Genitourinary Syndrome of Menopause

The Story of Mrs. X: One of Many

Mrs. X, despite all her conscious efforts, could not enjoy the weekend celebration which her spouse's friends had organized for both of them as an anniversary gift! When their friends gave this as a surprise gift to them, both of them gratefully accepted it and were actually very excited to spend some quality time together. In fact, Mrs. X thought that this was a perfect opportunity to rejuvenate their 30-year-old married life! The resort was beautiful, the environment serene, the food awesome, and her spouse in his usual chirpy mood. However, persistent discomfort in her perineal region, constant itching, frequency of micturition, and dysuria continuously troubled Mrs. X. As if this was not enough, her dyspareunia strained their mood and the holiday ended abruptly before the weekend was over! Although she tried to discuss her problems with her spouse, he also could not understand them fully. Mrs. X had had her menopause 6 years back and was suffering from these symptoms for the last 1 year. She discussed these with her family physician but was not given any definitive advice. Now, her quality of life had started getting significantly affected.

The story of Mrs. X is not hers alone. There are millions of postmenopausal women who suffer from a condition called genitourinary syndrome of menopause (GSM).

Genitourinary Syndrome of Menopause: Nomenclature

Earlier names for this condition were vaginal atrophy, vulvovaginal atrophy (VVA), and atrophic vaginitis. The term GSM was coined at a 2013 terminology consensus conference by The International Society for the Study of Women's Sexual Health and North American Menopause Society. GSM describes the genital, sexual, and urinary changes in the lower genital tract associated with menopause. It describes the constellation of lower urogenital tract signs and symptoms associated with a low-estrogen state.[1]

Pathophysiology

The female genital tract and lower urinary tract share a common embryonic origin, both arising from urogenital sinus. Hence, both are affected by estrogen deficiency after menopause.[2] Estrogen receptors (both α and β) are present in the lower urogenital tract. Their levels decline with menopause and may be restored by estrogen treatment.[3] Estrogen deficiency after menopause causes reduction in the content of collagen, hyaluronic acid, and elastin, leading to thinning of epithelium, alterations in function of smooth muscle cells, and increase in the density of connective tissue and fewer blood vessels. These changes reduce elasticity of the vagina, increase vaginal pH, lead to changes in vaginal flora, diminish lubrication, and increase vulnerability to physical irritation and trauma.[4] Pathophysiologically, evidence shows that both circulating estradiol and its androgen precursors dehydroepiandrosterone (DHEA)/DHEA sulfate, androstenedione, testosterone, as well as their local metabolites, are vital to maintain normal structures and function of the vagina and surrounding urogenital tissues.[5]

Dr. Ranu Patni

Prevalence and Diagnosis: The Dilemma

Affecting nearly 50% of postmenopausal women, GSM also occurs in other low-estrogen states, such as postpartum, during lactation, and with certain medications, such as aromatase inhibitors (AIs).[6]

GSM is a chronic condition which does not reverse by itself, requires individualized management, and definitely affects the quality of life of the patient (and her spouse) if not treated adequately.

The majority of postmenopausal women have signs of VVA upon physical examination but less than half of the postmenopausal women report VVA symptoms as bothersome in international surveys.[7] There is a lack of understanding surrounding vaginal health[8] and elderly women do not discuss VVA symptoms so easily because sexual health is a sensitive topic.[9] In addition, the condition is believed to be transient and part of the aging phenomenon.[10] A study by Sinha and Ewies showed that only a few women attributed symptoms to menopause or hormonal changes, most women do not consult a gynecologist about their symptoms, considering them to be part of normal aging.[11] Gupta *et al*. studied the prevalence and severity of urogenital complaints in postmenopausal women at a tertiary care hospital in Delhi, India. A total of 200 postmenopausal women (two groups: Group A - less

than 5 years postmenopausal, Group B - more than 5 years postmenopausal) were screened and followed for urogenital complaints over 1 year. They found that the overall prevalence of urogenital symptoms was 67%. The most common symptoms were vaginal dryness (Group A - 62%, Group B - 48%), vaginal discharge/infection (Group A - 28%, Group B - 25%), and dysuria (Group A - 15%, Group B - 13.6%) in that order.[12]

The Study of Women's Health Across the Nation in the USA reported that women with sexual dysfunction considered vaginal dryness to be an important factor associated with masturbation, pain, arousal, physical pleasure, and emotional satisfaction.[13] VVA symptoms have an approximately linear relationship with sexual functioning,[14] and VVA correlates with sexual inactivity in the Hormone Therapy (HT) Trials of the Women's Health Initiative.[15]

Management Options

The primary aim of treatment of GSM is relief of symptoms. Lifestyle changes and nonhormonal and hormonal treatments are the main options. Tobacco abuse has been associated with increased atrophic vaginal changes as well as menopause at younger age.[16] Apart from avoiding tobacco consumption, regular sexual activity, maintaining vaginal hygiene, and avoiding use of chemicals/fragrances in and around perineal area might also help to a certain extent.

Nonhormonal therapies for GSM include vaginal lubricants and moisturizers. These may be sufficient for patients with only mild symptoms. Other nonhormonal options such as black cohosh or soy have not been shown to improve GSM.[17]

Vaginal estrogen is still the gold standard pharmacologic treatment for GSM, especially for patients who are not suffering from systemic symptoms of menopause.[18] If systemic HT does not provide relief after a certain time, vaginal estrogens may be added to that too.

Vaginal estrogen users had similar rates of endometrial cancer, invasive breast cancer, and pulmonary embolism/deep vein thrombosis as nonusers. In fact, risks of coronary heart disease, fracture, and all-cause mortality were lower in vaginal estrogen users.[19] Addition of progestins is not required with low-dose vaginal estrogen use. Contraindications to vaginal estrogen use include unexplained uterine bleeding, endometrial hyperplasia or cancer and use of AIs.

Ospemifene, a selective estrogen receptor modulator (SERM), is approved for the treatment of dyspareunia due to GSM as a daily oral tablet. Studies have demonstrated improvement in GSM symptoms compared to placebo.[20]

Lasofoxifene, a SERM, and prasterone, a vaginal DHEA, are also being studied for their effects on GSM. Fractional carbon dioxide laser therapy popularly called "vaginal rejuvenation" is also being studied but not yet FDA approved.

Women with breast cancer and other gynecological malignancies are at an increased risk of VVA and associated symptoms. Endocrine chemotherapy, surgery, and/or radiation may induce profound changes at urogenital levels which have to be timely recognized in oncologic care.[21] Compounding the situation, the use of adjuvant endocrine therapy with Gonadotropin Releasing Hormone (GnRH) agonists, AIs, or SERMs (e.g., tamoxifen, raloxifen) has increased from 69.8% in 2004 to 82.4% in 2013 in women with hormone positive cancers.[22] Even though data regarding efficacy are limited, vaginal moisturizers and lubricants are considered the initial and mainstay treatment options for GSM for women with breast cancer.[6] The safety of local estrogen therapy, when nonpharmacologic and nonhormone therapies have failed in women with or at high risk of breast cancer, has not been definitely established, and recommendations for use remain controversial.[23]

GSM, though very common, does not receive the desired attention. Hence, it becomes a chronic condition which can compromise the quality of life of an otherwise healthy lady. It should therefore be proactively managed by healthcare providers to preserve urogenital and sexual health as long as possible through hormonal, nonhormonal, and lifestyle measures.

Ranu Patni[1,2]

[1]Division of Gynaecologic Oncology, Prayaas Clinic, [2]Eternal Heart Care Centre and Apex Hospital, Jaipur, Rajasthan, India
E-mail: prayaas40@hotmail.com

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