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REVIEW ON ADENOMYOSIS IN WOMEN WITH INFERTILITY

Gynaecology

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ABSTRACT

Adenomyosis uteri is often encountered during the workup of infertile women especially who are in their thirties – be it primary or secondary infertility. There are many mechanisms by which adenomyosis results in infertility eg. dysregulation of the myometrial architecture and functioning along with alteration in the receptivity. Adenomyosis and endometriosis have similar pathogenesis, therefore they co-exist frequently and cause infertility in conjunction with each other. Transvaginal ultrasonography, MRI, HSG, hysteroscopy and laparoscopy aid in diagnosing adenomyosis in symptomatic women presenting with infertility. It is seen that early diagnosis followed by minimal surgical eg. Adenomyomectomy or non-surgical methods eg. MRgFUS for focal adenomyosis carry favourable prognosis in respect to future reproductive potential and good pregnancy outcome whereas diffuse severe adenomyomatosis usually carry poor reproductive prognosis.

KEYWORDS

adenomyosis, adenomyoma, adenomyomectomy, endometriosis, infertility.

INTRODUCTION:

Adenomyosis, also called endometriosis interna, is a benign condition where endometrial tissue (glands and stroma) invade into the myometrium, resulting in a diffusedly enlarged uterus. (1). Microscopically there are evidences of ectopic, non-neoplastic, endometrial glands and stroma which are surrounded by hypertrophic and hyperplastic endometrial tissue (2).

Women who suffer from adenomyosis often complain of dysmenorrhoea and heavy menstrual bleeding with enlarged tender uterus evidenced on physical examination. It can be diagnosed in symptomatic women by ultrasonography – transvaginal or transabdominal.(3)

Adenomyosis is often encountered in many women during their infertility workup – especially who are in their thirties. Many women with or without endometriosis may also have co-existing adenomyosis at an earlier age. Adenomyosis alone , or with co-existing endometriosis, can result in infertility in these women. It has been observed that these women when treated for adenomyosis have resulted in pregnancies. (3) (4)

The Mechanisms By Which Adenomyosis Might Cause Infertility:

- Dysregulation of the normal architecture and functioning of the endometrium.

The junctional zone (the area of myometrium underlying the endometrium immediately) – is abnormally thickened in adenomyosis. (5,6,7). The junctional zone undergoes architectural damage and impairs the rapid sustained and well-directed sperm transport. The utero-tubal transporting capacity decreases progressively with increase in the severity of the disease.(8)

- Alteration in the endometrial receptivity which results from abnormal inflammatory response resulting in impaired and defective implantation (8).
- Abnormalities in the intraendometrial metabolism due to increased expression of Estrogen, increased local Estrogen production, defective Progesterone production, defect in the Progesterone receptors and their hypofunction.

This explains subfertility and IF in women with adenomyosis and also why they respond poorly to pro gestational agents used for therapy.

- **Expression of Hoxa 10 gene is decreased.**

It is an established fact that proper expression of Hoxa 10 gene is necessary to maintain the viability of the preimplantation embryo.

In adenomyosis, there is decreased expression of Hoxa 10 gene during the secretory phase of the menstrual cycle. (8)

ADENOMYOSIS AND ENDOMETRIOSIS:

Adenomyosis and endometriosis frequently co-exist (9). Since they have similar basic pathogenesis – so much so that adenomyosis is known as Endometriosis Interna – these two entities cause IF by compounding each other's effect. Both the entities occur because of an exaggeration of the basic physiological process of tissue injury and repair, which involves local estrogen production and is magnified in an hyperestrogenic environment controlled by the ovaries. Chronic hyper-peristalsis of the endometrial – myometrial interface and trauma cause dislocation of the basal endometrium into the peritoneal cavity and also into the depth of the myometrium. (10)

ADENOMYOSIS INTERNA AND EXTERNA:

- Adenomyosis Interna (Internal adenomyosis) occurs within the uterus evidenced by focal or diffuse invasion of endometrial tissue into the myometrium and also myometrial hyperplasia.
- Adenomyosis Externa (External Adenomyosis) is evidenced by thickened nodular rectovaginal septum, caused by endometrial glands, stroma and fibromuscular hyperplasia of the septum. (10, 11).

FOCAL AND DIFFUSE ADENOMYOSIS:

Focal Adenomyosis (Adenomyoma) is a circumscribed infiltration of the endometrial glands and stroma into the myometrium whereas diffuse adenomyosis is diffuse or generalized invasion of the endometrial glands and stroma within the myometrium.

Focal adenomyosis or adenomyoma might be mistaken for a leiomyoma on ultrasound. Therefore, all patients with fibroid and dysmenorrhoea should be evaluated for the possibility of adenomyosis. (9)

ADENOMYOSIS ON USG (TVS) :

Diagnostic criteria for Adenomyosis at USG are **:**

- Globular enlargement of the uterus (10,11,12,13).
- Asymmetric enlargement of the anterior and posterior myometrial wall (posterior > anterior) .
- Heterogeneous mottled/salt and pepper appearance or texture of the myometrium.
- Anechoic lacunae or cystic spaces of varying sizes within the myometrium.
- Venetian blind shadowing effect – myometrial hypoechoeic linear striations.
- Indistinct myometrial – endometrial interface.
- Functional zone thickening with infiltration and distortion.
- Adenomyosis has ill-defined border with increased vascularity within the mass whereas fibroids appear as hyperechoeic masses with well-demarcated borders with prominent vascularity at the periphery.
- Thickened junctional zone is the most sensitive feature evident on 3D-USG. On 2D-USG, the most specific finding is the presence of myometrial cysts and the most specific finding is the presence of

heterogeneous myometrium. (10,11)

MRI AND ADENOMYOSIS :

Features suggestive of adenomyosis on MRI are :

- The junctional zone is widened to > 12 mm and > 40% of the myometrial thickness.
- Poorly defined low signal intensity areas with high signal intensity foci subadjacent to the endometrium. (11,12).

In a meta-analysis by Champeneria R et al (14) it was stated that for diagnosing adenomyosis, TVS has 72% sensitivity 81% specificity as compared to MRI which has 77% sensitivity and 69% specificity (14). Therefore, though both TVS and MRI are good non-invasive diagnostic aids for adenomyosis, but MRI gives a more concrete diagnosis. (1).

ADENOMYOSIS AT HSG (HYSTEROSALPINGOGRAPHY) :

The *features on HSG suggestive of adenomyosis are* :

- Multiple tiny spicules with saccular endings extending from the endometrium and going into the myometrium.
- A focal accumulation of the dye in the myometrium, sometimes giving a honey-comb like mottled appearance.

- **ADENOMYOSIS AT HYSTEROSCOPY :**
- ***Features suggestive are :***
- Globular enlarged uterus with either anterior or posterior wall bossing.
- The boggy uterine texture may allow marked indentation of the myometrium with a probe. (16)

MEDICAL MANAGEMENT OF ADENOMYOSIS :

Medical management of adenomyosis consists mainly of hormonal treatment just like in endometriosis.

These include :

- Progesterone
- Continuous combined OCPs
- Danazol
- Progesterone antagonists
- GnRH agonists
- Anti estrogens
- Aromatase inhibitors

- **SERM (Selective Estrogens Receptors Modulators)**

These agents provide symptomatic relief of varying and unpredictable degree and are usually restricted to the duration of the treatment. (17,18).

Patients who are not good candidates for surgery can be offered LNG-IUS, which showed quiet good results. Danazol-releasing-IUS (D-IUS) also has very good results and there have been reports of pregnancies after D-IUS treatment. (4,5).

COMBINED SURGICAL AND HORMONAL TREATMENT :

Cytoreductive surgery followed by hormonal treatment with GnRH agonists have shown very good results and there have been many case reports of resultant pregnancies in such patients. (4).

CONSERVATIVE SURGERIES FOR ADENOMYOSIS :

Conservative surgical procedures include :

- Laparoscopic / surgical adenomyoma resection.
- Hysteroscopic adenomyoma resection (if no desire for future pregnancy).
- Laparoscopic myometrial electro coagulation (the width of the scar is more extensive than that of surgical excision, therefore there is more risk of uterine rupture in early pregnancy). (19,20,21)
- Uterine Artery Ablation (UAA) under fluoroscopic guidance (especially if fertility is not desired).
- MRgFUS-MRI-guided focussed ultrasound in focal adenomyosis (21,22)

RESECTION OF ADENOMYOMA (ADENOMYOMECTOMY) :

- Here the area of focal adenomyosis i.e. the adenomyoma is excised or removed surgically.
- The part of the uterus with maximum bulge is excised with electrocautery followed by the excision of the adenomyotic lesion. Haemostasis is maintained by bipolar electrocautery. The adenomyoma is grasped and pulled and gradually excised till healthy normal myometrium is reached. Utmost care is taken so as not to open the uterine cavity or create too large a defect which will render it difficult to approximate the defect and suture adequately without much tissue tension so as to achieve optimum results. (11,12)

ADENOMYOSIS ASSOCIATED INFERTILITY AND FUTURE FERTILITY :

- Conservative surgical approaches eg. Adenomyomectomy of a focal adenomyoma offers good results with favourable future pregnancy potential with approx. 50% pregnancy rates.
- Patients who have diffuse adenomyosis should be counselled about the poor outcomes of fertility treatment and should be guided to opt for IVF and surrogacy. Or if not feasible then go for adoption or hormonal treatment for symptomatic relief. (11)

CONCLUSION :

Adenomyosis is a fairly frequent finding in women coming for infertility workup. This is a debilitating disease with increasing incidence among infertile group of women. Though hysterectomy remains the definitive treatment for debilitating adenomyosis, this is not easy to accept by women who are desirous of pregnancy and come seeking treatment for their infertility. With the availability of high resolution and improved non-invasive imaging techniques, it is now easy to diagnose adenomyosis. For women coming with infertility and desirous of infertility, conservative management options for adenomyosis should be offered.

ABBREVIATIONS:

- MRgFUS : MRI-guided Focussed Ultrasound In Focal Adenomyosis
- D-IUS: Danazol Releasing Intra Uterine Contraceptive Device
- MRI : Magnetic Resonance Imaging
- SERM : Selective Estrogen Receptor Modulator
- LNG-IUS : Levonorgestrel Releasing Intrauterine Contraceptive Device
- TVS : Trans Vaginal Ultrasonography
- HSG : Hysterosalpingography
- UAE : Uterine Artery Embolisation
- OCP : Oral Contraceptive Pills

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