Review Article:

Endometriosis in Postmenopausal Women

ABSTRACT

Whenever there is functional endometrial tissue anywhere than uterine cavity and uterine mucosa with a proclivity for infiltration and invasion it is labelled as endometeiosis. It is a chronic inflammatory condition. It can occur anywhere but most common site is ovary. It is also labelled as endometrioma or Chocolate cyst. Other common sites for endometriosis are pouch of Douglas (POD), posterior leaf of broad ligament, uterosacral ligament, fallopian tube. Barin is the least common site for Endometriosis. Endometriotiosis is never seen at spleen. This condition, which impacts 10–15 percent of women of childbearing age, is characterised by pelvic pain and infertility. Dysmenorrhoea, adnexal mass and infertility is the classical triad of clinical features. This classical triad is mostly seen in the women of childbearing age but can also be seen in the women after menopause. Endometriosis is an estrogen-dependent condition that tends to go away on its own or after surgery. It tends to regress after menopause because it is an estrogen-dependent condition. Endometriosis is associated with cellular and humoral immunity also. Impaired immune function may contribute for the development of endometriosis. Despite this, up to 2.2 percent of women after menopause are affected. Endometriosis in postmenopausal women is seen mostly after elevated systemic estrogen concentrations or excess exogenous estrogen intake. In the majority of women, symptomatic endometriosis after menopause begins more than 10 years after menopause in the absence of elevated systemic oestrogen concentrations or exogenous oestrogen intake. This is necessary to understand the pathophysiology and management of endometriosis after menopause.

KEY WORDS - endometriosis, menopause, estrogen.

INTRODUCTION

Endometriosis is ectopic functional endometrial glands and stroma in sites other than the uterine mucosa. Endometriosis is the disorder of contrast. It is a chronic inflammatory condition. Endometriosis is benign but locally invasive and disseminates widely. Endometriosis is now being seen in both premenarchal and postmenopausal women, thanks to paradigm change from idea that it solely affects women of reproductive age. Higher circulating oestrogen levels, especially in the form of phytoestrogen and hormone therapy, may exacerbate postmenopausal disease.

OBJECTIVES

- To provide basic information about endometriotiosis in postmenopausal women.
- Identification of causes contributing to postmenopausal endometriosis.

- Providing accurate information for prevention and management of postmenopausal endometriosis.

ETIOPATHOGENESIS

In the majority of women, symptomatic endometriosis in postmenopausal women begins more than 10 years after menopause in the absence of elevated endogenous oestrogen concentrations or excess oestrogen intake. In postmenopausal women this is required to understand the pathophysiology of endometriosis in women after menopause. Although there have been hypotheses made about the etiology and pathophysiology of endometriosis, no definitive explanation of the pathophysiological mechanism involved has yet been identified. The theory of cell transplantation, the theory of metaplasia, and the theory of the endometrial-subendometrial unit or "archimetra" are all being debated. Other theories like Sampson theory of implantation expine why ovary and Pouch of Douglas (POD) are most common and second most common sites respectively. Immunological, endocrinological, genetic, and inflammatory condition have significant role in pathogenesis of endometrios. Endometriosis is associated with cellular and humoral immunity. Impaired immune function may contribute for the development of Endometriosis in women after menopause. Endometriosis is like a chronic inflammatory condition. Progesterone acts as an anti-inflammatory agent. So the level of progesterone decreses during endometriosis. Hormonal theory also suggest there is increse in the level of prostaglandins which is associated with symptoms of endometriosis. Increase in PGE2 causes inflammation and increase in the level of PGF-2 alpha leads to vasoconstriction and myometrium contraction which is associated with dysmenorrhoea. The results suggest that interleukins (IL1), Interleukin 2, Interleukin 6, Interleukin 8 and other inflammatory mediators (tumor necrosis factor alpha, interferon gamma, monocyte chemotactic protein1) may play a key role in the pathophysiology of endometriosis, since they allow the growth of ectopic endometrial cells. and develop or induce an etiopathogenic mechanism of coelomic metaplasia. We believe that many post-menopausal woman may had a state of immunosuppression that causes lesions to form and progress.[i] Estrogen dependency is thought to have a key role in the pathophysiology and duration of the lesions. There is still a scarcity of information in the literature about endometriosis after menopause, with the prevalence in postmenopausal women being the most studied and described. Endometriosis after menopause is thought to have a more complicated pathogenesis than premenopausal endometriosis. It is still unestablished if this is a recurrent condition or it continues from past illness or is new aliment. Endometriosis is promoted by excess estrogen in general. It's a common adverse effect of Hormone Replacement Therapy (HRT). After menopause there is a cessation of estrogen production at ovarian level but this estrogen deficit is balanced by production of estrogen in peripheral tissues from conversion of androgen to oestrogen . Estrone is the most common estrogen discovered in these patients. "Estrogen threshold," means, when a particular systemic estrogen levels is achieved and exceeded in women after menopause, it triggers undiscovered or transient foci for pathogenesis of endometriosis and it owes proper explanation about the pathogenesis of endometriosis in postmenopausal women. Although factually, the immunochemical profile of endometriosis is same before and after menopause and can reactivate when estrogen is stimulated, the lesions of endometriosis after menopause appear less frequently, rarely widespread and have got low activity level in majority of patients. Endometriosis in menopausal women manifests itself in a variety of ways, including pelvic discomfort, ovarian cysts, and digestive problems. Patients are

frequently suspected of having a neoplastic condition due to their age. On ultrasonography, if any abnormal mass is observed, specially after menopause, malignancy should be ruled out. After menopause, the decline in oestrogen levels reduces endometriosis-related symptoms in women who had endometriosis during their reproductive years. [ii]

DIAGNOSIS

Endometriosis after menopause carries the danger of recurrence and malignant change. Clear cell and endometrioid ovarian cancer are associated to endometriosis lesions. Ovarian endometriosis with a diameter of 9cm or more is a major predictor of ovary cancer happening in woman after menopause and 45 years or above. It is still a disease with a long latency period, particularly in older people. It is still a disease with a long latency period, particularly in older people. This is due to a scarcity of noninvasive technologies during initial phase of diagnosis. There is a persistent myth, that endometriosis solely affects women in child bearing age group. However, in past few years, attention has been diverted to the diagnose cases of endometriosis in women after menopause, as that pain can begin beyond menopause, and endometriosis has been reported in patients as old as 80. In women after menopause, endometriotic lesions are most commonly found in the ovaries. Regardless of age, laparoscopy and histopathologocal examination by biopsy of suspected lesions is currently the gold standard for diagnosing endometriosis. Laparoscopy is the primary method for investigating any abnormality in the pelvis, can diagnose and treat abnormalities at the same time. Magnetic resonance Imaging(MRI) and Ultrasonography are essential imaging technique however, it is extremely difficult to come to a conclusion and interpret in women after menopause than in women of reproductive age group patient because of heightened concern for a malignancy and unpredictable nature of endometriosis.

CLINICAL EXAMINATION

There is no direct relationship between symptoms and signs and the skeletal-surgical features of endometrial foci, and the patient's treatment history, diagnostic examination, or symptoms before operation play a restricted character in identifying the lenght of endometrial foci. Endometriotic areas have more pain sensitive nerve endings. Pain is related to the depth of the lesion. Severe pain is seen in deep infiltrating Endometriosis (DIE). Per vaginal examination shows retroverted flexed uterus which can't be corrected manually. Hormone replacement therapy (HRT) is routinely used to alleviate climacteric symptoms and prevent bone loss in postmenopausal women; however, in women with a history of endometriosis, Hormone replacement therapy (HRT) may reactivate endometriosis and induce malignant transformation. In extreme situations, however, first-line pharmacological therapy (including the oral contraceptive pill or progestogens) or laparoscopic excision of endometriotic lesions may be insufficient, and menopause induction via GnRH analogues or oophorectomy may be necessary.[iii] Many patients with severe lesions who are asymptomatic have a gap between the intensity of their symptoms and the degree of their lesions. This is a significant role in the 6 to 8-year delay between development of symptoms and diagnosis in both premenopausal and postmenopausal women. Endometriosis nodules found in the posterior compartment in lower part of pelvic can be identified with pelvic, vaginal and rectal examination, however clinically examination findings can be normal in significant number of patients who suffer from endometriosis which inflitrates deeply.

Imaging

Trans vaginal sonography is the first investigation done in suspicion of endometriosis. “Diagnostic laparo-scopy” is the gold standard, but it’sno longer the 1st choice of clinical-diagnosis, as non-invasive tests are becoming increasingly popular for early detection and progression of endometriosis.. On ultrasound, endometriomas appear as unilocular cysts, which are usually homogeneous in appearance and seem like ground glass.An endometrioma should aware the doctor to likelihood of average to advanced disorder. Ovary cysts with a "ground glass" appearances are corresponded with incidence of cancer in 44% of postmenopausal women.[iv]TVS can also be used to assess bladder and rectum diseases. Magnetic resonance imaging (MRI) is not routine investigation. It is done when not sure about nature of adnexal mass. It helps in diagnosis of deep infiltrating Endometriosis (DIE) and rectovaginal disease. “rectal endoscopic USG” ,“Transvaginal sonography”, “computed tomography”, “magnetic resonance imaging” , and “three-dimensional ultrasonography” are all imaging modalities that can be used to diagnose deep infiltrating endometriosis (DIE).Because it allows through pelvic exploration, and is widely available, cost-effective, and well tolerated.Transvaginal ultrasound has become popularity in past years and is now suggested as the 1st treatment approach for endometriosis. Magnetic resonance Imaging and Ultrasonography are essential imaging technique however, it is extremely difficult to come to a conclusion and interpret in women after menopause than in women of reproductive age group patient because of heightened concern for a malignancy and unpredictable nature of endometriosis. Magnetic Resonance Imaging is a noninvasive Deep Infiltrating Endometriosis diagnostic technology that allows for a thorough examination of the pelvic cavity with good accuracy, but at a higher cost. A new diagnostic approach in Deep Infiltrating Endometriosis (DIE) is sonovaginography with a saline solution “saline contrast sonovaginography” or “gel infusion sonovaginography”. Dessole et al. were the first to describe it, and it comprises of TVS mixed with the infusion of saline solution or gel into the vagina, which allows for a more thorough view of the vaginal walls and fornix, pouch Douglas, uterosacral ligaments, and rectovaginal septum.[v]

Biomarkers

To so far, no exact markers for endometriosis diagnosis have been discovered.When compared to normal women, endometriosis patients have altered CA-125, cytokines, angiogenic, and growth factor ranges, however all of these biomarkers are found in a variety of other illnesses and are not specific enough to diagnose endometriosis. When compared to single biomarker readings, a mixture of biomarkers may improve sensitivity and specificity.[vi] The results suggest that interleukins “(IL1), Interleukins2, Interleukins 6, Interleukins 8 “and other inflammatory mediators (tumor -necrosis factor alpha, inter-feron gamma, monocyte -chemotactic protein1) may play a key character in the pathology of endometriosis, since they allow the growth of ectopic endometrial cells and develop or induce an etiopathogenic mechanism of coelomic metaplasia. We believe that some females after menopause may have a state of immune-suppression that causes lesion to form and advance.

Treatment

Surgery:-As the diagnosis as well as threat of malignancy is unpredictable, exploration by surgery should be primary therapy option for women after menopause who are having symptoms suggestive of endometriosis. The surgical method, preferably laparoscopy or minimal access surgery, should be used to get histological confirmation of the illness as well as alleviation from uncomfortable symptoms. Histology may be required in some cases to diagnose endometriosis

and rule out malignancy.Histological confirmation is necessary in ovary endometriomas (> 4 cm in the diameter) and deep infiltration diseases to rule out a rare case of malignancy. Laparoscopy is used to diagnose and treat Deep infiltrating endometriosis and to remove any visible endometriosis implants, which is particularly important in women after menopause because of the potential of malignant transformation.After complete resection of all visible lesions, several studies have reported significant reductions in clinical symptom and a lower danger of cancer in females after menopause. Accurate preoperative images can help guide surgical therapy methods and achieve the best postoperative results.

Medical Therapy:- When surgery is unsuitable and there is a recurrence of disease following surgery, a medicinal treatment should be used.

There is lack of treatment options in women after menopause than with a women has had endometriosis in reproductive age group. The best plan for hormone replacement therapy (HRT) for menopausal women with a history of endometriosis is an important consideration. Combined "hormone replacement therapy" (estrogens plus gestagens) and, tamoxifen\ tibolone (which especially have an estro-genic result on symptoms of menopause and bone density, but has a gestagenic result on tissues) have been studied as treatment options in postmenopausal women with endometriosis and women with endometriosis in the reproductive age group. Administration of a lower-dose levonorgestrel intrauterine system along with a estrogen given systemically may be an alternative for women who cannot tolerate oral progestins. New combinations of hormone replacement therapy (HRT) containing oestrogens and dioenogest are proposed; The confirmation in the literature is still limited, but this method, as well as the levonorgestrel intrauterine system plus oral estrogens may be effective in regulating menopausal symptoms and preventing endometriosis from recurring.

The isoflavone which is given orally as a dietary additive has been linked to a lower incidence of endometriosis recurrence. The Aromatase Inhibitors action on extra-ovarian oestrogen production is the reason for their use.Treatment with the aromatase inhibitor reduced pain and, in some of the cases, reduced the proportion of the lesion. Due to the reduction of extra-ovarian oestrogen secretion, Aromatase inhibitors can cause secondary climacteric symptoms such as hot flashes, vaginal dryness, and decreased bone density.Add-back therapy with low-dose oestrogen could be an alternative. Neurotransmitter modulators such serotonin reuptake inhibitors and gabapentin are the most often utilised non-hormonal treatments for climacteric symptoms. These are just moderately better than placebo for the treatment of menopausal symptoms and are only half as effective as oestrogen.

Risk for malignant transformation

Endometriosis lesions have been reported to transform from benign into malignant lesions and can spread to the ovary on both side, intestines, and even to the lungs. The incidence of malignant conversion from endometriosis to ovarian cancer is estimated to be 2% to 3%. The incidence is little higher in patients receiving estrogen therapy. It's tough to tell the difference between benign and malignant tumours in postmenopausal women. It's important to remember that some endometrial lesions resemble cancerous lesions and can induce local and distant metastases as well as invade neighbouring tissues and organs. It is difficult to distinguish a benign tumor from malignant one after menopause in clinical practice as the danger factors for endometriosis and malignancy of ovary are similar such as lower parity, late first pregnancy, infertility and use of oral contraceptive pills for a short period of time . Endometrial cancer risk

is enhanced when oestrogen is stimulated without being resisted. Exogenous estrogens have been shown in certain investigations to increase the likelihood of endometriosis lesions malignancy transformation. 7-11

Clinical Implications

This article suggests that endometriosis in postmenopausal women is a disease, of which bulk part has not yet been discovered. After considering the studies which has been taken place till date it is suggestive of that Hormone replacement therapy should be avoided in women with the history of endometriosis as it increases the risk of malignant transformation. The article mentioned above will be helpful in early evaluation of endometriosis in females after menopause. Even if the patient does not have a history of endometriosis lesions, clinicians should evaluate risk of endometriosis in situations of unexplained pain in the pelvic region in females after menopause, although it rarely occurs.

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