Comprehensive management of severe Asherman syndrome and amenorrhea

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Objective: To describe a comprehensive approach to women with severe Asherman syndrome and amenorrhea, including preoperative, operative, and postoperative care and subsequent resumption menses, and pregnancy.
Design: Retrospective case series.
Setting: Tertiary care teaching hospital.
Patient(s): Twelve women with severe Asherman syndrome and amenorrhea.
Intervention(s): Preoperative administration of prolonged preoperative and postoperative oral E_2 to enhance endometrial proliferation, intraoperative abdominal ultrasound-directed hysteroscopic lysis of uterine synechia to ensure that the dissection is performed in the proper tissue plane, placement of a triangular uterine balloon catheter during surgery, and postoperative removal with placement of a copper intrauterine device (IUD) to maintain separation of the cavity and mechanically lyse newly formed adhesions during removal.
Main Outcome Measure(s): Resumption of menses, pregnancy, and delivery.
Result(s): All women resumed menses, although 5 of 12 had a preoperative maximal endometrial thickness of 4 mm or less, with follow-up ranging from 6 months to 10 years. Six of nine women less than age 39 years (67%) became pregnant, and four of six achieved a term or near-term delivery.
Conclusion(s): Comprehensive management provides the best possible outcomes in poor-prognosis women with severe Asherman syndrome. (Fertil Steril® 2012;97:160–4. ©2012 by American Society for Reproductive Medicine.)
Key Words: Asherman syndrome, amenorrhea, infertility, hysteroscopy, intrauterine adhesions, uterine synechia, intrauterine device, ultrasound

Asherman syndrome is an acquired condition characterized by the formation of adhesions in the uterine cavity. Women with this disease often struggle with infertility, menstrual irregularities including amenorrhea, hypomenorrhea, or dysmenorrhea, and recurrent pregnancy losses (1). Women with the most severe Asherman syndrome have dense adhesions affecting at least two-thirds of the uterine cavity and amenorrhea or hypomenorrhea.

Women with severe Asherman syndrome may require more than one imaging modality to establish the extent of disease and determine the prognosis for repair, and more than one approach to minimize recurrence of adhesions. Preoperative assessment of Asherman syndrome may include hysterosalpingography (HSG), hysteroscopy, transvaginal ultrasonography, or saline infusion sonohysterography (2–4). Many preoperative, intraoperative, and postoperative measures have been described to improve surgical outcomes, including hormonal manipulation with estrogen (E) to induce endometrial proliferation, ultrasound-directed hysteroscopic lysis of synechia, and mechanical separation of the endometrium (5–9).

Individually, these methods to assess preoperative prognosis, utilization of hormonal measures to promote endometrial healing, and application of mechanical methods to limit recurrence of uterine synechia may improved the prognosis for women with severe Asherman syndrome and amenorrhea. It is likely that the systematic application of all of these measures may provide optimal outcomes. In the present study, we report our experience and surgical outcomes using a comprehensive preoperative, intraoperative, and postoperative approach for women with severe Asherman syndrome and amenorrhea.

MATERIALS AND METHODS

A retrospective chart review was completed to identify women who underwent comprehensive treatment of severe Asherman syndrome and amenorrhea by one surgeon (B.S.H.) at Carolinas Medical Center from 2001 through 2009. Institutional Review Board exempt status was given for this retrospective study. Eight women experienced complete amenorrhea attributed to Asherman syndrome, and four reported only scant spotting, at most (Table 1). The diagnosis of

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TABLE 1

Patients with Asherman syndrome and outcomes.

Patient	Preoperative menstrual history	Etiology of Asherman	Prior repair attempts	Age at surgery (y)	Maximum preoperative endometrial thickness	Postoperative menstrual history	Other fertility factors	Pregnancy
1	Scant spotting	D&C	None	33	2.0 mm	Regular	Obesity, prior ectopic, APA, RPL	SAB at 6½ weeks
2	Amenorrhea	Multiple D&Cs for PP hemm	h/s × 1	32	3.0 mm	Regular	None	SAB at 9½ weeks, 69, XXY
3	Amenorrhea	D&C	None	35	3.7 mm	Regular	Endometriosis, adenomyosis	CS 34 wk breech
4	Scant spotting	Unexplained	h/s × 1	43	4.0 mm	Regular	Ov dysfxn	None
5	Scant spotting	CS	h/s × 2	34	3.0 mm	Regular	Note: postoperative IUD not used	Unknown; repeat HSG only slightly improved
6	Amenorrhea	Multiple D&Cs for incomplete Ab	h/s × 1	31	5.0 mm	Regular	RPL	Term CS; 24 wk CS
7	Amenorrhea	PP hemm, D&C 3w pp	h/s × 2; ut perf	32	6.0 mm	Regular	Endometriosis stage I; LAVH age 38 y	None
8	Amenorrhea	Multiple D&C	h/s × 2	41	6.0 mm	Regular	RPL; abd MM × 2, h/s MM; hyst age 45 y	None
9	Amenorrhea	CS	None	39	7.5 mm	Irregular	DOR (basal FSH 26)	None
10	Amenorrhea	PP D&C retained placenta	None	29	8.0 mm	Regular	Postoperative contraception desired	Limited follow-up
11	Amenorrhea	Cone biopsy, D&C	h/s × 1; ut perf	29	Hematometrium	Regular	None	Term repeat CS
12	Scant spotting	D&C	h/s × 1	35	8.0 mm	Regular (with ov induction)	PCOS, ectopic, pelvic adhesions	SAB × 2, term SVD × 2

Note: All patients had resumption of menses. Of the women under age 39 years, six of nine became pregnant, and four of these six had a live birth delivery at or near term. Ab = abortion; APA = antiphospholipid antibodies; CS = cesarean section; D&C = dilatation and curettage; DOR = diminished ovarian reserve; Hemm = hemorrhage; h/s = hysteroscopy; hyst = hysterectomy; LAVH = laparoscopy-assisted vaginal hysterectomy; LOS = lysis of synechia; MM = myomectomy; ov dysfxn = ovulatory dysfunction; PCOS = polycystic ovarian syndrome; POC = products of conception; PP hemm = postpartum hemorrhage; RPL = recurrent pregnancy losses; Ut perf = uterine perforation; SVD = spontaneous vaginal delivery.

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TABLE 2

Comprehensive management of severe Asherman syndrome.

Preoperative
- Hysterosalpingogram, saline sonohysterography, and/or hysteroscopy to confirm diagnosis and identify extent of adhesions
- Transvaginal ultrasound of endometrium to assess "baseline" endometrial thickness and evaluate pelvic anatomy
- Estrogen supplementation for 2–8 weeks to stimulate endometrial development
- Repeat transvaginal ultrasound of the endometrium preoperatively to reassess stimulated endometrial thickness

Intraoperative
- Abdominal ultrasound-directed cervical and uterine dilatation
- Ultrasound-directed lysis of uterine synechia
- Ultrasound-directed placement of triangular intrauterine balloon catheter, advanced to uterine fundus

Postoperative
- Continue estrogen supplementation for 4–10 weeks after surgery
- Remove balloon catheter within 1 week of surgery, replace with copper intrauterine device
- Reassess cavity by hysterosalpingogram, saline sonohysterography, or hysteroscopy and assess postoperative menstrual function

Myers. Management of severe Asherman syndrome. Fertil Steril 2012.

Asherman syndrome was confirmed by preoperative HSG, hysteroscopy, or both. These patients had the most severe disease, with scores ranging from 10–12, according to The American Fertility Society (AFS) Classification of Uterine Adhesions (10).

All women underwent a preoperative ultrasound to assess the uterus and measure maximal endometrial thickness (Table 2). All women identified with severe Asherman syndrome were treated with preoperative oral E_2 4–6 mg daily, beginning 4–8 weeks before surgery, to stimulate endometrial proliferation with a secondary goal to help identify the endometrium with abdominal ultrasound during hysteroscopy. All women underwent a preoperative ultrasound approximately 4 weeks after taking E, to assess the uterus and measure the maximal preoperative endometrial thickness to help determine the prognosis for repair (2). Oral E was continued for up to 8 weeks and ultrasound repeated when the endometrial thickness was <4 mm after 4 weeks.

When the maximal endometrial development was achieved, all women underwent abdominal ultrasound-directed hysteroscopic lysis of uterine synechia. The bladder was filled to improve visualization with abdominal ultrasound, and then an ultrasound-directed dilatation was performed, with progressively larger dilators advanced to the top of the endometrial cavity. Concurrent abdominal ultrasound was used to help direct the hysteroscopic lysis of uterine synechia (1). Hysteroscopic lysis of synechia was continued with hysteroscopy scissors using a controlled flow pump with saline or lactated Ringer's solution for distention until the cavity had been completely reopened and no evidence of residual adhesion or distortion of the cavity could be seen, as determined by hysteroscopy and by abdominal ultrasound. At the conclusion of the lysis of synechia, a triangular uterine balloon catheter (Cook Medical) was placed at the uterine fundus under abdominal ultrasound guidance, and the balloon inflated (2). This balloon catheter was removed 3–7 days after surgery, and a copper intrauterine device (IUD) (Duramed Pharmaceuticals) was immediately placed into the endometrial cavity. Oral E_2 4–6 mg daily was continued until the IUD was removed, approximately 4–10 weeks after surgery. Response to treatment was determined by subsequent resumption of menses, achievement of pregnancy, and live birth.

RESULTS

Preoperatively, the maximal measured endometrial thickness ranged from 3–8.5 mm, and age ranged from 29–43 years (Table 1). Eight of the 12 women reported amenorrhea, and the other four experienced scant spotting. A dilation and curettage (D&C) procedure after pregnancy was the underlying cause in eight women; two experienced amenorrhea and Asherman resulting from a cesarean section, one resulted from a cervical cone biopsy and D&C, and one case was unexplained by the history provided. Eight of these women had failed at least one previous hysteroscopic repair, and two of these ended in a uterine perforation. Several women had been advised to consider hysterectomy, as their condition was believed to be inoperable due to the severity of the disease. In preparation for surgery, all women underwent transvaginal ultrasound examinations, usually before and during treatment with oral E_2.

Intraoperatively, the abdominal ultrasound helped to provide safe dilation of the cervix and endometrial cavity. Uterine perforation did not occur during repair. Visualization by hysteroscopy was often poor during lysis of uterine synechia in these women with severe Asherman syndrome, as distention of the endometrial cavity was poor and even small amounts of bleeding often caused complete loss of the image. However, concurrent abdominal ultrasound allowed the surgeon to safely continue the hysteroscopic dissection in the proper tissue planes, even when hysteroscopic visualization was poor. In all patients, the procedure was continued until the endometrial cavity had been restored to a normal dimension by ultrasound and by hysteroscopy, when visualization was adequate. A balloon catheter was successfully placed in all women at the conclusion of the procedure, and advanced to the uterine fundus under ultrasound visualization.

Postoperatively, the balloon catheter was removed within 1 week of the initial procedure, and an IUD placed in all but one patient. The IUD was removed 4–6 weeks later, and oral E discontinued. All 12 women reported the resumption of

menses. Although eight women had additional infertility factors, six of the eight women who desired pregnancy, less than age 39 years, conceived, and four of these six women delivered at or near term. Follow-up was limited for two women. None of the three women more than age 39 years with severe Asherman syndrome conceived after surgery in this series, but all of these had additional infertility factors.

DISCUSSION

A standardized comprehensive approach using a combination of preoperative, intraoperative, and postoperative methods appears to provide optimal clinical outcomes for women with severe Asherman syndrome. Unlike a prior study that showed that pregnancy was unlikely in women who had a thin endometrium before surgery (2), postsurgical conception occurred in one woman who had a maximal endometrial thickness of only 2 mm, and for one woman with a 3-mm endometrium. However, both of these pregnancies resulted in first trimester losses. In the current study, 3.7 mm was the thinnest preoperative endometrium that resulted in a live birth after repair. Thus, the current series reinforces the theory that a functional endometrium is not likely if it has been largely denuded, even if the uterine cavity is open. Preoperative ultrasound remains an important but imperfect method to assess preoperative prognosis.

Although hysteroscopy is considered the gold standard for diagnosis, other less invasive modalities such as HSG, transvaginal ultrasound examination, or saline infusion sonohysterography can help determine the extent of uterine adhesions and may provide meaningful prognostic information (2). Severe cases may require more than one of these modalities to establish the extent of disease and prognosis for repair.

Transvaginal ultrasound is a noninvasive method to evaluate the endometrial cavity. In a woman with risk factors for Asherman syndrome, such as amenorrhea after an incomplete abortion, transvaginal ultrasound findings suggestive of uterine synechia may include an endometrium that measures less than 2 mm in the luteal phase of the cycle, asymmetry of uterine cavity on a transverse view, or an irregular echogenic pattern within the uterine cavity (3, 4). Furthermore, transvaginal ultrasound may be the best study to evaluate the endometrium of a woman whose scarred lower uterine segment precludes evaluation by either HSG or sonohysterography (2). There may also be a prognostic use for transvaginal ultrasound, with better surgical outcomes in women with a thicker presurgical endometrium.

Proposed methods to prevent postoperative formation of intrauterine adhesions and improve the outcome of surgical repair of severe Asherman syndrome have included a number of hormonal and surgical techniques. Estrogen is often used to promote endometrial proliferation and healing after surgery. Farhi et al. (5) evaluated E and P therapy administered after first trimester D&C and found that women treated with hormone therapy (HT) had 95% more endometrial volume at 1 month than untreated women. Several investigators advocate the placement of a device to provide mechanical separation of the opposing endometrial surfaces to reduce adhesion recurrence after hysteroscopic lysis of synechia (6–9). In one report, placement of an intrauterine balloon catheter after hysteroscopic correction of Asherman syndrome showed a trend to less intrauterine adhesion reformation (6). In another study, a copper IUD placed after hysteroscopic lysis of synechia was found to restore normal menses in 40 of 48 women with secondary amenorrhea treated for Asherman syndrome (7). When use of an intrauterine balloon was compared with copper IUD, Orhue et al. (8) found that both methods were effective, with 73% of women experiencing a return of menstruation, 31% conceived, and the term birth rate was 16%. More recently, intrauterine adhesion treatment with resectoscope or versapoint with subsequent HT and IUD placement showed to have an overall live birth rate of 41% (9).

The use of E before and after surgery provides several potential benefits (5). Before surgery, E promotes maximal endometrial growth, and allows surgery to be performed in the proliferative phase. Furthermore, as the hysteroscopic repair is performed under abdominal ultrasound guidance, prolonged E will help achieve maximal endometrial thickness, and this may help improve intraoperative visualization by abdominal ultrasound. After surgery, continued proliferation is needed to stimulate the endometrium to cover the denuded uterine cavity. It is likely that E facilitates each of these important steps and can be considered an important addition to surgery.

Perhaps the most technically difficult aspect of Asherman syndrome is the surgical management. Unless ultrasound guidance is used intraoperatively, it can be extremely difficult to determine whether the dissection is performed in the correct planes. Clearly, this had been an issue in the two women in the present series who had experienced uterine perforations in prior attempts. Distention of the uterine cavity is difficult to achieve for almost all cases of severe Asherman syndrome, but almost impossible once perforation has occurred. When blood is present and when a constricted cavity reduces hysteroscopic flow, visualization is even more limited. Concurrent abdominal ultrasound allows the surgeon to continue the procedure and complete the dissection safely, even when the procedure could not be safely continued by hysteroscopy alone. After the hysteroscopic lysis of synechia, abdominal ultrasound ensures that the uterine balloon catheter has been positioned properly at the uterine fundus.

A mechanical separation of the uterine cavity is recognized as an important aspect to improve surgical outcomes with Asherman syndrome (5, 6). In the present series, a triangle balloon catheter was placed during surgery instead of a round balloon, to minimize pressure points and tissue necrosis that may occur with a Foley catheter balloon. The balloon catheter was removed within 1 week of surgery, and a copper IUD immediately placed. Although it is possible that the copper in the IUD helps promote endometrial healing (6), it is also likely that the mechanical adhesiolysis that occurs each time a device is inserted into and removed from the cavity helps to reduce the incidence of recurrent adhesions. This is especially important with Asherman syndrome, as the opposing sides of the uterine cavity will almost certainly resume contact, unless separated mechanically.

Regardless of the mechanisms of action, all of the patients treated had resumption of menses. We were encouraged by our successes, especially the observation that six of eight women who desired pregnancy were able to conceive, and four of six gave birth at or near term. However, even with the comprehensive approach proposed for severe Asherman disease, we are frustrated by our failures, especially in women more than age 38 years and those who had a maximal preoperative endometrial thickness that measured less than 3.7 mm. The rarity of this condition and the difficulty in correcting the cavity in women with amenorrhea due to severe Asherman disease precludes a large randomized control trial, but the present series shows that women with severe Asherman syndrome treated in a comprehensive, standardized fashion can achieve favorable outcomes.

REFERENCES

1. Yu D, Wong YM, Cheong Y, Xia E, Li TC. Asherman syndrome—one century later. Fertil Steril 2008;89:759–79.
2. Schlaff WD, Hurst BS. Preoperative sonographic measurement of endometrial pattern predicts outcome of surgical repair in patients with severe Asherman's syndrome. Fertil Steril 1995;63:410–3.
3. Confino E, Friberg J, Giglia RV, Gleicher N. Sonographic imaging of intrauterine adhesions. Obstet Gynecol 1985;66:596–8.
4. Salle B, Gaucherand P, de Saint Hilaire P, Rudigoz RC. Transvaginal sonohysterographic evaluation of intrauterine adhesions. J Clin Ultrasound 1999;27:131–4.
5. Farhi J, Bar-Hava I, Homburg R, Dicker D, Ben-Rafael Z. Induced regeneration of endometrium following curettage for abortion: a comparative study. Hum Reprod 1993;8:1143–4.
6. Amer MI, El Nadim A, Hassanein K. The role of intrauterine balloon after operative hysteroscopy in the prevention of intrauterine adhesions; a prospective controlled study. Middle Eastern Fertil Soc J 2005;10:135–9.
7. Vesce F, Jorizzo G, Bianciotto A, Gotti G. Use of the copper intrauterine device in the management of secondary amenorrhea. Fertil Steril 2000;73:162–5.
8. Orhue AA, Aziken ME, Igbefoh JO. A comparison of two adjunctive treatments for intrauterine adhesions following lysis. Int J Gynaecol Obstet 2003;82:49–56.
9. Zikopoulos KA, Kolibianakis EM, Platteau P, de Munck L, Tournaye H, Devroey P, et al. Live delivery rates in subfertile women with Asherman's syndrome after hysteroscopic adhesion lysis using the resectoscope or the versapoint system. Reprod Biomed Online 2004;8:720–5.
10. The American Fertility Society classifications of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, Müllerian anomalies and intrauterine adhesions. Fertil Steril 1988;49:944–55.