Original article

Uterine preservation surgery for placental polyp

Koichi Hiraki[a], Khaleque Newaz Khan[a*], Michio Kitajima[a], Akira Fujishita[b], Hideaki Masuzaki[a]

[a]Department of Obstetrics and Gynecology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan; [b]Department of Obstetrics and Gynecology, Saiseikai Nagasaki Hospital, Nagasaki, Japan

Running head: Uterine surgery for placental polyp

*Address for correspondence:

Khaleque Newaz Khan,· MD, PhD

Department of Obstetrics and Gynecology

Graduate School of Biomedical Sciences, Nagasaki University

1-7-1 Sakamoto, Nagasaki 852-8501, Japan

Tel: 095-819-7363; Fax: 095-819-7365

Email: nemokhan@nagasaki-u.ac.jp

Abstract

Aim: To examine clinical and surgical performances of cases with placental polyps in which uterine preservation surgery was conducted.

Materials and Methods: During the period between September 2002 and April 2009, we examined eight cases (hysteroscopic resection, 6 cases; laparotomy, 1 case; dilatation & curettage, 1 case) diagnosed with placental polyp had treated with polyp extraction surgery. Imaging evaluation was done using magnetic resonance image (MRI) and two-dimensional (2D) ultrasound.

Results: Three of eight cases (37.5%) had first-time pregnancies. Most of our cases experienced minimal surgical manipulation after medical abortion. Among them, 6 cases (75%) were in mid-term medical abortions, one case (12.5%) received no treatment after spontaneous abortion, and one case (12.5%) had post surgical abortion (D&C). All cases showed variable amount of blood flow in the internal mass and myometrium by color Doppler ultrasound. MRI angiography showed contrast effects in the intrauterine cavity and myometrium in selected cases. The average duration from diagnosis to surgery was 32 days (range: 11-105 days). Color Doppler revealed a reduction in blood flow in 5 cases during the waiting period until surgery with an average blood loss of 10 g (range: 0-20 g) during surgery.

Conclusions: Use of color Doppler ultrasound may be useful in diagnosing placental polyp. Although hysteroscopic resection of placental polyp is effective in patients hoping for uterine preservation, delaying timing of surgery may reduce blood loss during operative procedure.

Key words: Placental polyp, medical abortion, color Doppler, hysteroscopic resection, delayed surgery

Introduction

A placental polyp is an intrauterine polypoid mass occurring from residual placental fragments following surgical abortion, Cesarean section, or vaginal delivery, and as the polyp enlarges due to accumulation of blood clots and fibrin products over several weeks to several months after delivery, uterine bleeding occurs as the main symptom with this disease. The detection rate of blood flow within the placental polyp is high[1] with the use of color Doppler ultrasound, and an increasing trend of neovascularity, which is representative of arteriovenous fistula (AVF), can be observed. The sudden occurrence of uterine bleeding is thought to be a result of the rupture of this abnormal blood vessel. This clinical event could be life-threatening for the patient and sometimes may require an emergency hysterectomy. However, there are numerous cases where uterine preservation is requested, and in such cases, selection of a proper treatment method seems to be difficult.

Recently, placental polyp removal surgery[2] and uterine artery embolization have been proposed[3] as surgical methods with the intention to preserve the uterus, and in some cases, a combination of these procedures has been chosen as a treatment method[4-7].

Two dimensional (2D) ultrasound and MRI have been used for diagnosis. Recently, there are some reports indicating that 3D CT angiography can be useful in diagnosing placental polyps and in determining a treatment plan[7-10]. However, details of uterine preservation surgery in women with placental polyp are not well described.

Therefore, we examined the clinical backgrounds, duration of surgery, blood flow after surgical delay and surgical outcome of eight cases who underwent uterine preservation surgery following a diagnosis of placental polyp.

Subjects and Methods

During the period between September 2002 and April 2009, we retrospectively examined eight cases had diagnosed with placental polyp and had treated with polyp extraction surgery at Nagasaki University Hospital. In all 8 cases, uterine preservation surgery was possible following a diagnosis of placental polyp. Among eight cases, 6 cases underwent hysteroscopic resection, one case had a laparotomy for polyp extirpation, and the remaining one case had dilatation & curettage.

Our current study is in accordance with the guidelines of the Declaration of Helsinki and was performed with the approval by the Institutional Review Board of Nagasaki University. An informed consent was obtained from all participated women.

We performed MRI and 2D ultrasound (Mochida SIEMENS SONOVISTA FX, Tokyo, Japan) including color Doppler for the evaluation of all eight cases. Presence of blood flow by color Doppler was graded as absence (-), mild to moderate (1+), high (2+) and remarkable (3+). Remarkable blood flow was defined as the continuation of abundant blood flow within polyp with the myometrial blood flow (Figure 1). Serum hCG level in all cases was measured by immulite system (Siemens Healthcare Diagnostics Products Ltd. UK). In order to preserve uterus, trans-cervical hysteroscopic resection (TCR) was performed whenever possible. Despite reports related to the usefulness of uterine artery embolization (UAE) [3-7], we did not perform UAE in our cases to avoid possible adverse effects on normal myometrium and ovarian function[11]. With the speculation in mind that waiting longer period until surgery may reduce intra-polyp blood flow, resection procedure was delayed as longer as possible, in cases showing imaging evidence of increased blood flow within myometrium/placental polyp, in an attempt to reduce blood loss during surgery.

Symptoms, prior pregnancy, clinical profiles, pre-operative imaging diagnosis, serum hCG level, surgery period, and surgery results were examined. A resectoscope (Karl Storz, Germany) was used for the hysteroscopic resection (TCR). A bipolar resectoscope was introduced in February 2009 at Nagasaki University Hospital.

Results

The clinical backgrounds of eight cases with placental polyp are shown in Table 1. The mean age was 28.5 ± 8.5 years old ($\pm$ SD, range, 17-43 years old), and in all cases, uterine preservation was requested. With the preceding pregnancies, five of 8 cases had artificial abortions (cases 1-5) and 3 cases had spontaneous abortion (cases 6-8). In six cases where 5 had artificial abortions and one had spontaneous abortion, medical abortion (PGE_2 induced) was conducted at 13 weeks to 20 weeks of pregnancy with minimal post-abortion surgical manipulation. In the remaining two cases of spontaneous abortion, surgical abortion (dilatation & curettage, D&C) was performed in one case and no treatment for another. Although variable amount of uterine bleeding was observed in all cases, they were admitted 9-107 days (median: 32.5 days) after surgical abortion (6 cases with sudden massive bleeding and 2 cases with constant small amount of bleeding). The median hemoglobin level on the first visit was 10.3 g/dl (range: 5.9-14.2 g/dl), and some cases had concentrated red blood cell transfusion due to severe anemia.

Hemoglobin level was measured in all 8 cases before operation and five of 8 cases showed improvement after surgical delay. Serum hCG level was measured in all cases and median hCG level was 2.7 IU/L (range: 1.8-59 IU/L) with 3 cases where levels were below 1.0 IU/L. We did not measure serum hCG levels after operation in any of these

cases. Pre-operative methotrexate (MTX) was administered into 3 out of the 8 cases, and hCG level was declined in all 3 cases (Table 1).

A 2D vaginal ultrasound was performed in all cases, and a polypoid mass was detected in the uterine cavity. The median polyp diameter was 26 mm (range, 18-50 mm). Blood flow within the polyp or myometrium was observed in all cases with the use of color Doppler ultrasound, and a high (2+) to remarkable (3+) increase in blood flow was detected in 5 of 8 cases. MRI was performed on 6 cases, and a polypoid mass in the uterine cavity was visualized as low signal and high signal nodule with T1-weighted image and T2-weighted image, respectively. Four cases underwent a contrast enhanced MRI examination, and contrast effect was observed in these polyps (Table 2).

In an attempt to control bleeding during operative procedure, surgery was planned with possible delay from first hospital visit with the anticipation of reduced blood flow within the placental polyp. The median period from first hospital visit to surgery was 32 days (range: 11-105 days) (Table 3). During the waiting period, a reduced blood flow within the mass was observed using color Doppler ultrasound in 5 cases out of the 8 cases (Figure 2/Table 2). Mass extraction of polyp by hysteroscopic resection was conducted in 6 cases. Hysteroscopic resection was switched to laparotomy in one case (case 4) and surgical abortion in one case (case 7) due to inadequate view of operation field being caused by massive bleeding (Table 3). The median amount of bleeding during surgery in 7 cases was 10 g (range: 0-120 g) with the exception of case 4 where bleeding was massive (340 g).

Tissue samples were collected from all extracted polypoid mass and presence of chorionic villi was histologically confirmed in all cases. Intra-operative complication was observed in none of the cases. To prevent intrauterine adhesion following surgery, IUD

was inserted in 5 cases and an EP agent was administered in one case. Preventive measures against intrauterine adhesion were not taken in two cases (case 3 and 7) without occurrence of any postoperative adhesion (Table 3).

Discussion

We successfully conducted uterine preservation surgery for the first time in eight cases with placental polyp had artificial medical abortion instead of surgical abortion. Although massive uterine bleeding at first hospital visit may be an indication of emergency surgery or uterine artery embolization, we found that prolonged delaying in operative procedure after onset of abortion could be an attractive approach to reduce pre-operative blood flow or intra-operative bleeding. In fact, after confirming reduced intra-polyp blood flow by color Doppler before surgery, we also found remarkable decrease in intra-operative blood loss in five of eight cases after surgical delay.

Although the onset of placental polyp is thought to occur during various timing of pregnancy as a result of surgical abortion (D&C) from first trimester to natural delivery or Cesarean section, information regarding the frequency of placental polyp development after medical abortion is unknown. In fact, 6 cases (75%) out of 8 cases developed placental polyp after medical abortion (PGE_2 induced) in our study which is of high frequency and noteworthy.

With regards to placenta formation during 8-18 weeks of pregnancy, the outer chorionic trophoblast extends from the basal deciduas into the myometrium, followed by villus infiltration. The cell layers of the cytotrophoblast and syncytiotrophoblast of the villus during this period are thick compared to the final stage of pregnancy and is tightly adhered to the surrounding myometrium. Although medical abortion was conducted

during 13 weeks to 20 weeks of pregnancy in our cases that developed placental polyps, incomplete detachment of placenta after medically induced labor and consequent retention of placental fragments may be the possible cause of placental polyp development in our cases. Serum hCG levels depend on the activity status of trophoplastic cells and this may explain the reason why serum hCG levels in three cases was below detection level in our current study.

Although the development mechanism of placental polyp is still not fully understood, it has been reported[12] that placental polyp may occur due to the retention of a portion of placenta and eventually forming an adhered placenta. In addition, it has also been reported[8] that the removal of the myometrium may be required to completely remove the placental polyp by means of a hysteroscopic resection. We could histologically confirm the presence of chorionic villi in tissue samples derived from polypoid mass in all cases. This may strengthen the controversial opinion that the naming of the term "placental polyp" does not depend on gestational age (8 weeks in case 8 of our study) rather on histological findings.

The use of color Doppler ultrasound[1] can be a suitable tool to detect presence of blood flow within the placental polyp or myometrium. This procedure was extremely useful in terms of being able to observe changes in the blood flow over time. Although variable blood flow was observed in the polypoid mass of all 8 cases using color Doppler in our study during the first visit, an absence of blood flow was detected in 5 cases before surgery (Table 2). Our results corresponded with the reduced intra-operative blood loss (0-20g) in these five cases (case 1, 2, 3, 7, 8)(Table 3). We could not measure blood loss in these cases during the first visit. The most interesting findings in our study is that delaying timing of surgery after first hospital visit and diagnosis (11-105 days delay)

markedly reduced intra-polyp blood flow by color Doppler as well as intra-operative blood loss in all these five cases (0-20g). These findings are the first report in our current study. We presume that detection of blood flow within polypoid mass after medical or surgical abortion could be a good parameter to decide the timing of uterine preservation surgery by TCR.

The exact mechanism of reduced blood flow by color Doppler and decreased intra-operative blood loss during surgery is unclear. This may be explained as follows: (1) time-dependent disappearance of AV fistula within polypoid mass that often occurs during the initial development of a placental polyp. (2) time-dependent vasospasm as caused by the release of some macromolecules such as PGE_2 and/or $PGF_{2\alpha}$ in response to tissue hypoxia that may occur secondary to blood loss during first hospital visit.

The relationship between MTX and blood flow of placental polyp is unclear. Serum levels of hCG is a marker of activity of trophoblastic cells within placental villi and not a measure of increased or decreased blood flow. We observed in our current study that in some cases, blood flow was not changed even hCG level was decreased by MTX. Whereas, in some cases, hCG was still positive when blood flow within polyp was reduced after MTX treatment. The persistence of blood flow with reduced hCG level may be explained by insufficient time-dependent disappearance of AV shunt that had appeared within placental polyp at initial screening. In contrast, reduced blood flow with persistence of serum hCG level after MTX treatment may be explained by effective resolution of AV shunt but still presence of some active trophoblastic cells in placental villi. Therefore, careful interpretation should be made regarding the effectiveness of MTX treatment on blood flow and serum hCG levels in placental polyp or any other trophoblastic disease.

Application of MRI (T1 and T2-weighted image) is not useful to differentiate placental polyp from endometrial polyp, because both of these polyps display similar signal intensity. We took contrast enhanced MRI in four cases and found that high contrast enhancements corresponded with the high (2+, cases 2, 4, 6) to remarkable (3+, case 5) intra-polyp blood flow as detected by color Doppler ultrasound. The cases showing minimal blood flow by color Doppler failed to reveal contrast enhancement by MRI (cases 1 and 8). We propose that color Doppler ultrasound might be useful in clinical practice to detect variable amount of blood flow within placental polyp during diagnosis, follow-up and also before surgery.

There are some limitations in our study. (1) We could not take contrast enhanced MRI after surgical delay. Therefore, it is difficult to estimate clinical value of MRI in detecting decreased intra-polyp blood flow in comparison to color Doppler ultrasound. (2) In order to reduce the cost performance in this retrospective study, we did not measure serum hCG levels in five detectable cases after operation. Since most of the cases already showed reduced intra-polyp blood flow and intra-operative blood loss, after effective removal of placental polyps by TCR, we planned to follow-up all these cases only by 2D Ultrasound and failed to detect any further appearance of polyp. (3) Presence of retained placenta could be another bias in selecting all 8 cases in our current study. There is scanty information on how to differentiate placental polyp from retained placenta. From our clinical experience, retained placenta is an early event with gradual time-dependent decline of blood flow and serum hCG levels. In our five cases (cases 2-6) with placental polyp, we could still detect high to remarkable intra-polyp blood flow by color Doppler even after a delay of 9-107 days from starting of bleeding onset and first hospital visit. Serum hCG level was still higher in these five cases (12.2-59 mIU/ml) during initial

screening. Three of these five cases (case 2, 4, 6) took intramuscular injection of methotrexate. Serum hCG level was undetected (<0.01 mIU/ml) in three cases at initial screening (case 5, 7, 8) and was at minimal level in another case (case 1, 1.8 mIU/ml). Therefore, we could exclude the bias of retained placenta in selection criteria of our cases in this retrospective study.

In conclusion, we propose that color Doppler may be clinically useful in diagnosing placental polyp even with minimal blood flow within polypoid mass. When uterine preservation is requested, our non-invasive surgical procedure of hysteroscopic resection may be suitable to completely remove the placental polyp. Careful application of this procedure has the advantage to avoid any intra-operative complications and to prevent any endometrial adhesion with proper measurement (Table 3). Although UAE can be an alternative approach to preserve fertile uterus, we did not perform UAE in our cases before hysteroscopic resection in order to avoid adverse effects on ovary and myometrium[13,14]. We also suggest that except emergency cases with massive bleeding, delaying of surgical timing could be an attractive approach to reduce intra-polyp blood flow and to decrease blood loss during operative procedure. Further multi-center clinical studies with increased number of cases may strengthen our current findings.

Disclosure: The authors report no conflict of interest related to this paper.

References

1. Palat P, Suma S, Kantarcy M, Alper F, Levent A. Color Doppler US in the Evaluation of Uterine Vascular Abnormalities. *RadioGraphics* 2002,22: 47-53.

2. Jimenez JS, Gonzalez C, Alvarez C, Munoz L, Perez C, Munoz JL. Conservative management of retained trophoblastic tissue and placental polyp with diagnostic ambulatory hysteroscopy. *Eur J Obstet Gtnecol Reprod Biol* 2009,145: 89-92.

3. Yang JJ, Xiang Y, Wan XR, Yang XY. Diagnosis and management of uterine arteriovevou fistulas with massive vaginal bleeding. *Int J Gynecol Obstet* 2005,89: 114-119.

4. Takeuchi K, Sugimoto M, Kitao K, Yoshida S, Maruo T. Pregnancy outcome of uterine arterial embolization followed by selective hysteroscopic removal of a placental polyp. *Acta Obstet Gynecol Scand* 2007,86: 22-25.

5. Takeuchi K, Ichimura H, Masuda Y, Yamada T, Nakago S, Maruo T. Selective transarterial embolization and hysteroscopic removal of a placental polyp with preservation of reproductive capacity. *J Reprod Med* 2002,47: 608-610.

6. Greenberg JA, Miner JD, O'Horo SK. Uterine artery embolization and hysteroscopic resection to treat retained placenta accreta: A case report. *J Mini Invas Gynecol* 2006,13: 342-344.

7. Takeda A, Koyama K, Imoto S, Mori M, Sakai K, Nakamura H. Placental polyp with prominent neovascularization. *Fertil Steril* 2010,93: 1324-1326.

8. Takeda A, Koyama K, Imoto S, Mori M, Sakai K, Nakamura H. Computed tomographic angiography in diagnosis and management of placental polyp with neovascularization. *Arch Gynecol Obstet* 2010,281: 823-828.

9. Umezu T, Iwase A, Ota T et al. Three dimensional CT Angiography Is Useful for Diagnosis of Postabortion Uterine Hemorrhage: 3 Case Reports and Review of the Literature. *J Minim Invasive Gynecol* 2010,17: 246-251.

10. Takeda A, Koyama K, Mori M, Sakai K, Mitsui T, Nakamura H. Diagnostic computed tomographic angiography and therapeutic emergency transcatheter arterial embolization for management of postoperative hemorrhage after gynecologic laparoscopic surgery. *J Minim Invasive Gynecol* 2008,15: 332-341

11. Pron G, Bennett J, Common A, Wall J, Asch M, Sniderman K. The Ontario Uterine fibroid reduction and symptom relief after uterine artery embolization for fibroids. *Fertil Steril* 2003,79: 120-7, 2003

12. Swan RW, Woodruff JD. Retained Products of Conception. Histologic Viability of Placental Polyps. *Obstet Gynecol* 1969,34: 506-514.

13. Maassen MS, Lambers MD, Tutein Nolthenius RP, van der Valk PH, Elgersma OE. Complications and failure of uterine artery embolization for intractable postpartum haemorrhage. *BJOG* 2009,116: 55-61.

14. Berkane N, Moutafoff-Borie C. Impact of previous uterine artery embolization on fertility. *Curr Opin Obstet Gynecol* 2010,22: 242-247.

Figure legends

Figure 1. Shows pattern of blood flow within polypoid mass by color Doppler ultrasound and was graded as mild to moderate (1+, A), high (2+, B), and remarkable (3+, C), where there is continuation of abundant blood flow within polyp with the myometrial blood flow.

Figure 2. (A) Color Doppler ultrasound showing prominent blood flow within placental polyp during first visit to our hospital. (B) Color Doppler ultrasound showing disappearance of vascular flow from the mass of placental polyp after 28days of surgical delay and before hysteroscopic resection.
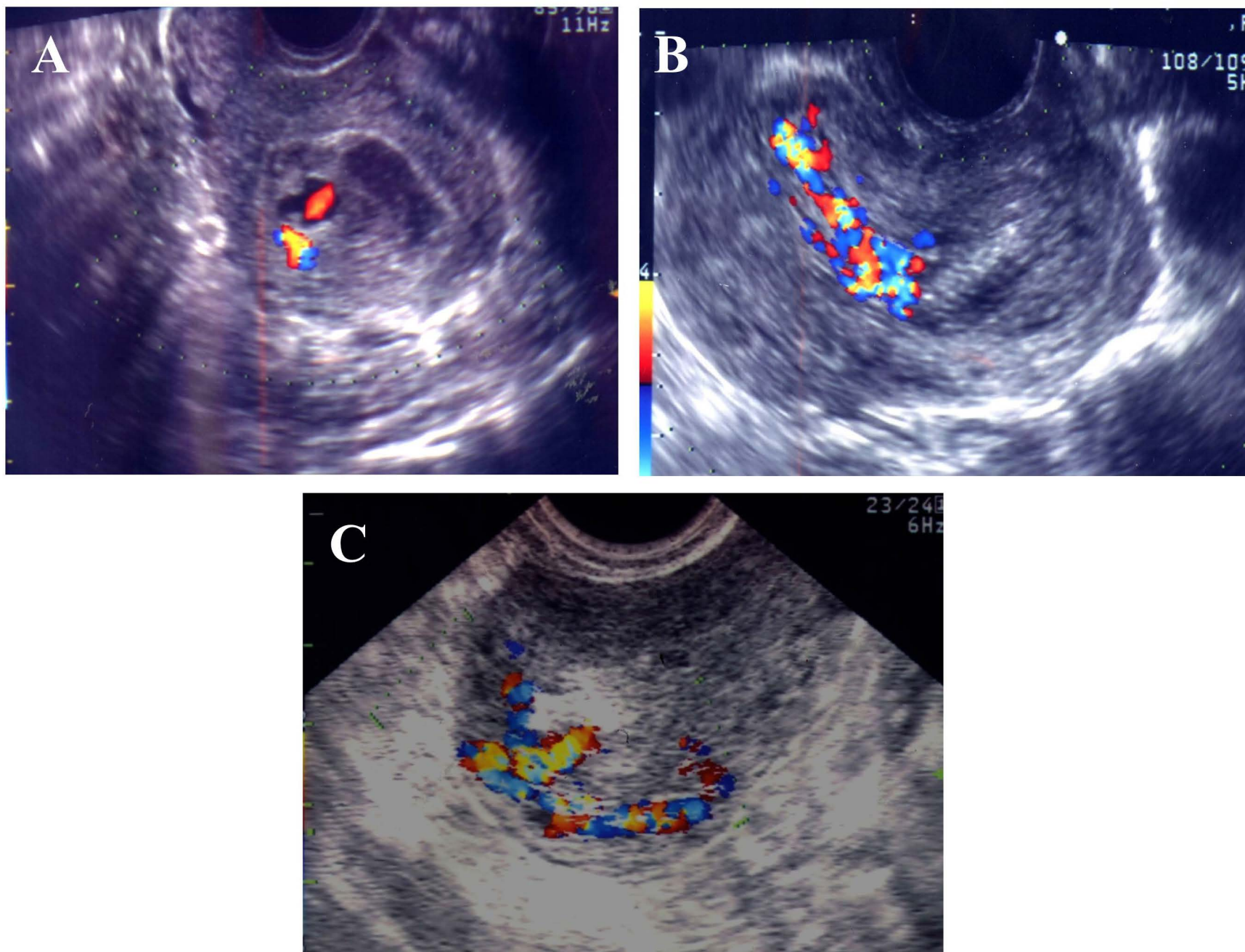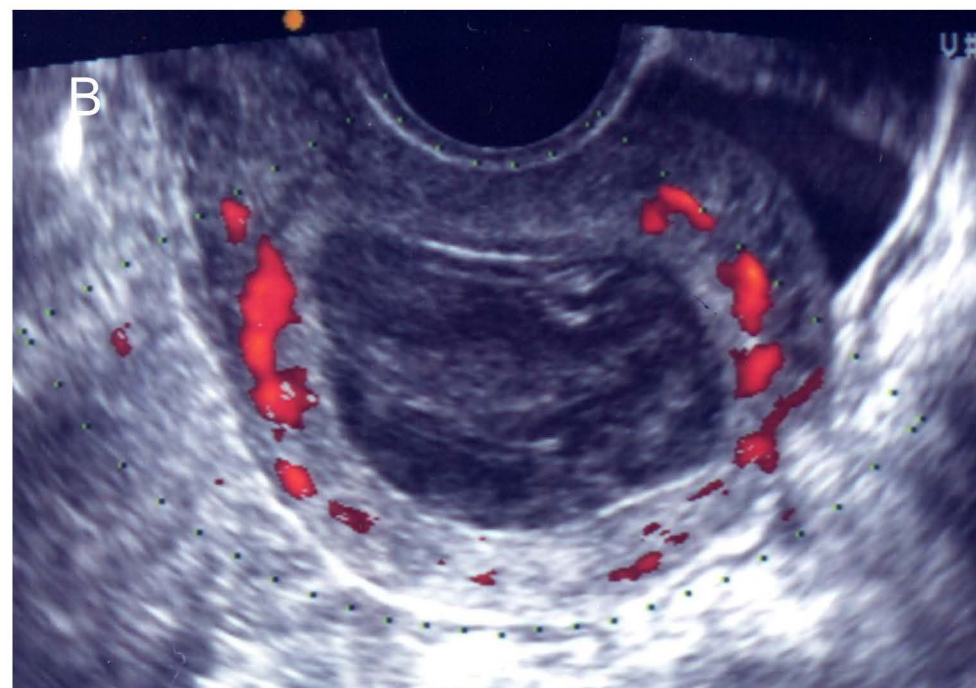
Figure 1.

Figure 2.

Table 1. Clinical profiles of patients with placental polyp

Case	Age (yrs)	Gravidity/ Parity	Type of abortion	Gestational age at abortion	Days of first visit after onset of abortion	Hb (g/dl) at first visit	Hb (g/dl) at operation	Serum hCG (mIU/ml) at first visit	Serum hCG (mIU/ml) at operation	Preoperative medication
1	17	G1P0	artificial abortion	14 weeks	57 days	5.9	7.7	1.8	-	-
2	22	G1P0	artificial abortion	15 weeks	20 days	7.7	9.4	3.6	1.4	MTX
3	43	G3P2	artificial abortion	20 weeks	17 days	10.3	12.4	59	1.7	-
4	31	G2P1	artificial abortion	16 weeks	9 days	10.3	12.0	49	7.8	MTX
5	24	G1P0	artificial abortion	13 weeks	107 days	10.4	10.2	<1.0	-	-
6	34	G3P1	spontaneous abortion	12 weeks	90 days	9.3	10.4	12.2	<1.0	MTX
7	36	G2P1	spontaneous abortion	18 weeks	44 days	14.2	14.4	<1.0	-	-
8	35	G2P1	spontaneous abortion	8 weeks	45 days	11.9	11.9	<1.0	-	-

hCG, human chorionic gonadotropin; MTX, methotrexate

Table 2. Ultrasonography and MRI findings of placental polyp

cases	size (mm)	Color Doppler image		MRI findings		
		Blood flow in polyp at first visit	Blood flow before surgery	T1-weighted image	T2-weighted image	enhancement
1	20×10	(1+)	(-)	–	–	–
2	40×30	(2+)	(-)	Low	High	High
3	23×22	(2+)	(-)	Low	High	
4	38×17	(2+)	(2+)	Low	High	High
5	50×25	(3+)	(3+)	Low	High	High
6	23×15	(2+)	(2+)	Low	High	High
7	18×11	(1+)	(-)	Low	High	
8	29×21	(1+)	(-)	–	–	–

Blood flow within polyp by color Doppler was graded as absent (-), mild to moderate (1+), high (2+) and remarkable (3+).
Remarkable blood flow is defined as the continuation of abundant blood flow within polyp with the myometrial blood flow.

Table 3. Summary of operation

Cases	Days of first visit after onset of abortion	Days delayed until TCR	Surgery	Duration of operation (min)	Intra-operative blood loss (g)	Intra-operative complication	prevention of endometrial adhesion
1	57	11	TCR	Uncertain	10	None	EP
2	20	28	TCR	55	10	None	IUD
3	17	105	TCR	19	0	None	None
4	9	78	TCR→conversion to laparotomy	260	340	None	IUD
5	107	14	TCR with uterine artery clamping	Uncertain	120	None	IUD
6	90	36	TCR	23	50	None	IUD
7	44	81	D&C	12	10	None	None
8	45	17	TCR	17	20	None	IUD

TCR = transcervical resection; IUD = intrauterine device