Case Report

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Primary Headache Associated with Sexual Activity Presenting with Persistent Genital Arousal Disorder: A Case Report

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Abstract

Persistent genital arousal disorder (PGAD) is characterized by unwanted and distressing genital sensations that are not associated with concomitant sexual interest or thoughts. Several etiologies have been proposed, but the underlying mechanism of the condition remains unclear. In this report, we describe a case of PGAD presenting with primary headache associated with sexual activity (PHASA). A 57-year-old female with no history of headache experienced recurrent, unwanted episodes of genital arousal lasting 3 to 5 days for 4 years. One day, she began to experience intense genital arousal that she had never experienced before. On the fourth day of arousal, while attempting intercourse with her partner, she experienced an abrupt explosive headache, which was repeated during another session of intercourse a week later. The patient underwent laboratory tests, as well as brain magnetic resonance imaging (MRI) and magnetic resonance angiography, all of which showed normal findings. She was referred to a sexual medicine specialist and prescribed amitriptyline, escitalopram, and propranolol with a diagnosis of PGAD. Her sexual arousal gradually diminished, and when she stopped all medications 3 months later, all symptoms had disappeared. On further investigation, spinal MRI revealed a Tarlov cyst. She has been in remission for three years. This case illustrates the co-occurrence of PHASA and PGAD and suggests a possible common pathophysiology shared between these two rare disorders.

Keywords: Arousal, Clitoris, Headache, Orgasm, Sexual behavior

INTRODUCTION

Persistent genital arousal disorder (PGAD) is a rare condition characterized by intrusive, unwanted, and distressing sensations of prolonged genital arousal that occur spontaneously, without sexual desire or stimulation.[1] Since the first report of a case series in 2001, approximately fifty reports have been published.[2] As PGAD becomes increasingly recognized, it has been registered and categorized as "Other Specified Sexual Arousal Dysfunction" in the

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International Classification of Diseases, 11th edition by the World Health Organization.[3]

Due to its rarity, no clinical trials for treatment of PGAD have been conducted. However, some reports illustrated a few successful modalities, like neuromodulation, electrical stimulation, surgery, or medications such as antidepressants or dopaminergic drugs.[4]

The pathophysiology of PGAD remains largely unknown, but both psychiatric and medical aspects seem to be involved.[5] Many patients with PGAD report psychiatric comorbidities, such as anxiety and depression, while structural lesions like sacral Tarlov cysts have been observed in many cases.[6,7] Herein, we report a case in which a thunderclap headache occurred during sexual intercourse shortly after the onset of PGAD, potentially providing some insight into the mechanism of PGAD.

CASE REPORT

Ethics approval has been waived due to the nature of this retrospective case report. Written informed consent was obtained from the patient by the corresponding author, and a scanned copy has been submitted to the editor.

A 57-year-old female had been experiencing recurrent episodes of unwanted and distressing genital sensations since 2017 (Figure 1). The main symptom was discomfort with heightened tension around the clitoris, preceded by a tightening sensation around the anus. These episodes started without any provoking factors, and lasted three to five days. She thought the symptoms as a result of postmenopausal syndrome, as they began after her menopause. Having been sexually inactive for over a decade, she managed these arousals through rigorous exercises, hoping the episode would end soon.

In March 2021, she encountered an intense episode unlike any previous ones. The symptoms were exacerbated by minimal stimuli, such as slight vibrations while driving or the sound of prayers in church. Topical anesthetics had no effect. On the fourth day of the episode, she attempted to have sexual intercourse with her husband for the first time in a decade, not out of sexual desire, but in the hope that it might alleviate her symptoms. However, she experienced a sudden, severe headache just before reaching orgasm. The headache was bilateral, explosive, and peaked within seconds, which was followed by shortness of breath and tremors. The remnant pulsating headache worsened with Valsalva maneuvers and persisted for 2 days. A week later, another attempt of sexual intercourse resulted the same explosive headache.

She visited a neurology clinic. She was examined and evaluated according to the standard protocol with particular attention to the thunderclap headache. The patient's past medical history was unremarkable except for white-coat hypertension. She denied any prior history of head-

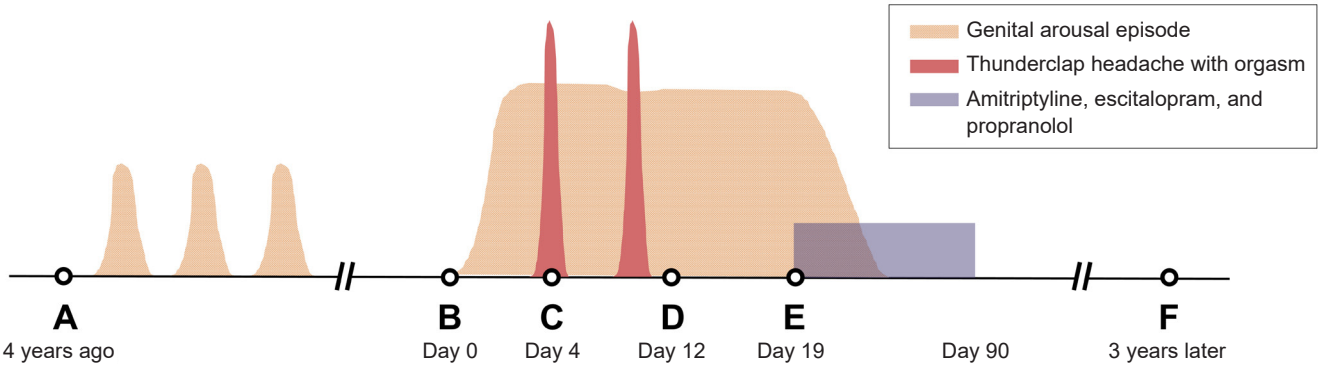

Figure 1. Timeline of the patient's illness. A: Recurrent distressing episodes of genital arousal for 4 years. B: Onset of an intense episode of genital arousal. C: On day 4, she experienced an abrupt, explosive headache while attempting sexual intercourse. D: On day 12, no abnormalities were found on a neurological examination, laboratory tests, or brain magnetic resonance imaging and magnetic resonance angiography; she was diagnosed with primary headache associated with sexual activity. E: On day 19, she visited a sexual medicine specialist and was diagnosed with persistent genital arousal disorder; medical treatment proved successful. F: After 3 years of follow-up, she remains in remission.

ache, including migraine. Her neurologic examination, laboratory tests, and brain magnetic resonance imaging (MRI)/magnetic resonance angiography showed no remarkable finding (Figure 2A). She was diagnosed with primary headache associated with sexual activity (PHASA), according to the International Classification of Headache Disorders, 3rd edition.[8] The neurologist suggested taking indomethacin before sexual activity; however, her chief complaint was genital arousal, not the headache.

She was subsequently referred to a sexual medicine specialist and diagnosed with PGAD. Treatment with amitriptyline, escitalopram, and propranolol was initiated. Her symptoms of genital arousal gradually subsided, allowing her to discontinue the medications within 3 months. As she no longer felt the need to engage in sexual activity, the explosive headaches did not recur.

A year later, a spine MRI revealed a Tarlov cyst at the sacrum (Figure 2B). Her follow-up was ended without further medication, and she has remained in remission for 3 years.

DISCUSSION

PGAD is a rare disease entity characterized by repetitive genital arousals.[1] A recent expert consensus from the International Society for the Study of Women's Sexual Health (ISSWSH) has suggested diagnostic criteria for PGAD (Table 1).[5] Unlike hypersexuality, genital arousal in PGAD does not accompany intrusive sexual thoughts and fantasies.[9] Patients with PGAD often seek relief through sexual intercourse or masturbation to alleviate unwanted tension, but not for pleasure or sensual experience. To the best of our knowledge, this is the first case report of PGAD and PHASA occurring in close temporal relation.

PHASA is characterized as a headache occurring only during sexual activity, increasing in intensity with increasing sexual excitement, and peaking abruptly just before or during orgasm.[8] The lifetime prevalence of PHASA in the general population is estimated to be around 1%.[10] Pathophysiologically, it is thought that the headache arises from vessels innervated by the trigeminal nerve, which is caused by vaso-neuronal coupling damage.[11] PHASA shares a bidirectional relationship and some pathophysiological aspects with other typical secondary thunderclap headaches, such as reversible cerebral vasoconstriction syndrome (RCVS), which includes factors like sympathetic overactivity, endothelial dysfunction, and oxidative stress.[11]

We propose two mechanisms linking PGAD with PHASA in this case. First, sympathetic overactivation seems to be a significant contributing factor in both disorders. The human sexual response involves a hypersympathetic response, during which norepinephrine levels increase in

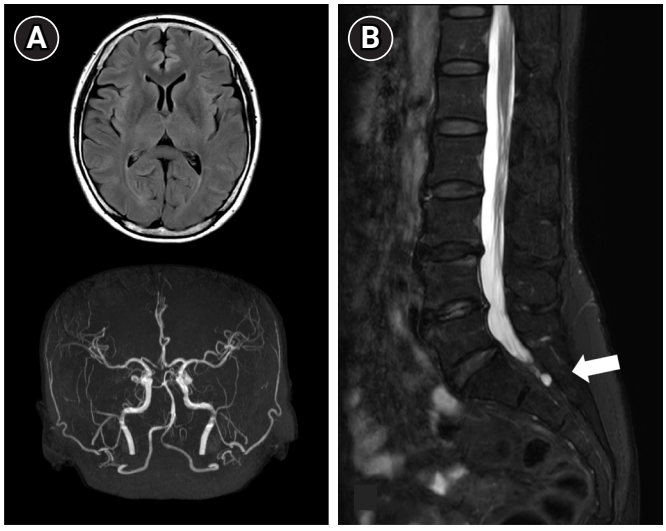

Figure 2. Imaging findings of the patient. (A) Normal brain magnetic resonance imaging (MRI) and magnetic resonance angiography taken 8 days after the initial thunderclap headache. (B) Spine MRI revealed a Tarlov cyst (white arrow), which is commonly reported in patients with persistent genital arousal disorder.

Table 1. 2021 ISSWSH consensus expert opinion on criteria for PGAD[5]

Criteria	Persistent or recurrent, unwanted or intrusive, distressing sensations of genital arousal
	Duration of ≥3 months
	May include other types of genito-pelvic dysesthesia (e.g., buzzing, tingling, burning, twitching, itch, pain)
	Most commonly experienced in the clitoris but also in other genito-pelvic regions (e.g., mons pubis, vulva, vestibule, vagina, urethra, perineal region, bladder, and/or rectum)
	May include being on the verge of orgasm, experiencing uncontrollable orgasms, and/or having an excessive number of orgasms
	Not associated with concomitant sexual interest, thoughts, or fantasies

ISSWSH, International Society for the Study of Women's Sexual Health; PGAD, persistent genital arousal disorder

both plasma and cerebrospinal fluid.[12] A study comparing vaginal pulse amplitude and heart rate variability reported moderate increases in sympathetic nervous system activity associated with higher genital arousal, indicating that patients with PGAD under attacks are likely in a hypersympathetic state.[13] Furthermore, some authors have suggested that negative appraisals of genital arousal may also lead to increased sympathetic nervous system activity in patients PGAD.[14] While many aspects of PHASA's pathophysiology and disease nature remain unclear, the fact that it is triggered during sexual activity suggests that an increased sympathetic tone would play a critical role in the generation of headaches.[15] Second, serotonergic dysfunction could be a key component in both PGAD and PHASA. Studies using functional MRI, found that while clitoral self-stimulation activates the paracentral lobule in the somatosensory cortex of healthy controls, symptomatic PGAD patients show hyperactivation of the paracentral lobule without any genital stimulation.[16,17] Sensorimotor integration in the paracentral lobule is regulated by 5-HT2A and D2 receptors.[18] This association is also supported by the fact that some cases of PGAD or RCVS are induced by the sudden withdrawal of selective serotonin reuptake inhibitor/serotonin–norepinephrine reuptake inhibitor medications.[19,20]

In conclusion, PGAD can occasionally co-occur with PHASA. Diseases related to sexual behavior may require a multidisciplinary approach.

AVAILABILITY OF DATA AND MATERIAL

Copies of the original medical records, specific imaging studies, and informed consent documents are available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS

Conceptualization: WSH; Data curation: WSH, HKB; Resources: WSH, HKB; Supervision: HKB; Visualization: WSH; Writing–original draft: WSH; Writing–review & editing: HKB; Approval of final manuscript: WSH, HKB.

CONFLICT OF INTEREST

Woo-Seok Ha has been the Junior Editor of *Headache and Pain Research* since August 1st, 2023, and was not involved in the review process of this article. All authors have no other conflicts of interest to declare.

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