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Review article

An update on adenomyosis uteri

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ABSTRACT

Adenomyosis is a gynecological condition commonly encountered in clinical practice. It is defined as the presence of endometrium within the myometrium. The prevalence of this condition in asymptomatic women is unclear, and a large proportion of these women may have associated pathology such as leiomyomas, endometriosis, endometrial polyps, and hyperplasia. Most of the time, diagnosis is made on histological examination of specimen following hysterectomy or adenomyomectomy. We will look at the role of various imaging modalities, such as pelvic ultrasound and magnetic resonance imaging, and their value in improving the accuracy of preoperative diagnosis. Various medical and surgical therapies will also be discussed. Careful counseling on the available treatment options form an important component of clinical care. Hysterectomy is the definitive treatment for women who no longer desire fertility.

Introduction

Adenomyosis is a gynecological condition commonly encountered in our clinical practice. It is defined as the presence of endometrial glands and stroma deep within the myometrium associated with myometrial hypertrophy and hyperplasia.[1] General consensus is that adenomyosis occurs when there is a disruption of the normal boundary between the endometrial basal layer and the myometrium. As a result, the endometrial glands invade the myometrium, resulting in ectopic intramyometrial glands, which cause adjacent myometrial hypertrophy and hyperplasia. Adenomyosis can be diffuse, where islands of adenomyosis may be found throughout the myometrium, or it can be localized in the form of adenomyomas.

Epidemiology

The exact prevalence of this condition in asymptomatic women is unclear, and the reported prevalence in surgical series varies widely due to the differences in histological diagnostic criteria used and number of tissue sections analyzed. Estimated prevalence of histologically confirmed adenomyosis in surgical series ranges from 5% to 70%.[2] A large proportion of these women may have associated pathology such as leiomyomas (80%), endometriosis (6.3–24%), endometrial polyps (2.3–14.7%), endometrial hyperplasia (3.5–13.6%), and adenocarcinoma (2.2–5.3%).[3] Adenomyosis is most common in women aged 35–50 years, and many cases occur in multiparous women.

Pathogenesis

The exact cause and pathogenesis of adenomyosis has not been well established. One theory states that adenomyosis originates from the basalis (deeper layer) of the endometrium, which grows between the smooth muscle bundles in the myometrium due to the action of specific enzymes. This repeated process of regeneration and re-epithelization leads to a loss of the interface between the endometrium and myometrium and there is myometrial hypertrophy around the foci of endometrium. The reason for this is unclear, however, it may involve the invaginating endometrium pushing aside the smooth muscle bundles or the body's response to control this invagination. Other factors also contribute to the pathogenesis, namely hormonal, genetic, and immunological factors.[4,5] Hyperestrogenism at the local level in addition to circulating estrogens may be another contributing factor. Adenomyosis grows and regress in an estrogen-dependent fashion due to the presence of estrogen receptors in adenomyotic tissues.[6]

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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Symptomology

Some patients may be asymptomatic, where it is an incidental finding on examination, imaging studies, or histopathology specimens, after hysterectomies. Others can have menorrhagia (40–50%) or metrorrhagia (10–12%), dysmenorrhea (30%), dyspareunia, chronic pelvic pain, or abdominal bloating.[7] The frequency and severity of symptoms correlate to the extent and depth of adenomyosis. Physical examination may reveal a tender enlarged uterus.[8]

Work-up

At present there is no single diagnostic test that is both sensitive and specific for adenomyosis. There is a lack of a reliable and diagnostic test for this condition at present, even though diagnosis is important in order to decide on the appropriate mode of management for the patient, and would greatly impact on patient counseling.

Pelvic ultrasound

Transvaginal ultrasound (TVS) is superior to transabdominal ultrasound in evaluating features of adenomyosis uteri. Sonographic appearances include uterine enlargement, asymmetric enlargement of the anterior or posterior myometrial wall, lack of contour abnormality or mass effects, heterogeneous, poorly circumscribed areas within the myometrium, hyperechoic islands or nodules, finger-like projections or linear striations, indistinct endometrial stripe, and anechoic lacunae or cysts of varying sizes. The accuracy of TVS reported in studies on the accuracy indices of sensitivity and specificity ranges between 53–89% and 50–99%.[9] There are some reports[10] on the use of three-dimensional TVS and three-dimensional power Doppler studies in adenomyosis, looking at vessel distribution and branching, and differences in perfusion patterns in affected areas.

Hysterosalpingography

Hysterosalpingography has a low sensitivity and specificity for the diagnosis of adenomyosis. Features include multiple small spicules extending from the endometrium into the myometrium and local accumulation of contrast in the myometrium giving a honeycomb appearance.[11]

Magnetic resonance imaging

Magnetic resonance imaging (MRI) features of adenomyosis include a focal or diffuse thickened junctional zone due to uncoordinated proliferation of the inner myometrial cells causing junctional zone hyperplasia. Areas of low signal intensities representing smooth muscle hyperplasia and foci of increased high signal intensity in the junctional zone representing heterotopic endometrial tissue can be seen on MRI.[12]

MRI as an imaging modality for adenomyosis has been compared with transvaginal ultrasound. Some studies found that both modalities have similar sensitivities and specificities, whereas others showed that MRI was a good complement to ultrasound when ultrasound is indefinite or in difficult cases with presence of other abnormalities (such as leiomyomas and endometriosis). In such situations, MRI may add more information and increase the diagnostic accuracy.[12]

Treatment options

Increasingly, the diagnosis of adenomyosis is being made before surgery due to the improvement in imaging modalities and this gives women with this condition the option of medical therapy. However, because of the diagnostic challenges of adenomyosis, there are not many large or well-designed trials that look at the treatment of this disease itself. Many treatment options are aimed at symptomatic relief, with hysterectomy being the main treatment option for those who have completed their families.

Medical

Nonhormonal treatments are targeted at symptomatic relief. Nonsteroidal anti-inflammatory drugs such as mefenamic acid are effective for relief of symptoms such as dysmenorrhea and heavy menstrual bleeding. Tranexamic acid, which is an antifibrinolytic, is used in cases of menorrhagia.

Hormonal treatment is aimed at inhibiting gonadotrophin release from the pituitary, estrogen surge midcycle and cyclical changes of ovarian steroids. However, the effects of these treatments are variable and tend to wear off after discontinuation of treatment, leading to symptom recurrence. Progestogens, levonorgestrel (LNG) intrauterine system, oral contraceptive pills, gonadotrophin-releasing hormone analogs, and danazol-loaded intrauterine devices (IUDs) are the different types of hormonal treatment available.

Progestogens and oral contraceptive pills have limited effectiveness as adenomyosis is largely an estrogen-mediated disease, but may be effective in symptomatic relief of menorrhagia and dysmenorrhea.

LNG-IUD use in women with adenomyosis results in less menstrual blood loss, reduction in uterine size, and improvement in dysmenorrhea.[13] The main disadvantage of this treatment is the irregular menstrual bleeding in the first few months of treatment.

Gonadotrophin-releasing hormone analogs induce medical menopause and leads to atrophy of adenomyotic nodules resulting in reduction of uterine size and symptomatic relief. Its use is limited to short term (3–6 months) because of its menopausal and skeletal side effects. Once the treatment is discontinued, the condition recurs.

Oral danazol is no longer commonly used because of its side effects. Danazol-loaded IUDs have been shown in some studies to improve symptoms such as dysmenorrhea and hypermenorrhea. Serum danazol levels were undetectable and the patients did not experience the systemic side effects associated with oral danazol.[14,15]

Surgical

Hysterectomy has been the definitive treatment for adenomyosis as well as for definite diagnosis until recently.[16] However, this option is only for patients who have completed their families.[17] Excision of affected myometrium can be performed in patients where the extent of disease is well-defined. This is a viable option in patients who still desire fertility. However, in cases where large or multiple areas of the uterus is affected, there is a risk of future obstetric complications such as uterine rupture, and risk of adhesion formation. Endomyometrial ablation or resection is an option for patients with superficial disease, however, deep-seated disease is associated with a risk of failure of treatment. Desire for future fertility is a contraindication. Uterine artery embolization is an option in patients with concurrent fibroids for which it is an accepted treatment. Laparoscopic uterine artery ligation has not

been well studied and available studies have not shown it to be effective.[9]

Conclusion

Adenomyosis is a common condition encountered by gynecologists. Its symptomology is poorly defined and severity of symptoms sometimes correlates poorly with severity of disease. The etiology of the disease is unclear and the exact prevalence of this condition in asymptomatic women is not known. Advancement in imaging modalities such as MRI can help to establish the diagnosis of adenomyosis more accurately and this will lead to better patient counseling before surgery and more directed treatment. Hormonal treatment can relieve symptoms and reduce the progression of the disease, but is limited by the side effects. Long-term studies regarding the effectiveness of hormonal treatment as well as long-term outcomes such as fertility and pregnancy are awaited. Hysterectomy and LNG intrauterine system is still the cornerstone of treatment.

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