

Postmenopausal endometriosis: An enigma revisited

Endometriosis is a common gynecological disorder associated with infertility and chronic pelvic pain and traditionally been considered as a disease of the premenopausal years.^[1] For pelvic disease alone, three clinical forms have been described: superficial implants on the pelvic peritoneum and ovaries, ovarian endometriotic cysts and rectovaginal nodules.^[2] Besides pelvic disease, extra pelvic disease has also been reported.^[3] Many theories have been proposed to explain the cause of endometriosis, but no single theory is capable of explaining the pathophysiology of endometriosis in its various forms. It has been suggested that the three different presentations of pelvic endometriosis may be caused by three different mechanisms.^[4] As no single mechanism has been elucidated for premenopausal disease, it is highly unlikely that one single theory could account for postmenopausal disease.

There are no sensitive markers for the diagnosis of endometriosis, except for diagnostic laparoscopy, which is the gold standard for its diagnosis. It is possible that women in their premenopausal years may have had asymptomatic endometriosis or there could be women who had symptoms, but did not undergo a laparoscopy, and in both these groups, the disease progressed in their postmenopausal years. It is also known that discovery of a lesion in a premenopausal woman does not always guarantee progression of disease in the menopause. And on the other hand, a previous negative laparoscopy does not always mean that there would be no later development of the disease just prior to the menopause. Evidence suggests that postmenopausal endometriosis could have arisen in patients with a premenopausal history of the disease.

Laparoscopic evaluation of chronic pelvic pain in endometriosis has shown poor correlation with symptoms and extent of disease.^[5] Endometriosis has also been detected laparoscopically in 70% of fertile, asymptomatic, multiparous women in whom a previous diagnosis of endometriosis has not been made based on either symptoms

or investigations.^[6] Endometriosis once established can persist in the presence of low circulating levels of estrogen as seen in the postmenopausal period. Local estradiol production by the endometriotic lesions drives the disease through autocrine and paracrine effects. If endometriosis does occur in the postmenopausal period, it is less common, is present in smaller volumes and is less active. Yet it has the same immunochemical profile as the disease occurring in premenopausal women and has the potential to reactivate when given the appropriate stimulation.^[7]

Postmenopausal disease could be enhanced in the presence of higher circulating levels of estrogen especially in the form of phytoestrogens and hormone therapy (HT). Phytoestrogens have been known to exert estrogenic effects on the uterus, breast and pituitary^[8] and support growth of endometriotic deposits.^[2] As these are over-the-counter drugs, their use is indiscriminate and could be responsible for perpetuating preexisting premenopausal endometriosis in the postmenopausal period, when used for menopausal symptom relief. This can occur as density of estrogen receptors in endometriotic tissue appears to be unchanged in older patients.

Limited data are available on the effect of type of HT in women with previous endometriosis. Tibolone has been proposed to be a safe treatment in such women. Unopposed estrogen therapy was found to reactivate symptoms of pelvic pain and deep dyspareunia^[8,9] after Total Hysterectomy with Bilateral Salpingo (TAH and BSO) for endometriosis.^[10] HT immediately after TAH + BSO or 6 weeks after surgery did not change the risk of recurrent pain.

Endometriosis is in some ways similar to malignant disease. It can cause local and distant metastases, attach to, invade and damage adjacent tissues. In 1925, Sampson was the first to describe malignant transformation and reported an incidence of 1%.^[11] The risk of malignant transformation of endometriosis deposits is higher in postmenopausal women,^[7] especially in women with long-standing history of ovarian endometriosis.^[12] Hence, clinicians should be alert to the possibility of endometriosis in any postmenopausal patient with symptoms of the disease. If endometriosis is confirmed on investigation, a careful follow-up of such women on a long-term basis is necessary for future adverse outcomes. Obesity and unopposed estrogen are 2 risk factors, which have an additional effect for significantly

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increasing the risk of cancer in endometriosis,^[3] hence combined HT is recommended. The risk of extra ovarian malignant transformation is low, the most common site being the vagina.^[13]

The treatment of postmenopausal endometriosis that was first reported in 1950 is primarily surgical, but medical treatment may be a future option. Use of GnRh analogues, danazol and progesterone, appears to be ineffective in postmenopausal endometriosis.^[14] AI's may be a new promising method, which could potentially improve symptoms and treat these patients either as first-line treatment when surgery is contraindicated or as a second-line treatment for recurrences following surgical treatment. AI's could significantly impair bone mineral density and increase the rate of bone fractures, hence need to be supplemented with bis-phosphonate therapy. HT has more benefits than risks in women who are premenopausal at the time of radical operation. Unopposed estrogen therapy (ET) following menopause might increase the risk of persistence or reoccurrence of endometriosis. Furthermore, ET may potentially increase the risk of neoplastic transformation of the residual tissue whilst HT may have a lower risk. More data are needed to confirm this. It is important to follow-up all patients operated for endometriosis who have been subsequently prescribed HT, on a long-term basis.

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