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Review Article

Adenomyosis in Infertile Women : A Review

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Abstract:

Adenomyosis is found during infertility work up in many women who delay pregnancy till their late thirties and in some women in their early age. Dysregulation of myometrial architecture and function and altered endometrial receptivity are among the possible mechanisms by which adenomyosis causes infertility. Adenomyosis and endometriosis may have similar pathogenesis as they have frequent association in women. Adenomyosis can be reliably diagnosed in symptomatic infertile women by non invasive means such as transvaginal ultrasound and magnetic resonance imaging as well as hysterosalpingography, hysteroscopy and laparoscopy. Early diagnosis by non-invasive means followed by surgical (adenomyomectomy) or non-surgical (MRgFUS) treatment of focal adenomyosis have promising effect on future pregnancy whereas diffuse severe adenomyosis have poor prognosis.

Keywords: *adenomyosis, endometriosis, infertility*

Adenomyosis is a benign invasion of endometrium into myometrium, producing diffusedly enlarged uterus. Microscopically there are ectopic, non-neoplastic, endometrial glands and stroma surrounded by a hypertropic and hyperplastic endometrium[1].

Women with adenomyosis suffer from dysmenorrhoea and menorrhagia and have enlarged tender uterus on examination. Adenomyosis can be diagnosed in symptomatic women by noninvasive means such as transvaginal ultrasonogram or magnetic resonance imaging[2].

Many infertile women are found to have adenomyosis during their infertility work up. This is because an increasing number of women delay their first pregnancy until their late thirties. Many women with or without endometriosis also have adenomyosis at an earlier age. Adenomyosis itself is associated with infertility in these women. There are reports of pregnancy in infertile women after being treated for adenomyosis[3].

Adenomyosis as a cause of infertility

a) Dysregulation of myometrial architecture and function:

   The area of myometrium immediately underlying the endometrium is called the junctional zone, which is demarcated on imaging. There is no recognizable protective layer or membrane underlying the endometrium[4-6]. Junctional zone myometrium is abnormally thickened in adenomyosis. The destruction of the normal architecture of junctional zone myometrium impairs the rapid, sustained and accurately directed sperm transport in uterus. The utero-tubal transport capacity progressively decreases with increasing severity of the disease [7].

b) Altered endometrial receptivity

   In women with endometriosis, an abnormal inflammatory response seems to exist in endometrium and impair implantation[7].

c) Abnormal intraendometrial metabolism

   Increased expression of estrogen, increased local estrogen production, a defect in progesterone production, a defect in progesterone receptor and their reduced function all explain the poor response to progestational agents in women with adenomyosis [7].

d) Hoxa 10 gene expression

   Proper expression of Hoxa 10 gene is necessary to maintain viability of the preimplantation embryo.

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In women with adenomyosis, Hoxa 10 gene expression is decreased during the secretory phase of the cycle [7].

Adenomyosis and endometriosis

Adenomyosis is frequently associated with endometriosis[8]. Endometriosis and adenomyosis may have similar pathogenesis. Both endometriosis and adenomyosis result from the exaggeration of the basically physiologic mechanism of tissue injury and repair. This involves local estrogen production and is magnified in an estrogen sensitive environment controlled by ovaries. There is a chronic hyper-peristalsis at the endometrial myometrial interface and traumatization causing dislocation of fragments of basal endometrium into the peritoneal cavity as well as into the depth of myometrium[9].

Internal and external adenomyosis :

Internal adenomyosis is within the uterus. There is focal or diffuse invasion of endometrium into the myometrium and myometrial hyperplasia. External adenomyosis is thickened nodular rectovaginal septum, due to endometrial glands, stroma, and fibromascular hyperplasia in the septum.

Focal and diffuse adenomyosis:

Focal adenomyosis, also called adenomyoma is a mere circumscribed infiltration of endometrial glands and stroma into myometrium. Diffuse endometriosis is diffuse invasion of endometrial glands and stroma within the myometrium.

Focal adenomyosis or adenomyoma at ultrasonography can be mistaken for fibroid. Patients with fibroid and dysmenorrhoea must be scanned for the possibility of adenomyosis before surgery. Patients should be counseled about the possibility of having adenomyosis before fibroid surgery especially if patient has dysmenorroea[8].

Associated endometriosis is common in adenomyosis but not in fibroid. Surgeon must evaluate carefully for evidence of endometriosis around pelvic organs in all cases of surgery for fibroid. If adenomyosis is missed before surgery, continuing dissection may result in opening of uterine cavity, very difficult suturing or hysterectomy—a disastrous consequence for an infertile patient[8].

Adenomyosis on transavaginal ultrasound

Diagnostic criteria of adenomyosis at ultrasound[9-12] include

- Globular enlargement of uterus
- Asymmetric enlargement of anterior and posterior myometrial wall
- Heteorgenous mottled/salt in pepper appearance or texture of the myometrium.
- Anechoic lacunae or cysts of varying size within the myometrium.
- Venetian blind shadowing effect—myometrial hypoechoeic linear striations
- Indistinct myometrial endometrial interface
- Thickening of junctional zone with infiltration and distortion
- Adenomyosis has poorly defined border with increased vascularity within the mass whereas fibroids are hypoechoic masses with well defined border, vascularity predominant at the periphery of the mass.
- Thickened junctional zone is the most sensitive feature on 3D ultrasound. On 2D ultrasound the presence of myometrial cysts is the most specific and heterogenous myometrium is the most sensitive finding[9].

Adenomyosis on magnetic resonance imaging

In adenomyosis the junctional zone is widened to more than 12mm and more than 40% of myometrial thickness. Other MRI features of adenomyosis are poorly defined low signal intensity areas with high signal intensity foci subadjacent to endometrium[10,11].

A meta-analysis[13] reveals that at diagnosing adenomyosis TVS has 72% sensitivity and 81% specificity whereas MRI has 77% sensitivity and 69% specificity. So both TVS and MRI show high level of accuracy for the non-invasive diagnosis of adenomyosis whereas a concrete diagnosis is more often obtained with MRI.

Adenomyosis at hysterosalpingography

Adenomyosis can be diagnosed at hystero-salphingography of infertile women by the following features[3]:

- Multiple small spicules with saccular endings extending from endometrium into myometrium
- A focal accumulation of contrast material in the myometrium sometimes providing a honeycomb appearance.

Adenomyosis at hysteroscopy

The best time for detection of adenomyosis is immediately after menstruation. The possible findings are dark or bluish depressions of variable sizes, muscular hyperplasia, hypertrophy and fibrosis causing distortion of endometrial cavity, gaping tubal ostia and a trabeculate appearance of uterine fundus[14].

Adenomyosis at laparoscopy

- Globular enlarged uterus with anterior or posterior bossing
- The boggy uterine texture may allow marked indentation of myometrium with a probe[15].

Medical treatment of adenomyosis

Hormonal or medical treatment of adenomyosis is similar to that of endometriosis. Hormonal treatment for symptomatic relief include progesterone, continuous oral contraceptive pill, danazol, progesterone antagonist, GnRH agonists, antiestrogens, aromatase inhibitor and selective estrogen receptor modulators. Variable and unpredictable degree of symptomatic relief is usually restricted to the duration of treatment[16,17].

Levonorgestrel releasing intrauterine system (LNG-IUS) can be given to women, who are not good candidates for surgery. Though there have been some reports of pregnancy following danazol releasing IUS[3], there has been so far no reports of pregnancy after use of LNG-IUS.

Combined surgical and hormonal treatment

Cytoreductive surgery followed by hormonal treatment with GnRH agonists have resulted in pregnancy[3].

Conservative surgical treatment

Conservative surgical treatment modalities include laparoscopic / surgical adenomyoma resection, hysteroscopic adenomyoma resection (if no desire for future pregnancy), myometria excision, laparoscopic myometrial electrocoagulation (width of scar more extensive than that of surgical excision, so risk of rupture in early pregnancy)[18,19].

Other modalities are uterine arterial ablation under fluoroscopic guidance (if no desire for future pregnancy)[20],and MRI guided focused ultrasound (MRgFUS) in focal adenomyosis[21].

Resection of adenomyoma (adenomyomectomy)

Part of the uterus with maximum bulge is excised with monopolar needle followed by excision of adenomyotic lesion. Hemostasis is achieved using bipolar electro-surgery. Adenomyotic lesion is grasped and pulled and gradually excised till normal healthy myometrium is reached. Care should be taken that the uterine cavity is not opened or a large defect is not formed. Then it becomes very difficult to approximate the defect and suture adequately[10].

Fertility after adenomyosis associated infertility

Conservative surgical techniques like adeno-myomectomy of focal adenomyosis seems to offer good results . A pregnancy rate of around 50% has been reported. Patients with diffuse adenomyosis should be counseled about poor outcome of fertility treatment . Those with severe adenomyosis should be advised for in vitro fertilization and surrogacy. If not possible they should be advised for adoption or treatment closure and hormonal treatment for symptomatic relief[10]

Adenomyosis is a fairly frequent and debilitating disease with increasing incidence in infertile women. Hysterectomy is the definitive treatment for debilitating adenomyosis. This is not an easy option for infertile women. Improved and high resolution imaging techniques have made it possible to diagnose adenomyosis by non invasive techniques. For infertile women and for those who want to pursue fertility, conservative treatment options for adenomyosis need to be confirmed in larger series.

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