Clinical Features (Signs and Symptoms)

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Intrauterine adhesions cause total or partial obliteration of the endocervix and/or uterine cavity, resulting in hypomenorrhea or amenorrhea, infertility, and pregnancy loss. The majority of patients with IUAs present with menstrual abnormalities, usually hypomenorrhea or secondary amenorrhea. Others may have relatively normal menses and in which case a high index of suspicion is needed to make diagnosis.

Endometrium is composed of two layers, the functional layer (adjacent to the uterine cavity) which is shed during menstruation, and an underlying basal layer (adjacent to the myometrium), which is necessary for regenerating the functional layer.

Trauma to the basal layer, typically after a dilation and curettage (D&C) performed after a miscarriage, or delivery, or for surgical termination of pregnancy, can lead to the development of intrauterine scars resulting in adhesions that can obliterate the cavity to varying degrees. In extreme cases, the whole cavity may be scarred and occluded. Even with relatively few scars, the endometrium may fail to respond to estrogen.

Dan Yu et al. proposed the following criteria for the diagnosis of Asherman's syndrome [1]:

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1. One or more clinical features: amenorrhea, hypomenorrhea, subfertility, recurrent pregnancy loss, or a history related to abnormal placentation including previa and accreta
2. The presence of intrauterine adhesions by hysteroscopy and/or histologically confirmed intrauterine fibrosis

3.1 Clinicopathological Association

The clinical features are closely associated with pathologic findings like depth of fibrosis, location of adhesions, and extent of pathologic changes.

The location of the adhesion can include the cervical canal, uterine cavity, or both cervical canal and uterine cavity.

Obstructive amenorrhea is a consequence of intracervical adhesions or stenosis, and patients often present with amenorrhea with periodic abdominal discomfort. There may be a normal uterine cavity and thus a good prognosis after treatment. The most common variety is when the adhesions are in the uterine cavity.

3.1.1 Subcategories

- *Central intrauterine adhesion without constriction of the cavity*: Patients with central intrauterine adhesions always have some normal endometrium and a relatively normal cavity. Therefore, the prognosis after treatment is usually good.
- *Partial obliteration of the cavity with constriction*: Patients with partial obliteration of the cavity have a reduced and irregular cavity.
- *Complete obliteration of the cavity*: No cavity is found and it results in amenorrhea.

In all of these conditions, the patient may present with any symptoms and the extent of disease can be confirmed by hysteroscopy. The extent will influence the prognosis.

The prognosis for pregnancy in these patients is often poor.

In some cases, the adhesions can be located in both cervical canal and cavity of the uterus. The patient may present with any symptoms, including menstrual abnormalities, infertility, and pregnancy complications, and the outcome (such as normal menses and fertility) depends very much on the severity and extent of the adhesions.

3.2 WHRIA's (Women's Health & Research Institute of Australia) Stages of Asherman's Syndrome

3.2.1 Stage I

- Minor scarring in either the cervical canal or the uterine cavity.
- Unless this involves isthmus, there will be little impact on the normal function of the uterus and treatment is not essential.

- If the scar involves the isthmus, there can be a significant impact on the function of the endometrium.
- Most women are able to conceive.

3.2.2 Stage II

- Patients frequently present at this stage of the condition.
- There will be an obstruction of the internal os.
- In some women this obstruction involves only a fraction of a millimeter; in others it can stretch over several centimeters.
- If the scarring involves the isthmus, there will be no menses and pain, or there will be mild cramps with no bleeding.
- Women with stage II Asherman's syndrome have more than a 60% chance of conceiving again.

3.2.3 Stage III

- The uterus will normally contract and more than 50% is blocked by scar tissue.
- There may also be an obstruction of one of the tubal orifices.
- The greater the extent of scar formation, the more difficult it is to treat.
- Typically, women have less than a 30% chance of successfully conceiving and delivering a child.

3.2.4 Stage IV

- More than 75% of the uterus is blocked and it is smaller in size.
- Treatment at this stage requires multiple visits and has a low success rate.
- Stem cell technology may improve the outcome.

3.3 Spectrum of Clinical Features

3.3.1 Gynecological Features (Fig. 3.1)

3.3.1.1 Menstrual Disorders

Menstrual disorders appear in 48–75% [2] of the patients with intrauterine adhesions. It is characterized by a decrease in flow and duration of bleeding (amenorrhea, scanty bleeding, or infrequent bleeding). Menstrual abnormalities are not always related to the severity of the disease.

- ***Hypomenorrhea*** may be caused by the replacement of normal endometrium by fibrosis, as well as endometrial trauma where damaged endometrium does not

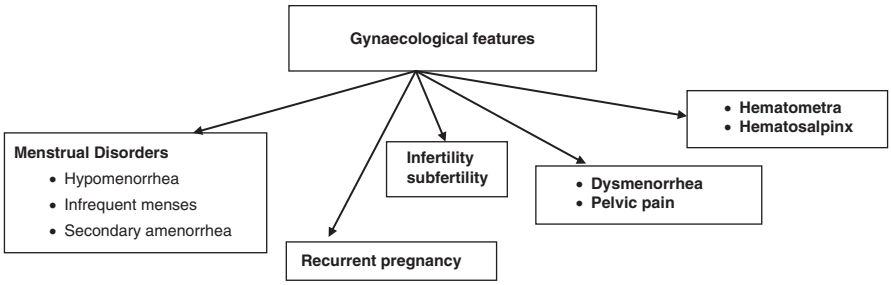

Fig. 3.1 Gynecological features

respond to estrogenic stimulus, as it would under normal conditions. The vascular damage to the tissues may precede the development of Asherman's syndrome.

- ***Amenorrhea***
  1. Cervical adhesions blocking menstrual flow.
  2. Severe endometrial fibrosis leading to destruction of the entire basal layer of the endometrium.
- ***Dysmenorrhea*** is occasionally present (3.5%).
- ***Atretic amenorrhea***: Mechanical obstruction of the internal cervical os could lead to secondary amenorrhea, periodic discomfort or pain, hematometra [3], and even hematosalpinx.

3.3.1.2 Infertility

Infertility appears in about 50% of patients diagnosed with Asherman's syndrome [3]. It may occur when the endometrium fails to respond to hormonal stimulation, as well as a restricted endometrial area [3].

Infertility could be due to occlusion of the tubal ostia, uterine cavity, or cervical canal caused by adhesions, which could prevent the migration of sperm or implantation of the embryo.

3.3.1.3 Recurrent Pregnancy Loss

The World Health Organization (WHO) defines recurrent pregnancy loss as two clinical pregnancy losses, not necessarily consecutive. Intrauterine adhesions and endometrial damage result in a restricted endometrial area and lead to abnormal placentation associated to recurrent pregnancy loss [4]. Some studies report early pregnancy loss (up to 13 completed weeks of pregnancy) in 25–40% [5] of these patients.

3.3.1.4 Causes for Recurrent Pregnancy Loss

1. Constriction of the uterine cavity caused by adhesions
2. Insufficient amount of normal endometrial tissue to support implantation and development of the placenta
3. Inadequate vascularization of the residual endometrial tissue due to fibrosis

3.4 Obstetrical Problems (Fig. 3.2)

Upon achieving pregnancy, obstetrical complications are more frequent.

Schenker and Margalioth [6] reported that among 165 pregnancies in women with untreated Asherman's syndrome, the rate of spontaneous miscarriage was 40% (66 out of 165), preterm delivery was 23% (38 out of 165), term delivery was 30% (50 out of 165), placenta accreta was 13% (21 out of 165), and ectopic pregnancy was 12% (2 out of 165).

The defective placentation may lead to fetal growth restriction (FGR). There have been several cases of FGR described in pregnant women with Asherman's syndrome after endometrial ablations. The defective uterine endometrium and obliterated uterine cavity may also predispose women to ectopic tubal and cervical pregnancies.

3.4.1 Fetal Growth Restriction (FGR) and Low Birth Weight

Endometrial trauma and restricted placental and uterine blood flow result in fetal growth restriction and low-birth-weight babies.

A retrospective research [7] conducted on 56 women, 14 cases, and 42 examinations concluded that pregnant patients diagnosed with Asherman's syndrome gave birth to children weighing less (2.23 ± 0.28 kg) than healthy pregnant women (3.13 ± 0.383 kg).

3.4.2 Abnormal Placentation

Endometrial damage leads to abnormal placentation, increasing the risk of placenta previa, ectopic pregnancy, and placenta accreta [8]. Placenta accreta would be caused by basal layer of the endometrial trauma leading to an increased invasion of the trophoblasts. Schenker and Margalioth [6] found an incidence of placenta

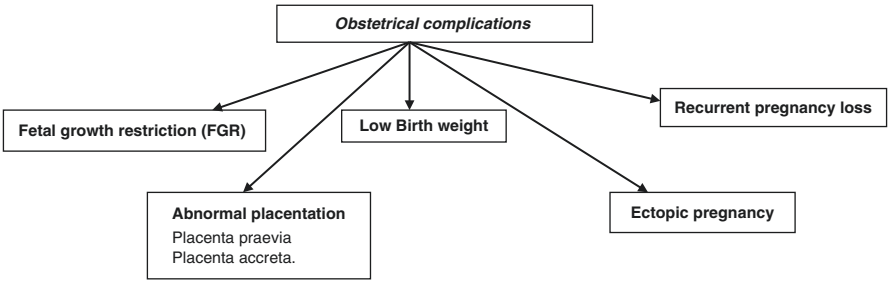

Fig. 3.2 Obstetrical complications

accreta in 13–14% of patients with previous Asherman's syndrome. Roy et al. [9] reported an incidence of postpartum hemorrhage due to adherent placenta in 12.5% of the women who had undergone hysteroscopic adhesiolysis due to Asherman's syndrome.

Any patient with a previous history of intrauterine surgery or Asherman's syndrome should be thoroughly examined by a skilled sonographer for possible abnormal placentation. In case of any suspicion of abnormal placentation, the patient should be scheduled for planned cesarean section with a setup of skilled clinicians due to risk of severe postpartum hemorrhage.

3.4.3 Ectopic Pregnancy

Asherman's syndrome, preceding uterine curettage, previous delivery by cesarean section, and cervix or uterine surgery are considered as underlying risk factors of ectopic pregnancy [10]. These conditions are associated to tissue damage leading to an abnormal placentation. The obliteration of the uterine cavity is also an underlying cause of tubal and cervical ectopic pregnancy.

3.4.4 Differential Diagnosis

Symptoms of the following disorders can be similar to Asherman's syndrome. Comparisons may be useful for a differential diagnosis:

- ***Primary amenorrhea***: Failure of menstruation by the age of 15 years or failure of breast development and menses by 13 years of age. Most often this disorder is a result of immaturity of hypothalamo-pituitary-gonadotropin axis. Symptoms of primary amenorrhea may be the absence of secondary sex characteristics, incomplete or underdeveloped external genitalia and breasts, ovarian deficiency, underactive pituitary, and an absence of menstruation. Secondary amenorrhea occurs in Asherman's syndrome, following D&C or acute endometritis.
- ***Endometriosis***
- ***Pelvic Inflammatory Disease (PID)***
- ***Stein-Leventhal Syndrome***

Key Points

1. Asherman's syndrome results in hypomenorrhea, amenorrhea, and infertility.
2. Patients with Asherman's syndrome may experience pelvic pain and/or hematometra.
3. Obstetrical complications are more frequent among patients with Asherman's syndrome.
4. Endometrial trauma may result in fetal growth restriction, low birth weight, and abnormal placentation.

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