Graft–versus-Host Disease of the Female Genital Tract

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Chronic Graft-versus-host Disease (cGVHD) of the Vulva and/or Vagina

• Immune disorder that occurs as late complication of stem cell transplant
• Vulvovaginal GVHD can cause pain and long term complication of scarring in vaginal canal
• Adverse effects on intimacy, sexual function and quality of life
• Can co-exist with disruption of ovarian function, often misdiagnosed as menopausal condition
Genital GVHD

- Can affect genital tract in females in 25-49% of stem cell transplant survivors
- Vulvar symptoms can occur first: median 7-10 months post-transplant
- Vaginal disease can occur years later, latest reported case 8 yrs post-transplant
- Vulva only (68%), Vulva and vagina (26%)

Genital GVHD-Background

- GVHD of female genital tract first described in 1982
  - 5 cases of severe vaginal scarring that required surgery
  - Menstrual flow blocked by scar tissue blocking vaginal canal
  - Successfully treated with surgery (to remove scar tissue) and use of estrogen and vaginal dilators post-operatively

Corson SL et al. Obstet Gynecol
1982;60;488-492
Vulvovaginal GVHD: Symptoms

- Dryness
- Burning
- Itching
- Tender to touch (vulva)
- Painful intercourse (with penetration of vaginal opening and/or with deep penetration of vagina)
- Amenorrhea, cyclic pelvic pain, unable to insert tampon (due to severe vaginal scarring—less common)

Vulvovaginal GVHD: Signs

- Redness of vulvar tissue (patchy or diffuse)
- Tenderness of gland openings in the vulvar vestibule (when touched with a Q-tip)
- Erosions or fissures, open sores (can look like genital herpes)
- Vulvar scarring (fusion of labia, clitoral hood)
- Scarring of vaginal canal: thin, filmy scar tissue vs. dense scarring

Genital Atrophy

- Atrophy of vulva and vagina can occur with disruption of ovarian function, at time of menopause or due to chemo/radiation
- Due to low estrogen levels
- Thinning and decreased elasticity of vaginal walls
- Decrease in vaginal lubrication
- Scarring not typical
## Genital Atrophy vs GVHD: Symptoms

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<th>Atrophy</th>
<th>GVHD</th>
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<tr>
<td>• Dryness</td>
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<td>• Painful intercourse</td>
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<td>• Itching (more common if co-existing infection)</td>
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Genital atrophy vs GVHD

**Atrophy**
- Pale pink vaginal walls
- Vaginal tissues bleeds easily with contact (severe)
- Labia “thinner”, sometimes fuse together (long term)

**GVHD**
- Redness of vulva
- Erosions, sores, fissures
- Tenderness of vulvar glands
- Scarring
Genital GVHD: Management

• **Key is to recognize the problem!**
  – History of vulvar or vaginal symptoms
  – Careful physical exam: inspection of vulva, vagina and area between vagina and anus (“perineum”)
  – Assessment of redness of glands in vulva (“vestibular glands”), tenderness if touched with cotton tipped swab
  – Gentle digital vaginal exam—scarring, size of opening, length of vagina
Genital GVHD: Management

- Examine vagina using speculum: rule out infection, obtain pap smear of cervix if due
- Culture any open sores/erosions of vulva or vagina for herpes simplex virus (HSV)
- Biopsy not always necessary (if vulva very tender)
GVHD: Treatment

• Topical steroids
• Topical immunosuppressants (cyclosporine, tacrolimus)
• Estrogen therapy
  – Can be applied locally to vulva and vagina
  – Cream, ring or vaginal tablet
• Vaginal dilators
• Surgery (if severe scarring)

Spiryda 2003, Stratton 2007
Genital GVHD: Treatment

• May see improvement in up to 2-4 weeks with daily application of topical steroid ointments
• May taper to 2-3x/week once area healing
• Erosions and fissures may take 6-8 weeks to fully heal
• Long term use of local estrogen important to prevent thinning of skin and mucosa—*but not a treatment for GVHD alone!*

Genital GVHD: Summary

• GVHD of vagina and vulva can lead to reduced quality of life due to pain and sexual dysfunction

• Early recognition of GVHD is key in preventing long term complications in the genital tract

• Estrogen therapy alone is not sufficient treatment

• Combination of topical therapies (steroids), estrogen and vaginal dilators can resolve pain and restore sexual function