

CASE REPORT

Restless Legs Syndrome Associated with Quetiapine in Elderly Patient

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ABSTRACT

Restless legs syndrome (RLS) is a sleep-related disorder characterized by abnormal sensations in the legs at rest in which the patients feel an urge to move the legs; beginning or worsening during inactivity; relief by movement; preponderance in evening or night. The drugs implicated were mainly psychotropic, especially neuroleptics and many others. Drug induced RLS generally resolves when the dose is reduced or the drug is withdrawn.

We report a case of bipolar mood disorder presented to our emergency department with insomnia and we added quetiapine 100mg at bed time for his disturbed sleep, patient reported on third day complaining with "itchy", "Pins and needles", "creepy crawly" feeling in the legs. The sensations are usually worse at rest and night due to which he is unable to sleep. Awareness and proper diagnosis by all primary care practitioners is necessary for effective management of RLS as well as clinicians are encourage to be aware of the potential for quetiapine to cause RLS.

Keywords: Restless legs syndrome, quetiapine, iron deficiency, akathisia

INTRODUCTION

Restless legs syndrome (RLS) is a neurologic movement disorder of the limbs that is often associated with a sleep complaint. Patients with RLS may report sensations, such as an almost irresistible urge to move the legs; that are not painful but are distinctly bothersome. RLS can lead to significant physical and emotional disability. According to *DSM-5* criteria for RLS are; an urge to move the legs that is usually accompanied by or occurs in response to

uncomfortable and unpleasant sensations in the legs, characterized by all of the following: the urge to move the legs begins or worsens during periods of rest or inactivity; the urge is partially or totally relieved by movements; and the urge to move legs is worse in the evening or at night than during the day or occurs only in the evening or at night (American Psychiatric Association, 2013). RLS affects approximately 10% of the population, prevalence increasing with age (Comella, 2002). Familial RLS is described with 63% at least one of their first-degree relatives (Montplaisir, Boucher, & Poirier, 1997). Patients with hereditary RLS have a significantly younger age of onset of disease than those with a negative family history (Winkelmann, Wetter, & Collado, 2000). The pathophysiology of primary RLS is associated with dopaminergic dysfunction and abnormal brain iron metabolism, and secondary RLS is commonly associated with iron deficiency (Allen, 2004).

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RLS occurs as an illness in its own right with major genetic factors as an etiological background but also in a secondary form with iron deficiency, pregnancy, kidney diseases and rheumatic diseases, magnesium deficiency, vitamin-B-12 deficiency, amyloidosis, diabetes mellitus, lumbosacral radiculopathy, Lyme disease, uremia, frequent blood donation as the most important risk factors (Ekbom, & Ulfberg, 2009). Beyond this, multiple drugs have been described to induce or to exacerbate RLS, among them dopamine D2 receptor antagonists, histamine receptor antagonists, antidepressants, lithium, beta blockers, alcohol and caffeine (Satija, & Ondo, 2008).

Dopaminergic dysfunction and a change in the regulation of iron homeostasis can lead to iron depletion in the central nervous system and are thought to be involved in the pathophysiology of RLS (Buturak, & Yazici, 2012). Drug-induced RLS remains an underdiagnosed condition, although it is associated with sleep deprivation, substance abuse and medication non-adherence (Michopoulos, & Ferentinos, 2014). Restless legs syndrome is a common side effect of both antidepressant and antipsychotic medications (Celebi, & Soyata, 2014).

Diagnostic criteria, based on the clinical interview questions, were developed in 1995. Although RLS is common with a general population prevalence of 5–15% (Bjorvatn et al., 2005), it is frequently undiagnosed or misdiagnosed in primary medical settings (Van der Vijver, Walley, & Petri, 2004; Hening et al., 2004). Studies have not been performed to determine the prevalence of RLS diagnosis in non-medical primary contact settings; nevertheless, it is essential that all primary contact practitioners be aware of this condition to ensure proper and efficient management. RLS has a female preponderance (Kushida, 2007; Zucconi, & Ferini, 2004). The exact pathophysiology of this condition is still largely unknown but theories and new knowledge are developing with the recent increased research interest. While studies have demonstrated a lack of awareness among primary medical practitioners (Van der Vijver, Walley, & Petri, 2004; Hening et al., 2004), 65% of patients with RLS also reported using complementary and alternative services in one report (Cuellar et al., 2004). Although studies have not determined the prevalence of

RLS awareness within other health care disciplines, it is important that all primary contact practitioners be aware of this common disorder. Approximately 85% of patients with RLS have periodic movements of sleep, usually involving the legs (periodic leg movements of sleep [PLMS]) (Krueger, 1990). PLMS is characterized by involuntary, forceful dorsiflexion of the foot lasting 0.5-5 seconds and occurring every 20-40 seconds throughout sleep.

Other features commonly associated with RLS but not required for diagnosis are sleep disturbances, daytime fatigue, and involuntary, repetitive, periodic, jerking limb movements: either during sleep or while awake and at rest. All patients with symptoms of RLS should be tested for iron deficiency (Gamaldo, & Earley 2006; Hening, 1999). If a secondary cause of RLS is suspected on the basis of history, abnormal findings on neurologic examination, or poor response to treatment, other laboratory tests should be done. These include a complete blood count (CBC) and measurement of blood urea nitrogen (BUN), creatinine, fasting blood glucose, magnesium. RLS is often unrecognized or misdiagnosed (Gamaldo, & Earley 2006; Evidente & Adler, 1999). Many patients are not diagnosed until 10-20 years after symptom onset. RLS may begin at any age, even as early as infancy, but most patients who are affected severely are middle-aged or older. The sensations of RLS usually are worse during inactivity and often interfere with sleep, leading to chronic sleep deprivation and stress (Silber, 1997).

Once correctly diagnosed, RLS can usually be treated effectively, and in some secondary cases, it can even be cured. Drug therapy for primary RLS is largely symptomatic, since cure is possible only in secondary disease. Medications used in the treatment are dopaminergic agents, benzodiazepines, opioids, anticonvulsants, presynaptic alpha2-adrenergic agonists, iron salt, and non-pharmacologic treatment are sleep hygiene measures, avoidance of caffeine, alcohol, and nicotine in patients with mild RLS who are sensitive to these substances, discontinuation, when possible, of medications that cause or exacerbate RLS, such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs),

diphenhydramine, and dopamine antagonists, exercise, physical modalities before bedtime, such as a hot or cold bath, whirlpool bath, limb massage, and vibratory or electrical stimulation of the feet and toes.

CASE REPORT

A 60-year-old, good body built male patient, belonging to low socioeconomic status, presented with recent complaints of difficulty falling asleep. He is known case of bipolar mood disorder, since 20 years and was on sodium valproate 1000mg per day and clonazepam 2mg at bed time. He was asymptomatic since long so he stopped his medications without consulted his psychiatrist. He had any medical history and was on any medication. He was no family history of psychiatric illness. He did not have any history of kidney diseases and rheumatic diseases, amyloidosis, diabetes mellitus, lumbosacral radiculopathy, lyme disease, uremia, iron, magnesium or vitamin-B-12-deficiency. He had no history of tobacco, drug and alcohol abuse and excessive caffeine consumption. Due to his sleep disturbances we started quetiapine XR 100mg at bed time and given appointment after three day to attend out-patient department for complete work up. He attended OPD on 4th day with complaining severe paresthesia, intractable pain, restlessness inside his bilateral thighs and urge to move his legs, he describing it as a "itchy", "Pins and needles", "creepy crawly" feeling in the legs. This sensation and involuntary movements of his legs disappear upon standing up and walking. According to clinical interview and DSM-4 criteria we diagnosed him quetiapine induced restless leg syndrome. These symptoms gradually faded away over a week after stopping quetiapine. He had no prior history or family history of leg movement disorders and no comorbid physical illness. Neurological examination did not show any abnormalities. The laboratory findings did not reveal any evidence of renal failure or anemia. His iron and ferritin levels were within normal limits. His previous medications restarted due to fear of relapse of his psychiatric symptoms now he is well settled with sodium valproate 1000mg per day and clonazepam 2mg at bed time.

DISCUSSION

This case report discusses RLS in an elderly patient caused by use of low dose quetiapine XR. There are many case reports of RLS due to Quetiapine. One paper reported a case of RLS after low dose quetiapine administration (Celebi, & Soyata, 2014). One elderly patient developed RLS symptoms after addition of 50 mg/d quetiapine to preexisting 20 mg/d citalopram treatment. Another patient developed RLS after a single dose of quetiapine was added to preexisting low-dosed paroxetine (Buturak, & Yazici, 2012). One patient developed RLS after combination therapy with lithium and quetiapine but symptoms were reduced by changing the times of administration without reducing the dose of quetiapine (Demirci, & Sert, 2014). In one case, the combination of quetiapine and venlafaxine was associated with RLS (Celebi, & Soyata, 2014).

In clinical practice, psychotropic medications are extensively used for various off-label indications such as sleep, eating or personality disorders and psychosis. Quetiapine is commonly prescribed for treatment of insomnia in clinical practice (Coe, & Hong, 2012). We ruled out an etiological manifestations such as pregnancy, kidney diseases and rheumatic diseases, iron, magnesium and vitamin-B-12 deficiency, amyloidosis, diabetes mellitus, lumbosacral radiculopathy, lyme disease, uremia, frequent blood donation. The laboratory findings did not reveal any evidence of renal failure or anemia also he had no history of tobacco, drug and alcohol abuse and excessive caffeine consumption, no family history of RLS. That's why in our patient, we thought that the etiology of RLS was dopaminergic receptor blockade by quetiapine. There are clinical similarities between RLS and dopamine antagonist-induced akathisia. As for differential diagnosis, the cardinal feature of RLS is the circadian pattern of symptoms predominating at night. In akathisia, the symptoms do not improve when the patient moves his legs. Antipsychotic-induced RLS has been reported rarely, yet it is important to distinguish RLS from akathisia. Quetiapine then only appeared as causative as it is used mostly as an adjunct therapy augmenting a pre-existing insomnia in this report.

CONCLUSION

Clinicians should always watch for these uncommon side effects during antipsychotic treatment. There is a great possibility for physicians to encounter various well-known side-effects of psychotropic medications during conventional use, but off-label use of these drugs may provoke some very rare and uncommon side-effects. In conclusion, our observations indicate that

quetiapine as an adjunct therapy for sleep might increase the risk for RLS. However, clinicians need to be aware the potential for quetiapine to cause RLS should be able to differentiate it from akathisia. The pathophysiologic mechanisms remain obscure. Further investigations concerning the frequency and possible pathof mechanisms are necessary and more research is needed to clarify underlying mechanisms of antipsychotic induced RLS.

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