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CASE REPORT

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Autonomic dysfunction in a patient with primary headache associated with sexual activity: case report and literature review

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Abstract

Background Primary headache associate with sexual activity (PHASA) is a relatively rare clinical condition and characterized by thunderclap headache exclusively triggered by sexual activity. The suggested involvement of autonomic dysfunction with altered cerebrovascular tone may contribute to the underlying mechanism of PHASA. However, the utilization of head-up tilt test (HUT), a valuable tool for assessing autonomic function, has not been employed in patients with PHASA.

Case presentation We present a typical case of PHASA with positive HUT response.

Conclusion Autonomic dysfunction and compensatory vasodilation due to cerebrovascular autoregulation may be part of the mechanism of PHASA.

Keywords Primary headache associated with sexual activity, Head-up tilt test, Pathophysiology, Autonomic system, Case report

Introduction

Primary headache associate with sexual activity (PHASA) is a relatively rare clinical condition with estimated 1–1.6% lifetime prevalence and often characterized by abrupt, explosive, bilateral headache lasting several minutes to 24 h [1–3]. The diagnosis of PHASA must fulfill criteria that sexual activity is the only trigger and pain intensity is in temporal relation with sexual excitement or thunderclap headache during or before orgasm [1, 4]. It is crucial to rule out some severe secondary causes such as reversible cerebral vasoconstriction syndrome (RCVS), subarachnoid hemorrhage, arterial dissection and cerebral venous thrombosis [1, 5]. Although the underlying mechanism of PHASA remains largely unclear, an aberrant cerebral vascular tone due to sympathetic overactivity is considered to play an important role in the disease pathophysiology [1, 6–8]. However, additional precise and comprehensive evidence is still needed to further elucidate this hypothesis. The head-up tilt test (HUT) is a valuable tool for evaluating the integrity of autonomic regulation through heart rate and blood pressure analysis [9–11]. Hence, we present a typical case of PHASA with a positive reaction of tilt test and attempt to shed light on the pathogenesis of this disorder.

Case presentation

A 45-year-old female attended to our department in September 2020 with a complaint of thunderclap headache during orgasm for three times in previous month. Her headache reached its peak less than 1 min involving the whole head especially the occipital area. The intensity of the pain was 8–9 described by visual analogue scale with explosive and throbbing quality. The severe headache often lasted for several hours following with a mild dull

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pain persisted almost one day. The patient noticed that headaches predominantly occurred in an upright position of the upper body. No accompanying symptoms were reported such as nausea, vomiting, photophobia except mild discomfort of her neck. Past history revealed occasionally headache attacks located in bilateral temporal and occipital area and dull in quality assumed to be tension type headache. She had no obvious emotion problems according to Hamilton Anxiety/Depression Scale and Self-rating depression scale. General physical and neurological examination was unremarkable. The Schellong test was negative. Blood tests including routine, biochemistry, c-reactive protein, coagulation tests, autoimmune antibody, thyroid function were normal. Catecholamine of both urine and blood was normal. Electrocardiograph and cardiac ultrasonography showed sinus bradycardia (Heart rate 53 bpm). Brain magnetic resonance imaging, angiography, venography and computed tomography angiography (carried out six days after the last thunderclap headache attack) detected no abnormalities which ruled out cerebral vasoconstriction and venous thrombosis. Ultrasound of extracranial arteries were unremarkable. The lumbar puncture revealed normal intracranial pressure and cerebral spinal fluid levels. A diagnosis of PHASA was confirmed. Ultrasound of bilateral jugular vein did not demonstrate retrograde venous flow during Valsalva-like maneuvre. Parameters of heart rate variability collected by 24-h Holter monitor was within normal range. Further, head-up tilt test was performed and revealed a positive response provoked with 0.25 mg nitro-glycerin. The patient developed symptoms of presyncope (dizziness, blurred vision, nausea and confusion) and soon afterwards experienced a moderate headache with short duration. Blood pressure analysis was consistent with vasodepressor type of reflex syncope instead of cardioinhibitory type (Fig. 1). Indomethacin was recommended but she refused for worrying about the side effects. Since the patient discharged, no headache had occurred after acupuncture therapy (Fengchi point and auricularis point) in year 2021. While within the next three years, she still suffered approximately 5 episodes of PHASA per year. In year 2024, about 10 h after her headache attack, Brain MRA scan was performed and revealed nothing. Head-up tilt test was conducted again and revealed the same result as last time.

Discussion

The current female case of PHASA presents typical characteristics: onset in the mid-forties, only precipitated by and occurring during orgasm, thunderclap quality and lasting several hours, localized in bilateral occipital area, seldom accompanying symptoms as previously reported [4, 5, 8, 12–14].

The primary finding of this particular case is the positive response observed in the head-up tilt test, which, to our knowledge, has not been examined in previous cases of PHASA. The significant reduction of blood pressure together with symptoms of presyncope in our patient resembling those observed in vasodepressor-type reflex syncope suggest the presence of autonomic dysregulation [9, 10]. Although some healthy subjects exhibit a positive response during HUT, a study has demonstrated that individuals without a history of syncope who display positive HUT results share similar hemodynamic and autonomic responses with confirmed cases of vasovagal syncope [15]. The physiological response to upright posture involves the sequential occurrence of blood redistribution and vagal cardiac response, followed by vagal withdrawal/sympathetic effect, which subsequently triggers neural and humoral compensatory mechanisms to maintain cerebral perfusion [9]. Elevated levels of norepinephrine in both plasma and CSF, indicative of a heightened sympathetic response, were observed during human sexual arousal and orgasm [16]. During sexual activity, there is a significant increase in blood pressure, heart rate, and intracranial pressure due to physical exertion

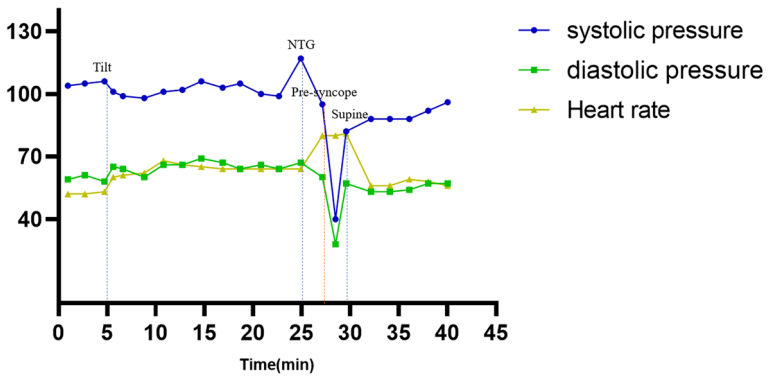

Fig. 1 The trends of blood pressure and heart rate changes in the patient during HUT

and the Valsalva maneuver. These hemodynamic changes can strain cerebral vasculature, potentially leading to PHASA. A positive HUTT reflects an abnormal hemodynamic response to orthostatic stress, suggesting impaired vascular compensation. This impaired response might also contribute to abnormal cerebral blood flow regulation during sexual activity, increasing the risk of PHASA. Although the HUTT primarily assesses systemic vascular and cardiac function, it can indirectly reflect cerebral vascular autoregulation. Additionally, Stefan Evers and his colleagues found that patients with PHASA exhibit impaired metabolic cerebral vasoneuronal coupling as evidenced by the acetazolamide test and stress Doppler sonography [7]. In fact, the balance between the sympathetic and parasympathetic nervous systems can be likened to a spring, whereby excessive compression results in an exaggerated rebound response. Thus, in patients with PHASA, it can be postulated that heightened sympathetic activity during orgasm, followed by a transient reversible dysfunction of baroreceptors and subsequent sudden withdrawal of sympathetic activity, leads to an augmentation in vagal tone. Consequently, compensatory vasodilation occurs due to cerebrovascular autoregulation in response to low blood pressure and the influence of neuroendocrine factors such as nitric oxide, which may contribute to the pain sensation.

The association between body position and the occurrence of headaches may also provide hints for investigating PHASA pathogenesis. According to our patient's report, headaches predominantly occurred in an upright position of the upper body.

In a German cohort, 8.4% of patients experienced headache during a specific position of sexual intercourse, while 51% reported alleviation of the headache by assuming a more passive role during sexual activity or keeping the neck lower than the trunk [12, 17]. In the earliest version of ICHD, PHASA was categorized into three subtypes, with type 3 specifically denoting a postural headache following orgasm and part of type 3 patients exhibited normal cranial pressure levels [12]. Recent studies have also observed a correlation between headache and orthostatic intolerance, encompassing orthostatic hypotension (OH), neurally mediated hypotension, and postural tachycardia syndrome [18, 19].

Headache often manifests during HUT with a brief duration, similar to our case [18, 19]. The headache associated with OH is referred to as coat-hanger ache (CHA) due to its impact on the neck and shoulder region [20]. Interestingly, many patients with PHASA may experience concurrent neck pain [4]. Collectively, the upright posture is somewhat associated with the occurrence of headache, suggesting potential involvement of the autonomic nervous system.

Exhaustive examination to exclude secondary etiologies is mandatory at first onset of PHASA, especially RCVS [1, 5]. However, distinguishing between RCVS and HSA poses a challenge due to the overlap in their clinical presentations [5]. Wang et.al proposed that the two diagnostic entities may be spectra of the same disorder and identified autonomic dysregulation through heart rate variability analysis in RCVS [13, 21]. It is suggested that PHASA may have potential overlap with primary exertional headache (PEH). A MRV study revealed the presence of venous abnormalities, such as jugular vein stenosis, in both PHASA and PEH patients [22]. Additionally, an ultrasonography study demonstrated internal jugular vein valve incompetence during Valsalva-like manoeuvres (VM) [23]. However, our patient exhibited normal findings on MRV and ultrasound with VM. The relationship between PHASA and RCVS/PEH requires further elucidation through additional mechanistic studies.

Our patient manifested as a relapse episodic course. Studies reported that 40% of individuals with PHASA have a prolonged course exceeding one year, suggesting the necessity of prophylactic treatment [4, 5, 24]. Propranolol as a recommended prophylactic drug for PHASA that acts by blocking β receptors [1, 6], may also exert its effects through modulation of autonomic nervous system. Our patient underwent 10 sessions of acupuncture therapy (with the refusal to consider indomethacin prior to sexual activity) and experienced one year without any occurrences of PHASA. A case report presented a successful manual therapy treatment for PHASA, which demonstrated sustained remission effectiveness at the 12-month follow-up [25]. Nevertheless, further validation of these non-pharmacologic treatment is warranted.

We conducted the Schellong test and the result was negative. The patient did not have orthostatic hypotension or tachycardia. We speculate that the autonomic nerve function of the patient is only a mild dysfunction. Therefore, routine tilt test was negative while provoking test was positive. We did not do the Cerebrovascular reserve test due to the equipment malfunction. This is the limitation of our case.

In conclusion, we present a representative case of PHASA with a positive head-up tilt (HUT) test, indicating the presence of autonomic dysfunction in the pathophysiology of this disease.

Conclusions

Autonomic dysfunction and compensatory vasodilation due to cerebrovascular autoregulation may be part of the mechanism of PHASA.

Clinical implications

Autonomic dysfunction may play a role in the underlying mechanism of primary headache associated with sexual activity.

Primary headache associated with sexual activity, reversible cerebral vasoconstriction syndrome and headache associated with orthostatic intolerance are similar in some clinical aspects and may share a common underlying mechanism involving autonomic dysfunction.

Abbreviations

PHASA	Primary headache associate with sexual activity;
HUT	Head-up tilt test
RCVS	Reversible cerebral vasoconstriction syndrome
CSF	Cerebral spinal fluid
ICHD	International classification of headache disorder
OH	Orthostatic hypotension
CHA	Coat-hanger ache
PEH	Primary exertional headache
VM	Valsalva-like manoeuvres

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Authors' contributions

YM was responsible for data collection, reviewing the literature, and writing the manuscript. HR was responsible for Conceptualization and revision of the manuscript. SY was the principal investigator who was responsible for study design, supervision and revision of the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Chinese PLA General Hospital, Beijing. Participants had to sign informed consent before participating.

Consent for publication

Informed consent was signed by our patient who agreed that all clinical data was allowed to be published.

Competing interests

The authors declare no competing interests.

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