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REVIEW ARTICLE

Asherman Syndrome

Alka Bhaurao Patil[1], Harshali Rajiv Tuknait[2], Prachi Vilas Saner[3]

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ABSTRACT

Asherman syndrome is the presence of adhesions in the endometrial cavity that can result in infertility or recurrent spontaneous abortion with or without amenorrhea. It can present with pain, menstrual abnormalities, recurrent pregnancy loss and infertility. These synechiae may be detected on a hysterogram or sonohysterogram, but are best shown with diagnostic hysteroscopy.

Management includes hysteroscopic guided lysis of adhesions and attempt to restore uterine cavity anatomy. Platelet rich plasma, stem cells, growth factors, tissue engineering are being explored for endometrial regenerative therapy. Preventive measures need to be explored more. Efforts are needed in reducing adhesions post instrumentation especially in gravid uterus.

KEYWORDS

• Asherman syndrome • Amenorrhea • Adhesions • Endometrium

INTRODUCTION

Intrauterine adhesions or intrauterine synechiae is a condition in which scar tissue develops within uterine cavity. When this is accompanied by symptoms of infertility, amenorrhea it is known as Asherman syndrome.

Named after Joseph Asherman of Tel Avires Hadassal hospital, who studied adhesions of cervical canal, cervical stenosis and intrauterine adhesions published in 1948 who called it amenorrhea traumatica.[1]

Asherman syndrome is an acquired condition, that makes it very important to study the causes and care to be taken to avoid dreadful outcomes like recurrent pregnancy loss, infertility and menstrual disorders like amenorrhea or hypomenorrhoea.

AUTHOR'S AFFILIATION:

[1] Professor and HOD, Department of Obstetrics and Gynecology, ACPM Medical College and Hospital, Dhule, Maharashtra 424002, India.

[2] Junior Resident, Department of Obstetrics and Gynecology, ACPM Medical College and Hospital, Dhule, Maharashtra 424002, India.

[3] Junior Resident, Department of Obstetrics and Gynecology, ACPM Medical College and Hospital, Dhule, Maharashtra 424002, India.

CORRESPONDING AUTHOR:

Harshali Rajiv Tuknait, Junior Resident, Department of Obstetrics and Gynecology, ACPM Medical College and Hospital, Dhule, Maharashtra 424002, India.

E-mail: harshalituknait@icloud.com

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RISK FACTORS

Any process with potential to damage basalis layer can be a risk factor.

1) Pregnancy: It is and independent risk factor distinct from intrauterine surgery. Patients who underwent curettage after a pregnancy loss at a more advanced gestational age have increased prevalence of IUA compared with early pregnancy loss.[1] Follow-up examination of 141 patients by Erikson *et al* reported higher risk of intrauterine synechiae formation in women who underwent postpartum curettage 2-4 weeks after delivery compared with early postpartum period. 20% prevalence was noted in a meta-analysis of 10 Prospective studies by hysteroscopy done within 12 months in women who underwent curettage post pregnancy loss.[2] There is increased susceptibility due to low estrogen state during postpartum and postabortion time. Antagonistic effects from. elevated prolactin levels associated with breastfeeding or post pregnancy physiological changes that make basalis layer more susceptible to injury.[3,4]

2) Intrauterine procedures: Apart from it's Association with pregnancy, intrauterine manipulations can result in formation of adhesions after procedures such as myomectomy or curettage of non-gravid Uterus. Hysteroscopic myomectomy of multiple fibroids is associated with higher risk of IUA than removal of one fibroid . Intrauterine devices can be used as a preventive measure rather than being a causative agent or risk factor.[5,6]

3) Inflammation or infection: Genital TB is associated with intrauterine adhesions, which are often severe resulting in complete obliteration of uterine cavity secondary to chronic inflammation of endometrium. Studies assessing chronic endometritis in women with known IUA, 35% had chronic endometritis confirmed by histology. However, it was a cause or the sequelae of adhesions is not known.[6-8]

4) Uterine compression sutures: B-lynch sutures for severe PPH shows Association with development of IUA.[9]

EPIDEMIOLOGY

True prevalence is difficult to establish because it is often asymptomatic and requires invasive procedure for diagnosis.

According to NCIB stats, Ashermans syndrome is found in

1-5% women doing HSG for infertility

5-39% women with recurrent pregnancy loss

31% women with previous hysteroscopic resection of leiomyoma

46% women with post 2nd hysteroscopic resection[10]

PATHOPHYSIOLOGY

Normally, the endometrium is divided into a functional layer, which lines the endometrial cavity, and a basal layer which regenerates the functional layer with each menstrual cycle. Destruction of the basal endometrium prevents endometrial thickening in response to ovarian steroids. Thus, no tissue is produced or subsequently sloughed when steroid hormone levels fall at the end of the luteal phase.

Endometrial damage may follow vigorous curettage usually associated with:

- Postpartum haemorrhage
- Miscarriage
- Elective abortion complicated by infection

In a study conducted by Schenker and Margalioth of 1856 women with Asherman syndrome, 88 percent followed postabortal or postpartum uterine curettage, risks for intrauterine adhesions rise with number of D and Cs for spontaneous first trimester abortion. In one prospective study, the risk was 16 percent after a single termination. The rate rose to 32 percent and with progressively more dense adhesions following three or more procedures.[12]

Damage may also result from other uterine surgery, including metroplasty, myomectomy, or cesarean delivery, or from infection related to an intrauterine device. Although rare in the United States, tuberculous endometritis is a relatively common cause of Asherman syndrome in developing countries. It can also be an intentional outcome following uterine ablation for heavy menstrual bleeding.

Depending on the degree of scarring patient may describe amenorrhea; or recurrent pregnancy loss due to inadequate placentation. In their evaluation 292 women with intrauterine adhesions, Schenker and Margalioth noted delivery of term pregnancies in only 30% of 165 pregnancies. Remaining

pregnancies either were spontaneously aborted or delivered prematurely.

Damage may result from other uterine surgery including:

- Metroplasty
- Myomectomy
- Cesarean delivery
- Infection related to intrauterine device

–Any trauma to basal layer of endometrium in opposing areas within uterine cavity.[10] Trauma->triggers inflammation -> formation of adhesion bands

–Low estrogen state makes endometrium more vulnerable to injury

–2 layers of endometrium become undifferentiated, loss of distinction between basal and functional layer of endometrium

–Abnormal placentation below basal layer

–Endometrial stroma is largely replaced by fibrous tissue and glands are lined by inactive cubocolumnar epithelium of endometrial type, there is no active inflammation.

–Replacememt of endometrium by epithelial monolayer-there can be calcification or even ossification in stroma and glands dilated or inactive.[17]

–Basalis layer is most susceptible to damage in first 4 postpartum and postabortal weeks.

–VEGF is an important modulation of endometrial stromal fibrosis which is downregulated in women with Asherman's syndrome

–Endometrial damage and scarring compromises vascularisation which in turn accounts for menstrual abnormalities, frequent dysmenorrhea, infertility and RPL.

SPECTRUM

Minimum	Maximum
Thin strings of tissue	complete obliteration
Minimal disease	Severe disease, anterior wall adhered to posterior wall
Flimsy string of endometrial tissue	Consists of Entirely connective tissue
Spotty	Confluent

Characteristics of adhesions:

Adhesions are usually avascular.

They may arise from endometrium, myometrium or connective tissue.[17]

Marginal adhesions	Mucosal adhesions	Fibrous adhesions	TB
Crescent shaped or like a curtain	**Same color** as endometrium and fragile	**Pale, strong**	**Honeycomb appearance**

Intrauterine fibrous adhesions cross the endometrial cavity. Synechiae form a mesh or spider's web within the uterine lumen, may cause infertility, hypomenorrhoea or amenorrhoea, better seen with sonohysterography.

Fibrous strands may calcify, with a characteristic sonographic appearance.

CLINICAL PRESENTATION

1) AUB/amenorrhea/hypomenorrhoea after an intrauterine procedure. 91-99. 2% occurs in previous pregnancy related intrauterine procedures.
2) Infertility - HSG, SIS, hysteroscopy are routinely done in view of infertility. IUA block sperm , destruction of endometrium prevents implantation of blastocysts. Impaired fecundity seem even after treatment of IUA in cases with recurrent D and C for miscarriages.
3) Dysmenorrhe/cyclic pain due to hematometra or obstruction to menstrual flow associated with amenorrhea or hypomenorrhoea.
4) Recurrent pregnancy loss: due to abnormality of implantation in areas of insufficient vascularisation or deluded endometrium.
5) Incidental finding: USG(A+P), SIS, HSG, hysteroscopy indicated for infertility or AUB.

DIAGNOSIS

1) History of:
   - Prior pregnancy, uterine procedure, menstrual changes dysmenorrhea.

- TB

2) ***Examination:*** Bimanual pelvic examination shows normal findings.
3) ***USG:*** Abnormally thin endometrium following amenorrhea and/or endometrial irregularity known as skip lesions with hyperechoic regions is suggestive of IUD but not Definitive.
4) ***Estrogen/Progestin withdrawal test:*** it takes time and delays diagnosis. 2 months process where first progestin is given alone followed by estrogen+progestin.

   Estrogen withdrawal - no withdrawal bleeding post conjugated equine estrogen 1. 25mg daily × 21days and progestin(MPA) 10mg daily for last 5-7 days. This demonstrates end organ endometrial failure.[18]
5) ***Sonohysterography:*** This is done by using saline contrast, which is pushed through the cervix by a paediatric Foley's or feeding tube under transvaginal scan visualisation. This is an excellent, easy, non-invasive, quick and reliable method to evaluate uterine cavity for Asherman's disease, polyps, submucous fibroids, focal lesions or even malignancy.
6) ***Hysteroscopy:*** Direct visualisation of presence, extent and morphological characteristics of IUA and allows treatment/lysis in same setting. Therefore it is gold standard.
7) ***SIS:*** water or air infusion can help to visualise tubal patency. Saline infusion sonography (SIS) provides excellent alternative. Intrauterine adhesions characteristically appear as irregular, angulated filling defects within the cavity.
8) ***Schistosomiasis:*** egg of parasite in urine, feces, rectal scrapping, menstrual discharge or endometrial aspirate.
9) ***MRI:*** useful in cases with cervical stenosis where other modalities needing per cervical instrumentation cannot be used.
10) ***TB:*** endometrial biopsy, nucleic acid test on endometrial aspirate.

SIS	HSG
No radiation	Radiation required
Office setting	Radiology suite required

- Radiological evaluation should be done if intrauterine adhesions are suspected.
- Hysterosalpingography allows to evaluate tubal patency and information about both uterine cavity.
- Uterine polyps, leiomyomas, air bubbles, and Blood clots may masquerade as adhesions.
- Definitive Diagnosis requires hysteroscopy.

DIFFERENTIAL DIAGNOSIS

1. Uterine anomaly
2. Endocrinology pathology
   a. Thyroid disease
   b. Hypothalammic dysfunction
   c. Pituitary dysfunction
   d. Androgen secreting ovarian/adrenal tumor
3. PCOD
4. Premature menopause
5. PID

TREATMENT

To improve fertility rates or to relieve symptomatic hematometra hysteroscopic lysis of adhesion is the preferred surgical treatment. Treatment of Asherman syndrome involve hysteroscopic lysis of the scar tissue.

Regenerative endometrial therapies:

Operative hysteroscopy-lysis by scissors, electrodissection, laser or sharp dissection(most preferred) as has low risk of further injury.

Hysteroscopy with laparoscopy or USG guidance helps to maintain orientation in grossly distorted uterus and decrease risk of perforation.

Intrauterine balloon catheter for 7-10days post adhesiolysis can decrease recurrence.

Broad spectrum antibiotic- doxycycline 100mg bd, NSAID decrease risk of infection and uterine cramping due to catheter.

High dose exogenous estrogen treatment for 4 weeks post surgery causes rapid endometrial re epithelisation and proliferation.

2.5mg conjugated equine estrogen 2-3 times daily or equivalent and progestin in final week

Follow up HSG post operatively gives us 2nd look and can allow lysis or early recurring

adhesions when still thin.

PROGNOSIS

Anatomically uterine cavity can be reconstructed after surgery but normal endometrial lining may lag for sometime or never recur. Chances of conceiving and delivery are lesser in moderate to severe disease.

Adhesions may recur even after adhesiolysis.

Menstrual function normalises in 52-88%.

Live birth in 25-35% with risk of preterm labour, placenta previa, placenta accreta, PPH 20-60% recurrence rate.

Risk of endometrial adenocarcinoma, because symptoms of endometrial cancer are masked due to adhesions. Therefore followup should be regularly done.

PATIENT EDUCATION

Proper and timely use of contraceptive can surely decrease rate of legal abortions, decrease uterine adhesions.

CONCLUSION

Asherman syndrome is an acquired condition which results in complications and symptoms lasting lifelong with no definitive permanent treatment. Therefore it is as important to focus and study the preventive measures and create awareness as is reviewing newer treatment advances. Patients undergoing procedures with risk of Asherman syndrome in future should be closely followed up to decrease the incidence of endometrial cancer in pre and post menopausal patients Constitutional component behind the occurrence of Asherman's syndrome in few individuals without any prior endometrial trauma should be studied. Also, during vulnerable period, that is, 2nd, 3rd and 4th postpartum week, hysteroscopic resection under direct visualisation of uterine cavity allows removal of RPOC with Minimal damage to endometrium.

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