Adenomyosis and Reproduction

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Introduction

Adenomyosis, very precisely described as internal endometriosis, is characterized as ectopic endometrial tissue within the myometrium in the uterus. It is the most inaccessible disease for preoperative histopathological diagnosis. Its diagnosis is always accomplished retrospectively after hysterectomy. Interestingly hysterectomy is usually done in multiparas and infrequently in infertile patients. Older literature supports the view that adenomyosis is a disease of multiparas. However increasing number of hysterectomies done for endometriosis show the presence of adenomyosis in the uterus. Hence the effect on reproduction is possible. Due to lack of high resolution imaging technics in earlier era, the preoperative diagnosis was impossible. But today we can have early diagnosis and offer treatment.

Effect of adenomyosis on reproduction

It is well known that endometriosis is frequently associated with various autoimmune phenomena. In adenomyosis, a series of immune responses is activated, including changes in both cellular and humoral immunity, i.e. a strong expression of cell surface antigens or adhesion molecules, an increased number of macrophages or immune cells, and deposition of immunoglobulins and complement components. The disease exhibits high frequency of autoimmune phenomena in peripheral blood. Thus, an immunological vicious circle is formed in the endometrium in adenomyosis. Endometrial cells seem to be under immunological stress, protecting themselves by exposing health shock proteins. The endometrial environment in adenomyosis differs widely from that in normal fertile women. These abnormal immune responses might be involved in poor reproductive performance in adenomyosis.

Hormone response of the endometrial junctional zone differs in adenomyosis. Evidence has been provided that pelvic endometriosis is significantly associated with uterine adenomyosis and adenomyosis may be the major cause of infertility in such conditions. Mild peritoneal endometriosis of the fertile woman, premenopausal adenomyosis of the parous and nonparous women, and adenomyosis in association with endometriosis of the infertile woman constitute a pathophysiological continuum that is characterized by the dislocation of basal endometrium. Due to the postponement of childbearing late into the period of reproduction, premenopausal adenomyosis might increasingly become a factor for infertility in addition to adenomyosis associated with endometriosis of younger women. In any event, the presence or absence of uterine adenomyosis should be examined in a sterility work-up.

A study of 160 patients with endometriosis and 67 without endometriosis showed a prevalence of adenomyosis of up to 90% on MRI. Uterine adenomyosis is significantly associated with pelvic endometriosis and constitutes an important factor for sterility in endometriosis presumably by impairing uterine sperm transport.

Adenomyosis may also affect fertility by altered contractility of the myometrium, possible effects on implantation, and poor placentation. These factors may be responsible for poor reproduction in patients with endometriosis.

Peristaltic activity of the nonpregnant uterus serves fundamental functions in the early process of reproduction, such as directing transport of spermatozoa into the tube ipsilateral to the dominant follicle, high fundal implantation of the embryo, and possibly retrograde menstruation. Hyperperistalsis of the uterus is significantly associated with the development of endometriosis and adenomyosis. In women with hyperperistalsis, fragments of basal endometrium are detached during menstruation and transported into the peritoneal cavity. Hyperperistalsis induces the proliferation of basal endometrium into myometrial dehiscencies. This results in endometriosis...
associated adenomyosis with a prevalence of approximately 90%. Adenomyosis results in impaired directed sperm transport and thus constitutes an important cause of sterility in women with endometriosis. The principal mechanism of endometriosis/adenomyosis is the paracrine interference of endometrial estrogen with the cyclical endocrine control of archimyometrial peristalsis exerted by the ovary, thus resulting in hyperperistalsis. 4.

**Effect of reproduction on adenomyosis**

It is not very well described as yet but histopathologically proven adenomyosis is seen more often in multiparas. Hence the possibility of pregnancy promoting the invagination of basal endomtrium and producing endometrial nests in the myometrium is considered. These cell nests are having high hCG/LH receptors. But majority of these cells are devoid of progesterone receptors and hence do not respond to endogenous or exogenous progesterone, whereas pregnancy is known to arrest the progress of external endometriosis.

**Clinical features of adenomyosis**

The typical symptoms include pelvic pain, dysmenorrhea, and menorrhagia. However, these symptoms are nonspecific and can be encountered in disorders such as dysfunctional uterine bleeding, leiomyoma, and endometriosis.

Examination reveals an uniformly enlarged tender uterus or rarely a nodular uterus or a thickened nodular rectovaginal septum. This is felt when there is external adenomyosis i.e. endometrial glands, stroma, and fibromuscular hyperplasia in the septum. This may present as dysparunia as well.

**Diagnosis**

The current preoperative diagnosis of adenomyosis is based on the clinical methods, and does not include authentic and specific laboratory markers.

Advanced imaging technics like sonography and MRI have enabled a better diagnosis. The typical gross appearance of adenomyosis is due to accompanying smooth muscle hyperplasia and corresponds to areas of decreased echogenicity at endovaginal ultrasonography and areas of decreased signal intensity at MRI. Endovaginal sonography also shows heterogeneity of the myometrial echotexture, which corresponds to small echogenic islands of heterotopic endometrial tissue surrounded by the hypoechoic smooth muscle. On T2-weighted MR images, bright foci are seen in areas of abnormal low signal intensity within the myometrium in approximately 50% of patients. Various signs include myometrial cysts, myometrial nodules, linear striations, pseudowidening of the endometrium, and poor definition of the endomyometrial junction. Pitfalls in diagnosis of uterine adenomyosis include leiomyoma, endometrial carcinoma, myometrial contractions, and muscular hypertrophy.

Serum levels of VEGF-A in patients with adenomyosis are significantly higher and could be used as a biochemical marker. However this is still under research. There seems to be a dysregulation of angiogenic activity in the eutopic endometrium of women with endometriosis.

**Importance of imaging in adenomyosis**

Imaging helps not only diagnosis but also can be used to guide the treatment. The correct diagnosis is established with imaging. Uterus conserving therapy is possible in cases of leiomyoma, whereas hysterectomy is the definitive treatment for debilitating adenomyosis. Imaging is performed to determine the extent and depth of myometrial penetration. Symptoms have been shown to correlate with the extent of disease. Determining the depth of myometrial penetration is important for treatment planning because superficial adenomyosis responds significantly better to endometrial ablation than deep adenomyosis. Imaging is also used to monitor the evolution of the disease in patients receiving conservative therapy.

**Postoperative diagnosis**

Histopathology forms the gold standard for the final diagnosis. Uterine adenomyosis is a common gynecologic condition that is characterized by the presence of heterotopic endometrial glands and stroma in the myometrium with adjacent smooth muscle hyperplasia.

**Treatment modalities**

Uterine artery embolization, laparoscopic or surgical adenomyoma resection, hysteroscopic endomyometrial resection, assisted reproductive technics, and therapy with Gn Rh agonist and antagonists have been found useful with variable responses.

**Conclusion**

Adenomyosis has adverse impact on reproduction and may be the factor responsible for infertility in cases of endometriosis. There is increasing evidence to support this concept. Because of improved and high resolution imaging technics, it is possible to diagnose the condition today and we can offer a ray of hope to these women who are infertile and want to preserve the fertility.
References


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