Trakia Journal of Sciences, No 1, pp 77-80, 2023

Available online at:
http://www.uni-sz.bg

ISSN 1313-3551 (online) doi:10.15547/tjs.2023.01.013

Case Report

DO WE RECOGNIZE RESTLESS GENITAL SYNDROME AND DO WE KNOW HOW TO TREAT IT?

T. Radeva[1, 2]*

[1]II Psychiatric Clinic, UMHAT "St. Marina"- Varna, Bulgaria
[2]Department of Psychiatry and Medical Psychology, Medical University "Prof. Parskev Stoyanov"- Varna, Bulgaria

ABSTRACT
The following presentation introduces a case of a patient with the restless genital syndrome. This is a rare, usually undiagnosed condition, in which significant organ damage and/or dysfunction is absent, the finding is defined as functional and the patient is referred for treatment of his neurosis in a psychiatric practice. The complaints include feeling of arousal and tingling in the genital area, which is not accompanied by subjective sexual arousal and is a harrowing experience for the patient. Masturbation and sexual activity do not manage to affect the symptoms. Symptoms of restless leg syndrome are often involved too, which puts the hypothesis for a common etiology of both of the syndromes that is associated with the dopaminergic mediation. In the literature, there are individual cases of patients with the syndrome, who have been administrated treatment with pramipexole. The patient in the present case report has also undergone treatment with pramipexole and has been observed for a period of two years.

Key words: restless genital syndrome, hypothesis, etiology, treatment

INTRODUCTION

Restless genital syndrome is a somatosensory disorder, characterized by unpleasant feelings of pulsing and tingling in the genital area and pelvis. It has a sudden onset- at rest and most often in the evening time or during the night, without apparent stimulation in this area and is experienced as unpleasant genital arousal, which is not accompanied by sexual desire on interest. It was first mentioned in 2001, when there were five cases, described as persistent sexual arousal syndrome (1). In 2003 it was found that it is about sensory disturbances in the genital area, and not about an irresistible sexual desire, wherefore the term undergoes a change and becomes persistent genital arousal disorder – PGAD (2). The term restless genital syndrome was introduced in 2009, after establishing a link between the condition and restless leg syndrome. In fact, this somatosensory abnormality can be observed in different regions of the body, where besides restless leg syndrome and restless genital syndrome, restless arms, restless hands, restless arms and legs, restless abdomen, restless pelvic, bladder syndromes are also known (3). Symptoms appear or worsen at rest and are relieved, but do not go away with movement or massage of the affected area. It is typical for complaints to appear or intensify in the evening or at night. Often, in about 85% of cases, they are accompanied by complaints of sleep disturbance and a concomitant feeling of fatigue during the day. In some of the cases, the symptoms appear 2-3 times a week, while in others they are daily. The sensations are not painful, but are extremely disturbing for the patient and, due to insomnia, often lead to serious physical and emotional exhaustion, even to anxiety and depression.

Incidence data are uncertain because patients turn to doctors with a primary complaint of insomnia,

***Correspondance to:** *Tatyana Radeva, 1, blvd Hristo Smirnenski, UMHAT "St. Marina", II Psychiatric Clinic, Varna, dr_usheva_radeva@abv.bg, +359897501581*

but it is estimated to affect 2-15% of the Earth's population (3). The period from the onset of symptoms to the diagnosis is 10-20 years, as the frequency of cases increases with age. There are also described cases of occurrence in childhood. Early onset was more often associated with more severe symptoms. The restless syndrome usually progresses slowly to daily symptoms and severe sleep disturbances after age 50, resulting in decreased daytime alertness. Patients with the familial form of the syndrome tend to have the onset of symptoms before the age of 45. Women are affected more often than men, by a ratio of almost 2:1, with nulliparous women having the same risk of developing the syndrome as men. Research shows that it affects African-Americans less often than Caucasians. Compared to the general population, the frequency among patients with Parkinson's disease is higher - up to 25% (4). The etiology is unclear, but nonspecific neuropathy of sensory nerve endings has been suggested. In the specific case of restless genital syndrome - neuropathy of the n. pudendus or of n. dorsalis clitoris in women (5,6). When it comes to the primary state of the syndrome, it can be familial in 25-75% of cases, following an autosomal or recessive inheritance pattern. In familial cases, there is a trend toward an earlier age of onset (<45 years) and slower disease progression. A progressive decrease in the age of onset with successive generations (i.e., genetic anticipation) has been described in some families (7).

Pathogenetic mechanisms are unclear, with various hypotheses being discussed for restless syndrome regardless of location. Currently, the most widely accepted mechanism involves a genetic component, along with abnormalities in central subcortical dopamine pathways and impaired iron homeostasis. It is dopamine transmission that helps control muscle activity, regulation and coordination of movements (8). Dopamine levels follow their circadian rhythm and naturally decline at the end of the day, which may explain why symptoms of restless syndrome often worsen in the evening or at night. The results of performed SPECT analyses suggest a deficiency of dopamine D2 receptors. Studies show that after taking dopamine receptor antagonists in patients with the syndrome, symptoms worsen or reactivate. Assumptions about the importance of iron metabolism abnormalities can be deduced from the measurements of its parameters in the cerebrospinal fluid. Of note is the reduced availability of serotonin transporter in the brainstem, which supports the hypothesis that increased serotonin transmission in the brain may exacerbate symptoms of the syndrome. Other neurotransmitters suspected in the development of the syndrome are glutamate and opioids. Restless syndrome can be a manifestation of a number of diseases: anemia, diabetes mellitus, kidney failure, venous stasis, Parkinson's disease, multiple sclerosis, fibromyalgia, rheumatoid arthritis, thyroid gland pathology, peripheral neuropathy (radiculopathy), myelopathy, Sjogren's syndrome, amyloidosis, folate, B-12 or magnesium deficiency, frequent blood donation. The restless syndrome can be observed in one in five pregnant women after 27 gestational week and most often subsides about 4 weeks after birth. It can also be observed after taking certain medications, related to their mechanism of action, involving directly or indirectly dopamine neurotransmission - beta-blockers and Ca-channel blockers, some antihistamines, and antiemetics, antidepressants, antipsychotics, excessive alcohol intake, coffee, and smoking. These data require exploring the complaints of the patient, medical statements through his life span and his family, also conducting research as a necessity to confirm that it is a primary restless genital syndrome (9).

CASE REPORT

A 52-year-old Caucasian woman, a nurse by profession, married with two children but living in an independent household with her husband. She shares that her life is in order and there is nothing to worry about personally or professionally. For about ten years, she has been treated with various antidepressants for recurrent depressive disorder. Chief complaints are increased anxiety and unmedicated insomnia. In the course of the examination, with great concern, she reveals the main cause of his insomnia: in the evening, when lying in bed, discomfort appears in the genital area, swelling as with sexual arousal, but without feeling it. The complaints arose about a year after the second birth when she was in her thirties. After the delivery, which ended with an episiotomy, the patient recovered

quickly. In the beginning, the complaints were for a few days, passing after masturbation or sexual intercourse. She had spontaneous periods of absence of complaints but did not establish a cause-and-effect relationship for their cessation or renewal. She visited many obstetricians and gynecologists and was treated with various antibiotics and antimycotics - local and systemic due to a finding in the vaginal discharge without any effect on the complaints. The sensation of tingling and numbness in the evening at rest became daily, did not go away from the usual techniques, and only walks relieved her. When she tried to lie down, the tingling would reappear. The forced walks at night interfered with her sleep, during the day she had reduced concentration and was anxious from the onset of the evening, which affected her overall functioning. The patient has difficulty finding words to explain the complaints - sensations of swelling and tingling, which are not related to sexual desire or conscious arousal. They no longer transition from intercourse or masturbating, they get a little relief from her walking around the room. They pile up daily, in the evening when lying down or sitting, and continue for hours when she falls asleep sitting up tired. The biochemical tests performed did not reveal any abnormalities, MR of a small pelvis - without deviations. Family burden data - mother with Parkinson's disease. Started treatment with pramipexole up to 0.18 mg in the evening about 2 hours before going to bed. After one week of treatment the patient reported a reduction in the frequency and intensity of complaints, and a month later - their complete suspension. Up to now, the patient has been monitored for two years without reporting a breakthrough in symptoms.

DISCUSSION

The restless genital syndrome is a somatosensory and not a sexual disorder, the complaints cause discomfort and stress for the patient without being accompanied by sexual interest or desire. It probably refers to dyseshesia in the genitopelvic area, as the term vulvodynia is not identical, because the disease also occurs in men and is associated with discomfort rather than pain (10). From a pathogenetic aspect, pelvic congestion, pelvic varices or neuroprathy of pudendal nerve are discussed. It is often seen as a comorbidity of restless legs syndrome, and restless genital syndrome is discussed in the literature as its phenotypic variant with a common dopanergic mechanism. In support of the role of dopamine in the onset of the syndrome is the circadian nature of complaints, duplicating the circadian rhythm of dopamine, the worsening of symptoms by taking antipsychotics and other dopamine antagonists, and the influence of dopamine agonists, such as pramipexole for example. According to the current guidelines of the International Society for the Study of Women's Sexual Health for Consensus Nomenclature and Process of Care for the Management of Persistent Genital Arousal Disorder/Genito-Pelvic Dysesthesia (PGAD/GPD) (11), diagnostic criteria include:

1. persistent or recurrent, unwanted or intrusive, distressing sensations of genital arousal
2. duration of 3 months
3. 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)
4. may include being on the verge of orgasm, experiencing uncontrollable orgasms, and/or having an excessive number of orgasms
5. not associated with concomitant sexual interest, thoughts, or fantasies

As additional criteria: limited or no resolution, or aggravation of symptoms by sexual activity, compromised orgasm quality (eg, aversive, impaired, altered frequency, intensity, timing, and/or pleasure), aggravation of genito-pelvic dysesthesia by certain circumstances (eg, sitting, car driving, music or sounds, general anxiety, stress, or nervousness), despair, emotional lability, catastrophization, and/or suicidality and absent evidence of genital arousal (genital lubrication, swelling of clitoris or labia) on physical examination.

Medications with varying degrees of credibility, from different generations of anticonvulsants, dopamine agonists, antidepressants, hypnotics, including intramuscular botulinum toxin, as well as cognitive behavioral therapy to reverse the discomfort, have been recommended.

CONCLUSION

In conclusion, it is appropriate to add that the disease is unknown and often underestimated in

the presence of significant distress in patients and diagnosis after the onset of symptoms for ten to twenty years. It is useful for the diagnostic-therapeutic process to take place in a multidisciplinary team, with an individualized approach to the patient, influenced by the biopsychosocial approach. There are still mostly individual cases reports in the literature, and systematic clinical studies are missing.

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