

図3

告では、long protocolの方が採卵数、受精卵数および移植あたり妊娠率において有意に良好な成績を示した²⁰⁾。また、異なる時期に行った、long法とhMG(rhFSH)-GnRH antagonist法とのRCTにおいては、やはりlong法を用いた方が、採卵数、治療周期および胚移植あたりの妊娠率において、有意に良好な成績を示した²¹⁾。ただし、彼らが対象としたのは血中FSH値が10IU/mL以下の症例のみで、卵巢予備能の十分な症例だけを対象としていることに留意すべきであり、FSH高値例を含めた高齢不妊症例一般にあてはめて考えるべきでないと思われる。ただ、40歳以上の症例でFSH値が低く、調節卵巢刺激の効果が期待できる場合にはlong法が最も有効な治療法かもしれない。

2001~2007年の自施設における検討では、40歳以上の症例に対して行われた391採卵周期のうち310周期が胚移植に至り、うち52周期で臨床妊娠が成立(移植周期あたり臨床妊娠率16.8%)、30周期が生産に至った(採卵周期あたり生産率7.7%)。当科においては、卵巢予備能が十分であると評価された症例についてはlong protocolを、予備能が低下している症例では主としてhMG-Antagonist法を用いている。次に、卵巢刺激プロトコールによる生産率を比較した(図2)。40歳以上の症例に対しては、198周期(50.6%)でlong protocol、100

周期(25.6%)でhMG-GnRH antagonist法が用いられていた。それぞれのプロトコールにより生産に至った周期はそれぞれ17周期(8.6%)、10周期(10.0%)であり、有意差はないものの、hMG-GnRH antagonist法の方がやや良好な成績を示した。なお、34歳以下、35~39歳の症例では有意差はないものいずれもlong protocolの方がやや良好な成績を示しており、高齢症例に対してGnRH antagonist法の有用性を示唆する結果となった。

次に、採卵数と生産率を各年齢層で比較したところ、34歳以下、35~39歳の症例では採卵数7~8個以上では生産率がほぼプラトーに達したの比べ、40歳以上の症例では採卵数7~8個の場合にもっとも生産率が高く、9個以上の群ではむしろ低下する傾向にあった(図3)。40歳以上の症例において、採卵数と生産率の関係をさらに誘発別に検討したところ、採卵数9個以上の群での成績低下は、hMG-antagonist群でより顕著であり、採卵数9~14個の群では生産症例がみられなかった。

近年、GnRH antagonistの導入とともに調節卵巢刺激法の多様化が進んでいるが、自施設における成績から推察されるように、hMGを中心とした卵巢に対する過度の刺激は、40歳以上の症例においてはむしろ逆効果である可能性が示唆されている。今後、特に卵巢機能の低下

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Assisted Reproductive Technology (ART) for aged infertile patients

Akihisa FUJIMOTO

Department of OB/GYN, Faculty of Medicine, University of Tokyo

Key words : aged patients · ART · hMG-GnRH antagonist

索引語 : 高齢不妊症, ART hMG-GnRH antagonist

Successful management of a ruptured endometrial cyst in acute leukemia

Ayumi Taguchi, M.D.,^a Kaori Koga, M.D., Ph.D.,^a Yutaka Osuga, M.D., Ph.D.,^a Akihisa Fujimoto, M.D., Ph.D.,^a Aki Miyasaka, M.D.,^a Tetsu Yano, M.D., Ph.D.,^a Minieo Kurokawa, M.D., Ph.D.,^b and Yuji Taketani, M.D., Ph.D.^a

^a Department of Obstetrics and Gynecology and ^b Department of Hematology and Oncology, University of Tokyo, Tokyo, Japan

Objective: To report a case of acute abdomen due to rupture of ovarian endometrial cysts, manifested as a first symptom of acute leukemia.

Design: Case report.

Setting: University hospital.

Patient(s): A 28-year-old Japanese woman with acute abdomen.

Intervention(s): A diagnosis of rupture of endometrial cysts was made by ultrasonography and magnetic resonance imaging. A diagnosis of acute myeloid leukemia (FAB M5a subtype) was made by bone marrow aspiration.

Main Outcome Measure(s): Remission-induction chemotherapy for leukemia was initiated. Meanwhile, endometrial cysts were managed expectantly. Once complete remission was achieved, laparoscopic surgery was attempted to remove ovarian cysts and abdominal fluid.

Result(s): Patients tolerated laparoscopy with favorable postoperative course. Consolidation chemotherapy commenced without substantial delay.

Conclusion(s): Accurate diagnosis, optimal timing of surgery, and minimally invasive surgery with laparoscopy enabled us to manage this high-risk case to a favorable outcome. (*Fertil Steril*® 2011;95:292.e1-e3. ©2011 by American Society for Reproductive Medicine.)

Key Words: Endometriosis, ovary, cyst, rupture, acute abdomen, acute leukemia, laparoscopy

Acute abdomen complicated with leukemia is rare, but it has a high mortality rate. We report herein the successful management of acute abdomen due to a sudden progression of endometriosis manifested as a first symptom of acute leukemia.

CASE REPORT

An approval of our Institutional Review Board was obtained for reporting this case. A 28-year-old woman presented to a local hospital with acute onset of severe abdominal pain which had developed 1 day earlier. Her past history was unremarkable. Her mother had died of ovarian clear cell carcinoma.

She had regular menstrual cycles, and the onset of symptoms fell on the second day of menstruation. She was not sexually active and had never had a gynecologic check-up until then. On examination, the abdomen was hard and distended. Computerized tomography revealed peritoneal fluid and enlarged ovaries. Laboratory tests revealed remarkable leukocytosis (100,000/mm³) and thrombocytopenia (14,000/mm³). She was transferred to our hospital on suspicion of abdominal hemorrhage complicated by acute leukemia.

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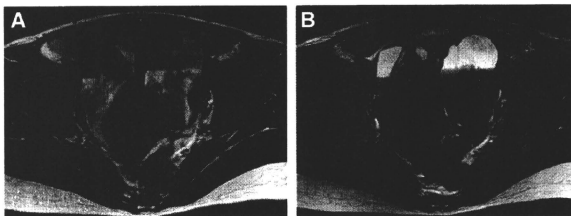
Reprint requests: Kaori Koga, M.D., Ph.D., Department of Obstetrics and Gynecology, University of Tokyo, 7-3-1 Hongo Bukyo, Tokyo, Japan 113-8655 (FAX: 81-3-3816-2017; E-mail: kawotan-ky@umin.ac.jp).

Her abdomen showed a strong muscle defense. On gynecologic examination, she had strong pain in the perimetrial area and cystic tumors palpable in both adnexa. Ultrasonography revealed peritoneal fluid as well as enlarged bilateral ovaries with heterogeneous echogenicity. To assess further, magnetic resonance imaging (MRI) was performed (Fig. 1). Ovarian cysts, 9 cm in diameter, were detected in each ovary with a moderate amount of peritoneal fluid. The cystic lesions indicated fluid-fluid levels and heterogeneous intensity; some parts exhibited hyperintensity on T1-weighted image (WI) and hypointensity on T2WI, a typical feature of endometrial cysts, hyperintensity on both T1WI and T2WI, or hypointensity on T1WI and hyperintensity on T2WI. There was no solid part enhanced by contrast media. The peritoneal fluid indicated intensity compatible with blood. Collectively, a diagnosis of bilateral endometrial cysts, containing various phases of clotting, accompanied by peritoneal fluid due to a leak from ruptured cysts, was made. The peripheral white blood cell count was 100,400/mL with 99% blasts. Her hemoglobin was 7.0 g/dL and platelet count 17,000/mL. The serum CA125 and CA19-9 levels were 1,933 U/mL and 2,255 U/mL, respectively, and the plasma D dimer level was 8.4 µg/mL. Bone marrow aspiration was conducted in the hematology clinic, and a diagnosis of acute myeloid leukemia (FAB M5a subtype) was made.

Her condition was considered to be acute abdomen owing to an acute progression of endometrioma with rupture, which occurred as a manifestation of acute leukemia. Given a high mortality rate for surgery in leukemia with nonremission status, we chose an expectant management for endometriosis and initiated remission-induction

FIGURE 1

Magnetic resonance images obtained on admission: (A) T1-weighted image; and (B) T2-weighted image. Bilateral ovarian cysts 9 cm in diameter in each were detected. The cystic lesions showed fluid-fluid levels, and each component showed heterogeneous intensity. The peritoneal fluid showed intensity compatible with blood.



Taguchi. Endometrioma rupture in acute leukemia. *Fertil Steril* 2011.

chemotherapy for leukemia. Combination chemotherapy with idarubicin and cytarabine started immediately in the hematology clinic. The patient was carefully monitored under intensive care; blood transfusions of concentrated red cells and platelets were given for anemia and prevention of hemorrhage, and analgesics for pain control. Signs of deterioration of endometriosis or infection were not observed. The patient tolerated the chemotherapy, and complete remission was achieved on day 31 of chemotherapy. Subsequent consolidation chemotherapy was requested for maintenance of the remission. Knowing that consolidation chemotherapy may inevitably cause severe pancytopenia, we scheduled a surgical removal of endometriosis with peritoneal lavage before chemotherapy to reduce a risk of further bleeding and/or an abdominal infection. A laparoscopic approach was considered to minimize the invasiveness. Five days after the complete remission was confirmed, we performed laparoscopy: The abdominal cavity was filled with a chocolate-colored fluid; ~250 mL, suggesting the earlier rupture of endometrioma.

Adhesion was seen between two ovaries as well as between each ovary and the posterior wall of the uterus. There was an endometrial cyst in each ovary, each with a diameter of ~10 cm. These cysts contained not only chocolate-colored fluid typically found in endometrial cysts but also large "fresh clots" presumably developed after the onset of leukemia. The total amount of cyst fluid was ~800 mL. There was no evident site of rupture, suggesting that the site had been already sealed. After adhesiolysis, the cyst capsules were removed, the abdominal cavity was cleaned, and hemostasis was achieved by bipolar coagulation and suturing. Histologic examination of the resected specimens indicated endometriosis without evidence of leukemic cell infiltration.

The patient's postoperative course was favorable. On postoperative day 12, consolidation chemotherapy with cytarabine was begun. Despite severe pancytopenia (white blood cell count 100/mL, platelets 14,000/mL), she successfully completed chemotherapy with no complication such as abdominal bleeding or abdominal infection.

DISCUSSION

Acute abdomen due to a sudden progression of endometriosis manifested as a first symptom of acute leukemia is extremely rare. To our knowledge, only one English-language article has previously described this complication. Cepicky and Feyerreislova (1) described

a case of a 23-year-old woman with a ruptured ovarian endometrial cyst as a first symptom of acute myeloid leukemia. In that report, the patient died in the postoperative period. Our case is the first report of successful management of this complication.

There are differential diagnoses that can cause abdominal fluid retention with ovarian pathology in acute leukemia, such as ovarian infiltration of leukemic cells and hemorrhage from corpus luteum. Nishimoto et al. (2) described a case of hemoperitoneum manifested as a first symptom of acute myeloid leukemia, complicated with ovarian infiltration. Habek et al. (3) reported a case of acute abdomen caused by a rupture of the corpus luteum, also a first symptom of acute lymphatic leukemia. In the present case, ovarian infiltration of leukemic cells was ruled out according to the MRI findings: No solid part enhanced by contrast agent was detected. We also excluded hemorrhage from the corpus luteum because of the bilateral pathology and onset was not in the luteal phase. The accurate diagnosis was crucial to determine further managements. In the present case, MRI findings as well as careful history taking was critical to reach the correct judgment.

Abdominal surgery for patients with leukemia is associated with extremely high mortality rates, ranging between 27% and 58% (4-8). The cause of death in most cases is sepsis or hemorrhage. It is therefore particularly valuable to report the present successful management of acute abdomen complicated by acute leukemia. One of the critical points to minimize the risk of perioperative complication is the timing of surgery.

In this context, two decisions were made in this case. First, we chose expectant management and commenced remission-induction chemotherapy instead of conducting emergency surgery. It has been shown that postoperative mortality rate is extremely high when the surgery is conducted while the patient with leukemia is not in remission. Vaughn et al. (4) reviewed intra-abdominal operations in acute leukemia and reported that the mortality rates for patients not in remission and for those in remission were 50% and 38%, respectively. Similar results were shown by Koretz et al. (5), such that the mortality rate for patients not in remission was 78%, whereas all patients in remission survived. Given this evidence, we decided to choose expectant management despite its inherent risks of intra-abdominal hemorrhage and/or infection in endometriosis. The patient was carefully monitored and given intensive care

during chemotherapy, resulting in complete remission without any complication of endometriosis.

Second, we scheduled surgery before the consolidation chemotherapy. If the abdominal pathology had not been treated, the risk of intra-abdominal hemorrhage and/or infection within endometriosis, with pancytopenia inevitably caused by chemotherapy, would have remained. Indeed, there is a report of acute abdomen, due to endometriosis, during chemotherapy for acute myelocytic leukemia (9). Thanks to these decisions, the surgery was completed without any complication and consolidation chemotherapy was conducted safely.

Our surgical management using a laparoscopic approach as a choice of minimally invasive surgery was also beneficial. Ustun (10) reports a case of acute leukemia where appendicitis developed during chemotherapy. Laparoscopic appendectomy was performed without any complication and chemotherapy was continued as scheduled. This favorable outcome is in contrast to the result of open surgery, which shows a high mortality rate even in appendectomy (5). In the present case, the laparoscopic approach was challenging because severe peritonitis with extensive adhesion was suspected. However, all of the procedures were completed laparoscopically.

The patient showed rapid recovery and was able to take the consolidation chemotherapy without substantial delay.

In this case, it is difficult to know the actual progression of endometriosis during the onset of leukemia, because information about disease status before the onset is lacking. However, given that the cysts contained fresh clots and chocolate-like fluid, it could be speculated that there might have been preexisting endometrial cysts and that the acute thrombocytopenia may have caused further hemorrhage within the cysts and their rupture. Interestingly, menstruation, which began the day before onset, was as usual in volume and duration. This may indicate that ovaries affected by endometriosis are vulnerable to bleeding compared with healthy organs, resulting in sudden hemorrhage.

In summary, we report a case of acute abdomen due to rupture of ovarian endometrial cysts, manifested as a first symptom of acute leukemia. Accurate diagnosis, optimal timing of surgery, and minimally invasive surgery with laparoscopy enabled us to manage this high-risk case to a favorable outcome.

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POLYPS

Sessile polyps and pedunculated polyps respond differently to oral contraceptives

OSAMU WADA-HIRAIKE, YUTAKA OSUGA, HISAHIKO HIROI, AKIHISA FUJIMOTO, MASANORI MARUYAMA, TETSU YANO, & YUJI TAKETANI

Department of Obstetrics and Gynecology, Graduate School of Medicine, The University of Tokyo, Tokyo, 113-8655 Japan

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Abstract

Endometrial polyp is the lesion frequently found by hysteroscopy. The presence of endometrial polyp is associated with abnormal uterine bleeding and is probably associated with infertility. Until today, clinical guidelines for endometrial polyp remain elusive. The aim of this preliminary study was to estimate whether the shape of endometrial polyps affects the response to the treatment with an oral contraceptive (OC). We performed a retrospective case series study on 50 women diagnosed as endometrial polyps by hysteroscopy and managed by the administration of OC. Hysteroscopy was performed in the follicular phase of the menstrual cycle before medical treatment. Endometrial polyps were classified as pedunculated polyps ($n=25$) or sessile polyps ($n=25$). After diagnosis, OC was administered for 2–5 months (median 3 months) intermittently. To quantify the regression rate of lesions, the area index of endometrial polyps was assessed. In the study group, when comparing the efficacy of treatment with OC, there was a statistically significant difference in the regression rate between sessile polyps and pedunculated polyps (76% vs. 44%, $p=0.042$). We conclude that sessile polyps are more sensitive to OC treatment than pedunculated polyps, implying usefulness of the hysteroscopic classification of the shape of polyps in the management of endometrial polyps.

Keywords: *Endometrial polyps, oral contraceptive, pedunculated polyps, sessile polyps*

Introduction

Endometrial polyp is the lesion most frequently found by hysteroscopy [1]. The frequency is 10% in asymptomatic premenopausal women older than 30 [2]. The aetiology of endometrial polyp is proposed to be related to estrogenic stimulation [3], which is manifested by induction of polyps after the treatment with tamoxifen that provides an estrogenic stimulus to the endometrium [4]. Polyps can be histologically characterised as localised hyperplastic overgrowths of glands and stroma. In menstruating women, they may cause abnormal uterine bleeding, hypermenorrhea, and infertility. Hysteroscopic polypectomy has been shown to improve fertility rate, suggesting that endometrial polyp is an infertile factor [5–7]. In addition, endometrial polyp is recently suggested to be a risk factor for endometrial cancer and the

presence of endometrial polyp should be carefully followed up to prevent disease progression [8].

Polyps can be surgically removed using curettage or hysteroscopy while some may regress on their own [9]. Although natural history of endometrial polyp is poorly understood, one study that followed seven asymptomatic women with endometrial polyps for 2.6 years demonstrated that both two women who had taken hormonal medications had regression of their polyps whereas two in five women who had not used any hormonal medications had spontaneous regression of their polyps [10].

We introduced an oral contraceptive (OC) for the treatment of endometrial polyp to confirm its expected effect to decrease the volume of endometrial polyp by suppressing endogenous estrogen. Conducting this treatment, we noticed that the response of polyps to OC appears to be different depending on the

Correspondence: Dr. Osamu Wada-Hiraike, Department of Obstetrics and Gynecology, Graduate School of Medicine, The University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo, 113-8655, Japan. Tel: + 81-3-5800-8657. Fax: + 81-3-3816-2017. E-mail: osamu.hiraike@gmail.com

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shape of polyp, i.e. pedunculated polyps and sessile polyps. Here we report the different regression rate by OC treatment between the two groups.

Materials and methods

We reviewed both electronic and paper medical records of all patients with endometrial polyps diagnosed at our institution between 1 January 2000 and 30 December 2008. The ultrasonographic evaluation with regard to the thickness of endometrium was assessed in all the patients. Indications for hysteroscopy were as follows, infertility screening, hypermenorrhea, abnormal uterine bleeding, and/or indicative findings for endometrial lesion (e.g. thick endometrial layer exceeding 15 mm). Prior to the hysteroscopy, endometrial cytology or biopsy was obtained and no malignancies were detected in all the subjects. In total, 212 women between 21- and 48-years old were diagnosed as endometrial polyp by hysteroscopy. Seventy-eight patients were treated by primary hysteroscopic resection of polyps and 46 patients were carefully observed without any interventions (Figure 1). These patients were randomly allocated to the treatments under informed choice of each patient. Of 88 patients that were treated by OC (Sophia A, a tablet containing norethisterone 1.00 mg and mestranol 0.05 mg, ASKA Pharmaceutical Co., Ltd., Tokyo, Japan) and were without hormonal medications before the administration of OC, 38 patients were excluded because of several reasons listed in the Figure 1 (reasons for dropout). The remaining 50 patients were subdivided into two groups according to the shape of polyps, i.e.

pedunculated polyps or sessile polyps. No patients possessed both pedunculated and sessile polyps in this study. The patients took OC (1 tablet/day) for 21 days with subsequent withdrawal bleeding. The cycle of OC intake was between 2 and 5 (median 3.0). Follow-up included clinic visits and repeated hysteroscopy and transvaginal ultrasound examination including sonohysterography just after OC cycle in the follicular phase of the menstrual cycle. The measurement of polyps was done by transvaginal ultrasound. After defining the largest sagittal view of the lesion, the longest part of the lesion (A) and the orthogonalising part (B) was measured, and then $A \times B$ was calculated (Figure 2). The sum of $A \times B$ of all polyps was calculated in each patient and defined as an 'area index' of polyps to estimate the volume of these lesions. To evaluate the efficacy of treatment, the reduction percentage of this index more than 90% was defined as 'regression' of the lesions. Less than 90% reduction was defined as the ineffective treatment. This report was exempt from the Institutional Review Board approval because the treatment required for these patients is a standard procedure for the treatment of endometrial polyps.

All procedures with regard to hysteroscopy were performed in the early follicular phase of the menstrual cycle on an outpatient basis. Each patient was discharged within 60 min. A 3.1-mm continuous-flow mechanical office hysteroscopy (Olympus, Tokyo, Japan) was inserted to the uterine cavity using atraumatic technique. Uterine cavity was distended with normal saline infusion. Uterine distension was achieved with a pressure cuff around the irrigation bag (25–35 mmHg). The cavity was systematically

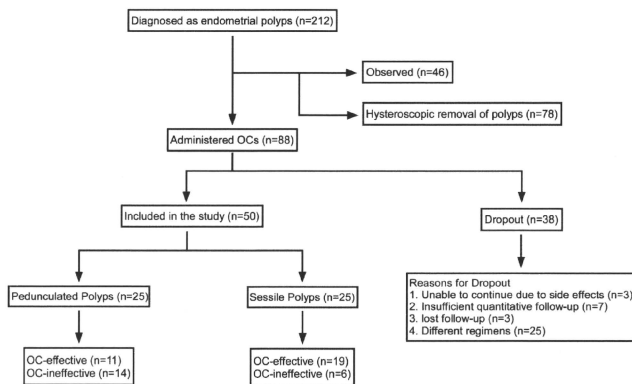


Figure 1. Flow chart of subjects in the study.

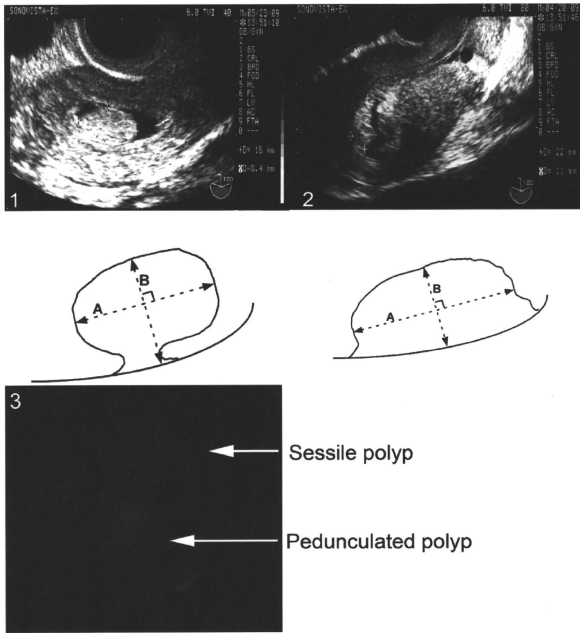


Figure 2. Representative size measurement and appearance of endometrial polyps. (1) Pedunculated polyps. (2) Sessile polyps. Schematic description of A and B is shown below. (3) Representative hysteroscopic appearance of polyps.

inspected for any abnormal findings. Good visualisation of the entire cavity with no structural abnormalities or hypervascularisation and the uniformly thin, homogenous-appearing endometrium without variations in thickness was considered normal. The typical appearance of pedunculated endometrial polyps was a well defined, homogenous, and smooth surface polypoid lesion attached to the uterine wall by a thick and short pedicle. These lesions were hemispheric, linguiform or coniform in shape. Even though the macroscopic appearance of sessile polyp was similar to that of the pedunculated ones, pedicle of sessile polyps was broad-based or flat as described in the previous report [11] and this atypical appearance of polyps was frequently observed. Most patients had no anesthesia during diagnostic hysteroscopy.

Statistical analysis was performed using Fisher's exact test for comparing the categoric variables between groups. The difference was analysed by Mann-Whitney's *U*-test for comparing continuous variables between groups. For all tests, a *p* value of

less than 0.05 was considered to be statistically significant.

Results

The characteristics of the subjects are summarised in Table I. Sessile polyps were tended to be multiple and the number of lesions was higher in women with sessile polyps compared to those with pedunculated polyps (3.32 vs. 1.48, $p < 0.0001$). There were no statistically significant differences in the parity, age, and the frequency of abnormal uterine bleeding between the two groups. Patients with sessile polyps were significantly complicated by hypermenorrhoea compared to those with pedunculated polyps (64% vs. 36%, $p = 0.022$, Table I).

After the OC treatment, the thickness of endometrium was decreased and the frequency of symptoms such as hypermenorrhoea and abnormal uterine bleeding was also decreased in most of the patients. Hysteroscopic and sonographic findings after the

Table I. Patient demographic and treatment characteristics.

	Pedunculated polyp (n = 25)	Sessile polyp (n = 25)	p value
Age (year)	35.2 ± 7.1	32.8 ± 4.7	0.183*
Parity	0.32 ± 0.74	0.28 ± 0.61	0.899*
Abnormal uterine bleeding	36% (9/25)	40% (10/25)	>0.999 [†]
Hypermenorrhea	28% (7/25)	64% (16/25)	0.022 [†]
Number of lesions	1.48 ± 0.77	3.32 ± 1.84	<0.0001*
Area index of lesions (mm ²)	142.3 ± 89.9 (range 36.2–319.8)	125.7 ± 64.0 (range 18.59–285.0)	0.826*
Regression [‡] by OC treatment	44% (11/25)	76% (19/25)	0.042 [†]

*Mann–Whitney U test.

[†]Fisher's exact test.[‡]The word 'regression' denotes the reduction rate more than 90%.

treatment with OC revealed that the rate of regression was higher in the group of sessile polyps compared with the group of pedunculated polyps (76% vs. 44%, $p = 0.042$, Figure 1 and Table I).

Discussion

The present study demonstrates that sessile polyps regress in a higher rate than pedunculated polyps under OC treatment. Several mechanisms can be speculated in OC-induced regression of the polyps. Apoptosis might be a mechanism in light of the finding that exposure to a monophasic OC for 30 days significantly increases endometrial apoptosis both in epithelial and stromal cells [12]. Another mechanism could be that the establishment of a steady estrogen-progesterone milieu induces endometrial quiescence, leading to the regression of endometrial polyps. Anti-inflammatory effects of progesterone might also be involved given that mast cell-associated inflammation is associated with endometrial polyp growth [13]. Nevertheless, it is difficult to speculate a specific reason why the sensitivity to OC is different between the two types of polyps. OC therapy is not without its own risks, particularly in an older (over 35-year old) population. Thus, it is debatable whether medical therapy is preferable. Furthermore, there is no longer-term follow-up as to how long the medical effects of the OCs will be maintained, even after cessation of this therapy. Given the average age of the populations studied, it is likely that the same endometrial environmental factors promoting the presence of the polyp(s) would still be extant at the completion of therapy. However, since there is no proper guideline for the treatment of endometrial polyp, it would be interesting to pursue the nature of endometrial polyp and therapeutic effect brought by OC.

Although the natural history of endometrial polyps is poorly known, one study demonstrated that smaller polyps regress with time and larger ones tend to persist [10]. The recent report speculated that polyps less than 10 mm may vanish [9]. In our study, as for pedunculated polyps, the size was tended to be small in OC-effective patients compared

to OC-ineffective patients (113.23 vs. 168.96 mm², $p = 0.123$) though the difference was not statistically significant. In contrast, sensitivity to OC treatment was unaffected by the size of polyps in patients with sessile polyps since the OC-effective patients possessed similar sized polyps compared with OC-ineffective patients (123.66 vs. 132.24 mm², $p = 0.496$). These findings may suggest that the difference of cellular characteristics between the polyps is relevant to the overall regression rate and polyps more than 10 mm can regress by the OC treatment, at least in part.

An association between endometriosis and the presence of polyps has been suggested. A retrospective study found endometriosis in 27 of 32 (84.37%) women with polyps or polyoids at hysterosalpingography, compared with endometriosis in 19 of 88 (21.59%) patients without polyps or polyoids [14]. Because of the limited number of cases, we cannot address the relationship between the types of polyps and endometriosis in this study. However, it may be intriguing to study the relationship between endometriosis and the shape of polyps.

Some argues that polyps spontaneously regress [9]. And it may be the weakness of our study that we did not include comparison/control group of non-OC-treated patients. Nevertheless, our finding has an impact by demonstrating that one can predict the response to OC according to the shape of the polyps and hysteroscopy is useful to judge the shape of the polyps precisely. Although the detrimental complication rate associated with hysteroscopic surgery is low [15], gynecologists should remember complications brought by the hysteroscopic surgery such as intravasation of distension fluid, uterine perforation, infection, and haemorrhage. The fact that the shape of the polyps would be informative in selecting the treatment of endometrial polyps might be especially helpful for managing patients who prefer to avoid surgical treatment.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Case of chronic ectopic pregnancy diagnosed in which the complete shape of the fetus was visible by ultrasonography

Miyuki Harada¹, Hisahiko Hiroi¹, Toshihiro Fujiwara², Akihisa Fujimoto¹, Akihiko Kikuchi³, Yutaka Osuga¹, Mikio Momoeda¹, Koji Kugu¹, Tetsu Yano¹ and Yuji Taketani¹

¹Department of Obstetrics and Gynecology, Faculty of Medicine, University of Tokyo, Tokyo, ²Center for Human Reproduction, Sanno Hospital, Tokyo, and ³Department of Obstetrics, Center for Perinatal Medicine, Nagano Children's Hospital, Nagano, Japan

Abstract

Preoperative diagnosis of chronic ectopic pregnancy is often difficult because of the high incidence of negative results on pregnancy tests as a consequence of the very small amount of live villi, subtle symptoms, and the poor specificity of ultrasonographic patterns. A 45-year-old woman was referred to our department for evaluation of a mass 8 cm in diameter with solid parts in the right adnexal area. Transvaginal ultrasonography showed a mass consisting of a cystic part with an irregular thick capsule distinct from the right ovary. In the center of the cystic part, a fetus-like image, 20 mm in length was seen. Preoperative diagnosis was confirmed by the laparoscopy, which revealed a swollen right tube containing a fetus with highly necrotic changes. This case was unique because chronic ectopic pregnancy was detected at an early stage before absorption of the conceptus occurred, which coincidentally is an appropriate time for morphological diagnosis.

Key words: chronic ectopic pregnancy, human chorionic gonadotropin, laparoscopy, magnetic resonance imaging, ultrasonography.

Case Report

A 45-year-old woman, gravida 4, para 2, presented to her primary gynecologist's clinic with complaints of lower abdominal distention for one month. She had no gastrointestinal symptoms, her appetite was normal and her bodyweight had not changed. Transvaginal ultrasonography revealed a mass, 8 cm in diameter, in the right adnexal area, similar to an ovarian neoplasm, and she was referred to our department. On gynecological examination, a fist-sized, immobile, tender, elastic hard mass was detected in the right side of the cul-de-sac, and no abnormal finding was shown in the left adnexal area. Transvaginal ultrasonography revealed that this mass consisted of a cystic part with

an irregular thick capsule distinct from the right ovary (Fig. 1a). There was no abnormal finding in the uterus or the left ovary, and free fluid was not observed by transvaginal ultrasonography. In the center of the cystic part, a fetus-like image, 20 mm in length, was seen. Magnetic resonance imaging (MRI) showed the lesion with central necrosis and a thick fibrous capsule (Fig. 1b). Tests for both human chorionic gonadotropin (hCG) and β -hCG were negative. The plasma α -fetoprotein (α FP) level (normal; 0–9) was elevated to 116 ng/mL. The plasma CA19-9 and CA125 levels were 17 U/mL and 13 U/mL, respectively. Hereafter, to clarify the clinical time course, we define the day of her first visit to our hospital as day 0. For example, one month before and 10 days after her first visit are

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Reprint request to: Dr Hisahiko Hiroi, Department of Obstetrics and Gynecology, Faculty of Medicine, University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. Email: hhroi-ky@umin.ac.jp

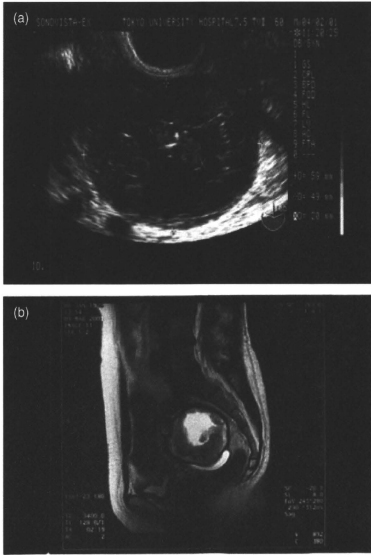


Figure 1 (a) Transvaginal ultrasonography revealed a right adnexal cystic mass with irregular thick capsule containing a fetus-like image. (b) Magnetic resonance imaging, T2-weighted. α FP, α -fetoprotein.

mentioned as -1 month (m) and $+10$ days (d), respectively. The clinical time course is indicated in Figure 2. Although the patient had a regular menstrual cycle of 28 days before -9 m, she had no menstruation in -8 m, -4 m (only spotting was observed), -3 m, and -1 m. The last sexual intercourse before consultation was during -4 m. On $+52$ d, the plasma α FP level dropped to 42 ng/mL and concomitantly, the size of the mass decreased to 5.5 cm in diameter, although no change was found in the shape of the fetus-like image. Taking these findings into consideration, we diagnosed the mass as a chronic ectopic pregnancy; however, we still couldn't exclude the possibility of an ovarian neoplasm with just these serological tests and images, in spite of the decrease in its size and the plasma α FP level within 2 months. In this context, with a thorough informed consent, we performed laparoscopy on $+53$ d in order

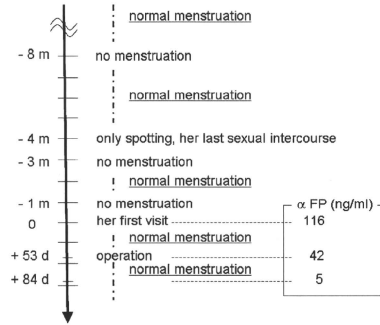


Figure 2 The clinical time course. The vertical line indicates the time course. d, day; m, month.

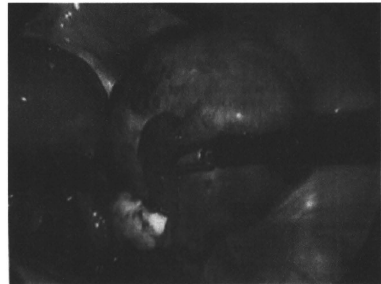


Figure 3 Laparoscopic view. The ampulla of the right tube enlarged.

to make a pathological diagnosis with a minimal invasive surgery. A 6-cm mass was noted in the ampullary portion of the right tube (Fig. 3). Filmy adhesion between the mass and the right ovary, surrounding mesentery, and the posterior broad ligament was found. The excised right tube is shown in Figure 4a. The mass was filled with brownish fluid, containing a fetus with highly necrotic changes (Fig. 4b). The crown-rump length of the fetus was about 2.0 cm. Histological evaluation confirmed a diagnosis of chronic right tubal pregnancy. The plasma α FP level gradually decreased thereafter, reaching normal limits one month after surgery.

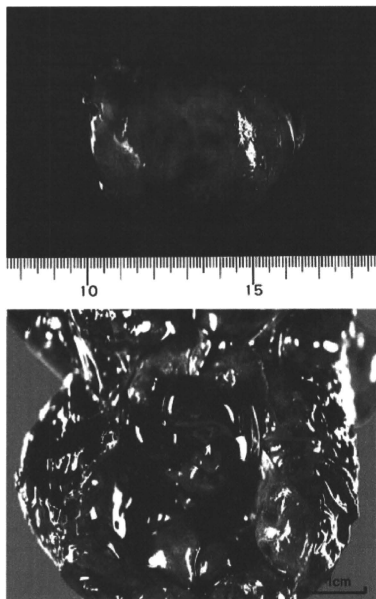


Figure 4 Macroscopic views of the excised right tube. (a) As a whole. (b) Inside the mass, a fetus of about 9 weeks of gestational age was found.

Discussion

This is the first case report of chronic ectopic pregnancy in which the complete shape of the fetus was visible. Chronic ectopic pregnancy is a tubal gestation that has undergone abortion or repeated minor bleeding episodes, in which the hemodynamic insult is subclinical and self-limiting.¹ Preoperative diagnosis is often difficult because of the high incidence of negative pregnancy tests as a result of a very small amount of live villi, subtle symptoms, and the poor specificity of ultrasonographic patterns.² Because hCG levels cannot reliably eliminate the risk of tubal rupture in the case of chronic ectopic pregnancy, it should be considered in the differential diagnosis of patients with an adnexal mass even with low hCG

levels and regular menses.³⁻⁵ Curry *et al.* reported the case of chronic ectopic pregnancy, diagnosed using hysterosalpingography, as a rare case.⁶ It was reported that an adnexal mass of chronic ectopic pregnancy, which was adherent to omentum, was demonstrated with extensive external vascularization, but with no internal blood flow on Doppler ultrasonography.⁷ In our case, there was only filmy adhesion around the right adnexal mass, indicating that Doppler ultrasonography might not give us useful information for diagnosis. The mass that occurs as the final form of chronic ectopic pregnancy is usually a conglomeration produced by adhesion between the inflamed tube after degeneration of the conceptus and surrounding structures, often containing blood and necrotic debris.^{8,9} In most cases, it occupies one adnexa and the cul-de-sac, yielding the heterogeneous echo pattern. Some cases, around 10% of the cases Turan *et al.* examined, revealed a predominantly solid pattern.⁸ Another ultrasonographic finding that may help diagnosis is simple fluid collection in the pelvic cavity resulting from old blood, although a big difference in its incidence has been seen depending on the report. In summary, the sonographic pattern of ectopic pregnancy is very similar to that of pelvic inflammatory diseases and ovarian neoplasms without any specific feature. That is why there are few papers reporting that ultrasound plays a key role in its diagnosis. Accordingly, the differentiation of chronic ectopic pregnancy without positive pregnancy tests from those other pelvic pathologies can only rely on a history of amenorrhea. Consequently, in almost all cases, diagnosis is possible only after pathological examination. In our case, however, the mass consisted only of the conceptus and a thick capsule, accompanied by infiltration of blood cells, fibrin deposition, and fibrotic change. We speculate that, if the natural course had been observed, it would have resulted in findings identical to those of other cases reported previously. This case was intriguing and novel because chronic ectopic pregnancy was detected at an early stage before absorption of the conceptus occurred, which coincidentally is an appropriate time for morphological diagnosis.

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子宮動脈塞栓術後の子宮鏡手術で切除した 胎盤ポリープの1例

A case of placental polyp treated with uterine arterial embolization and transcervical resection

東京大学医学部附属病院女性診療科・産科

Department Obstetrics and Gynecology, The University of Tokyo

北 麻里子 Mariko KITA	田 口 歩 Ayumi TAGUCHI	堤 亮 Ryo TSUTSUMI
平 池 修 Osamu HIRAIKE	廣 井 久 彦 Hisahiko HIROI	藤 本 晃 久 Akihisa FUJIMOTO
大須賀 穰 Yutaka OSUGA	矢 野 哲 Tetsu YANO	武 谷 雄 二 Yuji TAKETANI

概要 胎盤ポリープは分娩後や流産後の遺残胎盤組織が器質化することで発生し、しばしば大量出血を伴う。今回我々は帝王切開後胎盤ポリープによる大量出血をきたし、子宮動脈塞栓術後に子宮鏡を併用し胎盤ポリープを摘出した1例を経験したので報告する。症例は34歳、他院で妊娠37週5日に分娩停止のため帝王切開を施行。産褥29日目に経膈エコーで子宮内腔に5cm大の腫瘤を認め、外来で掻破を行うも大量の子宮出血を伴った。その後当院を初診、産褥58日目に大量出血を認め入院、エコーで子宮内腔に血流豊富な5cm大の高輝度腫瘤を認めた。dynamic CTで右子宮動脈から腫瘤への豊富な血流を認めたため、子宮動脈塞栓術を施行後、胎盤ポリープ摘出術を施行し子宮鏡下に止血した。術後は出血を認めず経過は良好であった。胎盤ポリープが血流豊富なものや大量出血を伴う場合子宮動脈塞栓後の子宮鏡下手術は妊娠能温存のためにも有用な治療法である。

Key words : placental polyp, uterine arterial embolization, transcervical resection

緒 言

胎盤ポリープは流産や分娩後に遺残胎盤が変性し、フィブリン沈着および硝子化により器質化しポリープ状に発育したものである¹⁾²⁾。症状としてしばしば大量出血を伴い、止血困難な場合従来は子宮摘出を考慮しなければならない疾患であったが、近年妊孕能を温存する治療法が普及しつつある。今回我々は帝王切開後胎盤ポリープによる大量出血をきたし、子宮動脈塞栓術(uterine arterial embolization : UAE)後に子宮鏡を併用し胎盤ポリープを摘出した1例を経験したので報告する。

症 例

症 例 : 34歳, 3経妊1経産 (2回人工中絶)。

既往歴 : 小児喘息があり、合併症として境界性人格障害のため妊娠前より抗鬱剤、抗不安薬を内服していた。

現病歴 : 自然妊娠し妊娠経過順調であったが、妊娠37週5日に分娩停止のため緊急帝王切開術を施行、胎盤の剝離は容易で胎盤遺残を認めなかった。産後の経過は順調であったが、産褥29日目の経膈エコーで子宮内腔に高エコー輝度の5cm大の腫瘤像を認めた。外来で子宮内掻破を行い出血量は多かったものの自然に止血した。摘出した組織の病理組織診断は変性壊死した胎盤組織であった。その後出血の持続なく経過、産褥48日目の外来受診時にも子宮内腔に同様の腫瘤像を認めたため再度掻破を施行したが、同様に大量出血を認め腫瘤は一部摘出されたのみであった。産褥57日目

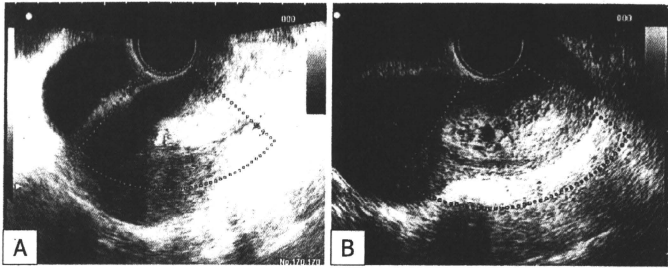


図1 初診時経陰超音波検査

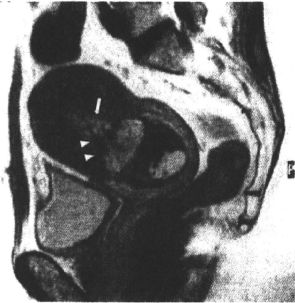


図2 MRI T2強調画像 矢状断
子宮底部側で子宮内膜が腫瘍と不連続
(矢印), flow voidを認め(三角印), 腫
瘍は子宮底部側を基部とし豊富な血流を
有する腫瘍であると考えられた

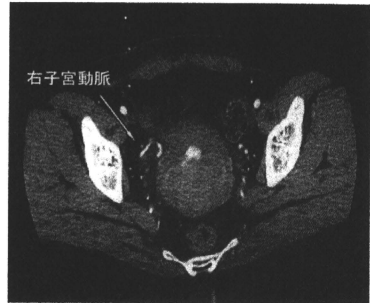


図3 dynamic CT 早期相

に当科紹介初診となった。

初診時、腔鏡診にて子宮出血はなかったが、外子宮口より腔内に突出する壊死様組織を認めた。経腔エコーにて50×40mm大の高輝度腫瘍像を認め、カラードップラーにて子宮底部から腫瘍へ流入する血流を認めた(図1A)。腫瘍内部にも一部豊富な血流を認めた(図1B)。子宮収縮剤投与にて経過観察としたが、翌日大量子宮出血を認め入院となった。入院時血圧110/93

mmHg、脈拍100回/分、体温37.8度。検査所見ではCRP453mg/dlと炎症所見を認めた。血中HCGは111.5mIU/mlであった。MRIで腫瘍はT2強調画像で低信号から高信号でflow voidを認め、T1強調画像で等信号を呈し、子宮底部側を基部とし豊富な血流を有する腫瘍と考えられた(図2)。dynamic CT早期相では右子宮動脈より腫瘍へ流入する血流を認めた。(図3)。現病歴および画像診断より右子宮動脈からの豊富な血流を伴う胎盤ボリーブと診断した。炎症所見を認めていたため早期の除去が必要と考えられた。本人および家族が妊娠性温存を希望したためUAEを施行し血流を遮断した後に子宮鏡を用い胎盤ボリーブを摘出

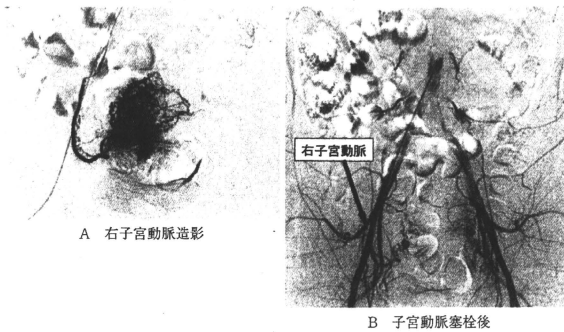


図4 子宮動脈血管造影

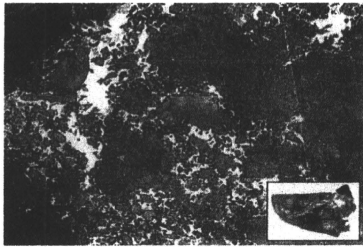


図5 摘出病理標本

する方針とした。

セルジnger法にて右大腿動脈よりカテーテルを挿入し、右子宮動脈から腫瘍内への豊富な血流を確認した(図4A)後、両側子宮動脈をゼラチンスポンジにて塞栓し、血流の遮断を確認した(図4B)。翌日カラードップラーにて腫瘍への血流が著明に減少していることを確認した。全身麻酔下で腔内の壊死した腫瘍を胎盤鉗子で捻除したところ、容易に5cm大の壊死組織が摘出できた。その後子宮鏡での観察で子宮後壁に基部様構造の壊死組織の断片および少量の出血を認めた。cutting loopを用い基部様組織の断片を切除し凝固止血した。術中出血は少量であった。術後出血少量のみ

で翌日退院した。術後病理組織診断は residual placenta of the uterus, 広範に壊死した絨毛を認め、出血、壊死、フィブリンの析出が目立つ所見であった(図5)。血中HCGは徐々に減少し術後1ヶ月で感度以下となった。現在外来にて経過観察中である。

考 察

胎盤ポリープの臨床症状の主な特徴は、産褥または流産後(数週~数ヶ月の間)に起こる大量出血であり、安易な子宮内掻爬術などにより止血困難になることがある。成因として癒着胎盤の存在が関与していると考えられている²⁾。胎盤ポリープのハイリスク因子として挙げられるのは癒着胎盤、人工中絶や流産手術の既往、子宮手術の既往(帝王切開術、子宮筋腫核出術)^{3,4)}、子宮奇形、子宮筋腫合併妊娠例である⁵⁾。本症例は2回の人工中絶既往があり、胎盤ポリープのハイリスク症例と考えられたが、前医では胎盤ポリープと認識されず、2回子宮内掻爬を施行し大量出血をきたした。

診断はエコー(カラードップラー法)が簡便で有用な検査である。子宮内に変性、壊死、出血を反映した高輝度~低輝度腫瘍として描出され、腫瘍内部および腫瘍基部に流入する血流を認めるのが特徴である⁶⁾。MRIではT1強調画像低信号~高信号、T2強調画像で高信号を示し、血流が豊富な場合 flow void(高輝度内の無信号域)を認める⁶⁾。また dynamic MRI, dynamic CTで腫瘍への流入血管が早期に造影され、流

入する血流の特定に有用である⁷⁾⁸⁾。本症例においてMRIは入院直前に他院で行いMRAやdynamic MRIで血流の評価が困難であったため、入院後造影CT撮影を行った。超音波検査、MRI、CT検査は胎盤ポリープの診断および流入血流の評価に有用であった。

胎盤ポリープは、大量出血がない場合保存的療法のみにて治療する症例も少なくないが⁹⁾、大量出血を伴い止血困難な場合は、従来は子宮全摘術を考慮せざるを得ない疾患であった。近年胎盤ポリープに対してUAEを行いその後病変が消失したとの報告や⁹⁾、UAE後にTCRを行うことで術中出血することなく安全に胎盤ポリープを切除できたとの報告が散見されるようになってきた¹⁰⁾¹¹⁾。Takeuchiらは持続する出血を認める胎盤ポリープ13症例に対しUAE後子宮鏡下手術(transcervical resection: TCR)を行い、出血なく安全に胎盤ポリープを切除したと報告している¹¹⁾。UAEは、子宮筋腫、産後大量出血に対して行われている治療で、血管造影により出血部位を特定し、塞栓物質を用い血流を遮断することで高い止血効果を発揮する。塞栓物質に遅延性吸収物質であるゼラチンスポンジを使用した場合その塞栓効果は数週間であることから長期的な子宮への影響は少なく、UAEはその後の月経周期や妊娠能に影響を与えないと報告されている¹²⁾。Takeuchiらは胎盤ポリープに対してUAE術後にTCRを施行した13症例中妊娠希望のあった11例のうち8例が妊娠し妊娠継続中の1例を除く7例で順調な胎児発育にて正常産に至り、産褥経過も良好であったと報告している¹¹⁾。

本症例では妊娠能温存の希望があり、画像診断で腫瘍への豊富な血流を認めたため、UAEを施行する方針とした。子宮鏡での子宮内の観察の前に胎盤鉗子で胎盤ポリープを捻除し、子宮鏡下止血および残存病変の摘出が可能であった。本症例のように胎盤ポリープが血流豊富なものや大量出血を伴う場合、UAE後TCRを行うことで妊娠能温存が可能であると考えられた。

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帝王切開術後3ヶ月に大量性器出血をきたした 子宮仮性動脈瘤破裂の1例

A case of uterine artery pseudoaneurysm after cesarean section

東京大学医学部附属病院産科婦人科

Department of Obstetrics and Gynecology, Tokyo University Hospital

磯野 涉	堤 亮	砂川 空広
Wataru ISONO	Ryo TSUTSUMI	Sorahiro SUNAGAWA
廣井 久彦	藤本 晃久	大須賀 稔
Hisahiko HIROI	Akihisa FUJIMOTO	Yutaka OSUGA
矢野 哲	武谷 雄二	
Tetsu YANO	Yuji TAKETANI	

概要 今回我々は帝王切開術後3ヶ月で子宮仮性動脈瘤破裂による大量性器出血をきたした1例を経験したので報告する。症例は40歳、2経妊1経産、妊娠40週分娩停止の診断で緊急帝王切開術を施行した。術後3ヶ月に大量の繰り返す性器出血を主訴に緊急入院し、入院後の出血量は2300gを超え、濃厚赤血球輸血を行った。造影CTで子宮頸部左側に仮性動脈瘤の形成・血管外漏出像を認め、子宮仮性動脈瘤破裂の診断に至った。緊急で子宮動脈塞栓術を施行し、止血を得た。塞栓物質はゼラチンスポンジを用いた。塞栓術後に再出血は認めず、術後4日目に退院となった。帝王切開時の血管損傷に起因した仮性動脈瘤と考えられた。

Key words: 子宮仮性動脈瘤, 帝王切開, 選択的子宮動脈塞栓術

緒 言

仮性動脈瘤は手術や外傷などで生じる動脈壁の損傷により発生する。子宮の仮性動脈瘤は子宮内容除去術・帝王切開術などの手術後の発症が報告されているが、稀である。しかし、破裂した場合は大量の性器出血をきたし、生命の危険にも及ぶ。今回我々は帝王切開術後3ヶ月で子宮仮性動脈瘤破裂による大量性器出血をきたした1例を経験したので報告する。

症 例

症 例: 40歳、2経妊1経産。
月経周期: 26日周期、順、持続5日間。
主 訴: 不正性器出血。
家族歴: 特記事項なし。
既往歴: 特記事項なし。
前回妊娠経過: 凍結融解胚移植で妊娠。妊娠10週から当院で妊婦健診を受けていたが、妊娠経過に異常は

なかった。妊娠40週2日妊娠高血圧症候群の診断で入院管理となった。妊娠40週3日前期破水・炎症反応の上昇を認めたため分娩誘発を行ったが進行が見られず、分娩停止の診断で緊急帝王切開術を施行した。4158gの男児娩出(Apgar score 8/9点)。手術時間65分、出血量は2400gであった。産後の経過は順調であり、1ヶ月健診で異常を認めなかった。

現病歴: 術後83日目から月経様の持続的出血を自覚していたが、術後3ヶ月に大量の性器出血・歩行困難を訴え緊急入院。経膈エコーで子宮頸部に12.3×4.6mm程度の大きさの血液貯留を認めるものの、入院後出血が減少したため、翌日退院した。退院13日後に外来で経膈エコー上に子宮頸部左側端に12mm大のanechoic lesion(図1)、カラドップラーエコーでその内部に動脈性の血流を認めた(図2)ため、鑑別診断として子宮動脈瘤奇形が考えられた。翌日午前6時頃に再び大量性器出血を認め、救急車を要請して来院し、緊

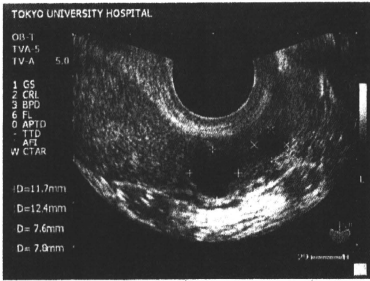


図1 外来時 経膈超音波検査

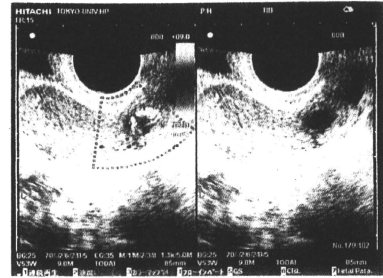


図2 外来時 カラードップラー超音波検査

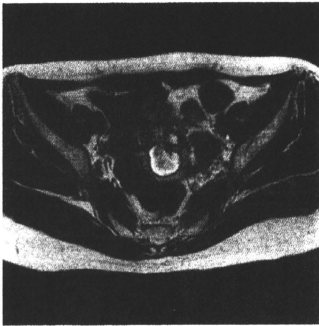


図3 入院後 緊急MRI検査

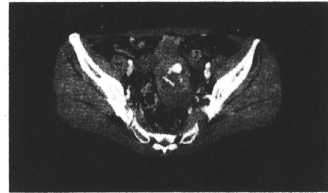


図4 入院後 緊急造影CT検査(冠状断)

急入院となった。

入院時検査所見：WBC 4.8千/ μ l, Hb 8.4g/dl, PLT 31.9万/ μ l, Alb 3.8g/dl, LD 168IU/l, AST (GOT) 20 IU/l, ALT (GPT) 19IU/l, γ -GTP 35IU/l, ALP 244 IU/l, T-Bil 0.4mg/dl, BUN 16.0mg/dl, Cre 0.54mg/dl, Na 142mEq/l, K 4.0mEq/l, Cl 109mEq/l, CRP 0.05 mg/dl, PT 10.8秒, PT 100.0%, PT INR 0.88, APTT 37.2秒, Fbg 285mg/dl.

経過：来院時出血は減少していたため、MRIで評価した後に動脈塞栓術を予定していたが、入院8時間後に再度1500gの大量出血をきたしたため、ヨードホ

ルムガーゼを挿入し緊急MRIを施行した。この際には子宮内腔と連続する異常な腔を認めたが、血管性病変か異胞性病変かは診断できなかった(図3)。血圧100/70mmHg、脈拍88回/分程度のプレショック状態となったため、濃厚赤血球4単位の輸血を施行すると同時に造影CTを施行。子宮頸部左側に造影剤の貯留と陰部に巨大血腫を認めた(図4、図5)ため、出血の原因は左子宮動脈上枝由来の子宮仮性動脈瘤破裂であると診断した(後日再構築された3D-CTを図6として示す)。同時に造影早期の異常血管の描出が見られないため動静脈奇形は除外された。また活動性出血所見であるpseudovesselの描出が、陰部血腫内部に見られた(図4)。造影CTから掃室後にも合計800g程度の凝血塊の排出を認め、CTでの血管外漏出像の所見と併せて緊急の止血術が必要と判断した。選択的子宮動脈