Clinical study on 7 cases of polypoid endometriosis. PEM: a mimic of malignancy, the symptoms of adenomyosis, endometrial polyps and infertility can assist in diagnosis

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Research Article

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Abstract

Objective: polypoid endometriosis (PEM) is a rare type of endometriosis (EMs), which is easy to be misdiagnosed. The purpose of this paper is to investigate the clinical features and diagnostic methods of PEM.

Methods: The clinical data of 7 patients with PEM who were treated at Fujian Provincial Maternity and Children's Hospital in China within July 2017 to December 2020 period were retrospectively analyzed, and their clinical characteristics, diagnosis, treatment and prognosis were summarized.

Results: The age of onset was 31-41 (38.00 ± 1.72) years. There were 5 cases with adenomyosis, 4 cases with endometrial polyps and infertility. The clinical manifestations were diverse. Most of them were pelvic mass, compression symptoms and signs, dysmenorrhea and abnormal uterine bleeding, and three of them were similar to malignant tumors. The gross pathological features were cysts, endogenous or exogenous polypoid masses, which were all composed of endometrioid glands and stromal components, but more diverse than ordinary em. All the 7 patients were confirmed by operation and pathology.

Conclusion: PEM is often complicated with adenomyosis, endometrial polyps and infertility. Pathological examination is the gold standard for diagnosis. Imaging examination is easy to be misdiagnosed. Abnormal increase of CA125 can assist in diagnosis.

Background

Endometriosis (EMS) is a disease of endometrial tissue (including glands and stroma) outside the uterine. Polypoid endometriosis (PEM) is a rare type of endometriosis. The lesion grows like endometrial polyps and is more active than ordinary endometriosis. It is easy to be misdiagnosed as malignant tumor or confused with other lesions. PEM was first named by Mostoufizadeh and Scully in 1980 [1]. At present, Parker[2] has the largest number of reported cases, with a total of 24 case series, while the rest of the reports are mostly cases misdiagnosed as malignant tumors [3-6]. The most common sites were the rectosigmoid colon and ovary. Both pathologists and surgeons performing abdominal surgeries should be aware of PEM because it mimics malignancy with its clinical, gross, and microscopic features[7]. Some report tamoxifen may have exacerbated the growth of multiple polypoid endometriotic implants[8].

This paper retrospectively analyzed the clinical manifestations and pathological features of 7 cases of PEM in our hospital in recent 5 years, and summarized the cases reported abroad in order to improve the understanding of PEM as a special type of endometriosis.

Materials And Methods

1.1 Clinical data. A total of 7 patients with PEM diagnosed by pathology were collected from July 2017 to January 2020 in the department of gynecology of Fujian Provincial Maternity and Children's Hospital in China.

1.2 Method. Clinical data of 7 cases were reviewed. The general situation, clinical characteristics, auxiliary examination, diagnosis and treatment process of the patients were analyzed retrospectively, and related cases reported abroad in the past 5 years were summarized.

Results

2.1 Baseline characteristics. Baseline characteristics of the patients are summarized in Table 1. The mean age of the 7 patients was 38.00 ± 1.72 years, ranged from 31 to 45 years. The duration of the disease varies from 1 month to 6 years.
All of them were married, including 2 cases of primary infertility and 2 cases of secondary infertility. Among the 7 patients, 1 patient (Case NO.7) received dydrogesterone tablets orally for 10 days due to abnormal vaginal bleeding, and 1 patient (Case NO.5) received mifepristone tablets orally for nearly half a year, while the rest had no special medication history.

| Case NO. | Age | course  | obstetrical history | Mode of delivery | Infertility | Drug use   |
|----------|-----|---------|---------------------|-----------------|-------------|------------|
| 1        | 40  | 3 months| 2-0-2-2             | both natural birth | -           | /          |
| 2        | 41  | 2 months| 2-0-0-2             | both natural birth | -           | /          |
| 3        | 36  | 2 years | 0-0-1-0             | natural delivery once | Primary    | /          |
| 4        | 35  | 2 years | 1-0-1-1             | natural birth, abortion once | Secondary  | /          |
| 5        | 45  | 6 years | 1-0-1-1             | natural birth, abortion once | -       | Mifepristone |
| 6        | 31  | 6 months| 0-0-0-0             | /               | Primary     |            |
| 7        | 38  | 1 month | 1-0-1-1             | natural birth, abortion once | Secondary  | dydrogesterone |

2.2 Clinical features

Clinical complications and symptoms are showed in Table 2. Pathological changes of clinical symptoms are mainly on pelvic mass or symptoms and signs of tumour oppression. Such as 4 cases of pelvic or abdominal mass, 1 case of vaginal bleeding because of lesions located in the cervical, 5 cases with ovulation dysfunction caused by abnormal uterine bleeding (AUB-O), 5 cases endometrial polyps, 5 cases with uterine glandular myopathy (imaging and pathological diagnosis), 5 cases were found in severe pelvic adhesion in operation and 1 case of PEM lesions located in the ureter, ovarian, uterine wall and the pelvic mass oppression ureter caused kidney sicker and waist pain. 5 patients with dysmenorrhea symptoms.
Table 2
Clinical complications and symptoms

| Cases | PEM parts                                           | Size (cm) | adenomyosis | dysmenorrhea | Pelvic adhesion | Other complications       |
|-------|----------------------------------------------------|-----------|-------------|--------------|-----------------|---------------------------|
| 1     | The left posterior wall of the uterus             | 4.2x3.7x4.4 | Y           | Y            | Y               | Multiple myoma            |
| 2     | Right fallopian tube                              | 2.7x2.1   | -           | -            | -               | Multiple myoma, AUB-O/EMP |
| 3     | The left ovary, The left fallopian tube           | 9.6x8.1x6.6,2.3x2.4x2.5 | Y           | Y            | Y               | AUB-O                    |
| 4     | Hysterosacral ligament, rectal fossa, the right fallopian tube | 11.7x7.1x7.3 | -           | Y            | Y               | EMP                      |
| 5     | The right ovary, uteropectal fossa tissue         | 4.5x4x4   | Y           | Y            | Y               | AUB-O/EMP                 |
| 6     | Ovary, posterior uterine wall, intestinal surface, left ureter | 8.1x5.0x5.8,4.0x1.1x3.5 | Y           | Y            | Y               | CIN2/AUB-O/Left hydronephrosis |
| 7     | The cervical                                      | 4.5x4.2x3.3 | Y           | -            | Y               | AUB-O/EMP/Endometrial atypical hyperplasia |

“Y” means YES, “-” means NO. “AUB-O” means abnormal uterine bleeding because of ovulation dysfunction. “EMP” means endometrial polyps.

2.3 Auxiliary examination

Auxiliary examination as tumor markers, Imaging examination, Intraoperative freezing pathology are showed in table 3.

2.3.1 Tumor markers. 7 cases all were detected tumor markers. CA_{125} was significantly increased by 103.8-762.6 (225.47±117.49) kU/L in 6 cases, and the normal one's PEM was located in the fallopian tube(Case NO.2), with CA_{125} 15.3 kU/L. 3 cases of CA_{199} elevated, others normal.

2.3.2 Imaging examination. 7 patients all had ultrasound examinations and all performed: the mass at the lesion site showed mixed echo with visible blood flow signal. The posterior uterine wall mass was misdiagnosed as fibroid degeneration with hemorrhage in case NO.1. It was diagnosed as endometriosis cyst in case NO.3 and 6. No definite diagnosis was suggested in the remaining 4 cases. 6 in 7 patients underwent CT or Magnetic resonance imaging (MRI)
examination, 2 patients underwent CT examination and both were ovary PEM misdiagnosed as ovarian cystadenoma. 4 patients underwent MRI examination, among which 1 case of cervical PEM was misdiagnosed as cervical cancer, 1 case of posterior uterine wall PEM was misdiagnosed as uterine fibroid degeneration, 1 case of ovarian PEM was diagnosed with EMs, and the other one case had no definite diagnosis.

2.3.3 Intraoperative freezing pathology. 6 cases had the intraoperative cryopathological examination showed: 3 cases were diagnosed as EMs; an ovarian PEM case suggested epithelial tumor of the right ovary and focal borderline dysplasia could not be ruled out (Case NO.5), the other ovarian PEM case suggested ovarian cystadenoma (Case NO.4), a cervical PEM case (Case NO.7) diagnosed mixed polyps.

| Cases | CA125  | CA199 | color ultrasound                         | CT/MRI                          | Intraoperative frozen          |
|-------|--------|-------|------------------------------------------|---------------------------------|--------------------------------|
| 1     | 112.2  | 462.03| Cystic-solid mass,                       | Myoma degeneration              | EMs                            |
|       |        |       | Myoma degeneration                       |                                 |                                |
| 2     | 15.3   | normal| Without reporting                        | not done                        | No reporting                    |
| 3     | 126.2  | normal| endometriosis                            | endometriosis                   | EMs                            |
| 4     | 460.4  | 313.53| Cystic-solid mass, nature to be determined| CT Endoheterosis, ovarian cystadenoma | Ovarian cystadenoma            |
| 5     | 762.6  | normal| Bilateral adnexal cyst                   | a cystic lesion in bilateral adnexal areas. The nature remains unknown | An epithelial tumor of ovary. Small borderline lesions. |
| 6     | 184.4  | 57.01 | Ovarian artful bursa                     | CT cystadenoma                  | Ovary & uterine posterior wall EMs |
| 7     | 103.8  | normal| The nature of the written                | Cervical cancer                 | Mixed polyps                   |

*: the unit of CA125 & CA199 were U/ml.

2.4 Histopathological features

2.4.1 General characteristics. 7 PEM cases all had different shapes and sizes of mass according to the different tumor lesions location. 3 cases were single and 4 cases were multiple. There were 3 cases of ovarian PEM, 1 case of cystic solid (Case NO. 4), cystic chocolate fluid, solid part of polypoid soft tissue, part of gray and white necrosis, 2 cases of cystic (Case NO. 5 and 6), brown serous or chocolate fluid. The PEM of posterior uterine wall and oviduct showed dark brown flocculent tissue or grayish yellow necrotic tissue. The cervix PEM presented vegetable pattern vegetations with red polyps in the deep, and acetic acid turn white when under colposcopy.

2.4.2 Postoperative pathological features. The histology of PEM is similar to that of endometrial polyps occurring in the uterine cavity. The pathological tissue of PEM is composed of endometrioid glands and interstitial components. It has the pathological characteristics of common EMs, but it is more diverse than that of common EMs. Ovarian PEM, sacral uterine ligament PEM, fallopian tube sample PEM performance for endometrial tissue sample (endometrial stromal and glandular) like polypoid (as Fig 1), may be accompanied by a small amount of active epithelial hyperplasia, gland cystic expansion, focal gland hyperplasia of dense, rich part of mesenchymal cells, and moderate alien (as Fig 2), nuclear
fission, or have borderline changes (Case NO.5). The cervical PEM case showed endometrioid glands and stroma, and focal metaplasia on the fallopian tube.

2.4.4 Immunohistochemistry

Only 2 cases (Case NO. 5, 7) underwent immunohistochemistry, and Case NO.5 showed CKPAN (epithelial +), EMA (epithelial +), ER(++), PR(++), Vinmentin(++), Cd (-), Ki67 (10%+); Immunohistochemistry of P16 (+), P63 (+), Ki67 (5%+) and P16 (+), P63 (-), Ki67 (20%+) was performed twice in Case NO.5.

2.5 Other cases reported these years

This paper also summarizes the international reports of 13 cases in recent 5 years, aged 20-62 (51.14±3.78) years. (Table 4).
Table 4
Polypoid endometriosis: review of the literature of recent 5 years

| Year | References | Age | Location | Hormonal status | Presenting complaint | Size | examination |
|------|------------|-----|----------|-----------------|----------------------|------|-------------|
| 2016 | Akiko Y[9] | 37  | Uterine serosa | Various          | Large cyst of the ovary | 20   | CA$_{125}$ 3263 MRI |
| 2016 | Takeuchi, M[10] | 52  | around the pelvic cavity | / | complex endometrial hyperplasia | NA   | CA$_{199}$ 482 CA$_{125}$ 123 |
| 2016 | Tham, WP[11] | 43  | post vaginal fornix | / | prolonged menstruation | 3    | MRI CEA |
| 2017 | Zhuang, L[12] | 62  | ureteric | tamoxifen | gross hematuria | 1.5-1.0 | CA$_{125}$ 37.6 |
| 2017 | Han, K[13] | 58  | Colonic | / | uterine bleeding | 13x7x4 | / |
| 2017 | Iida, Y[14] | 44  | ovary | / | müllerianosis of the pelvic lymph node | 3.0  | MRI |
| 2017 | Jaegle, WT[15] | 62  | endocervical, uterine serosal surface | tamoxifen | pelvic mass | 1.5–3.5 | CA$_{125}$ 37.6 |
| 2018 | Laopakorn, S[16] | 47  | Urinary Bladder | / | urinary urgency | NA   | / |
| 2018 | Tabakin[17] | 41  | Renal Cortical | / | flank pain and gross hematuria | NA   | CT |
| 2019 | Tsai, C[18] | 23  | ovary | GnRh OC | lower abdominal pain | 10   | CA125 1317 |
| 2020 | Carbone, F[19] | 53  | Endometrial stromal sarcoma | / | Endometrial stromal sarcoma | 13.9-10.9-21.9 | CA$_{125}$ 476 CA$_{199}$ 209 |
| 2020 | Ling, R[20] | 20  | Rectum and Vagina | Gestrinone, progesterone | menstrual abdominal pain, anal distending pain, stool frequency | 3× 2 | CA$_{125}$ 58.72 |
| 2020 | Ghafoor, S[21] | 60  | proctosigmoid | / | pelvic mass | 6    | MRI |

NA:not available, GnRh: gonadotropin-releasing hormone agonist, OC:oral contraceptive

Discussion

3.1 Pathogenic characteristics. Polyp like intrauterine membrane endometriosis is different from the traditional type of peritoneal, ovary, and deep infiltrating endometriosis, at present, the PEM most cases reported in literatures in the rectum and sigmoid colon, followed by the ovaries, uterus serous and cervical and vaginal tract of department of gynaecology,
individual in ureter, fallopian tubes, greater omentum and retroperitoneal region \cite{3,6,7,9}. As shown in Table 1, ovarian PEM accounted for 4 of the 7 cases in this group, followed by uterine serosal and cervical PEM. PEM is characterized by multi-site and multi-focal lesions with different lesions in size, with the largest case increasing from 3cm to 20cm in 6 months \cite{9}, and small cysts in part of the section were honeycombed. In our cases, 3 cases were single lesions and 4 cases were multiple lesions. The size of the tumor ranged from 2.1cm to 11.7cm, but the size of the tumor had nothing to do with the duration of the disease. Parker \cite{2} believed that PEM was common in elderly women, and 60% of the 24 PEM patients they observed were older than 50 years old (23-78 years old), with multifocal lesions, and most of the cases had a history of EMs. In addition, 13 international cases reported in the past 5 years, aged 20-62 (51.14±3.78) years old (as Table 4) \cite{10-21}, were summarized. Gunawardane DN reported a 50-year-old female had a hysterectomy and bilateral salpingo-oophorectomy for adenomyosis, uterine leiomyomas, ovarian and cervical endometriosis. Nine months later, a mass between the vagina and rectum was diagnosed the Pouch of Douglas PEM \cite{22}. But all of the 7 patients in our group were women of childbearing age, aged from 31 to 45 (38.00±1.72) years old. No such lesions were found in postmenopausal women, which may be due to the small sample size of the cases in this group or the difference in race. Some studies have shown that the average age of 10 cases with tumor pathomorphology similar to EMS is about 43.4 years old (29-58 years old), and the possible age of polyps with morphology similar to EMs tends to be postmenopausal, with an average age of 50.9 years old (42-74 years old) \cite{23}.

The clinical manifestations of PEM are related to the site and size of the disease, and the common manifestations are abnormal uterine bleeding, pelvic mass, and mass compression. Cervical and vaginal polypoid manifestations include irregular vaginal bleeding and contact bleeding in most cases, and there may be no symptoms in the pelvic and abdominal cavity, most of which are accompanied by adenomyosis and dysmenorrhea \cite{6,8}. This is related to the fact that PEM belongs to a special type of EMs. In addition, the patient also had endometrial polyps, and the clinical manifestations of prolonged menstrual period of PEM may also be related to adenomyosis and endometrial polyps. Colin Jr performed intrauterine endometrial biopsy on 5 cases of PEM with pathomorphology similar to endometrial polyps, and the results found that 3 cases had endometrial polyps \cite{23}, suggesting that PEM was also closely related to endometrial polyps. In this group, there were 6 cases of severe pelvic adhesion, complete closure of the uterorectal fossa, and even frozen pelvis (Case NO. 6), which was another factor causing infertility. 4 out of 7 cases in this group were infertile, which also reflected that infertility was one of the clinical manifestations of EMs. Large PEM masses may present symptoms of compression at relevant sites, such as abdominal pain, nausea, vomiting, constipation, etc. The symptoms of urinary system \cite{25} and digestive system \cite{20} were mostly reported by related departments. In this group, 1 case of PEM invaded the ureter and resulted in left hydronephrosis (Case NO. 6).

3.2 Cause of disease. Endometriosis is a benign estrogen-dependent disease, and PEM belongs to a special type of EMS. Most of the case literature suggests that it is related to the use of sex hormones, such as tamoxifen, non-antagonistic estrogen or gonadotropin-releasing hormone \cite{9,12,15,18}. Sex hormone drugs were used in 5 of the 13 cases reported in the last 5 years, as shown in Table 4. However, in this group of 7 cases, only 2 cases had a history of sex hormone use, and no correlation was suggested. One case had a history of mifepristone anti-progesterone use for 6 months, and one case had a history of drodrogesterone use for 10 days. Among the cases reported by Parker et al. \cite{2}, 45% were affected by exogenous or endogenous hormones, most of which were perimenopausal hormone replacement therapy, which is also the reason why the age of onset of the cases reported by Parker et al tended to be postmenopausal. Kaushal S reported a 27-year-old nulliparous woman who had no history of tamoxifen or oestrogen intake, but presented with large finger-like projections protruding from her vagina, and last was diagnosed multifocal PEM \cite{3}.

Syrcre et al. studied a 25-year-old vaginal PEM case and found that compared with normal vaginal tissue, the expression of ER-β in PEM polyp tissue was 10 times higher, while the expression of ER-α was 5 times lower. The expression of estrogen synthetase aromatase in polyps was 8 times higher, while the expression of 3β-hydroxysteroid dehydrogenase
was 400 times higher. The cell type localization of PR in polyps was altered and stromal cell proliferation was increased. It is considered that vaginal PEM tissue may be caused by increased local estrogen production \[26\]. Combined with the pathogenesis of EMT \[27\], abnormal expression of local estrogen progesterone receptor could not be ruled out, and ER(+) and PR(+) were suggested by immunohistochemistry in most cases reported \[6\]. Incidence of 1 immunohistochemical also prompt the ER (+ +), PR (+ +), and most with ovulation dysfunction caused by abnormal uterine bleeding (AUB - O) and endometrial polyps, or associated with menstrual extension, 6 regular checks on the sex hormones, including 4 cases of serum estradiol tip increases (116-323 pg/ml), does not exclude the PEM morbidity associated with excessive estrogen in the body. The recent research Altay AY \[7\] included 15 cases of polypoid endometriosis, which were diagnosed between 2005 and 2019 and conclude that loss of stromal CD73 expression, due to its effect on the extracellular ATP/adenosine balance, may contribute to the pathogenesis of this rare form of endometriosis.

3.3 Auxiliary examination. Tumor marker monitoring was performed in PEM patients. As shown in Table 1, CA\textsubscript{125} significantly increased (> 100 kU/L), which may be related to EMS. The clinical manifestations of adenomyosis, dysmenorrhea and infertility also support this reason. In addition, the cases reported internationally in the past 5 years also showed abnormal increase of CA\textsubscript{125}. Akiko Y reported 1 case of large ovarian PEM (tumor diameter was about 20cm), with serum CA\textsubscript{125} level up to 3263 U/ml (normal < 35 U/ml)\[9\]. In this group, 6 cases showed a significant increase in CA\textsubscript{125} by 103.8-762.6 (225.47±117.49) kU/L, and 1 case was found to be located in the fallopian tube during PEM operation, but imaging examination did not indicate it. CA\textsubscript{125} was 15.3 kU/L, about 2.7 x 2.1cm in size, and the clinical symptoms were not specific. In conclusion, the abnormal increase of CA\textsubscript{125} is helpful for the diagnosis of PEM, and the value of CA\textsubscript{125} may be related to the size of the tumor.

At present, there is still a lack of ultrasonic and imaging research summary of this disease, and color ultrasound and intraoperative freezing manifestations are mostly similar to EMs without specificity. Color ultrasound may have difficulty in diagnosis. Jacquot A\[6\] thought that MRI findings were useful for preoperative diagnosis and is the preferred imaging modality for these lesions. There was no functional sign of malignancy (no diffusion restriction, pronounced tumor enhancement, or metastasis).

In this group of cases, 6 cases underwent CT and MRI examination and 5 cases were misdiagnosed, indicating CT and MRI examination insensitivity to its diagnosis. Soleen Ghafoor reported a case of PEM in the posterior vaginal dome, which was misdiagnosed as cervical cancer by CT, but MRI could use the effect of diffusion weighted imaging to locate the tumor, whether the tumor was of tumor origin, and whether there were signs of proliferation around it to distinguish PEM from malignant tumors\[20\]. Yasushi summarized the characteristics of MRI examinations in 6 cases of misdiagnosis of ovarian PEM reported between 2003 and 2008: ovarian PEM showed low signal intensity margins on T2WI, and solid nodules showed rounded edges with smooth edges. However, in EMS-induced ovarian cancer, no such low signal intensity edge was observed on T2WI, and the nodular edge was irregular, which may help to distinguish PEM from EMS-related malignancy \[28\].

3.2 Clinicopathological features

The diagnosis of PEM depends on pathology. Based on the summary of the cases in this group and the literature reports, the general manifestations were all single or multi-focal cysts or exogenous masses of different sizes, which were connected to the surrounding tissues with pedles or broad bases of different thickness, and severe pelvic adhesion could be observed intraoperically. The PEM of the ovary was cystic and solid. The cystic portion of the tumor contained chocolate or brown serous fluid, while the solid portion of the tumor had a polypoid or malignant tumor or gray-yellow necrotic tissue appearance. The PEM of the vagina or cervix showed like cauliflower pattern or florid, and the deep part
showed red polyps. The PEM section of the serosal surface of the uterus was grayish white or grayish red. Cleo Tsai also reported a case of PEM behind pelvic uterus with the appearance of taupe florid polypoid soft tissue \[18\].

The term PEM (or "endometrial polyposis") was first coined by Mostoufizadeh and Scully for endometriosis \[1\]. Microscopy showed that the pathological morphology of the lesion was similar to that of endometrial polyps occurring in the uterine cavity. The pathological tissues were all composed of endometrioid glands and stromal components, which had the pathological characteristics of common EM, but were more diverse than that of common EM. The surface is erosive or covered with a single layer of columnar, cubic, or dwarf cubic epithelium. It may be accompanied by a small amount of active epithelial hyperplasia, cystic dilatation of the gland, intensive hyperplasia of the focal glands, abundant interstitial cells in some parts, moderate atypia, nuclear mitosis, or borderline changes, metaplasia of the fallopian tube, and atypical hyperplasia, which also bring great confusion for pathological examination \[22-24\]. At present, the immunohistochemical studies on PEM mostly suggest ER(+), PR(+), and Vinmentin(++) , as previously mentioned \[26,29\]. Two immunohistochemical examinations of 7 cases in this group showed P16(+). Colin JR, compares the 15 cases of PEM and 20 cases of PEM EMs (NPE) immune histology CD10 and p16 staining, and estimates the p16 positive proportion of stromal cells and epithelial cells, the results suggest: pathological morphology and immunohistochemical features of EMs is similar and NPE are similar, morphology and endometrial polyps similar 5 cases, the stromal cells and epithelial cells p16 expression \[23\]. Nicolae A also proposed that the metaplasia changes in the endometrium might be related to the increased expression of p16 \[30\].

In conclusion, PEM, a rare type of EMs, clinically easily misdiagnosed as malignant tumor, often with endometrial polyps, uterine adenomyosis, abnormal uterine bleeding, infertility and so on, auxiliary examination suggests higher abnormal CA_{125}, MRI is helpful to identify whether for EMs related to malignant tumor, pathological examination as the gold standard, immunohistochemical prompt ER (+), PR (+) and P16 (+). The clinician should combine the medical history, physical examination, tumor markers and other examination results to make comprehensive judgment.

**Declarations**

**Ethics approval and consent to participate**

The study was conducted following good ethical and scientific principles. The ethical review committee of Fujian Provincial Maternity and Children's Hospital approve that there were no ethical issues involved in this study.

After expressing objectives, assuring the participants about confidentiality of their data and possibility of withdrawing from the study, a written informed consent form will be signed by those participants who were willing to participate in this research.

**Consent for publication**

All participating patients signed the informed consent to participate in the study as well as their data and images (without personal identification) being used for diagnostic and scientific publication purposes.

**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Conflict of interest statement**
There is no conflict of interest associated with this manuscript. The author declares that they have no competing interests.

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**Authors’ contributions**

XHZ and YX proposed the study concept and design, assisted by CQL. YX, QBZ, RZ, and XJC acquired and checked the data. QBZ carried out the data analyses. XHZ drafted the manuscript. LJZ researched literature. All of the authors approved the final version of the manuscript.

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Figure 1

Hyperplasia of endometrial glands and stromal cells
Figure 2

Complex hyperplasia with secretory changes