infertility. This study aimed to determine the associations between CE and infertility.

Methods and Results: We performed a prospective study of 197 women with implantation failure and pregnancy loss after undergoing in vitro fertilization (IVF). The endometrium was examined with a hysteroscope, and a sample was taken for biopsy in areas suspected of having inflammation. Immunohistochemistry was performed for CD138 antibodies. Diagnostic criterion was more than 5 plasma cells per 10 high-power fields. Patients who were positive for CE were treated with antibiotics.

Among the 197 patients in our study, 115(58.4%) were positive for CE. Regarding the success of CE treatment and pregnancy after treatment, among the 115 CD138-positive patients, 32 became pregnant without IVF after treatment, while another 43 had successful pregnancies and childbirth with IVF. Thus, with treated CE, a successful pregnancy and childbirth was detected in 65.2% of cases, including spontaneous pregnancies and IVF.

Conclusion: Patients with infertility and those who have pregnancies lost in IVF have a high rate of CE. Failure to treat CE results in infertility and IVF failure. An efficient diagnosis and treatment of CE are important for a successful pregnancy. (International Journal of Biomedicine. 2023;13(2):273-276.)

Keywords: chronic endometritis • CD138 • infertility • IVF

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Introduction

Chronic endometritis (CE) is defined as inflammation of the endometrial mucosa characterized by the presence of leukocytes, plasma cell infiltration in the stroma, edema, and increased stromal density.^(1,2) Patients with this condition are usually asymptomatic but can present with chronic pelvic pain, dyspareunia, abnormal uterine bleeding, or persistent vaginal discharge.⁽³⁾ The presence of endometrial micropolyps in fluid hysteroscopy is significantly associated with endometrial inflammation and can be considered a reliable diagnostic sign for this pathology.^(4,5) In our experience, endometrial micropolyps are always associated with stromal edema,

homogeneous endometrial thickening, or, more frequently, non-homogeneous endometrial thickening and focal or diffuse periglandular hyperemia. These signs are also found in cases of CE.^(4,6)

The prevalence rate of CE is approximately 10%–11%, based on biopsies of patients who underwent hysterectomies because of benign gynecological conditions. Gynecologists and pathologists do not usually pay much clinical attention to CE because of the time-consuming microscopic examinations necessary to diagnose this condition, its mild clinical manifestations, and its benign nature.⁽⁷⁾

The possible relationship of CE with infertility and/or perinatal complications has recently emerged as an area of ongoing research.⁽⁸⁾ However, the definitive diagnosis for CE must be made by histopathology and immunohistochemistry.

Histopathological diagnosis is by the presence of plasma cells in the endometrium with or without accompanying acute

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inflammation and lymphocytes.⁽⁹⁾ Lymphocytes are a normal component of the endometrial stroma, and their number fluctuates with the phase of the cycle.^(10,11) Quantifying CD138+ cells by immunohistochemistry in women with a history of recurrent pregnancy loss is helpful in diagnosing CE and predicting subsequent reproductive outcomes.⁽¹²⁾

This study aimed to determine the associations between CE and infertility.

Materials and Methods

We performed a prospective study of 197 women with implantation failure and pregnancy loss after undergoing in vitro fertilization (IVF). The endometrium was examined with a hysteroscope, and a sample was taken for biopsy in areas suspected of having inflammation (Figure 1). Specimens were fixed with formaldehyde, embedded in paraffin, and subsequently sliced into 4- μ m sections and stained with hematoxylin and eosin. Immunohistochemical staining was performed by incubation of endometrial samples with a 1:100 dilution of mouse monoclonal antibodies against CD138 used for immunohistochemical staining. Diagnostic criterion was more than 5 plasma cells per 10 high-power fields (HPFs) (Figure 2). Patients who were positive for CE were treated with antibiotics.

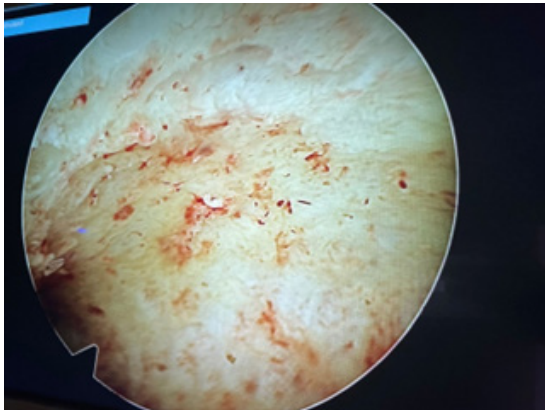


Fig. 1. Endometrial mucosa examined by hysteroscope. Endometrial mucosa appears thick, edematous, and hyperemic.

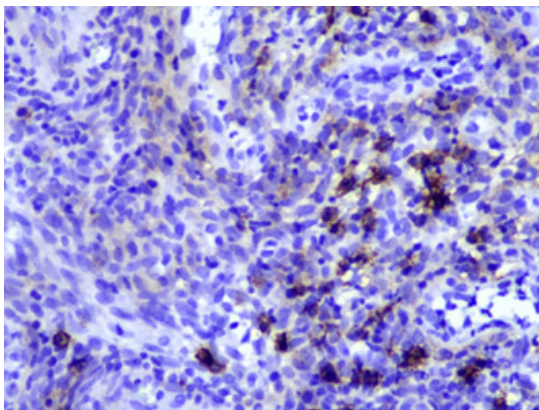


Fig. 2. Immunohistochemical CD138 expression in an endometrial biopsy: Groups of plasma cells stained with CD138 (X200).

Results

Among the 197 patients in our study, 115(58.4%) were positive for CE. When we divided the patients into age groups, the age group of ≤ 20 years included 3 patients (one with CE and 2 without CE), the age group of 21–30 years included 53 patients (32[60.4%] with CE and 21[39.6%] without CE), the age group of 31–40 years included 110 patients (71(64.5%) with CE and 39(35.5%) without CE), and the age group of >40 years included 31 patients (11(35.5%) with CE and 20(64.5%) without CE). These findings suggested that there was no difference in the incidence of CE between the age groups, except for the >40 group, which had fewer cases of CE than the 21–40 group.

Even after treatment at the second biopsy, among 115 patients who were CD138-positive, 20 had signs of endometritis. These patients were treated again. At the third biopsy, 3 patients still had signs of endometritis, while at the fourth biopsy, one of these patients was resistant to treatment. After treatment, this resistant patient was negative at the fourth biopsy (Table 1). Regarding the success of CE treatment and pregnancy after treatment, among the 115 CD138-positive patients, 32 became pregnant without IVF after treatment, while another 43 had successful pregnancies and childbirth with IVF. Another 40 patients had pregnancy loss even after IVF for other reasons. Thus, with treated CE, a successful pregnancy and childbirth was detected in 65.2% of cases, including spontaneous pregnancies and IVF.

Table 1.

Clinical characteristics of the CD138-positive/negative patients and successful pregnancy after treatment among the 115 CD138-positive patients.

Age (years)	Patients (n)	CD138-positive/negative	Positive for endometritis in the second biopsy	CD138-positive patients (n=115)	
				Pregnant without IVF	Pregnant with IVF
<20	3	1/2		1	0
21–30	53	32/21	3	11	14
31–40	110	70/39	13	20	23
>41	31	12/20	4	0	6
All	197	115/82	20	32	43

Discussion

CE is highly prevalent in patients with unexplained infertility. Many studies have suggested a close relationship between CE and reproductive impairment. Untreated CE may contribute to poor pregnancy outcomes, and this problem deserves further investigation in a large cohort.⁽¹³⁻¹⁵⁾ Our study found that the frequency of CE in women with unexplained infertility was higher than in the general population, and more than half of the patients had CE. We did not see a clear difference between the age groups, except for the >40 group, which had fewer cases of CE than the 21–40 group.

Most previous studies have shown that up to 40% of women with infertility are diagnosed with CE.^(13,16) The degree of inflammation of the endometrium in our study was higher than that in other studies, especially in the 21–40 age group. In addition to the treatment of other factors that cause infertility, another reason for this discrepancy between studies may be the determination of hysteroscopic criteria, such as hyperemia, a strawberry aspect as an atypical image of hyperemia, stromal edema, and micropolyps.⁽¹⁷⁻²⁰⁾

Many studies have shown that, for a more accurate diagnosis, immunohistochemical staining should be performed using CD138 antibody, which increases the sensitivity for detection in plasma cells.⁽²¹⁾ Additionally, studies have suggested the number of microscopic fields and plasma cells required to define CE. Five or more plasma cells per 10–30 HPFs were found in most previous studies.⁽²²⁻²⁴⁾ Our study agreed with the indicated data. CE is easy to diagnose even in 10 HPFs. These findings suggest that the presence of a group of plasma cells can be used to diagnose CE, while CE is an important factor in infertility.

In our study, after treating CE with antibiotics and verifying the elimination of plasma cells from the endometrium, a high pregnancy rate was observed. The greatest percentage of success was associated with age. At a younger age, curing endometritis leads to greater success in pregnancy, which suggests that endometritis was the most significant cause of pregnancy loss in these women.

Conclusion

Patients with infertility and those who have pregnancies lost in IVF have a high rate of CE. Failure to treat CE results in infertility and IVF failure. An efficient diagnosis and treatment of CE are important for a successful pregnancy.

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Competing Interests

The authors declare that they have no competing interests.

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