Chapter 4
Persistent Genital Arousal Disorder/ Genitopelvic Dysesthesia

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Learning Objectives
- To describe the definition, prevalence, and characteristics of Persistent Genital Arousal Disorder/Genitopelvic Dysesthesia (PGAD/GPD) to facilitate its understanding and aid in its efficient diagnosis.
- To illustrate the biopsychosocial influences involved in the expression of PGAD/GPD.
- To characterize PGAD/GPD as a multifactorial condition in which multiple, concurrent approaches are most likely to be effective in its management.

4.1 Introduction

Persistent Genital Arousal Disorder/Genitopelvic Dysesthesia (PGAD/GPD) is a highly distressing yet poorly understood condition affecting people of all ages and genders [1]. It is characterized by sensations of genital arousal (e.g., throbbing) that

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are persistent, unwanted, and distressing. These sensations occur in the absence of subjective feelings of sexual desire/arousal or feeling "turned on" [1]. Part of the reason that PGAD/GPD is not well understood is that the experience of genital "arousal" is usually interpreted to be time limited, wanted, and pleasurable [2]. Adding to the complexity of PGAD/GPD is the belief that "arousal" is a unified construct: the physical aspects of arousal are assumed to act in concordant ways with the subjective aspects [2]. However, decades of sexual psychophysiological research examining the main components of sexual arousal (genital response and subjective ratings of arousal) in response to sexual stimuli have indicated that the physiological and subjective components are not perfectly concordant [3]. In fact, there is much variation in sexual concordance (i.e., the relationship between the physiological and subjective components of sexual arousal) both between and within participants given various parameters, such as genital arousal measurement device, scales used for arousal ratings, and types of sexual stimuli (e.g., films versus audio stories) [3]. Thus, the experience of arousal is best conceptualized on a continuum—from not at all pleasurable to extremely pleasurable, for example. Applying this same perspective to the experience of orgasm, which is also assumed to be wanted and pleasurable, is useful in conversations with patients with PGAD/GPD because some patients experience repetitive, disruptive, and unpleasant orgasms [1]. Interestingly, the experience of non-pleasurable orgasms has also been reported in nonclinical and clinical (e.g., those with anhedonic ejaculation) samples [4, 5]. It is therefore essential to focus on the patients' experiences of their symptoms, avoid making assumptions about the valence of these experiences, and recognize the complexity of PGAD/GPD symptoms.

4.2 Definition of PGAD/GPD

Various names referring to PGAD/GPD have existed over the past two decades. It was first called Persistent Sexual Arousal Syndrome by Leiblum and Nathan (2001) [6]; however, it was changed to Persistent Genital Arousal Disorder (PGAD) to clarify that it was only the sensations of *genital arousal* (not "sexual arousal," which includes both physiological and subjective components) that were persistent [7]. The term PGAD was adopted by most sexual medicine experts [8] and by the International Classification of Diseases-11 [9], although some referred to it as Restless Genital Syndrome, drawing a parallel between PGAD and Restless Legs Syndrome [10]. In 2021, a consensus and process of care paper formally reconceptualized PGAD as PGAD/GPD, given that the genitopelvic sensations of arousal were unpleasant and atypical (i.e., a dysesthesia) [1]. This landmark paper defined PGAD/GPD as "persistent or recurrent, unwanted or intrusive, distressing sensations of genital arousal (e.g., feelings of being on the verge of orgasm and of lubrication and swelling, tingling, throbbing, contractions) that persist for 3 months or more and may include other types of genitopelvic dysesthesia (e.g., buzzing, burning, twitching, itch, pain)" (p. 668). In addition, it specified that the sensations of

PGAD/GPD are not associated with sexual interest, thoughts, or fantasies; that they can occur in various genitopelvic areas (e.g., clitoris, vulva, bladder) in the absence of observable signs of genital arousal (e.g., vaginal lubrication, vulvar or clitoral swelling); and that some people with PGAD/GPD experience uncontrollable orgasms or have an excessive number of orgasms. Furthermore, it states that PGAD/GPD symptoms may be resolved partially, not at all resolved, or even aggravated by sexual activity; may include dysesthetic orgasms (e.g., experienced as aversive); and may be aggravated by various factors (e.g., vibrations from a moving vehicle, music or sounds, stress). PGAD/GPD is also associated with various psychological experiences, such as despair, emotional lability, catastrophization, and suicidality [1].

4.3 Known Epidemiology

Studies examining the prevalence of PGAD/GPD in clinical and nonclinical samples indicate that up to 4.3% of individuals may be affected. Garvey and colleagues found that 1% (1 of 96) of women presenting at a sexual health clinic in London, UK reported distressing sensations of genital arousal in the absence of sexual desire [11]. In a study of more than 1500 undergraduate students attending a Canadian university, Jackowich and Pukall (2020) [12] reported prevalence rates of 0.6% (7 of 1267) in women and 1.1% in men (4 of 360), similar to the rate of 1.6% (11 of 679) of undergraduate women attending an Italian university [13]; none of the seven nonbinary participants reported PGAD/GPD symptoms [12]. In a representative US sample, Jackowich and Pukall (2020) [12] reported somewhat higher rates: 2.7% of women (14 of 514) and 4.3% of men (22 of 506) reported symptoms consistent with PGAD/GPD; 2 of 6 nonbinary participants reported mild intensity PGAD/GPD symptoms, with none reporting moderate to high intensity. Despite the study's finding that participants of all educational and cultural backgrounds endorsed at least one PGAD/GPD symptom, individuals who completed a high school degree/general educational development (as compared to those with less than a high school degree and those who completed post-secondary education) and Non-Hispanic Black and Hispanic/Latinx (as compared to non-Hispanic white) participants endorsed significantly more symptoms. The latter finding is consistent with prevalence patterns of other forms of genitopelvic dysesthesia, such as vulvodynia [12].

4.4 Clinical Presentation and Contributing Factors

Given that the bulk of research and published case studies have focused on samples of women with PGAD/GPD, little is known about the clinical presentation and contributing factors in men and individuals with trans and nonbinary identities; however, based on the clinical experience of the authors, all people with PGAD/GPD

symptoms can present with symptoms similar to those experienced in women and patients with a penis may also experience unwanted spontaneous ejaculation [14].

Distress is a key component to diagnosing PGAD/GPD [1](Goldstein et al., 2021). It is important to note that some individuals with persistent sensations of genital arousal do not experience distress associated with their experience; therefore, the diagnosis of PGAD/GPD would not be made in these cases. Those with PGAD/GPD report moderate to high levels of distress; in addition, suicidal ideation and high levels of worry, stress, and depression have also been reported [15]. Those with PGAD/GPD may experience a variety of symptoms related to orgasm (e.g., spontaneous orgasm, feeling on the verge of orgasm), urination (e.g., urgency, frequency), and pain (e.g., pain in the clitoris at rest) [15]. Therefore, a comprehensive assessment is critical, and accessible mental health support is essential.

The average age of PGAD/GPD onset for women is in their mid-thirties, but the range is wide, and PGAD/GPD can start at any age; in addition, most people with PGAD/GPD will report that the symptoms started suddenly (versus gradually) and that they are constantly (versus intermittently) experienced [15]. Triggers for symptoms range widely and include sexual (e.g., feeling sexual desire), nonsexual (e.g., driving), emotional (e.g., stress), and physiological (e.g., full bladder) states; not surprisingly, most patients with PGAD/GPD will report that their symptoms interfere with activities of daily living, such as work and social activities [15]. Fortunately, those with PGAD/GPD report that engaging in distracting activities, relaxation exercises, and solitary and partnered sexual activity, as well as sleeping and other activities, can alleviate their symptoms temporarily, although others report that some of the same activities (e.g., sexual activity, sleep) can trigger their symptoms [15]. It is important to note that some individuals with PGAD/GPD may engage in frequent sexual activity (solitary, partnered) to alleviate their symptoms; because of this, and because of the lack of knowledge about PGAD/GPD and the complexities of arousal, many individuals with PGAD/GPD may be diagnosed with hypersexual disorder. It is important to fully understand the motivations for high frequency of sexual activity and the criteria for PGAD/GPD and any differentials before a definitive diagnosis is made.

4.5 Possible Pathophysiological Mechanisms

Based on recent multidisciplinary research, it has become evident that organic pathologies play a significant role in PGAD/GPD [1]. As demonstrated by functional magnetic resonance imaging (fMRI) in women, there is a common representation of the dysesthesia of PGAD/GPD as spontaneous intense hyperactivity in the genital sensory cortex (paracentral lobule). A review of PGAD/GPD management has recognized that this hyperactivity in the genital sensory cortex can emanate from five specific body regions, categorized as Regions 1–5. These regions are the following: end organ (Region 1), pelvis/perineum (Region 2), cauda equina (Region 3), spinal cord (Region 4), and brain (Region 5) [1].

Region 1 end organ pathologies involve the clitoris, penis, vestibule, vagina, scrotum, prostate, urinary bladder, and urethra (e.g., dermatoses such as lichen sclerosus, infections, GSM, and inflammation) [1].

Upon physical examination, for patients whose PGAD/GPD trigger is related to clitoral pathology, the following histories may be observed. They may have a history of hypersensitivity of glans (e.g., "grain of sand" sensation), discomfort wearing tight clothing or contact during sexual activity, inability to see the glans, or traumatic injury to the vulva/clitoris from a straddle injury. Patients whose PGAD/GPD trigger is related to vaginal pathology may have a history of copious yellow discharge, chronic infection, severe allergic reactions (sensitive skin), or genitourinary syndrome of menopause (GSM) symptoms (e.g., vaginal dryness and introital dyspareunia) [1].

Region 2 pelvis/perineum pathologies include pudendal and/or pelvic nerve pathology, high tone pelvic floor dysfunction, vascular pathologies, e.g., arteriovenous malformation and pelvic congestion syndrome, in addition to hypertonic pelvic floor muscle, and pudendal nerve entrapment [1]. Patients whose PGAD/GPD trigger is related to neuropathy of pelvic nerve may have previously undergone a Loop Electrosurgical Excision Procedure (LEEP) for cervical dysplasia or a mid-urethral sling surgery (MUS) for stress urinary incontinence. In this latter case, we have shown that the mesh in a cadaveric study lies close to critical pelvic nerves in the anterior vaginal wall/periurethral prostatic tissue [16].

The report that Tarlov cysts, which form on the genital sensory nerve roots of the cauda equina (Region 3), occurred in 12 of 16 (66.7%) of women with PGAD/GPD raised the awareness that PGAD/GPD perceptual symptoms can be generated by neuropathy that occurs distant from the genitopelvic region [17]. These Tarlov cysts are cerebrospinal fluid-filled meningeal "blisters" that contain aberrant sensory nerve fibers and form on the genitopelvic sacral nerve roots. Region 3 pathologies also include herniation of the lumbosacral intervertebral discs, resulting in extrusion of the nucleus pulposus through the tear in the annulus of the disc, which produces inflammation of the pudendal, pelvic, and sciatic nerve roots in the cauda equina, typically at L5-S1 and/or L4-L5 [1]. Region 4 spinal cord pathology may result from cervical/thoracic herniated intervertebral discs or medication changes. The latter could produce an imbalance in spinal cord serotonin and/or norepinephrine, resulting from initiation and/or discontinuation of SSRIs or SNRIs, which could alter the function of the pain-gate mechanism that utilizes these neurotransmitters, thereby provoking or exacerbating the dysesthesias [1]. Region 5 represents direct brain mediation of PGAD/GPD symptoms resulting from, for example, epileptic seizures [17], medication changes (e.g., SSRI or SNRI discontinuation and even initiation in some cases), and/or psychological factors (e.g., sexual/emotional trauma, anxiety, hypervigilance, catastrophization), which can trigger or exacerbate PGAD/GPD symptoms, leading to suicidality [1].

4.6 Clinical Management, Including Biological-Psychological-Social Contributing Factors

4.6.1 Diagnosis

An accurate diagnosis is essential to the process of clinical management and will likely involve a multidisciplinary team and ruling out differentials (e.g., hypersexual disorder). To this end, a comprehensive biopsychosocial diagnostic evaluation is recommended; this process consists of taking a detailed symptom, psychosocial, and medical history through an extensive clinical interview and a multi-stage physical examination of all relevant regions. It may also involve referrals to other health care providers for full assessment of relevant regions [1]. In line with recent recommendations by an expert consensus panel [1], we recommend that the physical examination begin with a careful evaluation of Regions 1 and 2 given that these regions are symptomatic and are accessible to physical examination by most medically trained clinicians. Additional details about the physical examination are included in this section after the clinical interview is described.

During the clinical interview, the clinician should gather detailed information about the PGAD/GPD symptoms (e.g., arousal, orgasm), such as their location/s, intensity, pattern, and onset. Additional questions on any triggers, alleviators, and past and current treatment or management strategies should also be asked. Importantly, the impact of the symptoms on one's overall quality of life, including their work, family, social, and sexual activities, should be documented [1]. Mood, distress, and suicide ideation should be carefully assessed, and if the patient needs immediate support for their mental health, access to appropriate providers should be offered. Medical history, including any comorbid genitopelvic or other conditions (e.g., medical, psychiatric), as well as trauma history, should be documented. All medications and any medical or other interventions undertaken for any health-related complaints, including PGAD/GPD, should also be carefully documented [1].

The physical assessment includes conducting a comprehensive physical examination, which may take one or several appointments. Conceptualizing pathologies in patients with PGAD/GPD that could occur in five distinct body regions has been found useful in developing a systematic approach for the examination [1]. Since the presumptive pathophysiology of PGAD/GPD is sensory hyperactivity, the purpose of the comprehensive physical assessment is to assist the clinician in localizing the origin of the trigger(s) of this hyperactivity. This will enable the clinician to perform appropriate differential diagnoses and thereby rationale-based treatment(s) of patients with PGAD/GPD.

Region 1 Region 1 end organ pathologies involve the clitoris, vestibule, vestibular bulbs, vagina, cervix, Bartholin's glands, the glans penis, penile shaft, scrotum, prostate, epididymis/vas deferens, urethra, prostate, urinary bladder, rectum, and/or umbilicus [1]. For patients with clitoral pathologies, physical examination may generate the following findings: clitoral phimosis using vulvoscopy, keratin "pearls"

associated with balanitis from clitoral adhesions, vulvar dermatoses, inability to fully retract the prepuce, and inability to visualize clitoral corona [1]. On physical examination, patients with vaginal pathology may show erythema, induration, tenderness of vestibule and vaginal mucosa, leukorrhea, or cervicitis. Additional Region 1 pathologies are lichen sclerosus, lichen planus, vulvar inflammatory conditions (e.g., candidiasis), desquamative inflammatory vaginosis, GSM, and/or neuropathies of sensory branches of the pudendal nerve (e.g., dorsal nerve, perineal nerve, inferior hemorrhoidal nerve), and/or sensory branches of the pelvic nerve (e.g., clitoris, vestibule, vagina, cervix, and/or prostate) [1]. For patients with female genital anatomy who have other end organ pathologies, please see Goldstein et al. [1]. Examples of Region 1 pathologies in patients with male genital anatomy are genital dermatoses, balanitis secondary to phimosis, penile/scrotal inflammatory conditions, candidiasis, and sensory neuropathies of the branches of the pudendal and pelvic nerves [1].

Region 2 Region 2 pathology involves skin dysesthesia overlying the perineum and perianal area and/or high tone pelvic floor muscle dysfunction. This latter condition in patients with female genital anatomy is suspected if palpation of the pelvic floor musculature is reported by the patient as feeling tender or painful, specifically at the 4, 6, and 8 o'clock positions of the introitus and/or of trigger points within the deeper muscles of the pelvis [1]. In such cases, a pelvic floor physical therapist should be involved to manage the pelvic floor dysfunction. Region 2 pathology may also result from direct injury to the pudendal nerve, which courses through the pelvis in proximity to the bony pelvic structures (i.e., ischial spine, ischial tuberosity, ischiopubic ramus). It can be injured by trauma with or without entrapment resulting from bicycle/motorcycle riding, from childbirth, or from bony spicules resulting from pelvic fracture. This possible involvement of pudendal nerve can be assessed if the symptoms are attenuated or blocked by injection of local anesthetic at the ischial spine near the pudendal nerve entry into the pelvis, or medial to the ischial tuberosity, or at Alcock's canal, where the pudendal nerve divides into its three branches. Region 2 may also involve pelvic nerve neuropathology resulting in internal pressure/distension dysesthesia following radical cancer surgery of the bladder (cystectomy) or uterus (hysterectomy) and/or following intense pelvic radiation therapy. Additional Region 2 pathologies may include pelvic arteriovenous malformation and/or pelvic congestion syndrome. These can be accessed via pelvic radiologic imaging (e.g., internal pudendal arteriography).

Hormone Blood Testing (Regions 1 and 2) In patients with PGAD/GPD, hormone blood testing should be considered. Specifically, patients with PGAD/GPD and a history of combined hormonal contraceptive use should have their androgen status evaluated for hormonally mediated vestibulodynia as a potential trigger [1]. Menopausal patients typically have low testosterone and low estradiol, as GSM is a potential contributor to PGAD/GPD. In addition, as hyperthyroidism is a recognized contributor to premature ejaculation, it could be considered an excitatory condition similar to PGAD/GPD. Thus, in patients with PGAD/GPD, the following

laboratory tests should be considered: testosterone, free testosterone, sex hormone binding globulin, estradiol, and thyroid stimulating hormone.

Neurogenital Testing (Regions 1 and 2) In patients with PGAD/GPD, neurogenital testing should be considered [1]. Assessment of afferent pudendal nerve integrity involves determining vibration (A-beta), cold (A-delta), and warm/hot (c-fiber) sensory thresholds in the genitals compared to a non-genital control location (pulp of index finger). Assessment of afferent sciatic nerve integrity involves determining vibration thresholds in buttocks, posterior thigh, posterior calf, and feet compared to a non-sciatic control location (pulp of index finger). Bulbocavernosus reflex latency is subsequently determined. If both afferent pudendal nerve testing and bulbocavernosus reflex latency are abnormal, but afferent sciatic nerve testing response is normal, this suggests that the PGAD/GPD symptoms (e.g., clitorodynia, vestibulodynia, pudendal neuralgia) are associated with neuropathy (i.e., of the pudendal nerve dorsal branch, perineal branch, and pudendal nerve proper, respectively) located in Regions 1 and 2. Neurogenital testing is also applicable to diagnosis of Regions 3–5 pathology (see below).

End Organ Anesthesia Testing (Regions 1 and 2) Local anesthetization of the end organ (i.e., clitoris, vulva, and/or vestibule, penis and/or scrotum) or the pudendal nerve can help localize the pathology of PGAD/GPD to Regions 1 and 2. If this procedure temporarily results in clinically significant reduction of the PGAD/GPD symptoms, then the suspected location of the trigger of the symptoms can be considered to be located in Region 1 and/or Region 2. Thus, appropriate management of the end organ/pelvis/perineum pathology may help to alleviate PGAD/GPD symptoms. However, if in the seemingly paradoxical case in which local anesthetization of the end organ produces numbness to tactile stimulation, but at the same time, the bothersome dysesthesia (e.g., pain, itching) persists, then a more proximal ("farther upstream") trigger for the symptoms is probable.

Region 3 PGAD/GPD can result from sacral radiculopathy indicative of pathology in the cauda equina. Sacral radiculopathy is suspected if the following criteria are met: a) PGAD/GPD triggers in Regions 1 and 2 are ruled out, typically by a local anesthesia test that does not eliminate the PGAD/GPD symptoms; b) Neurogenital testing shows abnormal pudendal and sacral nerve responses and a prolonged bulbocavernosus reflex response; c) A lumbosacral MRI demonstrates pathology of the cauda equina, e.g., Tarlov cyst and/or herniated intervertebral disc(s) due to annular tear, typically at L4-5 and/or L5-S1. Since physical examination cannot occur of the cauda equina, it is important to recognize and emphasize the nature of the lesions causing the sacral radiculopathy. Sacral Tarlov cysts contain aberrant pudendal and/or pelvic sensory nerve root fibers, and their occurrence is highly correlated with PGAD/GPD symptoms [17]. Annular tears, particularly at the lumbosacral level, are a second type of pathology highly correlated with the symptoms [1]. A tear in the annulus fibrosus of the disc(s), particularly at the L4-5 and L5-S1 levels, allows the nucleus pulposus of the disc to be extruded, which can physically and chemi-

cally irritate and inflame the dura mater and adjacent genital sensory nerve roots of the cauda equina.

Suspected sacral radiculopathy is confirmed by administering an anesthetic (e.g., lidocaine) either via Trans-Foraminal Epidural Spinal Injection (TFESI) or caudal epidural. This diagnostic injection is administered at the suspected vertebral level indicated by the MRI. Anesthetic spinal injections are associated with risks of epidural hematoma, infection, nerve root damage/sciatica, dural puncture leak/headache, vomiting, dizziness, leg weakness/numbness. A clinically significant reduction in any or all PGAD/GPD symptoms would confirm the role of the Tarlov cysts (caudal epidural) and/or one or more annular tears (TFESI) as the PGAD/GPD trigger.

Region 4 At present, we are aware of no case of PGAD/GPD that has been attributed to pathology of the spinal cord. We believe, though, that the diagnostic evaluation of Region 4 would be similar to that of Region 3 [1]. This would involve ruling out other triggers, having abnormal neurogenital test findings, and an abnormal MRI in the thoracic or cervical region. Pathology in Region 4 could emanate from the genitopelvic nerve roots of the cauda equina that synapse at the S2-4 levels of the spinal cord in the conus medullaris (which is typically located at lumbar vertebral levels L1-2), from which the spinothalamic tracts transmit the genitopelvic sensory activity to the brain. It is possible that injury could occur to the spinal cord at any level, from lumbar to cervical, that would compromise the integrity of these genitopelvic sensory pathways. Such injury could include annular tears, nucleus pulposus herniation, spinal stenosis, facet synovial cyst, and others. These possible pathologies could be assessed by lumbar, thoracic, and/or cervical MRI. Furthermore, since serotonin and norepinephrine neural pathways descend from the brainstem to the spinal cord and modulate aversive sensory activity (e.g., via the "pain-gate" mechanism), SSRI/SNRI administration or withdrawal could iatrogenically affect PGAD/GPD symptoms via their action on the spinal cord [1].

Region 5 Although PGAD/GPD inevitably involves the brain, there is little evidence that any *specific* brain pathology is the initiating factor, except perhaps in the case of epileptic seizure, which was reported to correlate temporally with PGAD/GPD symptoms [18]. However, extrinsic factors that affect brain function, such as withdrawal from SSRI/SNRI therapy, can certainly trigger the onset of PGAD/GPD symptoms [1]. While not necessarily a brain-generated "cause" of PGAD/GPD, the following types of brain-involving factors have been reported to be associated with the symptoms and/or therapies.

- *Psychological factors*: Stress, depression, anxiety, and loss have been reported as initial triggers of PGAD/GPD symptoms in some patients. Exacerbating psychological factors include hypervigilance and catastrophizing [1].
- *Pharmaco-therapeutic factors*: In addition to PGAD/GPD symptoms being triggered by SSRI/SNRI withdrawal, discontinuation of trazodone has been associated with clitoral and penile priapism (persistent genital engorgement). PGAD/

GPD symptoms have also been associated with initiation of treatment with certain CNS-active medications (e.g., lamotrigine) [1].

- *Organic brain pathologies*: These include traumatic brain injury, arteriovenous malformations (AVMs), aneurysms, and/or other space-occupying lesions, which can be assessed by MRI, electroencephalography, and magnetic electroencephalography. Procedures that directly modify brain activity have included electroconvulsive therapy and transcranial magnetic stimulation, with inconsistent efficacy.

4.6.2 Treatment

Psychosocial Treatment The primary roles of a mental health care provider in the management of PGAD/GPD are to help the client cope with and manage their PGAD/GPD symptoms, aid in reducing the amount of distress they are experiencing, and, if desired, assist with connecting the client to their sexuality. A cognitive-behavioral therapy (CBT) approach is recommended, given that CBT has been useful for the treatment of genitopelvic dysesthesias characterized by pain [15]. A CBT approach would initially involve providing patients with information about their symptoms, the effects of the symptoms on sexual and nonsexual activities, and the role of psychological factors in maintaining the symptoms. Among other strategies, patients would be encouraged to keep track of their symptoms and any factors that may increase or decrease them, to engage in relaxation and mindfulness strategies, and to engage in cognitive restricting exercises to reduce their tendency to catastrophize about their symptoms given that catastrophization has been associated with negative outcomes (e.g., symptom intensity) [15]. Partners of those with PGAD/GPD are also encouraged to attend sessions to educate and involve them in the process. Other patients may benefit from trauma-informed therapy if trauma is a significant part of their history and if other strategies are not suitable for the patient at that time, and if distress is the key presenting factor, then a CBT approach focused on reducing distress, increasing social support, and targeting other urgent priorities is recommended [1].

Region 1 Patients with PGAD/GPD symptoms associated with clitoral and/or penile pain may have balanitis and/or adhesions between the prepuce and glans [1]. Treatment of underlying balanitis can be accomplished with appropriate medical management. Should adhesions be identified, these may be released in an office setting under local anesthesia using microfine Jacobson mosquito forceps. Another strategy could be dorsal slit surgery. Patients with traumatic dorsal nerve neuropathy (e.g., straddle injury) may be managed by local anesthesia/steroid nerve blocks. For patients with vestibulodynia, the following strategies may be employed based on the underlying triggering pathology: physical therapy, hormonal therapy, derma-

tological therapy using ultra-potent corticosteroids, medical therapy with oral neuroleptics (e.g., gabapentin) and/or topical agents (e.g., capsaicin), and complete vestibulectomy if neuroproliferation is thought to be the main contributing factor.

Region 2 In patients with PGAD/GPD, pelvic floor physical therapy may improve daily activity by treating overactive/hypertonic pelvic floor dysfunction and pudendal neuropathy [1]. Treatment consists of a combination of education, manual therapy, therapeutic exercises, and neuromuscular re-education. Symptom triggers include specific activities, positions, and movements (e.g., squatting, sitting), which can be modified/paced to reduce the severity of the dysesthesia. In addition, iatrogenic kinesiophobia and hypervigilant behavior are potential risks.

Pudendal nerve block (without patient sedation) may attenuate the PGAD/GPD symptoms and, if effective, can be used in conjunction with long-lasting steroid injection (e.g., triamcinolone acetonide 80 mg) [1]. This treatment may also improve voiding dysfunction and reduce pelvic pain. Other therapies for consideration are pudendal nerve entrapment surgery to release the nerve compression, and pudendal neuromodulation.

In patients suspected of having PGAD/GPD from pelvic congestion syndrome or pelvic arteriovenous malformation, referral to an interventional radiologist for diagnosis (i.e., pelvic MRI and selective venography/arteriography) and for treatment (i.e., embolization) [1].

Region 3 For patients with PGAD/GPD secondary to a lumbosacral annular tear, minimally invasive LESS (Lumbar Endoscopic Spine Surgery) procedure is optimal. During LESS, the extruded nucleus pulposus is morcellated via laser and removed by suction. For patients with PGAD/GPD secondary to a Tarlov Cyst, surgery involves laminectomy, draining, and imbricating the cyst(s) [1].

Region 4 If diagnostic procedures based on MRI and TFESI indicate pathology such as annular tear, the LESS procedure may be applied. In preliminary findings, administration of morphine to the conus medullaris has attenuated PGAD/GPD symptoms temporarily, suggesting that chronic dorsal root electrical stimulation may be indicated. In some cases of vertebral degenerative disc disease, however, the risk of surgical complications may be considered greater than the possible benefit [14].

Region 5 There are no medications approved for the treatment of PGAD/GPD. Off-label treatments that have shown inconsistent efficacy include varenicline, zolpidem, clonazepam, gabapentin, pregabalin, oxcarbazepine, topiramate, tramadol, hydrocodone, duloxetine, paroxetine, nortriptyline, amitriptyline, clomipramine, methocarbamol, cyclobenzaprine, baclofen, diazepam suppositories, and/or botulinum neurotoxin [1].

4.7 Conclusion

PGAD/GPD presents as a variable combination of abnormal sensations (dysesthesias: e.g., itching, burning, pain, "arousal") perceived as emanating from the clitoris/penis, vulva/scrotum, vestibule, vagina, urinary bladder, urethra, rectum, pelvic floor, buttocks, feet, legs, and/or lower back. In some cases, the condition results from pathology that is evident in the peripheral organs. However, many cases of PGAD/GPD are resistant to, and persist after, locally applied surgical, hormonal, and/or topical anesthetic therapy. In many of the persistent cases, pathology is found to originate in the pudendal, pelvic, and/or sciatic nerve roots, which originate in common at the S2 and S3 sacral foramina, where they join the cauda equina. There, they are subject to mechanical and/or chemical irritation, i.e., Tarlov cysts and/or herniated (annular tear) lumbosacral intervertebral discs. Thus, the PGAD/GPD sensations are perceived by the patient as emanating from the genitopelvic region, but are, in fact, due to radiculopathy remote from the perceived source. Psychosocial factors (e.g., depression, catastrophization) and iatrogenic factors (e.g., initiation or termination of anti-depression medication) can also initiate and/or exacerbate PGAD/GPD symptoms. Comprehensive biopsychosocial evaluation is recommended to optimize effective treatment of this complex condition.

Key Messages

- Because PGAD/GPD is relatively unknown by most health care providers, and because of the assumption that genital arousal experiences are pleasurable, PGAD/GPD is often misdiagnosed or undiagnosed.
- PGAD/GPD can affect up to 4.3% of the adult population, and it affects people of all gender identities even though most of the research focuses on women.
- A biopsychosocial, multidisciplinary approach is essential to the successful management of PGAD/GPD, and this process is complex, involving the careful and comprehensive assessment of symptomatology, and psychosocial, medical, and biological factors.
- Based on recent evidence, regional diagnostic and treatment approach to PGAD/GPD is suggested. This involves examining end organ pathologies (Region 1), pelvis/perineum pathologies (Region 2), pathologies affecting the lumbosacral region of the cauda equina (Region 3), pathologies affecting the spinal cord (Region 4), and factors affecting brain function and activity (Region 5).
- A multidisciplinary approach in the assessment, diagnosis, and treatment of PGAD/GPD is recommended.

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