Trauma Case Reports 11 (2017) 18–19

Contents lists available at ScienceDirect

Trauma Case Reports

journal homepage: www.elsevier.com/locate/tcr

Case Report

Venlafaxine-induced REM sleep behavioral disorder presenting as two fractures☆

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ARTICLE INFO

Keywords:
REM sleep
Parasomnia
Venlafaxine
Fracture

ABSTRACT

Rapid eye movement (REM) sleep behavioral disorder is characterized by the absence of muscular atonia during REM sleep. In this disorder, patients can violently act out their dreams, placing them at risk for traumatic fractures during these episodes. REM sleep behavioral disorder (RBD) can be a sign of future neurodegenerative disease and has also been found to be a side effect of certain psychiatric medications. We present a case of venlafaxine-induced RBD in a 55 year old female who presented with a 13 year history of intermittent parasomnia and dream enactment in addition to a recent history of two fractures requiring intervention.

Introduction

REM sleep behavior disorder is a condition in which the patient lacks atonia during REM sleep and therefore has the ability to physically act out dreams [1]. RBD can occur as a primary (idiopathic) disorder or secondary to obstructive sleep apnea, narcolepsy, α-synucleinopathies, or psychiatric medications [1]. Selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants are typically the causative agents of medication-induced RBD; however, antipsychotics may also be to blame [2]. Antidepressants have even been shown to increase muscle tone during REM sleep in people who do not have RBD [3]. There is also a theory that RBD due to medication may actually be an earlier presentation of RBD secondary to neurodegenerative conditions because those with medication-induced RBD have an increased risk of α-synucleinopathies compared to the general population [4].

The typical clinical presentation of a patient with RBD includes intermittent complex motor behaviors and/or vocalization during REM sleep. These movements appear purposeful and can range from gentle and subtle to violent and thrashing. Injuries during these episodes can be life and limb threatening as well as costly for the patient and the healthcare system as a whole; therefore, prompt recognition and treatment is necessary to forego these preventable risks and expenses.

Report of a case

A 55 year old Caucasian female presented to the sleep medicine clinic with a chief complaint of insomnia and sleepwalking. She complained of sleep onset and maintenance insomnia as well as waking up feeling unrefreshed and tired the following day. She also complained of sleepwalking and sleepeating, usually occurring around 2:30 in the morning. Her husband sleeps in another room every night because she frequently punches and kicks during sleep and had unknowingly hit him before. She sustained two fractures

☆ This work has not been presented at any meeting.

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http://dx.doi.org/10.1016/j.tcr.2017.10.017
Accepted 25 October 2017
Available online 28 October 2017

as a result of these nighttime behaviors. About one year ago, she fractured the base of her left fifth metatarsal and was treated with a fracture boot. She also sustained a comminuted, dorsally-displaced right distal radius fracture requiring open reduction and internal fixation with a plate and screws. She reported that all of these symptoms gradually began about 13 years ago. She admitted to decreased interest and pleasure in hobbies, feeling down, depressed and hopeless. She denied snoring, cataplexy, hypnopompic/hypnagogic hallucinations, and sleep paralysis. She has a past medical history of bipolar disorder, generalized anxiety disorder, attention deficit disorder, hypothyroidism and gastroesophageal reflux disorder. Past surgical history was positive for abdominoplasty, gastric bypass, and right wrist open reduction internal fixation. No one in her family had experienced any similar symptoms. The patient denied smoking, alcohol, and illicit drug use. She was taking lamotrigine, venlafaxine, ziprasidone, methylphenidate, levothyroxine, and pantoprazole. Physical examination was unremarkable.

Upon further questioning and medication review, it was ascertained that she started venlafaxine 13 years ago. It wasn't until after the start of this medication that her symptoms began. The patient underwent polysomnography which had no focal findings of an RBD episode. Venlafaxine was then cross-titrated with buproprion. She was originally taking venlafaxine extended release 150 milligrams (mg) which was decreased to 37.5 mg for 7 days and then stopped. Buproprion extended release was started at 150 mg for 6 days and increased to 300 mg. Methylphenidate 54 mg was tapered and stopped as well. She noticed her symptoms became less frequent and she was able to sleep longer and feel refreshed the next day. Upon stopping the medication she had complete resolution of her symptoms. She did, however, report starting having more vivid dreams. She denied nightmares but described these dreams as being exceptionally colorful and vibrant.

Discussion

The exact mechanism of RBD or medication-induced RBD has not yet been elucidated. However, there are theories of how atonia is lost during REM sleep in these conditions. Under normal conditions, motoneurons are hyperpolarized leaving the skeletal muscle unable to contract. Activation of both the GABA-ergic and glycinergic systems have been shown to account for this phenomenon [5]. Inhibition of excitatory cell systems such as glutamate, noradrenaline, and serotonin is another reason for REM sleep muscle atonia [5]. Therefore, inhibition of the GABA and glycine systems and overactivation of the excitatory systems are possible pathological mechanisms of RBD. However, the serotonergic system has been found to not be the etiology of this disease spectrum [6].

Our patient suffered from venlafaxine-induced RBD for around 13 years. Unfortunately, none of her other providers recognized her symptoms as possible side effects of her psychiatric medication. She even suffered through two fractures and had to undergo surgery because of it. She was treated by discontinuing the causative medication and starting another psychiatric medication from a different class in its place. Other possible treatments of RBD include pramipexole, clonazepam, and melatonin [5]. The gold standard of RBD diagnosis is a positive polysomnography (PSG) along with sleep history; however, the test-retest reliability of objective tests like PSG is low for RBD [7]. Our patient was diagnosed by sleep history alone and the diagnosis was confirmed when her symptoms resolved upon discontinuation of venlafaxine.

All medical professionals should be aware of REM sleep behavioral disorder and medication-induced RBD and should have a low threshold to refer to a sleep medicine specialist if their patients are experiencing concerning symptoms.

Conflict of interest statement

None.

Role of the funding source

None.

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