Persistent Genital Arousal Disorder (PGAD): Experience with Management in 35 Consecutive Cases

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Introduction: Persistent genital arousal disorder (PGAD) is a rare, unwanted and intrusive sexual dysfunction associated with excessive and unremitting genital arousal and engorgement in the absence of sexual interest.

There are no recognized safe and effective evidence-based treatments.
Persistent Genital Arousal Disorder: During PGAD Symptoms

Homuncular genital representation

Normal clitoris projection

PGAD attack
Persistent Genital Arousal Disorder is a persistent or recurrent, unwanted or intrusive, bothersome or distressing, Genital Dysesthesia unassociated with sexual interest, with the following characteristics:

1. Symptoms may lead to despair, frustrations, emotional lability, and/or catastrophizing thoughts
2. Symptoms may be associated with overactive bladder and restless leg syndrome
3. Orgasm may be spontaneous, recurrent, aversive, absent, delayed, muted, and or not associated with pleasure or satisfaction
4. Symptoms have limited, or no resolution, or even aggravation with orgasm
5. Symptoms may be caused by peripheral and central pathophysiology
Increased peripheral pudendal nerve sensory afferent input

Central sexual arousal reflex center that is overly excited and under inhibited
Pain and Orgasm Share Common Neurologic Pathways – Lateral Spinothalamic Tract

Nucleus acumbens
Amygdala
Hippocampus
Paraventricular Nucleus of the Hypothalamus
Ventral Tegmentum
Pain and Orgasm Share Common Neurologic Pathways – Lateral Spinothalamic Tract

The spinothalamic tract is a sensory pathway originating in the spinal cord.

The spinothalamic tract transmits afferent information to the thalamus about pain, temperature, itch, and crude touch.

The types of sensory information transmitted via the spinothalamic tract are described as “affective sensation” - the sensation is accompanied by a compulsion to act.

For instance, an itch is accompanied by a need to scratch, and a painful stimulus makes us want to withdraw from the pain.
Aim: We wished to assess characteristics of women who were diagnosed and managed for PGAD.

Methods: A retrospective clinical chart review was performed on the last 35 women who were assessed for PGAD.
Results 1: In this review, women (mean age 46 +/- 18 years) had symptoms of PGAD for a mean of 17 +/- 16 years.

In these women PGAD appeared secondary to the sum of two underlying pathophysiologies:

i) increased peripheral sensory afferent input

ii) central sexual arousal reflex center that was under inhibited.

In these women with PGAD, the central sexual reflex center of the brain appeared to falsely interpret the excess peripheral sensory information as sexual arousal - leading to the spontaneous arousal and orgasm and short refractory period post-orgasm.
Female Sexual Response Cycle


PGAD ?????? = limited resolution of the genital arousal
Results 2: The following conditions were observed to result in increased peripheral sensory afferent input in this population:

a) altered pre-menopausal hormone integrity – hormonally mediated provoked vestibulodynia; n = 6 (17%)
b) altered menopausal hormone integrity – vulvovaginal atrophy/genitourinary syndrome of menopause; n = 9 (26%)
c) increased nerve fiber density - genetic susceptibility leading to elevated levels of nerve growth factor substances; n = 2 (6%)
d) an injury to, or irritation of, the pudendal nerves that transmit pain and other sensations; n = 10 (29%)
e) abnormal response of tissues to Candida infection, or recognized allergies or non-specific allergies; n = 4 (11%)
f) dermatologic conditions: lichen sclerosus or lichen planus; n = 4 (11%)
g) vulvar granuloma fissuratum; n = 2 (6%)
h) peri-urethral glans pathology; n = 1 (3%)
i) clitorodynia; n = 4 (11%)
j) pelvic congestion syndrome; n = 1 (3%)
k) S2 Tarlov cyst; n = 3 (9%)
l) high tone pelvic floor dysfunction n = 30 (86%)
Persistent Genital Arousal Disorder (PGAD): Experience with Management in 35 Consecutive Cases

Results 3: Treatment of PGAD in this population was **individually based** and included strategies to:

i) reduce the excess peripheral sensory input – with conservative sex therapy/counseling, pelvic floor, pharmacologic, device and surgical treatments

ii) increase inhibitory regulation of the uninhibited central sexual reflex center

Successful PGAD management utilized all the strategies, to keep the PGAD condition manageable
Medical/Biologic Causes of PGAD

1. Altered pre-menopausal hormone integrity – Hormonally Mediated PVD
2. Altered menopausal hormone integrity – Vulvovaginal Atrophy
3. Increased nerve fiber density - genetic susceptibility leading to elevated levels of nerve growth factor substances
4. An injury to, or irritation of, the pudendal nerves that transmit pain and other sensations
5. Abnormal response of tissues to Candida infection, or recognized allergies or non-specific allergies
6. Dermatologic conditions: lichen sclerosus or lichen planus
7. Vulvar granuloma fissuratum
8. Peri-urethral glans pathology
9. Desquamative Inflammatory Vaginitis
10. Bartholin cyst
11. Clitorodynia
12. Pelvic Congestion Syndrome
13. Endometriosis
14. Pelvic Organ Prolapse
15. Interstitial Cystitis
16. Referral from Hip Disease
17. High tone pelvic floor dysfunction
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Hormonally Mediated Provoked Vestibulodynia

Treatment:
Stop hormonal contraceptives
Systemic testosterone – ideal calculated free testosterone 0.8 ng/dl
Local to vestibule estradiol 0.02%/testosterone 0.1% in methylcellulose BID
Expect no improvement for 6 weeks, 30-40% by 12 weeks

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**MENOPAUSE MANAGEMENT – FIVE TREATMENTS**

**Testosterone Therapy**
Use FDA-approved testosterone at 10% of male dose
1. Daily transdermal gel - 1/10th tube daily to calf/thigh
2. Weekly IM injections - 0.1 ml - 50 mg/ml testosterone enanthate/cypionate - into vastus lateralis muscle – anterolateral mid-thigh; 27 gauge needle; 1 ml syringe
3. 4-6 month subcutaneous testosterone pellet

**Estradiol Therapy**
Consider FDA-approved biologically identical estradiol
1. Daily oral (↑SHBG, ↑VTE, ↑lipids)
2. Daily transdermal gel, emulsion, spray
3. Twice weekly, weekly transdermal patch
4. Three month vaginal ring
5. Weekly IM injections - 0.1 ml – estradiol valerate 10 mg/ml; 5 ml bottle; vastus lateralis muscle – anterolateral mid-thigh - 27 gauge needle; 1 ml syringe

**Progesterone Therapy**
Consider FDA-approved biologically identical progesterone
1. Oral micronized progesterone 100 mg q MWF (intact uterus, q MTH hysterectomy)
2. Vaginal progesterone suppository – 6 per month
3. Compound progesterone cream

**Vestibular Hormonal Therapy**
Compound estradiol 0.02%/testosterone 0.1% in hypoallergenic base (methylcellulose); apply pea-sized volume x 2 (right and left sides; directly onto entire vestibule; QD – BID

**Intravaginal Hormonal Therapy**
1. Daily compound estradiol 0.02%/testosterone 0.1% in hypoallergenic base (methylcellulose); apply pea-sized volume directly into vagina
2. Daily vaginal estradiol cream – pea-sized amount
3. Daily 10 mg DHEA tablet/1% DHEA suppository
4. Three month vaginal ring
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TENS and Pudendal Neuromodulator
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INTROITAL DYSPAREUNIA
Vulvar granuloma fissuratum
Erosive Lichen Planus
Pelvic Congestion Syndrome Presenting as Persistent Genital Arousal: A Case Report

Catherine Thorne, MBBS,* and Bronwyn Stuckey, FRACP*††

Figure 1  Magnetic resonance imaging scan with contrast enhancement shows extensive varices involving the entire vaginal wall, contiguous with the prominent parametrial veins. Varicosities are also seen in the anterior abdominal wall and in the anterior thigh.

Figure 2  Venogram of the left ovarian vein shows retrograde flow and pelvic varices before embolization (left) and after embolization using stainless steel coils and 3% ethoxysclerol (right).
Persistent Genital Arousal Disorder (PGAD)

PGAD is likely always secondary to the SUM of TWO two underlying pathophysiologies:

- **Increased peripheral sensory afferent input**
- **Central sexual arousal reflex center that is overly excited and under inhibited**
High Excitation, Low Inhibition Sexual Dysfunction

**SEX THERAPY**
- Strategies to reduce anxiety
  - Conservative measures such as heating pad, warm bath, yoga and acupuncture

**PHYSICAL THERAPY**
- Pelvic floor relaxation strategies to reduce stress or anxiety that is associated with skeletal muscle pelvic floor relaxation

**Non-Pharmacologic Strategies That Decrease Neurotransmission**
- TENS/Inferential Stimulation
- Sacral Neuromodulation – Interstim
- Pudendal Neuromodulation – Interstim
- Pudendal Nerve Block – local anesthesia and steroid
- Electroconvulsive Therapy (ECT)

**DOPAMINE ANTAGONIST**
- Varenicline Tartrate 0.5 mg – 2 mg/day

**Hyperthyroidism**
- Methimazole 5 – 60 mg

**PHARMACOLOGIC AGENTS THAT DECREASE NEUROTRANSMISSION**
- Local Anesthesia, Tricyclic Antidepressants, Calcium Channel Blocking Agents, Sodium Channel Blocking Agents, Anticonvulsant Agents
  - Lidocaine – topical 1-5%
  - TCA – Amitriptyline – 25 – 150 mg
  - TCA – Nortriptyline – 25 – 100 mg
  - TCA – Desipramine – 25 – 300 mg
  - Ca⁺⁺ – Gabapentin – 100 – 2400 mg
  - Ca⁺⁺ – Pregabalin – 25 – 300 mg
  - Na⁺⁺ – Carbamazepine – 100 – 400 mg
  - Na⁺⁺ – Oxcarbazepine – 150 – 2400 mg
  - Lamotrigine – 25 – 200 mg

**EXCITATION – Central and Peripheral**
- SEX STEROIDS
- THYROID HORMONE
- DOPAMINE
- OXYTOCIN
- MELANOCORTIN
- NOREPINEPHRINE
- STRESS, ANXIETY
- PUDENDAL NEUROPATHY
- EXCESS STIMULATION FROM TISSUE SERVED BY PUDENDAL NERVE

**INHIBITION – Central and Peripheral**
- SEROTONIN
- OPIOIDS
- ENDOCANNABINOID
- PROLACTIN

**SEROTONIN AND NOREPINEPHRINE REUPTAKE INHIBITOR**
- Serotonin Reuptake Inhibitor and 5 HT1A Receptor Partial Agonist

- SNRI – Duloxetine - 20 – 120 mg
- SNRI – Venlafaxine – 75 – 225 mg
- SNRI – Desvenlafaxine – 50 – 100 mg
- SRISRPA – Vilazodone – 10 – 40 mg

**OPIOID AGONIST**
- Tramadol 25 – 200 mg
- Tapentadol 25 – 400 mg
- Hydrocodone bitartrate and acetaminophen – 5/500
- Oxycodone and Acetaminophen – 2.5/325 – 10/325

**CANNABINOID**
- Dronabinol – 2.5 – 20 mg

**VASCULAR CAUSES**
- Arterial Venous Malformation – Embolization
- Congestion Syndrome - Embolization

**NEUROLOGIC CAUSES**
- Cerebral space occupying lesion, CVA
- Spinal Cord injury, trauma, surgery

**PHARMACOLOGIC CAUSES**
- DISCONTINUE UNDER SUPERVISION:
  - Trazodone
  - Anti-psychotics - chlorpromazine
  - Anti-coagulants – heparin
  - Anti-hypertensives – alpha-blockers
  - Recreational drugs – cocaine
Conclusions: PGAD is not so rare

An estimated 20% of healthcare providers at numerous sexual meetings have claimed caring for individuals with PGAD

PGAD can be managed so that afflicted women can have excellent life quality

Patients diagnosed with PGAD and managed successfully are no longer suicidal or bothered/distressed after treatment(s)
Conclusions 2: PGAD seems to be caused BOTH by:
1) excess peripheral afferent stimulation from irritated genital, pudendal nerve, pelvic floor tissues or sacral nerve roots and 2) from a central sexual reflex that has limited central inhibition

PGAD may be acquired later in life after living many years with no hint of PGAD symptoms

PGAD can occur at a very young age; some people report persistent genital arousal all their lives and do not know any other form of sexual arousal