

Pramipexole with leuprolide: a treatment strategy for PGAD**Rajnish Raj^{1*}, Nisha Bhagat²**¹Department of Psychiatry,²Department of Obstetrics and Gynecology, Government Medical College, Patiala, Punjab, India**Received:** 01 May 2017**Accepted:** 27 May 2017***Correspondence to:**Dr. Rajnish Raj,
Email: dr rajnish_raj@yahoo.com**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.**ABSTRACT**

Persistent genital arousal disorder (PGAD) is described as the spontaneous, intrusive, and unwanted genital arousal in the absence of sexual interest and desire. Whether, its etiology is central or peripheral neurovascular in nature, it is still unclear. However, patient presents with symptoms of persistent engorgement of genital erectile and vascular tissue. The majority of women report PGAD as distressing. The symptoms usually occur in females in the age group 25-58 years especially in perimenopausal phase. The case is reported of PGAD in 19-year old female who was treated successfully with Pramipexole and Leuprolide.

Keywords: Impulse-control disorder not otherwise specific, Leuprolide, Non-paraphilic sexual addiction, Persistent genital arousal disorder, Restless genital syndrome

INTRODUCTION

Persistent genital arousal disorder (PGAD) is characterized by symptoms of physiological sexual arousal (i.e., genital vasocongestion, increased sensitivity of genitalias and nipples) in absence of feeling of subjective arousal.¹ These symptoms are described as intrusive, unpleasant; sometimes painful that result in great amount of distress and is associated with feeling of shame, isolation and suicidal ideation.² Although, it is a female syndrome but cases have also been reported in males.³ It was first described by Leiblum and Nathan, who proposed the following criteria:⁴

- Symptoms of physiologic sexual arousal (genital vasocongestion, increased sensitivity of genitalias and nipples with or without fullness or swelling)

that persist for hours or days and do not subside completely on their own (Physiological model).

- These symptoms do not resolve with ordinary orgasmic experience and may require multiple orgasms over hours or days to remit (Behavioral and adaptive model).
- Symptoms are usually experienced unrelated to any subjective sense of sexual excitement or desire (Psychological model; involuntary or unintentional production of symptoms).
- The persistent genital arousal can be triggered not only by sexual activation but also by non-sexual stimulus or by no apparent stimulus at all (Neurological model; trauma, arterio-venous malformation and drugs).

- Arousal symptoms are felt unbidden, intrusive, uninvited and unwanted (Psychiatric model of Obsession; ego-dystonic).
- The symptoms cause the woman at least moderate degree of distress (Self-Psychology model; Insight).

The words in square brackets have been added by authors after thorough deliberations and are recommended for delineating the phenomenological progression of logical thought in the development of scientific knowledge relating to sexual medicine.

Although, many etiological hypotheses have been proposed yet the exact cause of PGAD remains unknown. These etiological factors include meningeal and tarlov cyst, pharmacological drugs e.g., withdrawal of selective serotonin receptor inhibitors (SSRI), pramipexole and overactive bladder and soy diet.⁵⁻¹⁰

There is no standardized treatment algorithm for PGAD. However, various modalities include hypnotherapy, botulinum toxin injection, transcutaneous electrical nerve stimulation, electroconvulsive therapy, various oral medications like nicotinic receptor partial agonist (Varenicline), antidepressants like Fluoxetine, Paroxetine, Sertraline, Venlafaxine, atypical antipsychotics e.g., Olanzapine, Risperidone etc., antiepileptic drugs i.e., Carbamazepine, Valproic acid and sedatives. Deka et al, reported treatment of PGAD with Leuprolide.¹¹⁻¹⁷ The psychological intervention includes cognitive behavioral therapy (CBT) and mindfulness-based therapies (MBT).¹⁸⁻²⁰

The case of 19-year unmarried female is reported who suffered from PGAD and responded successfully to Pramipexole with Leuprolide.

CASE REPORT

A 19-year-old unmarried female reported to outdoor patient department (OPD) of Obstetrics and Gynecology, Government Medical College, Patiala with chief complaint of irresistible urge to have pelvic movement around her genitals that culminated to orgasmic release for the last 7 years. The activity started at the age of 12 years and gradually increased over time from one or two acts to 17 or 20 times. The time spent on this activity was more than 3 hours per day. She denied touching genitals manually or with objects. The pelvico-genital movement did not involve any erotic fantasy or preceding desire for sexual pleasure. She felt warmth inside her vagina with pulsations, tingling sensations, lubrication and sometimes discharge also. Whenever she tried to stop, she felt low on mood, irritable, lethargic, restless and distressed.

She attained menarche at the age of 13 years and had regular periods with menstrual flow for 3-4 days and cycle length of 28 days. She did not notice any accentuation or attenuation of her symptoms during the menstrual cycle. There was no history of any local

infection, drug intake i.e., selective serotonin reuptake inhibitor (SSRI) use or withdrawal, and neurological or endocrine dysfunction. Past history of medical disorder or mental illness was normal. She was first in birth order, full term normal vaginal delivery; breast fed and had normal milestones. During her childhood, she had age related role-play with peers and neither saw or touched nude body of same or opposite sex nor had any history of sexual abuse.

General physical and local examination was normal and secondary sexual characters were normally developed. Her haemogram, laboratory tests, hormone assays, which included estrogen, progesterone, follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin and testosterone, were within normal limits. Ultrasonography (USG) for pelvic organs, magnetic resonance imaging (MRI) and electroencephalography (EEG) of brain were within normal limits.

The patient was preoccupied with increased sexual sensations, feelings of guilt, shame, hopelessness and worthlessness. Therefore, the psychiatric consultation was sought for further evaluation and management. On mental state examination, she was conscious, well oriented to time, place and person. Eye-to-eye contact and rapport was established. Speech was normal, low on mood and affect was anxious. Thought process showed no circumstantialities but in thought contents there was compulsive- impulsive acts and the time spent was more than 3 hours per day that significantly interfered with her psycho-social functioning. Higher mental function, judgment, abstract thinking, insight to the illness were normal and reality contact was intact.

On ICD-10 the provisional diagnoses were predominantly compulsive acts F42.1; unspecified sexual dysfunction, not caused by organic disorder or disease (diagnostic code F52.9) and on DSM-IV TR sexual disorder not otherwise specified (302.9).^{21,22} However, authors preferred the diagnosis of impulse control disorder not otherwise specified (NOS) as they observed that compulsive behavior of the patient involved ritualistic acts contemplated in erotic thoughts whereas in OCD these compulsive ritualistic acts were an attempt to neutralize their sexual thoughts. Subsequently, to control for the bias of confounding with obsessive compulsive disorder (OCD); Y-BOCS scale was applied.²³ Obsession subtotal score was 4, compulsion subtotal score was 16 and Y-BOCS total score was 20, which revealed that compulsion was of moderate range. To ascertain the emotional aspect of the patient, she was screened for depressive and anxiety on Hospital Anxiety and Depression Scale-Anxiety (HADS-A) and Hospital Anxiety and Depression Scale-Depression (HADS-D) scales; clinical outcome on Clinical Global Impression-Severity Scale (CGI-S), which showed scores of 11, 15 and 6 respectively, indicating severe illness.^{24,25}

Initially, she was treated with Fluoxetine 20mg once daily for a week and then increased to 60 mg per day for the next week and Clonazepam 0.5mg twice daily for her compulsive acts. Y-BOCS total score, HADS-A, HADS-D and CGI-I scores were 19, 9, 13 and 4 respectively, which indicated no change. Fluoxetine was gradually tapered down and stopped. Pramipexole 0.25mg at night was started on 2nd week and then gradually titrated to 0.75mg in divided doses with Lignocaine gel for local application four times a day along with pelvic floor exercises and psychotherapy. Clonazepam was increased to 1.5mg per day in divided doses for the next 2 weeks. After 4 weeks, her Y-BOCS, HADS-A, HADS-D and Clinical Global Impression- Improvement Scale (CGI-I) scores were 17, 8, 7 and 3 respectively, indicating a marginal decrease in genital sensations as compared to baseline and response was less than 35%. So, injection Leuprolide 3.75mg (anti-androgen) was given subcutaneously after consultation with gynecologist. A few days after 1st Leuprolide injection, she reported decrease in sexual sensations. The adjunct Leuprolide was given from 4th week onwards and the regimen continued at an interval of one month for 5 months. Y-BOCS total, HADS-A, HADS-D and Clinical Global Impression- Improvement Scale (CGI-I) scores were 7, 6, 6 and 1 respectively, indicating very much improvement.

DISCUSSION

It is proposed that PGAD should be considered as Non-paraphilic sexual addiction (NPSA) and placed under the rubric of impulse control disorder NOS where there are “repetitive sexual acts involving conventional, normative, or non-deviant sexual thoughts or behavior that the person feels compelled or driven to perform, which may or may not cause distress.^{26,27} Paraphilic disorders are “recurrent, intense sexual arousing sexual urges or behavior that occurs over a period of at least six months” and nature of interest and arousal is not normophilic.²⁸ Paraphilic thoughts are ego-syntonic whereas OCD thoughts are ego-dystonic. In this case, patient had intrusive sexual fantasies or non-manual stimulation of genitals during the acts hence, a diagnosis of NPSA.

PGAD requires careful evaluation of sexual abuse, dietary factors like increased soy intake, initiation or discontinuation of medications that coincided with symptom onset i.e., antidepressants or dopaminergic medications and co-morbid conditions such as Parkinson’s disease, pudendal nerve injury, entrapment or lesion.^{29,30} It worsens on withdrawal of SSRIs or by giving Methyphenidate and antiparkinsonian drugs.³¹⁻³³ These could be attributed to an underlying bipolar disorder, where possibility of drug induced hypersexuality as a symptom is not uncommon.³⁴ Despite their behavioral similarity, hypersexuality is characterized by high subjective desire for sexual activity whereas PGAD is typically characterized by high level of genital arousal in absence of preceding desire, this statement is too narrow and should be construed as medicalization of

PGAD instead of applying the full proposed criteria as suggested by Leiblum et al.^{1,35}

Our patient responded marginally with Pramipexole along with local application of anesthetic Lignocaine gel and pelvic floor exercises. This improvement was significantly enhanced by adding injection Leuprolide, which is an agonist at pituitary gonadotropin-releasing hormone (GnRH) receptor that indirectly down regulates the secretion of gonadotropin-luteinizing hormone (LH) and follicular stimulating hormone (FSH).

This treatment regimen was in consonance with the treatment given by Deka et al, who successfully treated 53-year-old widow with Clomipramine, Fluoxetine, Clonazepam and Leuprolide.¹⁷ In our case, the age of the patient was 19 years and we initially used fluoxetine but had no response. It was stopped and then Pramipexole (dopamine agonist) was given. Our treatment was in line with Aquino et al, who treated an elderly patient suffering from Parkinson’s disease with restless genital syndrome (RGS) where they ascribed it as a phenotype of rest leg syndrome (RLS).⁹ After augmentation with Leuprolide, there was marked improvement. These benefits could be related to differential neurotransmitter receptor function, biochemical and endocrinal mechanism of action in PGAD, which requires further studies. It shouldn’t be considered as a standard treatment protocol amongst young patients because of GnRH agonist related effects and Good-Clinical judgement is required before prescribing.

Limitations

It’s a single case report that can contribute to scientific quest in ameliorating the problem of PGAD as its prevalence is suspected to be low and likely to be under-recognized and under-diagnosed.

Salient features and implication

This case report highlights the phenomenological, psycho-pathological and pharmacological differences and their variable responses to obsessive compulsive spectrum disorder (OCS), impulse control disorder NOS and establish PGAD as NPSA.

CONCLUSION

PGAD is NPSA and a variant of OCS. The diagnosis of impulse-control disorder not otherwise specific (NOS) may be appropriate, if the behavioral patterns and experiences of persons significantly interfere with their functioning for at least six months. However, the standard treatment regimen for OCD is SSRIs. NPSA being neuro-endocrinologically and biochemically distinct responded minimally to dopamine agonist (Pramipexole) and its results were enhanced by adjunct treatment with Leuprolide.

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