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Case Report

Post-orgasmic illness syndrome accompanied with testosterone deficiency: a case report

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Abstract

Post-orgasmic illness syndrome (POIS) is a rare disease that affects the quality of life of patients. Here, we report a case of a 27-year-old man who visited our clinic and presented with physical fatigue, muscle weakness, emotional irritability, memory difficulties, lack of attention, and flu-like state after ejaculation. The patient was diagnosed with POIS accompanied by testosterone deficiency (TD) and treated with antiallergic therapy combined with testosterone supplementation therapy (TST) and selective serotonin reuptake inhibitor (SSRI). After 3 months of medication, the patient's POIS symptoms, testosterone levels, and relevant questionnaire scores significantly improved. Antiallergic therapy combined with TST and SSRI treatment can effectively treat patients with POIS accompanied by TD.

Keywords: Post-orgasmic illness syndrome; Antiallergic therapy; Testosterone deficiency; Testosterone supplementation therapy

1. Introduction

Post-orgasmic illness syndrome (POIS) is a rare disease characterized by local allergic symptoms, such as nasal congestion, itchy eyes, and transient flu-like symptoms after ejaculation and lasts for 2–7 days [1]. After ejaculation, men with POIS develop symptoms, such as severe fatigue, weakness, nasal congestion, itchy eyes, lack of attention, irritability, depression, and flu-like state [1]. The pathogenesis and treatment of POIS remain unclear [2]. Here, we report a case of a patient with POIS accompanied by testosterone deficiency (TD) who was effectively treated with antiallergic therapy combined with testosterone supplementation therapy (TST) and selective serotonin reuptake inhibitor (SSRI) and provide clinical experience for the treatment of POIS.

2. Case report

A 27-year-old man visited the outpatient clinic of Peking Union Medical College Hospital on September 25, 2020 due to serious physical fatigue, muscle weakness, emotional irritability, memory difficulties, lack of attention, and flu-like state after ejaculation. The symptoms almost constantly appeared after ejaculation for approximately 5 min, and the symptoms were relieved after approximately 3–7 days. The patient had a history of allergic rhinitis, anxiety, and chronic gastritis. The patient showed no obvious abnormality on routine physical examination of the urinary system. Ultrasound examination of the urinary tract, hormonal laboratory tests, semen analysis, and total prostate-specific antigen (TPSA), Immunoglobulin E (IgE), and urine tests have been performed. Because of hospital limitations, free testosterone level was not determined. The ultrasound examination of the urinary tract and urine tests showed normal results. Hormonal results were as follows: follicle stimulating hormone (FSH), 4.10 IU/L; testosterone (T), 2.48 ng/mL; luteinizing hormone (LH), 3.19 IU/L; prolactin (PRL), 8.0 ng/mL; estradiol (E2), 26 pg/mL; and TPSA, 0.965 ng/mL. The results of the semen analysis showed that the density and activity of sperm were normal, and the blood IgE test also showed normal values (<0.35 KU/L). Based on obvious symptoms and examination results, the patient satisfied the five preliminary diagnostic criteria of POIS summarized in a previous study (shown in Table 1, Ref. [1]). The patient was diagnosed with POIS accompanied by TD. Moreover, the patient was examined using the Patient Health Questionnaire-9 (PHQ-9) depression screening scale, Generalized Anxiety Disorder 7-item scale (GAD-7) anxiety screening scale, International Index of Erectile Function 5 (IIEF-5), and the self-made POIS symptom scale (shown in Table 2) to evaluate the severity of various POIS-related symptoms. The IIEF-5 is a brief, reliable, validated, multidimensional scale for the assessment of male sexual function, including relevant domains of male sexual function, such as erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction [3,4]. Therefore, we used the IIEF-5 to test the patient's sexual function. Because there is no standard scale for the change in patients' clinical symptoms, the self-made POIS symptom scale is customized for this patient according to the patient's clinical symptoms and the five diagnostic criteria of POIS, which can reflect the change in patients' symptoms before and after treatment. The POIS symptoms scale is not a validated questionnaire. The results showed PHQ-9, GAD-7, IIEF-5, and self-made POIS symptom scores of 8, 9, 19, and 61, respectively.

Table 1. Five preliminary diagnostic criteria of POIS [1].

Criteria	Description
Criterion 1	One or more of the following symptoms: Sensation of a flu-like state, extreme fatigue or exhaustion, weakness of musculature, experiences of feverishness or perspiration, mood disturbances and irritability, memory difficulties, concentration problems, incoherent speech, nasal congestion or watery nose, and itchy eyes
Criterion 2	All symptoms occur immediately (within a few seconds), soon (within a few minutes), or within a few hours after ejaculation that is initiated by coitus or masturbation or spontaneously (e.g., during sleep)
Criterion 3	Symptoms occur always or nearly always (>90% of ejaculation events)
Criterion 4	Most of these symptoms last for approximately 2–7 days
Criterion 5	The symptoms disappear spontaneously

POIS, post-orgasmic illness syndrome.

Table 2. Self-made POIS symptom scale.

Symptoms	Description and score (1 to 10)
Symptom 1	Flu-like state (1 to 10)
Symptom 2	Extreme fatigue (1 to 10)
Symptom 3	Weakness of musculature (1 to 10)
Symptom 4	Experiences of feverishness or perspiration (1 to 10)
Symptom 5	Mood disturbances and/or irritability (1 to 10)
Symptom 6	Memory difficulties (1 to 10)
Symptom 7	Concentration problems (1 to 10)
Symptom 8	Incoherent speech (1 to 10)
Symptom 9	Congestion of nose or watery nose (1 to 10)
Symptom 10	Itching eyes (1 to 10)

POIS, post-orgasmic illness syndrome.

After diagnosis, the patient was treated with loratadine (antihistamine) 10 mg once daily as an antiallergic treatment, andriol testocaps 80 mg twice daily to increase testosterone levels, and sertraline 50 mg once daily for anxiety and depression. The patient was instructed to take medicine for 3 months and observe changes in the disease.

The patient was followed up after 3 months. During the medication, the average number of sexual activities per month was 7–8. The patient felt that the drug treatment was effective and the patient's physical fatigue, muscle weakness, emotional irritability, memory difficulty, lack of attention, and flu-like state after ejaculation, anxiety, and depression improved. The patient's male reproductive hormones were reexamined and showed the following results: FSH, 4.51 IU/L; T, 3.05 ng/mL, LH, 3.14 IU/L; PRL, 6.2 ng/mL; and E2, 20 pg/mL. The testosterone level was significantly higher than that obtained at baselie. The patient was again examined using the PHQ-9 depression screening scale, GAD-7 anxiety screening scale, IIEF-5, and the self-made POIS symptom scale. The results showed that the PHQ-9 score decreased from 8 to 3, GAD-7 score decreased from 9 to 4, IIEF-5 score increased from 19 to 24, and POIS symptom score decreased from 61 to 38. The patient was also tested for blood-specific IgE and underwent routine semen tests. The examination results before and after the treatment are summarized in Table 3, and showed that the patient's anxiety and depression symptoms, sexual function, and POIS-related symptoms improved. Moreover, the patient felt that the overall symptoms improved by approximately 50% after taking the medicine. Therefore, after systematic treatment, the patient's symptoms significantly improved, suggesting that the combined drug treatment was effective.

3. Literature review and discussion

To date, POIS remains a rare disease. The prevalence of POIS is unknown and difficult to determine may be because many people affected by POIS do not seek medical assistance, and most doctors are not aware of POIS [5]. POIS was first discovered in 2002 when Waldinger *et al.* [6] reported two cases of this disease, of which a series of symptoms in two men after ejaculation were described, including severe fatigue, flushes, generalized myalgia, and flu-like state. These symptoms appeared rapidly after ejaculation and disappeared after 4–7 days.

3.1 Diagnostic criteria of POIS

Waldinger *et al.* [1] proposed preliminary diagnostic criteria to evaluate POIS in a study involving 45 white men with POIS in the Netherlands. They thought that the symptoms of POIS were diverse, but five criteria covered most cases of POIS. Criterion 1 requires at least one of the following symptoms: flu-like state, extreme fatigue, generalized weakness, experiences of feverishness or perspiration, mood disturbances, memory difficulties, concentration problems, incoherent speech, runny nose, nasal congestion, and itchy eyes. Criterion 2 requires that all symptoms occur within seconds, minutes, or a few hours after ejaculation. Criterion 3 requires that symptoms occur in >90% of ejaculation events. Criterion 4 requires that most of these symptoms last for 2–7 days. Criterion 5 requires that the symptoms disappear spontaneously. The details are listed in Table 1.

At present, there are no widely accepted objective diagnostic criteria, but they are based on the subjective feelings of patients. The diagnosis of this case is also based on the subjective statement of the patient, which conforms to

Table 3. Examination results before and after treatment.

Examination	Results before treatment	Results after treatment
FSH	4.10 IU/L	4.51 IU/L
T	2.48 ng/mL	3.05 ng/mL
LH	3.19 IU/L	3.14 IU/L
PRL	8.0 ng/mL	6.2 ng/mL
E2	26 pg/mL	20 pg/mL
PHQ-9 score	8	3
GAD-7 score	9	4
IIEF-5 score	19	24
Self-made POIS symptom scale score	61	38
Blood specific IgE level	<0.35 KU/L	<0.35 KU/L
semen analysis	Normal	Normal

PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder; IIEF-5, International Index of Erectile Function 5; FSH, follicle stimulating hormone; T, testosterone; LH, luteinizing hormone; PRL, prolactin; E2, estradiol.

Waldinger's five diagnostic criteria. Therefore, the patient was diagnosed with POIS.

3.2 Pathogenesis of POIS

The pathophysiological mechanism of POIS remains unclear, but most scholars believe it to be related to autoimmune abnormalities. The most accepted hypothesis proposed by Waldinger *et al*. [1] is that POIS is an immunological phenomenon. They speculated that POIS is an autoimmune or allergic disease in which patients produce inflammatory responses to substances in their semen. This hypothesis is supported by the skin prick test (SPT) of autologous semen in patients with POIS. Harvested semen of patients with POIS was diluted to 1:40000 and injected intracutaneously to the volar side of the forearm and compared with placebo skin reaction with 0.9% of intracutaneous saline. Of the 33 men with POIS who were tested, 88% showed positive SPT reactions to their own semen, whereas none showed positive SPT reactions to the placebo. However, the serum IgE levels in patients with POIS were normal, indicating that POIS was not associated with any disease that causes an increase in IgE. Therefore, Waldinger *et al*. [1] concluded that type I and IV allergic reactions of patients to their own semen might be the main pathological mechanism of POIS. However, the pathological mechanism of POIS remains controversial. Jiang *et al*. [7] found that although patients with POIS had a positive SPT reaction to their own semen, there were no specific IgE antibodies in serum concentrations. They suggested that IgE-mediated semen allergy might not be the underlying mechanism of POIS and believed that POIS might have been caused by opioid withdrawal. This is because orgasm consumes many endogenous opioids, leading to opioid withdrawal symptoms. Therefore, they speculated that chemical imbalance in the brain might be the physiological basis of POIS, and psychological factors could be risk factors [7]. However, Depreux *et al*. [8] found that the SPT of autologous semen and serum IgE antibody reactions in patients with POIS were negative and thought that the immune mechanism might not be the mechanism of POIS; therefore, neurobiochemical mediators should be involved in the study of POIS. Amicis *et al*. [9] also found that immunological studies did not confirm the hypersensitivity reaction hypothesis in a patient with POIS. Moreover, the patient received specific immunotherapy with a transient clinical response and did not show clinical improvement of symptoms. Therefore, the pathophysiological mechanism of POIS remains unclear and warrants to be studied.

3.3 Treatment options of POIS

As POIS is a rare disease with complex pathogenesis and diverse clinical manifestations, the treatment options are also diversified, and clinical reports further verify the diversity of treatment options [2]. Therefore, there is no recognized treatment for POIS, and many scholars have explored desensitization therapy, which has become the main strategy.

Waldinger *et al*. [10] successfully treated two patients with POIS using autologous semen desensitization therapy at 31 and 15 months, with improvement rates of chief complaints of 60% and 90%, respectively. Another trial of therapy with nonsteroidal anti-inflammatory medication (diclofenac) successfully relieved the symptoms of POIS (the improvement rate was as high as 80%) and increased the frequency of sexual life of the patient with POIS from two times a month to four times a month [11]. Another study found that silodosin, a highly selective alpha1A-blocker, was effective in 57% of patients with POIS [12]. Intralymphatic immunotherapy is a new method of allergen-specific immunotherapy, and it is reported that a Korean patient with POIS received intralymphatic immunotherapy, which alleviated POIS-related symptoms, and the presence of semen-specific IgE also confirmed the immune mechanism of POIS [13]. Furthermore, some studies have found

that antihistamines, selective serotonin reuptake inhibitors, and benzodiazepines can also be used to treat patients with POIS-like symptoms [14]. Therefore, the treatment options for POIS are diverse.

3.4 Possible association between testosterone deficiency and the case

In this case, the serum testosterone level of the patient was 2.48 ng/mL, indicating TD. TD can affect multiple systems in the entire body and can cause male sexual dysfunction, decline in physical strength and energy, decrease in muscle and bone density, metabolism-related diseases, and cardiovascular system-related diseases [15]. Moreover, testosterone plays an important role in regulating the immune system. By affecting the innate and adaptive immune systems, testosterone acts on many branches of the immune system and plays the role of inhibiting immune responses [16]. Therefore, TD can lead to excessive activation of the immune system and increase the risk of autoimmune diseases. Bolanos and Morgentaler reported the first successful treatment of POIS using hCG to elevate serum testosterone, resulting in prompt resolution of POIS symptoms [17]. The success of this treatment also provided a basis for hormone therapy in patients with POIS. If the testosterone level of patients with POIS is low, hCG therapy or TST can be considered.

3.5 Treatment for this case

In this case, a 27-year-old man visited the outpatient clinic of Peking Union Medical College Hospital for treatment due to serious physical fatigue, muscle weakness, emotional irritability, memory difficulties, lack of attention, and flu-like state after ejaculation. The symptoms almost constantly appeared at approximately 5 min after ejaculation, and the symptoms were relieved after approximately 3–7 days. According to the five criteria proposed by Waldinger *et al*. [1] the patient was diagnosed with POIS. Examination showed that the patient's serum testosterone level was low. The PHQ-9 and GAD-7 scales suggested that the patient had mild anxiety and depression. The IIEF-5 score also indicated that the patient had mild erectile dysfunction. Considering the clinical diagnosis and related literature, the patient was administered 10-mg loratadine (antihistamine) once daily as an antiallergic treatment. Moreover, the serum testosterone level of the patient was low, and he was given andriol testocaps 80 mg twice daily for TST.

The emotional disorder is a widespread non-specific symptom of the disease due to discomfort and depression. The treatment of anti-anxiety and depression drugs has become an important combination therapy for this disease. Therefore, the patient was administered sertraline 50 mg once daily for anxiety and depression. Sertraline is a selective inhibitor of serotonin reuptake into presynaptic terminals and has been shown to have both antidepressant and anxiolytic effects [18]. The use of the SSRI may lead to side effects of sexual dysfunction, such as delayed ejaculation, reduced sexual desire, reduced sexual satisfaction, and impotence [19]. In this case, the patient did not suffer any sexual side effects, his sexual desire and sexual satisfaction improved, and he had more sexual activity than before.

After 3 months of treatment, the patient's symptoms significantly improved, and the examination findings also verified the effectiveness of the drug treatment. Therefore, for patients with POIS accompanied by TD, antiallergic therapy combined with TST and SSRI treatment can be used to improve the level of testosterone and relieve the symptoms of POIS. In this case, after TST, there was no significant change in FSH or LH levels, although the patient's total testosterone level increased. We speculate that this is because the function of the hypothalamic-pituitary function axis in this patient is reduced, resulting in the inability to secrete enough hormones in time to change the FSH and LH levels when the testosterone level changed.

This case provided clinical experience for the treatment of patients with POIS accompanied by TD.

4. Conclusions

Antiallergic therapy combined with TST and SSRI treatment can effectively treat patients with POIS accompanied by TD.

Author contributions

HS, YL, CM and HL were involved in the acquisition, analysis and interpretation of the data. HS, HL also contributed to the design and conception of the study. HS drafted the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Medical Ethics Committee of Peking Union Medical College Hospital (Study No. S-214). The patient provided consent to publish the details of his case.

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Conflict of interest

The authors declare no conflict of interest.

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