

The continuously complaining wife about chronic pain is not neurotic, but has endometriosis

Pelvic pathologies are not easily diagnosed, and females suffer for years before a diagnosis can be established

The significant dissimilarity between men and women covers the whole spectrum of health and disease. She experiences pain and shows emotional reactions different from his. Common illnesses, such as cardiovascular diseases, develop different characteristics in women compared to men (1). Certain diseases, such as gynecological malignancies, are restricted to occurring in only one sex. Pelvic pain because of chronic infection of the urinary tract and bladder, fungus infection of the vagina are examples together with irritable bowel syndrome and the frequent occurrence of dysmenorrhea is accounted for the female anatomical condition.

Noticeably, pelvic pathologies are often not easily diagnosed in chronic pelvic pain (CPP), and females suffer for years before a diagnosis can be established (2). Emotional reactions because of the continuous stress are aggravated because of the particular mental health burden a woman has to overcome throughout her lifetime. They might be ill-tolerated by their male counterparts (3). Instead of blaming a notorious female hypochondriac's overreaction, the presence of endometriosis, a benign disease, but a heavy burden on quality of life, should be considered.

Endometriosis

Endometriosis develops during the reproductive age, around the 25th to 35th years. The endometrium is the mucous membrane that lines the inner side of the uterus. The disease is defined as the presence of endometrial-type mucosa outside the uterine cavity, mainly in the pelvic cavity (4). Locations could also be in the ovaries, the fallopian tubes, the urinary bladder, the sigmoid colon, the appendix, the upper abdomen, or elsewhere (5). There are no particular symptoms for diagnosis; chronic pain and often infertility are present. The reasons for infertility, as well as the etiology of the disease, are still unknown, although several theories exist (6). Endometriosis is now outlined as one of the diseases that were neglected in the past because of the LGBTQ ideology and its widespread presence among females, estimated to affect 190 million women worldwide (7, 8).

Estimation of prevalence

For the United States, it is estimated that one in ten women suffers from endometriosis, thirty to fifty percent endure infertility, and chronic pain, and for most of the women, it takes eight to ten years to make a correct diagnosis (6). For Thailand, the prevalence of the illness is unknown; however, it is mentioned in almost all websites of high-ranking hospitals in Bangkok. A group of obstetricians from a number of leading university hospitals in Thailand introduced themselves as the 'Thai Interest Group for Endometriosis (TIGE) and tried to estimate the magnitude of the condition in the country. They report 8.6% from hospital-based data, 25.6% in infertile women, 30.5% in benign gynecological diseases, and 60.9% with chronic pelvic pain who underwent

laparoscopic surgery (9). Predilections for endometriosis were found mainly in the muscles and tissue in the uterus wall (uterine leiomyoma), tissue growing in the muscular wall of the uterus (adenomyosis), and ovarian cysts (10).

Symptoms

The symptoms a woman with endometriosis can suffer are seriously disruptive to her quality of life, including her relationship with her partner, daily activities, and productivity within her household and her workplace. The results of a prospective pilot study involving 214 patients in Germany tried to document this. Their diseases were diagnosed by transvaginal ultrasound. Out of the study group almost 90% suffered from dysmenorrhea, over 75% had severe pain, and might avoid intercourse (dyspareunia), nearly 80% complained about pelvic pain, over 65% complained of constipation (dyschezia), and 15% observed blood in her stool (hematochezia). Half of the study group endured infertility (11). Not surprisingly, depression, anxiety, and stress are psychiatric disorders highly observed in connection with the ailment (12). In addition, the economic aspects of the illness in terms of lost income and medical fees could be enormous, and were estimated to be about 10.000 EUR (approximately 380.000 THB) for one woman for a year (13).

Proposed factors in the development of endometriosis

The cause of the disease is still unknown. Several theories about its development have been suggested. The most common one is Simpson's 1927 (2470) proposal of the retrograde menstruation theory (14). The theory is based on the observation that during menstruation, blood and endometrial tissue flow back into the peritoneal cavity through the fallopian tubes and might give rise to the endometriotic lesions (15). One of the drawbacks of the theory is the fact that retrograde menstruation is quite common in healthy women, with 75 to 90% without the occurrence of endometriosis (13).

Another hundred-year-old theory, known as coelomic metaplasia, from 1924 (2467), refers to multipotent stem cells from bone marrow or endometrium itself, which, under the influence of hormonal or immunological factors, play a role, especially in cases of endometriosis found outside the pelvic cavity, such as lymph nodes, lungs, brain, and kidney (13, 16).

During the development of the female embryological organs, resulting in the uterus, fallopian tubes and upper vaginal are the Müller's ducts. An additional theory for endometriosis is the Müllerian embryonic remnant abnormalities. The theory suggests that during the formation of the different organs, disordered differentiation and proliferation occur (17). The findings of extra-pelvic endometriosis in women in 'sentinel' lymph nodes support the lymphatic and vascular metastasis theory (18).

In recent times, the endometrial stem cell implantation theory is favored. As mentioned above, the stem cells are thought to originate from the uterine endometrium and bone marrow (19). Hormones and factors of the tissue microenvironment enable the adhesion necessary for the establishment of endometriosis (20). The beauty of the theory is that multipotent cells, through

the retrograde menstruation, settle at different locations, which also helps explain deep infiltration endometriosis and the diseases in the abdominal cavity (13).

The multifactorial disease

Advances in 'omic' technology led to research in genetic and epigenetic changes in endometriosis (21). An introduction to recent research developments is provided by Franca et al. 2022 (13). Several genes related to endometriosis and ovarian cancer were identified with mutations that may have a role in the implantation of the tumor and extraovarian endometriotic lesions (22). An epigenetic mechanism was detected in a promoter gene named HOXA10 in the endometrium of patients with endometriosis compared to healthy women. The expression of the gene is intensely increased during the secretory phase of the menstrual cycle (23).

Besides genetic factors, dysfunction of the innate immune system seems to be involved in the development of the disease. Macrophage activation, cytotoxicity of killer cells, and the production of proinflammatory cytokines are implied (24). Another field of investigation concentrated on steroid hormones and endometriosis. The hormones have a key role in ectopic endometrial lesions in the interplay of resistance to progesterone and an increase in estrogen in connection with inflammation (25). Endometriosis appears to result from the interaction of several systems, making it a multifactorial disease (26).

Infertility

The complex circumstances in the etiology of the diseases probably contribute to the fact that, besides the polycystic ovary syndrome, endocrine/anovulatory age, advanced age, particularly endometriosis, are listed among the leading causes of infertility (27). Still, the ultimate reason for infertility is not yet fully known, and the population of infertile women with endometriosis is heterogeneous. It is estimated that a third of women suffering from endometriosis are infertile, which is twice the rate compared with women without the disease (28). To help women become pregnant, one of the difficulties is establishing the diagnosis of endometriosis.

Diagnostic capacities

The most accurate diagnosis is laparoscopy, which, in fact, is an operation as a diagnostic tool, and might not be very well accepted by women. The procedure still bears the possibility of some unexpected complications, such as bleeding and infection, and it also has to be paid for and might be expensive (13). Other diagnostic measures, uncertain whether they might detect the lesions, are transvaginal ultrasound (TV-USG) and magnetic resonance imaging (MRI). More sophisticated radiological techniques and scintigraphy are used as well. TV-USG and MRI are reported to have a sensitivity of 91% and a specificity of 98%. However, peritoneal lesions are too small to be detected by the mentioned techniques (26).

Several biological markers are currently discussed, such as cancer antigens CA-19.9, CA-125, and interleukin-9. Given a level above 30 units/ml, CA-125 might be used as an initial 'rule-in' test to suspect endometriosis. This test might be preferred instead of interleukin-9. However,

TIGE does not favor biochemical makers because of their low sensitivity and specificity, and does not recommend them (9). The diagnosis of the illness is challenging, as is the treatment.

Treatment

The TIGE recommends resorting to appropriate treatment, which depends on the patient's age, the disease's severity, and the patient's overall condition, including her economic status and fertility needs (9). Surgical treatment could mean the necessity to remove visible lesions, but could be demanding in case of deep infiltrating and extra-pelvic endometritis. For Thailand, TIGE recommends long-term medication to avoid surgery and disease progression. The first—and second-line medications list includes analgesics, steroidal anti-inflammatory preparations, and combined oral contraceptives (9).

The latter might not always be to the liking of the patients, as a request for advice from the South of Thailand indicates, who was not happy with the aspects of ‘being pumped with hormones for god knows how long’ (29). However, the pharmaceutical industry is jubilant, as endometriosis treatment in Thailand has an annual growth rate of 13.9% and will reach US\$20.9 million in 2030 (30).

Outlook:

Endometriosis, a disease well known over hundred years, is still surrounded by uncertainties as far as the causing factors are concerned, to get the final diagnosis the women has to be cut open, and the pharmaceutical sector sees a massive gain in income through a long-term hormonal therapy, hampered by possible side effects, and is a telling example for the deficiencies in putting the priorities right for women’s health and well-being.

A very positive aspect is the Thai Interest Group for Endometriosis (TIGE), which comes up with concise statements, information, and recommendations. The ball for improvements lies mainly in the medical field, but probably public health could assist. Help could be offered in improving the accuracy of the magnitude of the ailment within the population, to assist in working on the sensitivity and specificity of biomarkers, and through measures of primary health care to sensitize women in the reproductive age with unclear long time present abdominal pain to be transmitted with the suspicion of endometriosis to the gynecological medical service.

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Grammarly software was used to improve English, but the AI function was disabled.