MANAGEMENT OF SEXUAL COMPLICATIONS FROM CANCER DIAGNOSIS

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DISCLOSURES

- Medical Advisor - Madorra, a small tech start-up developing an ultrasound device to treat vaginal dryness

- Special thanks: Melissa Boll, MS, CNM, NAMS practitioner, AASECT certified sexual counselor, Manager, Midi Health

CASE STUDY

- 48 year old, recent diagnosis of locally advanced hormone positive breast cancer, status post unilateral mastectomy, AC/T chemotherapy, radiation, now on ovarian suppression, letrozole and Ibrance. Menses were regular prior to treatment and stopped with first round of therapy. Had a previously satisfying sex life with her male partner of the past 10 years. She has daily hot flashes and night sweats, marked vaginal dryness, pain and slight bleeding with penetrative sex, decreased libido, poor sleep, brain fog, fatigue and some mood changes and comes to you for treatment options.

UNIQUE ASPECTS OF CANCER HISTORIES THAT NEED TO BE ASSESSED AND CONSIDERED IN TREATMENT RECOMMENDATIONS

Pelvic surgery or radiation may cause vaginal or vulvar scarring that can lead to pain with touch or penetration and difficulty with lubrication

Surgery, radiation or chemotherapy induced menopause can impact vaginal dryness, arousal and desire

Chemotherapy can induce neuropathy that influences genital sensitivity and can impair arousal

Cancer surgeries like mastectomy, pelvic surgeries, vulvectomies, ostomy creation and issues like lymphedema can impact body image, well being and overall sense of sexual identity

UNIQUE ASPECTS OF CANCER HISTORIES THAT NEED TO BE ASSESSED AND CONSIDERED IN TREATMENT RECOMMENDATIONS

Stem cell transplants may cause graft-versus-host disease, leading to scarring, stenosis, ulcerations leading to sexual pain and impacts on arousal and desire

Lymph node dissection can lead to lymphedema with associated pain, impacting arousal and desire

Cancer treatments or cancer itself may cause pain, which can make any activity (including sex) difficult or impossible

Side effects of cancer medications may impact arousal and desire

Cancer-related stress, anxiety, and depression may impact overall well-being and interest in sex

SEXUAL FUNCTIONING IN CANCER SURVIVORS - GSM

- What is GSM? a broad term that describes the symptoms of vaginal and vulvar dryness, burning, irritation, lack of lubrication, dyspareunia, urinary urgency, frequency, dysuria, and frequent urinary tract infections (UTIs) that occur from hypoestrogenism

- " If it hurts to be touched or have penetration it will impact overall sexual functioning"

SAFE TREATMENT OPTIONS FOR ALL SURVIVORS - GSM

Vaginal Moisturizers – maintain moisture within the vaginal tissue, meant for long-term relief and recommended for regular use multiple times per week, many available, lack of head-to-head comparisons, low risk

Lubricants – meant for short term use, decrease pain with friction, come in water, silicone and oil- based formulations. Many available, water based less irritating but don't' last as long as silicone or oi

WHO recommends lubes with lower osmolarity, lower pH (similar to vaginal flora) so less irritating

pH-balanced gels – particularly helpful if associated discharge and altered genital flora

Topical oils – for both vulva and vagina- penetrate thin tissue and very soothing

Lidocaine- helpful for introital pain, can be applied prior to penetrative sex (4% solution)

TREATMENT OF GSM WITH VAGINAL HORMONES IN CANCER SURVIVORS

- Vaginal estrogens (estradiol) felt to improve GSM by increasing blood supply, improving tone, lubrication, normalize pH and prevent UTI's
- Come in cream, ring and suppository formulations. No one formulation felt superior and should be based on personal preference and cost
- Not thought to cause rises in systemic estradiol. No recommendation for checking estradiol levels
- For survivors with nonhormonal cancers AND those with gyn cancers, any formulation can be used

WHAT ABOUT VAGINAL ESTROGEN AND BREAST CANCER?

- Particular concern for breast cancer survivors on aromatase inhibitors as worse GSM and sexual dysfunction
- Why? Aromatase inhibitors work by shutting down all peripheral estrogen production so any systemic rises in estradiol might be harmful
- Limited trials show the ring and suppository formulations are safe, recommended by the National Comprehensive Cancer Network (NCCN)
- Small amounts of cream formulations can be applied to the vulva and introitus safely to alleviate discomfort
- Not thought to impact disease recurrence except for a single observational cohort (Danish) study
- Small studies suggest vaginal estriol safe formulation

PAIN WITH SEX – SAFE TREATMENTS FOR ALL CANCER SURVIVORS

- Aids and support:
  - Pelvic floor PT- can assess and treat any pelvic floor dysfunction that might be contributing
  - Vaginal dilators- can gently stretch the tissue in a nonsexual setting and help determine what hurts and what doesn't hurt
  - Tools like "ohnut rings" to limit the depth of penetration.
  - Sex Therapy referrals - The American Association of Sexuality Educators, Counselors, and Therapists provides information on certified sex therapists. (AASECT)

MEDICATIONS TREATMENTS FOR DYSPAREUNIA IN CANCER SURVIVORS

- Ospemifene – Oral SERM that is FDA approved for dyspareunia due to GSM
  - Preclinical studies showing an anti-estrogen at the level of the breast
  - Small studies showing no evidence of recurrence of BC but generally felt insufficient data to safely use in breast cancer survivors with HR+ disease

- Vaginal DHEA (Prasterone) – precursor to androgens and FDA approved for dyspareunia due to GSM
  - Limited trial data in cancer survivors. 2 in breast cancer survivors and one showing small rises in total testosterone so lack of safety data.

- Reasonable to use in survivors with non-hormonal cancers both - but the “oncologist is in charge”
- Note that these are not specifically FDA approved in cancer survivors

SUMMARY: ASSESSING PAINFUL SEX IN CANCER SURVIVORS

- Make sure to address overall pain- cancer related, surgical, etc
- Identify what hurts- the vulva, where in the vagina – entry, throughout, upper vault
- Target treatments to the areas of concern:
- Vulvar pain- use vulvar moisturizers and hormonal creams
- Vaginal pain-
  - Entry pain- topical anesthetics prior to penetration, hormonal creams rubbed into the vestibule
  - Mid pain- ensure atrophy is treated (vaginal hormones), treatments for dyspareunia
  - Upper vault- consider ohnut rings to limit depth of penetration

Remember supportive services like Pelvic PT and Sex Therapy

WHAT ABOUT ANDROGENS (TESTOSTERONE) IN CANCER SURVIVORS

- Not FDA approved for women but expert consensus groups support its use for improving sexual functioning (low libido) in postmenopausal women

- Concerns in HR+ breast cancer that testosterone can be “aromatized to estrogens”
- NCCN states to use with caution, particular for hormone sensitive cancers
- Dosing: need to use either compounded formulations or 1/10 of male hormone dosing
- Limited data on safety or efficacy in cancer survivors
- There are androgen receptors throughout the vulva and vagina and small amounts of creams can be used for pain without concern for systemic absorption (finger application)

FDA APPROVED DRUGS FOR LIBIDO AND CANCER SURVIVORS

- Flibanserin (Addyi) - nonhormonal, multi-functional serotonin agonist-antagonist that increases dopamine and norepinephrine and decreases serotonin
  - Studies showing benefits in PMP women but needs to be used off-label
  - Almost no data in cancer survivors - recent small trial presented at ASCO 2023 looked at 50 breast cancer survivors on endocrine therapy for their breast cancer and showed improvements in users of Addyi in multiple domains of sexual functioning

- Bremelanotide (Vyleesi) – peptide agonist of melanocortin receptors that acts to reduce inhibitor and increase excitement
  - No published data in cancer survivors

- Theoretically both drugs should be ok for use in cancer survivors but the “oncologist is in charge”

UNIQUE ASPECTS: RADIATION THERAPY AND SEXUAL FUNCTIONING

- Frequently a part of treatment for uterine, cervical, vaginal and anorectal cancers
- Can result in vaginal scaring, vaginal shortening and stenosis, grading systems for severity
- Mechanism – thought due to mucosal damage, collagen damage, cellular death
- Risks are age, dose/volume of radiation, additional chemotherapy tissue sensitivity
- Can see with both brachytherapy (BT) and external beam radiotherapy (EBRT)

UNIQUE ASPECTS: RADIATION THERAPY AND SEXUAL FUNCTIONING

- Treatments: Dilators recommended to stretch the tissue, breakdown adhesions and improve patency
- Mixed data on success of vaginal dilation, most studies show improvement in sexual functioning and is almost always recommended
- Lots of variation in terms of recommendation for when to initiate, frequency and instructions on use
- Most often initiate within 4 weeks from completion of RT, use a minimum of 3x per week, typically placed along the uppermost part of the vault and gently rotated, use for at least 5-10 minutes per session
- Can see light bleeding with use
- Use with water soluble lubricant
- Some studies suggest vaginal estrogen may improve outcomes, possibly hyaluronic acid

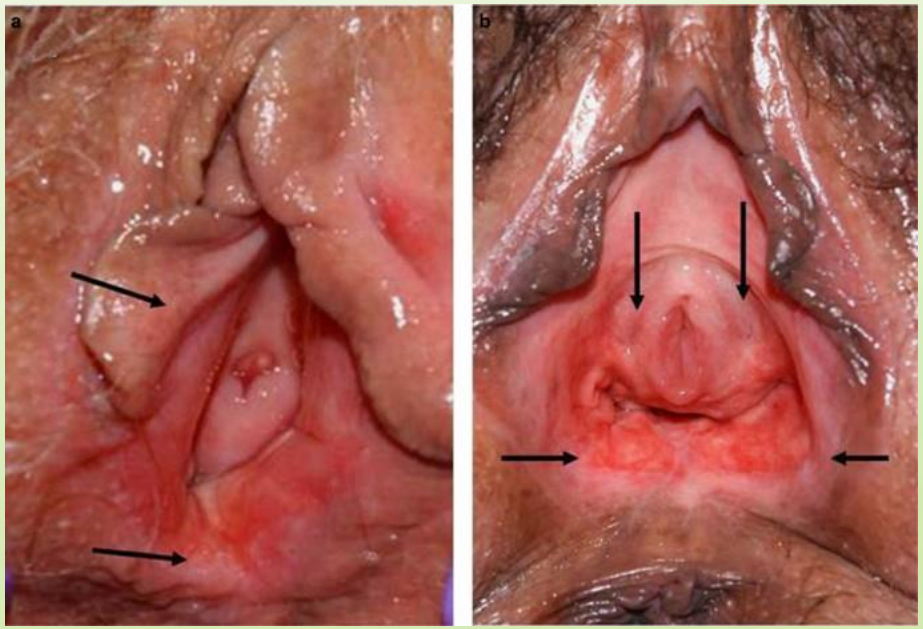
GRAFT VS HOST DISEASE

- Graft-versus-Host Disease (GVHD) - a complication following hematopoietic stem cell transplantation (HSCT) and occurs when immunocompetent donor T cells recognize host tissue as foreign
- Genital GVH is one of the least common areas and reported incidence from 20-50% post HCT
- Risk factors unclear but genital GVH most often seen with GVH elsewhere
- Higher likelihood of seeing assoc. dysplasia
- Symptoms overlap with GSM: vulvovaginal dryness, burning, discharge vulvar pain, and dyspareunia.
- NIH grading system having do do with severity and biopsy findings
- Diagnosis based on exam and biopsy

GRAFT VS HOST DISEASE

Exam findings:

- erythema and/or tenderness to palpation over Bartholin's or Skene's
- vulvar erythema, local mucosal paleness, and white/reticulated patches or plaques.
- can look similar lichen sclerosis or lichen planus



GRAFT VS HOST DISEASE

Treatments:

- Topical immunosuppression (clobetasol and vaginal steroid suppositories for vaginal GVH)
- Start dilator use early if vaginal involvement
- Adjuvant topical estrogen
- Rarely surgery to address scarring or to access the cervix
- Co-management with transplant team/hematologist if planning systemic steroids
- Important to diagnose early and initiate treatment to prevent scarring/stenosis

SEXUAL FUNCTIONING IN METASTATIC DISEASE

- Misconception that survivorship issues like sexual health only apply to those who are likely to have long life expectancies
- Limited literature but small studies suggest that patients with advanced cancer aren't asked about sexual functioning and when they are they don't have their concerns fully addressed
- Some may prioritize sexual intimacy more than sexual activity. One study showed that women with advanced cancer asking about sexual concerns were just offered lubricants and their full concerns were not addressed
- Sexual health issues should be addressed regardless of cancer stage or life expectancy

SUPPORTIVE TREATMENTS AND SEXUAL FUNCTIONING IN CANCER SURVIVORS

- Lifestyle changes that reduce fatigue and stress may result in positive effects on sexual functioning (diet, exercise, etc)
- Integrative therapies (Yoga, meditation, and mindfulness) may improve sexual functioning by decreasing pain and improving overall sense of well-being
- Therapy referrals for patients- individual and/or couples
- Pelvic floor PT
- Sex Therapy

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HOW TO APPROACH: "FIX WHAT YOU CAN FIX"

- Hot flashes/night sweats – prescription alternatives to hormones (Gabapentin, Venlafaxine, Fezolinetant)
- Vaginal pain – OTC moisturizers, vaginal estradiol, introital lidocaine, vaginal dilators
- Decreased Libido – see response to GSM treatment, if lack of benefit consider bupropion or off-label Flibanserin, Bremelanotide
- Poor sleep – see response to treating night sweats, add magnesium glycinate, ? Ashwaganda, CBT-I
- Brain fog and fatigue- work on sleep first, discuss lifestyle- exercise recommendations, review diet,
- Mood Changes- see if resolves with treatment of other issues, consider Venlafaxine as maybe can help with both
- Additional support- consider therapy or sex therapy pending on response to treatments

MOST IMPORTANT TAKE AWAY…..

- You may be the only one discussing sexual health - oncology may not bring up
- There is no need for any cancer survivor to just “live with the side effects”
- There are always treatments that can be offered
- Discussions regarding sexual health should be brought up frequently
- Intimacy is possible!

PATIENT RESOURCES

- ASCO patient information site cancer.net has informational resources on sexual functioning and cancer
- Breastcancer.org – has general information and guides to cancer institutes with specific programs
- Pelvic floor PT referrals –
- pelvicguru.com provides pelvic health information and resources
- Herman & Wallace Practitioner Directory, pelvicrehab.com for practitioner data base

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THANK
YOU