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Persistent genital arousal disorder – the present knowledge

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Summary

Persistent genital arousal disorder (PGAD) is a relatively recently described sexual disorder, characterized by symptoms of spontaneous genital arousal which persist in the absence of sexual desire and may affect women and men. Epidemiological studies conducted so far indicate that the prevalence of PGAD in the population may reach 1–4%. The etiology of PGAD remains unclear and complex, hypothesized causes include vascular, neurological, hormonal, psychological, pharmacologic, dietary, mechanical factors or a combination of these factors. Proposed methods of treatment include pharmacotherapy, psychotherapy, electroconvulsive therapy, hypnotherapy, injection of botulinum toxin, pelvic floor physical therapy, application of anesthetizing agents, reduction of identifiable factors exacerbating the symptoms, and transcutaneous electrical nerve stimulation. There is no standardized treatment algorithm for PGAD due to lack of clinical trials (evidence-based medicine). The classification of PGAD is under discussion: it could be classified as a separate sexual disorder, a subtype of vulvodynia or a disorder with pathogenesis similar to overactive bladder (OAB) and restless legs syndrome (RLS). Due to specificity of symptoms, patients may feel shame and discomfort during the examination or even delay reporting symptoms to the specialist. Thus, it is crucial to spread knowledge about this disorder, which would allow doctors to diagnose and help PGAD patients sooner.

Key words: persistent genital arousal disorder, restless genital syndrome, restless legs syndrome

Introduction

First cases of persistent genital arousal disorder (PGAD) were reported by S.R. Leiblum and S.G. Nathan in 2001 [1]. The study included descriptions of five patients who presented similar symptoms defined as "spontaneous, intrusive and unwanted genital arousal (pulsation, swelling, tingling) in the absence of subjective sexual

desire and sexual fantasies" [2, p. 229]. Due to the fact that PGAD is a relatively new and poorly understood condition, it has not yet been included in the ICD-10 or DSM-V classification and both its treatment and etiology remain unclear. Initially it was suspected that PGAD affects only women, however, in the following years, first descriptions of similar symptoms among men appeared [3–6].

The following diagnostic criteria for PGAD were proposed in 2010 [7]:

1. Presence of physiological symptoms of sexual arousal (for example, congestion, tingling, throbbing, genital tactile sensitivity) that persist for hours, days or months.
2. Genital arousal is unrelieved by orgasm.
3. Genital arousal is not accompanied by sexual interest and desire.
4. Genital arousal is unwanted and intrusive.
5. Persistent genital arousal causes anxiety.

Pukall et al. [8] noticed that genital pain is a frequent symptom accompanying PGAD and proposed classification of genitopelvic dysesthesias, including subcategories of unpleasant sensations based on patients' main complaint: arousal, arousal and pain, or pain, which could be helpful in choosing proper treatment depending on the prevailing symptom. PGAD patients used terms such as "throbbing" or "itching" to describe their symptoms. These expressions are also used to describe pain, for example, in the McGill Pain Questionnaire (MPQ) [9], which emphasizes the complex connection between pain and arousal, as well as the necessity of having a detailed medical history of a patient for a thorough understanding of their condition.

It should also be noted that PGAD is not the same as hypersexuality. Unlike hypersexuality, PGAD is not accompanied by intrusive, recurrent sexual thoughts and fantasies. The feeling of genital arousal occurs despite the lack of sexual desire and people suffering from PGAD seek relief from sexual intercourse and masturbation in order to get rid of unwanted tension, not for pleasure and sensual experience.

This article reviews the literature on PGAD in order to systematize knowledge about this little-known disorder. A review of sources from 2001 to 2020 archived in, e.g., Pubmed and Researchgate was conducted, using key words.

Epidemiology

The exact prevalence of PGAD has not been precisely established. In 2009, Garvey et al. [10] conducted a survey among 96 women attending a sexual health clinic. 33.3% of patients presented one symptom of PGAD, in 2% of women four symptoms of PGAD were found, while one woman met all diagnostic criteria of PGAD. An interesting phenomenon observed during this study was a large percentage of woman (33.3%) experiencing spontaneous genital arousal in the absence of sexual desire, however, this feeling was not persistent and not as bothersome as in PGAD.

Another research aimed at determining the prevalence of PGAD was conducted by Dèttore and Pagnini [11] in 2020 on a group of 679 students. 11 of them (1.62%)

met all 5 PGAD diagnostic criteria. Furthermore, 109 women (16.05%) reported spontaneous genital arousal in the absence of sexual desire or fantasies, 63 women (9.28%) reported that genital arousal lasted for hours or days and 39 women (5.74%) described these symptoms as unwanted and intrusive.

In the same year Jackowich and Pukall [12] examined two groups of people. One of them consisted of 1,634 Canadian students (1,267 women, 360 men and 7 non-binary individuals) and the second was a representative group consisting of 1,026 American citizens (514 women, 506 men and 6 non-binary individuals). 1.1% of men and 0.6% of women from the group of students met all criteria of PGAD diagnosis and described the severity of symptoms as moderate or high, along with 4.3% of men and 2.7% of women from the group of American citizens. The mean age of patients fulfilling all criteria of PGAD diagnosis was 38.06 years and ranged between 17 and 76 years, which may suggest that the prevalence of PGAD increases with age. However, it should be taken into consideration that the 1–4% prevalence resulting from the research may be understated. PGAD is associated with feelings of embarrassment and anxiety which may result in reluctance to reveal those symptoms both in the survey and during medical appointment.

Another – online – study involving 111 women suffering from PGAD disclosed that almost half of them searched for specialist's help after more than 6 months from the onset of their symptoms and 11.9% decided to do so after more than 10 years. In addition, 64.2% of patients felt discomfort when talking about their symptoms with a doctor and 54.2% of patients required consultations with 3 or more specialists [13], which may indicate that knowledge about PGAD is poorly spread. This may extend the diagnostic process or even discourage help-seeking among patients.

Etiology and comorbid conditions

Although there have been many hypotheses about etiology, the cause or causes of PGAD remain unclear. Current hypotheses include vascular changes, central or peripheral neurological damage, Tarlov cysts, psychological, pharmacological, dietary, and hormonal factors, disturbances in neurotransmission, mechanical pressure against genital structures or combinations of above [14].

In 2009, Waldinger et al. [15] examined 19 women with PGAD, performing routine and hormonal laboratory testing, electroencephalography (EEG) and magnetic resonance imaging (MRI) scan examination of the brain and pelvis. Additionally, transvaginal ultrasound (TVUS) and MRI with contrast were performed in patients with MRI abnormalities. Routine blood and hormonal tests as well as EEG did not reveal any significant changes and no abnormalities were found in MRI brain scans, apart from a pericallosal aneurysm (diagnosed previously) in one woman and postoperative findings of meningioma surgery in another woman. MRI of the pelvis implied presence of pelvic varices in 55% of the examined women, which was confirmed by TVUS in 9 patients. In three of these nine patients, an additional MRI with contrast

was performed and revealed mild to moderate dilation of ovarian veins. In addition, 7 women (39%) had varices of one or both lower limbs, of which 5 had underwent variceal surgery before developing PGAD symptoms. Comparing the prevalence of pelvic varices among the examined women (55%) with the prevalence among the general population (9.9%), it seems likely that they may play a role in the pathogenesis of PGAD. According to the authors of the cited article, the verification of this hypothesis requires further research involving a larger group of people.

Waldinger and Schweitzer [16] also showed that PGAD often coexists with restless legs syndrome (RLS) and overactive bladder (OAB) – out of 18 examined women, 67% had symptoms of both RLS and OAB. The prevalence of RLS (67%) among examined patients with PGAD is much higher than the prevalence of RLS (3–19%) in the general population [17], which may suggest an association between these conditions. Moreover, some women confirmed that severity of PGAD symptoms is related to body movements – sitting position exacerbated PGAD symptoms in 72% of female patients, which is also the case in RLS [18]. A common pathogenesis for these conditions has been suggested and an analogical name has been proposed for symptoms of genital arousal – restless genital syndrome (RGS). Other authors came to similar conclusions, observing comorbidity of PGAD and RLS [19]. 30 (26.1%) out of 115 female patients with PGAD reported symptoms of RLS, furthermore 42 (36.5%) women were diagnosed with irritable bowel syndrome (IBS), 22 (19.1%) women suffered from chronic pelvic pain and 21 (18.3%) women complained of chronic constipation.

The results of another study conducted by Waldinger et al. [20] suggested that sensory neuropathy of the pudendal nerve and the dorsal nerve of the clitoris (DNC) may play a role in the etiology of PGAD. In all 23 examined women, sensory testing disclosed hyperesthesia in the dermatome area of the pudendal nerve and the DNC. Moreover, the possible role of pelvic varices in the pathogenesis of PGAD was pointed out once again – MRI revealed pelvic varices in the vagina, labia minora and/or majora and uterus respectively in 21 (91%), 8 (35%) and 7 (30%) women. The possible role of small fiber sensory neuropathy (SFSN) in the etiology of PGAD is also indicated by the case of a woman in whom clitoridectomy did not eliminate the primary symptoms [21].

In 2009, Filler [22] described the methods of treating patients with entrapment of the pudendal nerve, some of whose clinical pictures contained symptoms we may associate with PGAD. This suggests the pudendal nerve entrapment as another possible source of PGAD. On the other hand, Anzellotti et al. [23] suggested a central mechanism of developing PGAD – they noticed increased functional connectivity (FC) between different brain areas such as left middle frontal gyrus, left inferior and superior temporal gyrus and left inferior parietal lobe, in a patient presenting symptoms of PGAD. Additionally, an epileptic focus was found remaining in FC with above mentioned regions. After the administration of the antiepileptic drug, PGAD symptoms disappeared in this patient. A central mechanism of developing PGAD may also be indicated by the fact that in one of female patients, symptoms worsened significantly during sleep [24]. In healthy people, sexual arousal during REM sleep occurs regard-

less of whether dreams have sexual content [25], but it usually disappears after a few minutes. Perhaps some dysfunction of the locus coeruleus, involved in the regulation of REM sleep, has a significant role in the pathogenesis of PGAD.

In 2017, Komisaruk and Lee [26], during the lumbosacral MRI examination, found that out of 18 women suffering from PGAD, 12 (66.7%) had Tarlov cysts. In addition, two PGAD patients were diagnosed with multiple disc herniations impinging on the cauda equina. After successful treatment of the herniated discs, the symptoms of PGAD disappeared. Feigenbaum and Boone [27] also discussed the role of Tarlov cysts in pathogenesis of PGAD and examined 11 female patients with symptoms of PGAD and Tarlov cysts. In 91% of patients, PGAD symptoms resolved completely or partially after surgical removal of the cysts.

Meanwhile, Leiblum and Chivers [28] proposed a psychological mechanism of female body's response to symptoms of PGAD, according to which anxiety would intensify the perception of genital arousal as intrusive and unwanted by increasing autonomic nervous system activity and narrowing attention to genital sensations [28]. Researchers also noted a higher coexistence of anxiety disorders (27.6%) and obsessive-compulsive behaviors (15.8%) with PGAD, which may suggest a helpful role for antidepressants and anxiolytics in the treatment of this disorder.

In the previously cited Waldinger's study from 2009 [16], it was also observed that the manifestation of PGAD symptoms often occurs after menopause, before menstruation or during pregnancy, which may indicate the role of significant changes in hormone levels in the etiology of PGAD. Due to the beneficial effect of clonazepam, oxazepam and tramadol in the reduction of PGAD symptoms, another hypothesis on the role of GABA and μ-opioid receptors in PGAD etiology was proposed.

Under consideration there is also involvement of pharmacological factors, such as selective serotonin reuptake inhibitors (SSRI), serotonin-norepinephrine reuptake inhibitors (SNRI) [29, 30] and even increase in atrial natriuretic peptide (ANP) following SSRI discontinuation [31]. Along with the SSRI discontinuation, the activity of serotonin reuptake is restored which combined with desensitization and a decrease in the density of serotonin transporters may lead to serotonin deficiency [32]. Serotonin is a central mediator that inhibits the sexual response, while dopamine stimulates this response [33]. PGAD may thus result from an imbalance between neurotransmitters that inhibit and stimulate the sexual response.

Other described cases included a woman with PGAD symptoms associated with excessive consumption of soy [34] or patients who reported that the symptoms of PGAD appeared for the first time or were aggravated by mechanical pressure on the genitals, e.g., when driving a car or bicycle [30, 35].

Psychosocial functioning and sexual life of PGAD patients

In 2005 a survey was conducted including 103 female patients meeting one or more diagnostic criteria for PGAD [35]. In this study Female Sexual Function Index (FSFI)

was used along with a questionnaire consisting of 46 questions about basic information (such as age, marital status, educational level), health history and menopausal status, details about PGAD complaints (such as onset of symptoms, factors that exacerbate and alleviate symptoms), anxiety and fear resulting from the symptoms, treatment interventions and their results, as well as an open-ended question in which patients could clarify and describe their symptoms. Obtained data showed that the occurrence of PGAD was associated with distress, anxiety and depressive mood. Moreover, patients suffering from PGAD complained of feelings in regard to their symptoms such as distraction (75.73%), frustration (65.05%), anxiety (51.46%), and embarrassment (50.49%). Using the FSFI scale, patients mostly reported moderate levels of sexual satisfaction, while having a sexual partner contributed to reduced suffering resulting from PGAD.

In some cases, however, persistent genital arousal was not associated with explicitly negative emotions – in 2002, Leiblum and Nathan [36] described a female patient who led a satisfactory sexual life due to constant arousal, had multiple intercourses daily and had sexual relations with over 400 different male partners.

In 2013, Carvalho et al. [37], using the Sexual Dysfunctional Beliefs Questionnaire (SBDQ) and the Sexual Modes Questionnaire (SMQ), analyzed responses of 43 female patients with PGAD symptoms concerning their beliefs about sex and their sex life. They showed that, compared to the control group, these patients more often present conservative views on sex and dysfunctional sexual beliefs, such as perceiving sexual desire as a sin. Moreover, thoughts about sexual abuse and feeling of lack of partner's affection were more common during sexual activity. Sexual thoughts and fantasies occurred much less frequently than in women without PGAD symptoms. In this study the Positive and Negative Affect Schedule questionnaire was also used, which disclosed that patients with PGAD presented significantly more negative affect during sexual activity compared to women without PGAD symptoms.

In 2019, Jackowich et al. [38] analyzed the impact of PGAD on psychosocial functioning and sexual life of 72 female patients over 18 years of age (mean age 45.42 years) using the following scales: Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventory (BAI), Pain Catastrophizing Scale (PCS), Female Sexual Distress Scale (FSDS), Relationship Assessment Scale (RAS), and FSFI. Compared to the control group, PGAD patients reported significantly more depressive and anxiety symptoms. Moreover, more than twice as many women in the PGAD group (54.2%) reported suicidal thoughts as in the control group (25.0%). Slightly more patients declared that their depressive and anxiety symptoms started before the PGAD onset (40.3% and 48.6%, respectively) and in 30.6% and 34.7%, respectively, they were observed later. Patients with PGAD also reported lower relationship satisfaction, compared to the control group. Data on sexual satisfaction remained incomplete as many women with PGAD did not answer all questions about sexual functioning. 18.1% of patients reported that they had not participated in any sexual activity in the previous 4 weeks, which is a high proportion compared to 8.3% of the control group. From the answer to

the open question: "How has PGAD influenced your sexual life?" it could be concluded that some of the patients increased their sexual activity to cope with the symptoms, but for some it led to an extremely opposite situation – avoiding sexual contact because of fear of inducing symptoms (e.g., "I cannot engage in any sexual activity without suffering dire consequences"; "PGAD has made me not want sex at all because sex only worsens PGAD symptoms"; "I'm too afraid of sex"). PGAD can negatively affect relationship [39] including causing guilt in patient's partner ("I am not enough for her") and provoking conflicts or exacerbating existing ones.

A study conducted in 2018 involving three groups of women – patients with PGAD, painful PGAD and vulvodynia [40] – showed that women with symptoms of genital arousal reported a significantly greater feeling of helplessness than patients suffering from vulvodynia. In patients with painful PGAD, their ailments were found to have a significantly greater impact on work performance than in the group of patients with vulvodynia. In addition, the FSQ (Functional Status Questionnaire) was used to assess the impact of disorders on activities of daily living, such as housework or driving. The greatest difficulties were reported by patients with painful PGAD.

Treatments for PGAD

Attempts to treat PGAD include reduction of identifiable factors exacerbating the symptoms, application of anesthetizing agents to numb the area, cognitive behavioral therapy (CBT) and mindfulness techniques (MBCT) [41], hypnotherapy [42], pelvic floor physical therapy [43], pharmacotherapy (e.g., mood stabilizing, anti-seizure medications, SNRI) [44–50], injection of Botulinum toxin [51], electroconvulsive therapy (ECT) [52, 53], variceal embolization [54], and transcutaneous electrical nerve stimulation. Due to the fact that PGAD is still a poorly understood disorder, there are no clinical trials testing the safety and effectiveness of proposed treatments, neither is there a recommended treatment algorithm.

Treatments with descriptions of the effects and the characteristics of patients are presented in Table 1 and 2.

Table 1. **Treatment methods and their effectiveness, selected clinical data for men**

Treatment	Treatment outcome	Proposed etiology/ circumstances of symptoms	Age	Medical history	Duration of symptoms	Clinical picture
Pregabalin 50 mg/d; diazepam 20 mg/d [3]	symptoms reduced in intensity	onset of symptoms after watching pornography, anxiety associated with this event	54	vasectomy 4 years earlier with minor complication of painful scrotum, UTI in the past	2 years	genital arousal increased in intensity and without sexual stimuli 2-3 times a day, temporary relief with an orgasm
Pramipexole 0.5 mg/d; gabapentin 600 mg/d [4]	resolution of symptoms	unknown	45	scrotal trauma 5 years earlier while playing sport, mother with RLS symptoms	2 years	genital arousal increased in intensity during night (tingling, pain), walking and low temperature ameliorated the symptoms, temporary relief with an orgasm
Transcutaneous electrical nerve stimulation (TENS) [5]	no resolution of symptoms (38-year-old patient) 90% reduction of symptoms (74-year-old patient)	small fiber sensory neuropathy (SFSN)	38, 74	sterilization at the age of 36, OAB (38-year-old patient); laparoscopic radical prostatectomy at the age of 73, varicocele around the spermatic cord, OAB (74-year-old patient)	4 years (38-year-old patient) unknown (patient 74-year-old)	genital arousal and spontaneous ejaculations, symptoms aggravated during resting, defecation, micturition, in a cold environment (38-year-old patient); genital arousal of being on the edge of an orgasm triggered by sitting, tingling in the absence of erection and ejaculation, temporary relief with an orgasm, symptoms reoccurred in a short time after orgasm (74-year-old patient)
Sertraline 100 mg/d; Clonazepam 0.5 mg/d [6]	resolution of symptoms	unknown	38	unknown	unknown	genital arousal, tingling, stinging, persistent feeling of impending ejaculation, temporary relief with an orgasm

Table 2. **Treatment methods and their effectiveness, selected clinical data for women**

Treatment	Treatment outcome	Proposed etiology/ circumstances of symptoms	Age	Medical history	Duration of symptoms	Clinical picture
psychotherapy [1]	no resolution of symptoms, but a patient (36-year-old) developed better awareness about situations which aggravated symptoms; no resolution of symptoms (61-year-old patient)	psychological (36-year-old patient); psychological (61-year-old patient), additionally obsessive-compulsive methods of coping with stressful situations	36, 61	unknown	7 years (36-year-old patient); 11 years (61-year-old patient)	genital arousal, anxiety and nervousness preventing from sleeping, relief with 6–11 orgasms (36-year-old patient); 61-year-old patient: additionally congested and sensitive breasts
Self-treatment attempts, including modification of the diet [1]	symptoms not fully remitted	onset of symptoms after hysterectomy	81	hysterectomy 6 years earlier	6 years	genital arousal preventing from daily functioning, aggravated at night, at first relief with an orgasm
topical application of lidocaine [1]	resolution of symptoms	unknown	38	unknown	2 years	genital arousal with remissions and relapses, symptoms aggravated by tight clothes, no relief after masturbation or intercourse (pain)
Clonazepam 0.5–1.5 mg/d or tramadol 50 mg/d [16]	20–90% reduction of symptoms, in 3 patients no resolution of symptoms, 60–100% reduction of symptoms after tramadol	among 18 examined women one of them had symptoms after SSRI discontinuation, one of them developed symptoms after smoking marijuana for the first time and one of them experienced symptoms during withdrawal of medical marijuana	30–70	depressive disorder (1), anorexia nervosa (1), burnout syndrome (1), alcohol abuse (1), adjustment disorder (1), hysterectomy (3), sexual abuse in the past (3) epilepsy (1), ectopic pregnancy in the past (1)	0.2–26 years	genital arousal at the clitoris, vagina and labia respectively in 14 (78%), 10 (55%) and 5 (28%) women; 8 (44%) women reported a combination of these localizations; severe and to very severe symptoms occurring during the day, time-varying symptoms

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Risperidone 2 mg/d [24]	symptoms reduced in intensity	arousal aggravated by initiation of sleep – possible central activation	66	unknown	5 years	genital arousal worsened during initiation of sleep, in resting position, temporary (2–3 minutes) relief with an orgasm
Dietary modification [34]	resolution of symptoms	excessive consumption of soy (>4 lb/d) one month before onset of symptoms, possible impact of fitoestrogens	44	uterine leiomyomas	unknown	pressure in the genitals, need for self-stimulation to orgasm 15 times a day
Hypnotherapy [42]	symptoms not fully remitted but treatment resulted in better quality of life and better 'control' over symptoms	increased dosage of pramipexole	71	Parkinson's disease	3 years	genital arousal aggravated at night, vaginal wetness and engorgement, temporary relief (few minutes) after intercourse
Pelvic floor therapy [43]	resolution of symptoms	onset of symptoms around 18th week of pregnancy, pelvic floor hypertonus	27	unknown	2 months	genital arousal aggravated by standing, temporary relief with an orgasm
Venlafaxine 150 mg/d sertraline 200 mg/d alprazolam 1 mg/d escitalopram 10 mg/d doxepin 100 mg/d systemic and cognitive behavioral psychotherapy (CBT) [44]	no resolution of symptoms after pharmacological treatment, symptoms reduced in intensity after psychotherapy	onset of symptoms after first intercourse	40	for 2 years "feeling of incomplete bladder emptying", tension-type headaches, personality disorder with a tendency toward anxiety and depression, history of alcohol abuse	21 years	genital arousal accompanied by itchiness, irritability and burning sensations, no resolution by orgasm, variable severity of symptoms; occasionally sleep disturbances and decreased concentration

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Quetiapine 100 mg/d; later olanzapine 5 mg/d [45]	resolution of symptoms	onset of symptoms 3 days after the initiation of zolpidem (10mg/d)	55	insomnia	7 days	genital arousal, genital fullness, throbbing, tingling without relief after orgasm
Ropinirole 1.5 mg/d [46]	resolution of symptoms	unknown	44	none	11 years	genital arousal, needle-like sensations extending to the anal area and coccyx, worsening during night and resting
Olanzapine 5 mg/d fluoxetine 60 mg/d CBT [47]	symptoms reduced in intensity	psychological background: borderline personality disorder (BPD), suicide attempts	35	two psychiatric hospitalizations with no effect, BPD, RLS, abundant venous plexus in the labia majora	15 years	long-lasting tension in the clitoris which appeared every two weeks and lasted for several days
Clomipramine 75 mg/d [48]	resolution of symptoms after 2 years	in 52-year-old patient onset of symptoms after menopause; other patients – unknown	26, 50, 52, 70	bipolar affective disorder (BPAD) (26-year-old patient), depressive symptoms (50-year-old and 52-year-old patients), mother with PGAD symptoms (52 y-old patient), depressive symptoms and NES (70-year-old patient)	1–45 years	constant genital arousal (26-year-old patient), other patients with genital arousal 1–5 times a day and spontaneous orgasms
Clomipramine 112.5 mg/d [48]	resolution of symptoms after 2 years	unknown	61	depressive symptoms, non-epileptic seizures (NES)	4 years	constant genital arousal, erotic dreams over the preceding 6 months

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Clomipramine 150 mg/d [48]	symptoms decreased to one spontaneous orgasm daily (40-year-old patient); resolution of symptoms after 2 years (43-year-old patient)	unknown	40, 43	depressive symptoms (43-year-old patient), 40-year-old woman: additionally obsessive-compulsive symptoms	24 years (40-year-old patient) 2 years (43-year-old patient)	genital arousal, 5–15 spontaneous orgasms daily
Duloxetine 60 mg/d [49]	resolution of symptoms after 4 months	unknown	36	OAB symptoms	4 years	genital arousal (stabbing pain in the clitoris), genital enlargement, spontaneous orgasms at night disturbing sleep
Pregabalin 175 mg/d psychodynamic therapy [49]	symptoms reduced in intensity and returned in only mild form for a few days before menstruation or under psychological pressure	onset of symptoms after the initiation of treatment with amitriptyline	41	depressive symptoms, OAB symptoms	unknown	genital arousal perceived as almost painful, symptoms aggravated during masturbation, driving a car; temporary relief after intercourse and cold compresses
Varenicline [50]	resolution of symptoms	unknown	46	hysterectomy, sigmoidectomy and partial rectum resection, ductal carcinoma in situ	32 years	genital arousal and enlargement, temporary relief after intercourse
pericilitoral injection of Botulinum toxin [51]	symptoms reduced in intensity (23-year-old patient); resolution of symptoms (38-year-old patient)	unknown	23, 38	none	unknown	persistent genital arousal and feelings of imminent orgasm

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Electroconvulsive therapy (ECT) once every 5 weeks; valproic acid 250 mg/d paroxetine 10 mg/d [52]	after each ECT session symptoms reappeared after 4 weeks, necessity of repeating ECT	paroxetine discontinuation and initiation of lamotrigine	52	BPAD	3 years	genital arousal significantly impeding daily functioning, inability to reach orgasm
ECT once every week [52]	after each ECT session symptoms reappeared after 1 week, necessity of repeating ECT	lamotrigine and paroxetine discontinuation	58	BPAD, Tourette syndrome	6 months	genital arousal and sensitivity, inability to reach orgasm
ECT (30 in 4 years) [53]	resolution of symptoms after 4 years, at the beginning necessity of repeating ECT sessions	discontinuation of paroxetine and initiation of lamotrigine	52	BPAD, OAB symptoms	2 years	genital arousal, throbbing, tingling, genital engorgement, symptoms worsened during exposure to heat, driving, physical activity
Endovascular coil embolization of the ovarian vein [54]	70% reduction of symptoms	pelvic congestion syndrome	62	nocturia, asthma	5 months	genital arousal, exacerbated by sitting, walking and standing, partially relieved by lying down; significantly disturbing sleep

Recapitulation

Although Leiblum and Nathan [36] reported the first cases of PGAD in 2002, the knowledge of this disorder is still mainly based on case reports. There is still discussion whether PGAD, often coexisting with pain, is one of the subtypes of vulvodynia or a separate sexual dysfunction [55]. The following question also remains valid: does PGAD belong to a clinical cluster together with RLS and OAB? In the case of a positive response, it seems more reasonable to term this disorder as restless genital syndrome. Large-scale evaluations are needed to clearly establish the nature of these disorders, and thus to choose the appropriate treatment and monitor symptoms in the long term.

Undoubtedly, the knowledge about PGAD is still not disseminated among primary care physicians and specialists in various medical fields, including urologists, gynecologists, psychiatrists, and neurologists. The aforementioned data show that PGAD symptoms may affect even 1–4% of patients. Due to the specificity of the symptoms and distress associated with them, patients may delay reporting their problems to a doctor and feel discomfort and shame during the examination; therefore sharing information about PGAD is crucial, same as doctor's understanding and empathy during the medical appointment.

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