Hysteroscopic endometrial biopsy with immunohistochemistry in the diagnosis of endometritis

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To the Editor: Chronic endometritis (CE) is a subtle type of inflammation characterized by the persistent presence of plasma cells in the stroma of the endometrium and is usually asymptomatic, only slight symptoms, such as abnormal uterine bleeding, pelvic pain, dyspareunia, or leucorrhea.

There are currently no universally accepted standardized definitions or established diagnostic guidelines for CE. Pathologist agree that the presence of multiple endometrial stromal plasmacytes is the most specific and sensitive finding in pathology.

Using conventional hematoxylin and eosin (H&E) staining, it is sometimes difficult to distinguish the plasma cells from the fibroblasts and monocytes of the endometrial stroma. In practical work, finding plasma cells is largely influenced by pathologist experiences and the quality of endometrial samples. The success rate of accurate diagnosis and treatment of CE is not high.

Kitaya *et al*[1] indicated that although inexperienced pathologists could not recognize plasma cells very well, they could recognize plasma cells by CD138/CD38 immunohistochemical (IHC) staining easily. CD138 (transmembrane heparin sulfate proteoglycan) and CD38 (type II transmembrane glycoprotein) are the specific markers of plasma cells. The markers of plasma cells (CD138/CD38) can help pathologists identify plasma cells and improve the clinical diagnostic rate of CE. Therefore, in current clinical practice, CD138/CD38 IHC staining is used for the detection of CE to improve its diagnosis rate.

Hysteroscopy is used to identify the visual signs of endometrial inflammation, and gynecologists attempt to use hysteroscopy to diagnose CE. Cicinelli *et al*[2] have proposed the following hysteroscopic criteria: hyperemia, strawberry aspect as atypical image of hyperemia, stromal edema, and micropolyps (small pedunculated, vascularized protrusions of the uterine mucosa measuring < 1 mm). The sensitivity of endometritis by hysteroscopy is largely influenced by the media of inflation and the cognition of the disease by the operator; however, it is still useful in positioning biopsy and providing high-quality samples for pathological examination.[3] Therefore, the purpose of this study was to explore the role of hysteroscopy and IHC in diagnosis.

A total of 306 cases were retrospectively analyzed at Urumqi Maternal and Child Health Hospital of Xinjiang Uygur Autonomous Region from January 2019 to January 2020; the average age was 37.9 ± 7.5 (31.0–48.0) years. The clinical presentations mainly included abnormal uterine bleeding (69 cases), repeated abortion (128 cases), and infertility and repeated implantation fail (109 cases).

The exclusion criteria included: (1) menstruation at the time of examination; (2) reproductive tract infection; (3) presence of intrauterine contraceptive device; (4) history or presence of endometrial carcinoma; (5) positive result on pregnancy test; and (6) use of hormone replacement therapy or hormonal therapy in the preceding 3 months.

Hysteroscopy and endometrium biopsy were performed in the daytime operating room. All biopsy samples underwent pathological examination by H&E staining and CD138/CD38 IHC staining.

This study was approved by the ethics committee of Urumqi Maternal and Child Health Hospital of Xinjiang Uygur Autonomous Region. Each patient signed a consent form for surgical and pathological examination.

A 4.5 mm and 6 mm hysteroscopy were selected (Shenyang Shenda Endoscope: DG-1 type dilation pressurizer, F-126D endoscope influence system, GL350-5 type cold light source, Shenyang, China). A 5% glucose injection was used as a dilation medium with a dilation pressure of 80 to 100 mmHg. The condition of the uterine cavity was observed, and the endometrium biopsy was performed.

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000001275

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Chinese Medical Journal 2021;134(9)
Received: 21-04-2020 **Edited by:** Li-Shao Guo

Specimens were fixed with 4% neutral formaldehyde, dehydrated and embedded in paraffin. They were subsequently, sliced into 3 to 4 μm sections, stained with H&E; immunohistochemical (IHC) staining was performed by incubation with a 1:100 dilution of mouse monoclonal antibodies directed against CD38 and CD138 (Beijing Zhong Shan Jin Qiao Company, Beijing, China) was used for IHC staining.

Hysteroscopic diagnostic criteria were one or more hysteroscopic criteria, hyperemia, strawberry aspect as atypical image of hyperemia, stromal edema, and micropolyps. Pathological diagnostic criteria were one or more plasma cells identified per 10 high power fields were graded as positive. All endometrial biopsy specimens were examined by a single histopathologist. IHC diagnostic criterium was that the membrane/cytoplasm of the plasma cells that appeared brown-yellow was defined as CD38/CD138 positive.

The SPSS 20.0 software (IBM) was used to statistically analyze the data. The main method used was consistency test: *Kappa* value < 0 very poor consistency; 0–0.20 very weak consistency; 0.21–0.40 weak consistency; 0.41–0.60 moderate consistency; 0.61–0.80 high consistency; 0.81–1.00 extremely strong consistency.

In accordance with the diagnostic standard of endometritis under hysteroscopy, 132 cases were diagnosed as CE out of 306 cases (43.14%), 110 cases were pathologically diagnosed by H&E staining out of 306 cases (35.95%), and 117 cases were diagnosed by IHC out of 306 cases (38.24%) [Table 1].

Traditional H&E staining was used as the reference standard; the sensitivity and specificity of hysteroscopy in the diagnosis of CE were 83.33% (110/132) and 89.91% (196/218), respectively.

The sensitivity and specificity of office IHC in the diagnosis of CE were 94.02% (110/117) and 96.55% (196/203), respectively. The *Kappa* value of consistency test for hysteroscopy *vs*. H&E staining and IHC *vs*. H&E staining were 0.91 and 0.97, respectively.

The prevalence of CE ranges from 8% to 72% in women of reproductive age.[4] This large variance among studies is thought to be caused by the relatively small number of patients and differences in the diagnostic criteria applied. The relationship between CE and infertility has recently emerged as an important clinical challenge; the prevalence of CE has been found to be 2.8% to 56.8% in infertile women.[5] The incidence of CE in abnormal uterine bleeding, endometrial hyperplasia, intrauterine adhesions, and other diseases was also significantly increased. Considering these high prevalence rates, CE is a condition that must not be ignored during gynecological diseases treatment.

Hysteroscopy is used to identify the visual signs of endometrial inflammation, according to the Cicinelli *et al* proposed hysteroscopic criteria: hyperemia, strawberry aspect, stromal edema, and micropolyps. In this study, CE is diagnosed by the presence of at least one feature, we got higher detection rate than H&E staining. Glucose was used as a dilatation fluid, no capillary rupture was caused by sudden dilatation of the uterine cavity, and all surgical were performed by senior surgeons; so in our study, the sensitivity and specificity of hysteroscopy in diagnosing CE exceeded 80%, and hysteroscopy and H&E staining had high consistency in diagnosis (*Kappa* = 0.91).

IHC staining for CD38/CD138 has been successfully used for years in diagnosis of plasma cell tumors, including multiple myelomas. Many studies now suggest that CD38/CD138 staining was used for the diagnosis of CE. CD38/CD138 IHC staining improves the sensitivity of plasma cells detection on microscopy, accelerates the plasma cell count, and decreases the false-negative rates limited by the pathologist's experience.

CE may occur throughout the endometrium or confined to local endometrium. The site and amount of tissue collected may affect the detection of plasma cells. Office hysteroscopy is a useful diagnostic tool, which locates the CE and provides high-quality endometrium samples.

In our study, the accuracy of localization biopsy under hysteroscopy combined with IHC staining in the diagnosis of CE was higher than H&E staining (38.24% *vs*. 35.95%), consistency test proved IHC staining and H&E staining had highly consistent (*Kappa* = 0.97).

In conclusion, hysteroscopy could fix the position of CE and endometrium biopsy; IHC staining could improve the recognition rate of plasma cells with lesser experience of pathologist. Therefore, we suggest that hysteroscopy, endometrial biopsy, and IHC staining should be used to improve the diagnosis rate of CE.

Table 1: Correlation between hysteroscopy features, immunohistochemical (IHC) staining, and hematoxylin and eosin (H&E) staining.

Items	H&E staining	Hysteroscopy	IHC
Positive, *n* (%)	110 (35.95)	132 (43.14)	117 (38.24)
Negative, *n* (%)	196 (64.05)	174 (56.86)	189 (61.76)
Sensitivity, % (*n*/N)	100 (110/110)	83.33 (110/132)	94.02 (110/117)
Specificity, % (*n*/N)	100 (110/110)	89.91 (196/218)	96.55 (196/203)
Kappa value		0.91	0.97

Conflicts of interest

None.

References

1. Kitaya K, Takeuchi T, Mizuta S, Matsubayashi H, Ishikawa T. Endometritis: new time, new concepts. Fertil Steril 2018;110:344–350. doi: 10.1016/j.fertnstert.2018.04.012.
2. Cicinelli E, Vitagliano A, Kumar A, Lasmar RB, Bettocchi S, Haimovich S. International Working Group for Standardization of Chronic Endometritis Diagnosis. Unified diagnostic criteria for chronic endometritis at fluid hysteroscopy: proposal and reliability evaluation through an international randomized-controlled observer study. Fertil Steril 2019;112:162–173.e2. doi: 10.1016/j.fertnstert.2019.03.004.
3. Song D, Li TC, Zhang Y, Xia E, Huang X, Xiao Y. Correlation between hysteroscopy findings and chronic endometritis. Fertil Steril 2019;111:772–779. doi: 10.1016/j.fertnstert.2018.12.007.
4. Kimura F, Takebayashi A, Ishida M, Nakamura A, Kitazawa J, Morimune A, *et al*. Affiliations review: chronic endometritis and its effect on reproduction. J Obstet Gynaecol Res 2019;45:951–960. doi: 10.1111/jog.13937.
5. Wang HY, Qiao J, Sun XX, Wang SY, Liang XY, Sun Y, *et al*. Epidemiological survey and risk factor analysis of recurrent spontaneous miscarriages in infertile women at large infertility centers. Chin Med J 2017;130:2056–2062. doi: 10.4103/0366-6999.213415.

How to cite this article: Zhang Y, Li WY, Lu J. Hysteroscopic endometrial biopsy with immunohistochemistry in the diagnosis of endometritis. Chin Med J 2021;134:1116–1118. doi: 10.1097/CM9.0000000000001275