Asherman Syndrome

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Asherman syndrome (AS) was first reported in 1894 by Heinrich Fritz, however it was not until 1948 that Joseph Asherman described the syndrome, frequency, and etiology based on a series of cases of intrauterine adhesions following curettage of a gravid uterus in 29 women with secondary amenorrhea (Asherman 1948; 1950).

4.1 Definition

Asherman syndrome is also known as uterine atresia, amenorrhea traumatica, endometrial sclerosis, and intrauterine adhesions or synechiae (Asherman 1950). AS arises due to trauma of the endometrium and produces partial or complete obliteration of the uterine cavity and/or cervical canal due to intrauterine adhesions (Asherman 1948; March 2011; Schenker and Margalioth 1982). Intrauterine adhesions are composed of fibrotic tissue and the extent of fibrosis can range from mild and superficial fibrosis in a small area of the uterine cavity to a severe fibrosis of a large area, extending deep into the myometrium and causing adhesion of the opposing surfaces in the uterine cavity. Fibrosis in the cervical canal can cause amenorrhea and retrograde menstruation.

AS can occur due to uterine and intrauterine surgery such as cesarean section, curettage, myomectomy involving the uterine cavity, endometrial ablation, and hysteroscopic removal of fibroids and polyps (Asherman 1950; March 1995, 2011; Yu et al. 2008a). However, intrauterine adhesions

O. Istre (ed.), *Minimally Invasive Gynecological Surgery*,
DOI 10.1007/978-3-662-44059-9_4, © Springer-Verlag Berlin Heidelberg 2015

are also seen as a consequence of endometritis, congenital uterine abnormalities, and genetic predisposition. It is well known that the endometrium is more susceptible to trauma in a gravid uterus and the incidence of intrauterine adhesions following curettage for retained tissue is reported up to 40 % 3 months after curettage (Westendorp et al. 1998).

4.2 Symptoms

Trauma of the uterine cavity results in dysfunction of the endometrium which presents in conditions such as menstrual abnormalities (secondary amenorrhea and hypomenorrhea), dysmenorrhea, infertility, and recurrent pregnancy loss (March 2011). Symptoms have a broad clinical spectrum from asymptomatic in cases with mild adhesions to complain of severe pelvic pain and secondary amenorrhea in cases with retrograde menstruations due to fibrosis in the cervical canal.

In women with infertility or recurrent pregnancy loss, treatment is required for optimal conception possibilities. AS is furthermore, a cause of abnormal placentation in subsequent pregnancies due to defects in the decidua basalis (Nitabuchs layer) which in a gravid uterus can give rise to placenta previa and placenta accreta (Yu et al. 2008a; Jauniaux and Jurkovic 2012).

4.3 Prevalence

The prevalence of AS varies from 1.55 to 20 % (Schenker and Margalioth 1982; Westendorp et al. 1998; Dmowski and Greenblatt 1969; Friedler et al. 1993) according to population, mainly due to different diagnostic criteria, the number of abortions in the population, choice of management, awareness of clinicians, and incidence of infections (genital tuberculosis and puerperal infections) (Schenker and Margalioth 1982). It is well known that the endometrium is more susceptible to trauma in a gravid uterus and the incidence of intrauterine adhesions following curettage for retained tissue is reported up to 40 % 3 months after curettage (Westendorp et al. 1998).

4.4 Diagnosis

AS should be suspected in any woman presenting with menstrual abnormalities and/or infertility and a history of previous curettage or intrauterine surgery. Accurate diagnosis of AS is possible by imaging the uterine cavity by a number of modalities.

Hysterosalpingography (HSG) has been the most widespread tool in diagnosis of AS. HSG can reveal filling defects described as sharply outlined intrauterine structures in the uterine cavity, however in the worst cases, HSG cannot be performed due to ostial occlusion. HSG has a high false positive rate and cannot reveal endometrial fibrosis, furthermore fibroids and polyps can be mistaken for intrauterine adhesions by the appearance at HSG. HSG has a sensitivity of 75 % and a positive predictive value of 50 % (Soares et al. 2000).

Transvaginal ultrasound is easily performed and can reveal an echo dense pattern with difficult visualization of the endometrium interrupted by cyst-like areas (Yu et al. 2008a). The diagnostic accuracy of ultrasound, however, allows visualization of the uterine cavity in cases where HSG and hysteroscopy cannot be performed due to obstruction of the cervix (Soares et al. 2000).

3D ultrasound and intrauterine saline infusion (3D-SHG) is another diagnostic tool for diagnosis of AS. 3D-SHG combined with 3D power Doppler has a sensitivity of 91.1 % and specificity of 98.5 % for detection of all kinds of intrauterine adhesions (Makris et al. 2007).

Magnetic resonance imaging (MRI) can be helpful as a supplementary diagnostic tool, especially when the adhesions involve the endocervix (Bacelar et al. 1995).

Despite the abovementioned diagnostic tools, hysteroscopy remains the golden standard in the assessment and diagnosis of AS. Hysteroscopy venables direct vision of the extent of lesions and adhesions and provides thorough planning of removal of adhesions by the surgeon (Figs. 4.1 and 4.2).

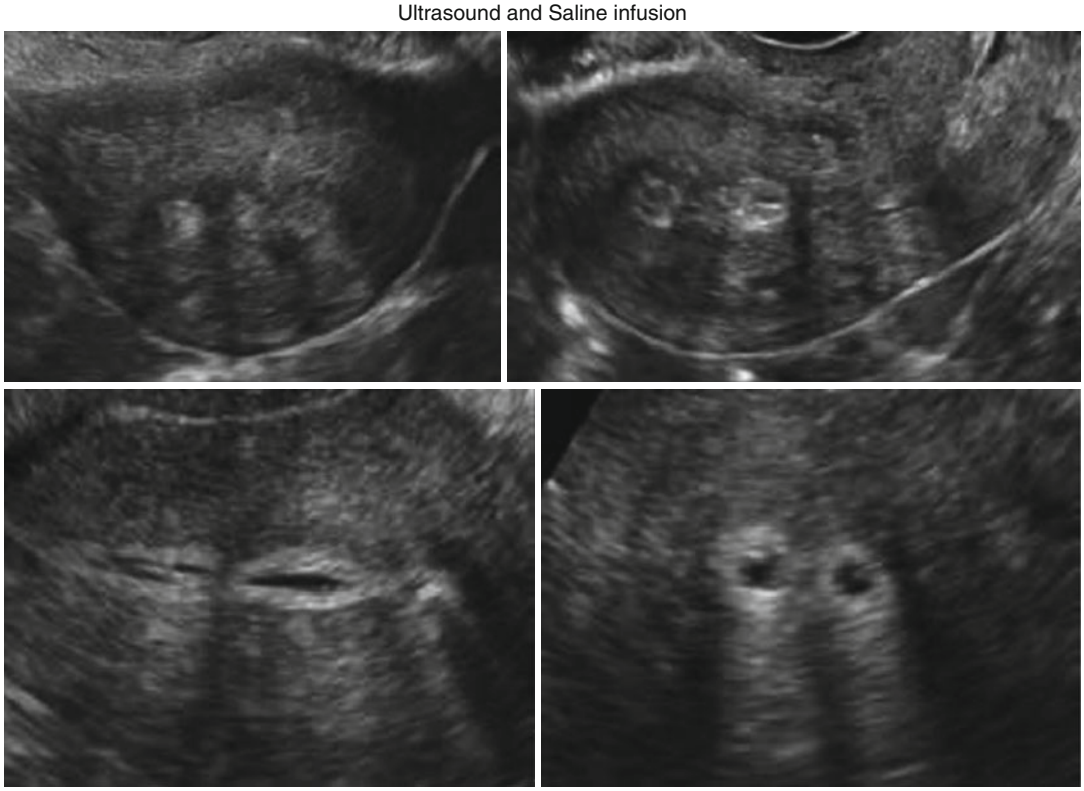

Fig. 4.1 Ultrasound and saline infusion revealing filling defects in a patient with AS

4.5 Classification

Since the description of AS was made in 1948, several attempts have been made to classify the extent of adhesions and lesions in patients with AS.

To date, several classification schemes are available for classification of the extent of Asherman disease. One of the most widely used is developed on behalf of the American Fertility Society and provides a classification of AS based on extent of the disease, menstrual pattern, and the morphological feature of the adhesions. Both hysteroscopy and HSG could be used for this kind of scoring system (Table 4.1).

More recently, a classification scheme published in 2000 by Nasr et al. illustrated an innovative way to classify AS (Table 4.2). This scoring system includes not only the menstrual symptoms but also the obstetric history of the woman (Nasr et al. 2000). According to this group, clinical history plays a more important role than the extent of the adhesions. The classification scheme provides good correlation in women with mild or severe disease, but not in those with moderate adhesions.

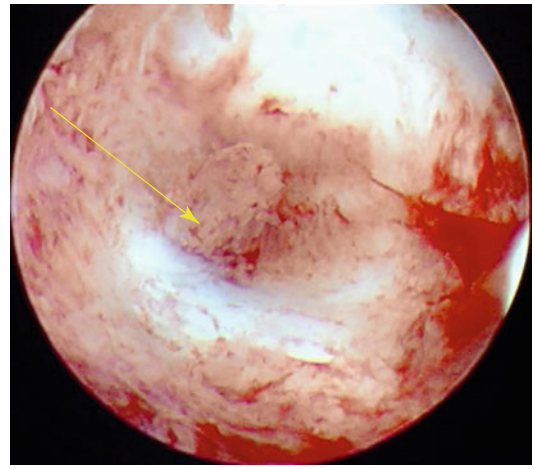

Fig. 4.2 Dense adhesion in the inner cervical area

Table 4.1 The American Fertility Society classification system for intrauterine adhesions

Classification		Score
Extent of cavity involved	<1/3	1
	1/3–2/3	2
	>2/3	4
Type of adhesion	Filmy	1
	Filmy and dense	2
	Dense	4
Menstrual pattern	Normal	0
	Hypomenorrhea	2
	Amenorrhea	4
Prognostic classification	Stage 1 (Mild): 1–4	
	Stage 2 (Moderate): 5–8	
	Stage 3 (Severe): 9–12	

Table 4.2 Clinico-hysteroscopic classification system for intrauterine adhesions

Hysteroscopic findings		Score
Isthmic fibrosis		2
Filmy adhesions	>50 % of the cavity	1
	<50 % of the cavity	2
Dense adhesions	Single band	2
	Multiple bands	4
Tubal ostium	Both visualized	0
	One visualized	2
	None visualized	4
Tubular cavity	Sound less than 6	10
Menstrual pattern		
	Normal	0
	Hypomenorrhea	4
	Amenorrhea	8
Reproductive performance		
	Good obstetric history	0
	Recurrent pregnancy loss	2
	Infertility	4
Stages	Mild	0–4
	Moderate	5–10
	Severe	11–22

4.6 Management

Treatment of AS should only be considered when there are signs or symptoms of pain, menstrual abnormalities, infertility, or recurrent pregnancy loss. The primary goal of intervention is to restore the volume and shape of the uterine cavity; to facilitate communication between fallopian tubes, uterine cavity, and cervical canal; and to restore reproductive function.

The management strategy of AS is based on four steps:

1. Surgical procedures
2. Prevention of the formation of re-adhesions
3. Restoring a normal endometrium
4. Postoperative assessment

4.6.1 Surgical Procedures

4.6.1.1 Hysteroscopic Adhesiolysis

Removal of adhesions can be performed by hysteroscopic adhesiolysis which is the current treatment of choice for AS (Pabuccu et al. 1997; Roy et al. 2010; Yu et al. 2008b). During hysteroscopy adhesions can be classified and adhesiolysis can be performed under direct vision. The procedure is minimally invasive. Adhesiolysis can be performed with the touch of the endoscope in cases of thin filmy adhesions or with the help of hysteroscopic scissors or cutting modalities as laser and diathermy in case of more dense adhesions.

Hysteroscopic adhesiolysis can be technically difficult even in the hands of a trained surgeon. The procedure is associated with risk of perforation of the uterus, especially in cases on cervical fibrosis. Approximately 2.5 % undergoing adhesiolysis experience perforation of the uterus; however, in severe cases the rate is as high as 10 % (Pabuccu et al. 1997).

In cases with extensive adhesions, one approach is to start with the wire loop of the smaller resectoscope and gradually remove the scarring tissue in the cervix until you reach the cavity. On this stage the loop is replaced by the knife, cold or warm, and then it is possible to open up the cavity.

In severe cases, in has been reported that concomitant laparoscopy may help the surgeon to avoid perforations, but simultaneous laparoscopy cannot prevent perforations of the uterine wall. Yet concomitant laparoscopy enables detection of perforations immediately and the prevention of trauma to other pelvic organs (Fig. 4.3).

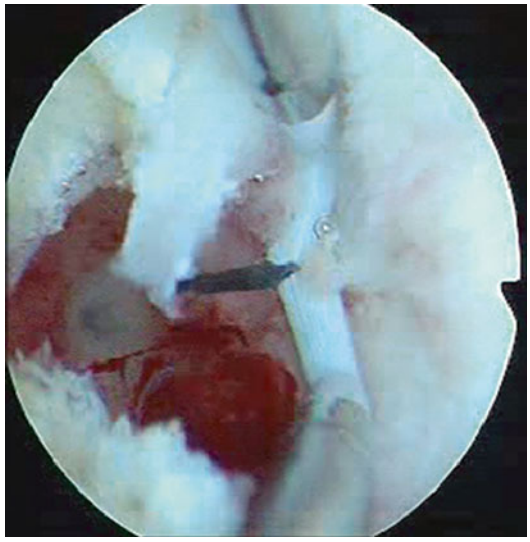

Fig. 4.3 Surgical treatment with resectoscopic needle

4.6.1.2 Myometrial Scoring Technique

Myometrial scoring technique is used in cases with dense adhesions and reduction of the size of the uterine cavity. The technique is used to restore the size of the cavity and to uncover functional endometrium by making six to eight longitudinal incisions into the myometrium, of which two to three are lateral incisions from the fundus to isthmus on both sides and two to three transverse incisions in the fundus. In the end of the procedure the cervical canal is dilated up to Hegar 12–18 in order to reduce the risk of cervical stenosis postoperatively (Protopapas et al. 1998).

4.6.2 Prevention of Reformation of Adhesions

Different techniques have been developed for the purpose of preventing reformation of adhesions following hysteroscopy.

Insertions of intrauterine devices (IUD), such as the loop IUD, have shown promising results in preventing reformation of adhesions. The loop IUD is placed in the uterus following hysteroscopy and is recommended to stay typically 1–3 months.

Intrauterine balloons have also been used to prevent adhesions, and the balloon is placed in uterus and is typically removed after 7 days. Balloons used have been Foley catheters as well as heart-shaped balloons.

Another technique for prevention of reformation of adhesions is installation of hyaluronic acid gel in the uterus following hysteroscopy. A recent study by Lin et al. compared the effect of cobber IUD, a heart-shaped balloon and hyaluronic acid in the prevention of reformation of adhesions in patients who had undergone hysteroscopic surgery for AS. The study demonstrated that treatment with balloon and IUD significantly decreases the extent of reformation of adhesions compared to the use of hyaluronic acid and no treatment following hysteroscopy. No difference in the extent of adhesions was found between patients who were treated with hyaluronic acid or the control group who received no postoperatively treatment (Lin et al. 2013).

Treatment with estrogen has shown good results preventing formation of adhesions following hysteroscopic surgery for AS. Use of per oral estrogen gives better fertility and menstrual outcome when given in combination with ancillary treatment (IUD, balloon, or hyaluronic acid). Estrogen therapy is favorable regardless of stage of AS and is typically given 4–6 weeks postoperatively (Johary et al. 2014).

4.6.3 Restoring a Normal Endometrium

Endometrium in AS can be sparse and fibrotic. Hysteroscopic treatment enables adhesiolysis and reformation size and function of uterine cavity. Yet, in order to reestablish a functioning endometrium and enable subsequent pregnancies, the standard treatment recommended to promote endometrial growth and reepithelialization of scarred surfaces is typically oral estradiol 2 mg daily for 30–60 days and medroxyprogesterone acetate 10 mg for the last 5 days of the estrogen therapy (Johary et al. 2014).

Restoration of a functioning endometrium by stem cells is a potential future treatment; however, the research and knowledge on treatment of AS with stem cells is still in its infancy.

4.6.4 Postoperative Assessment

Management of moderate and severe AS poses a challenge and repeat surgery is necessary in some cases, however does not always produce the desired outcome.

Postoperatively assessment of the effect of treatment is mainly reflected by the patient's symptoms. Ultrasound and repeat hysteroscopy can give an assessment of the uterine cavity, though reformation of adhesions is not always related to a poor outcome.

In those patients who succeed in achieving pregnancy, a thorough antenatal follow-up is necessary due to increased risk of abnormal placentation (March 2011).

4.6.5 Reproductive Outcome After Treatment

Infertility and recurrent pregnancy loss due to AS can be treated with good outcomes. A recent study by Roy et al. reported conception rates of 58 % in mild AS, 30 % in moderate AS, and 33.3 % in severe cases of AS following hysteroscopic adhesiolysis. Furthermore, the live birth rate reported was 86.1 %, the miscarriage rate 11.1 %, and the cumulative pregnancy rate showed that 97.2 % of the patients conceived within 24 months postoperatively (Roy et al. 2010).

References

Asherman JG (1948) Amenorrhoea traumatica (atretica). J Obstet Gynaecol Br Emp 55(1):23–30

Asherman JG (1950) Traumatic intra-uterine adhesions. J Obstet Gynaecol Br Emp 57(6):892–896

Bacelar AC, Wilcock D, Powell M, Worthington BS (1995) The value of MRI in the assessment of traumatic intra-uterine adhesions (Asherman's syndrome). Clin Radiol 50(2):80–83

Dmowski WP, Greenblatt RB (1969) Asherman's syndrome and risk of placenta accreta. Obstet Gynecol 34(2):288–299

Friedler S, Margalioth EJ, Kafka I, Yaffe H (1993) Incidence of post-abortion intra-uterine adhesions evaluated by hysteroscopy–a prospective study. Hum Reprod 8(3):442–444

Jauniaux E, Jurkovic D (2012) Placenta accreta: pathogenesis of a 20th century iatrogenic uterine disease. Placenta 33(4):244–251

Johary J, Xue M, Zhu X, Xu D, Velu PP (2014) Efficacy of estrogen therapy in patients with intrauterine adhesions: systematic review. J Minim Invasive Gynecol 21(1):44–54

Lin X, Wei M, Li TC, Huang Q, Huang D, Zhou F et al (2013) A comparison of intrauterine balloon, intrauterine contraceptive device and hyaluronic acid gel in the prevention of adhesion reformation following hysteroscopic surgery for Asherman syndrome: a cohort study. Eur J Obstet Gynecol Reprod Biol 170(2): 512–516

Makris N, Kalmantis K, Skartados N, Papadimitriou A, Mantzaris G, Antsaklis A (2007) Three-dimensional hysterosonography versus hysteroscopy for the detection of intracavitary uterine abnormalities. Int J Gynaecol Obstet 97(1):6–9

March CM (1995) Intrauterine adhesions. Obstet Gynecol Clin North Am 22(3):491–505

March CM (2011) Asherman's syndrome. Semin Reprod Med 29(2):83–94

Nasr AL, Al-Inany HG, Thabet SM, Aboulghar M (2000) A clinicohysteroscopic scoring system of intrauterine adhesions. Gynecol Obstet Invest 50(3):178–181

Pabuccu R, Atay V, Orhon E, Urman B, Ergun A (1997) Hysteroscopic treatment of intrauterine adhesions is safe and effective in the restoration of normal menstruation and fertility. Fertil Steril 68(6):1141–1143

Protopapas A, Shushan A, Magos A (1998) Myometrial scoring: a new technique for the management of severe Asherman's syndrome. Fertil Steril 69(5):860–864

Roy KK, Baruah J, Sharma JB, Kumar S, Kachawa G, Singh N (2010) Reproductive outcome following hysteroscopic adhesiolysis in patients with infertility due to Asherman's syndrome. Arch Gynecol Obstet 281(2):355–361

Schenker JG, Margalioth EJ (1982) Intrauterine adhesions: an updated appraisal. Fertil Steril 37(5):593–610

Soares SR, Barbosa dos Reis MM, Camargos AF (2000) Diagnostic accuracy of sonohysterography, transvaginal sonography, and hysterosalpingography in patients with uterine cavity diseases. Fertil Steril 73(2): 406–411

Westendorp IC, Ankum WM, Mol BW, Vonk J (1998) Prevalence of Asherman's syndrome after secondary removal of placental remnants or a repeat curettage for incomplete abortion. Hum Reprod 13(12):3347–3350

Yu D, Wong YM, Cheong Y, Xia E, Li TC (2008a) Asherman syndrome–one century later. Fertil Steril 89(4):759–779

Yu D, Li TC, Xia E, Huang X, Liu Y, Peng X (2008b) Factors affecting reproductive outcome of hysteroscopic adhesiolysis for Asherman's syndrome. Fertil Steril 89(3):715–722