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CASE REPORT

WILEY

A case of restless legs syndrome after BNT162b2 mRNA COVID-19 vaccination

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Abstract

Restless legs syndrome (RLS) can be secondary to several disorders. We present an 87-year-old woman who developed RLS 2 days after the first injection of BNT162b2 mRNA coronavirus disease 2019 vaccine. The symptoms of RLS tended to improve and eventually resolved with the administration of gabapentin.

KEYWORDS
BNT162b2 mRNA vaccination COVID-19, COVID-19, restless legs syndrome, sleep-related movement disorder

1 | INTRODUCTION

As of October 2021, BNT162b2 vaccine (Pfizer/Biotech), mRNA-1273 vaccine (Moderna), and ChAdOx1 nCoV-19 vaccine (AstraZeneca) had been approved in Japan for severe acute respiratory syndrome coronavirus 2 resulting coronavirus disease 2019 (COVID-19). Typical adverse events due to BNT162b2 mRNA COVID-19 vaccine are local injection-site reactions, fatigue, headache, myalgia, and chills.[1–3] We report a patient with restless legs syndrome (RLS) after BNT162b2 mRNA COVID-19 vaccination.

2 | CASE REPORT

An 87-year-old Japanese woman was injected 30 μg of BNT162b2 mRNA COVID-19 vaccine intramuscularly for the first time in June 2021. The only adverse event immediately after the vaccination was focal pain at the injection site; however, she developed a tingling and burning sensation in her legs and an uncontrollable urge to move them 2 days after the vaccination. The sensory symptoms started when she was at rest, especially at bedtime, and were relieved by walking. She felt difficulty falling asleep. Her symptoms tended to improve spontaneously 10 days after the vaccination but did not disappear. She consulted our hospital 26 days after the vaccination. She had a medical history of dyslipidemia, treated with 5 mg of atorvastatin, and pulmonary segmentectomy due to lung cancer 9 years ago. She had neither past nor family history of RLS.

On examination, she presented with mild hypopallesthesia in the legs; however, we observed neither cranial nerve abnormalities, pyramidal tract signs, ataxia, nor parkinsonism. The total score of the international RLS study group (IRLSSG) rating scale for the severity of RLS (Table 1) was 22, ranging from 0 to 40, with higher scores indicating greater severity.[4] Laboratory investigations showed mild elevation of HbA1c (6.6%), which did not exacerbate before the onset of RLS. Neither renal dysfunction nor iron-deficiency anemia was observed (BUN 17.4 mg/dL; Creatinine 0.79 mg/dL; Hemoglobin

TABLE 1 Neurological adverse events associated with BNT162b2 mRNA COVID-19 vaccine

Events	References
Acute transverse myelitis	2
Bell's palsy	3
Cerebrovascular disorders	3
Fatigue	1
Guillain-Barre syndrome	2
Headache	1
Lumbar radiculopathy	2
Myalgia	1
Paresthesia	1,2
Seizure	2,3
Syncope	3
Vertigo	3

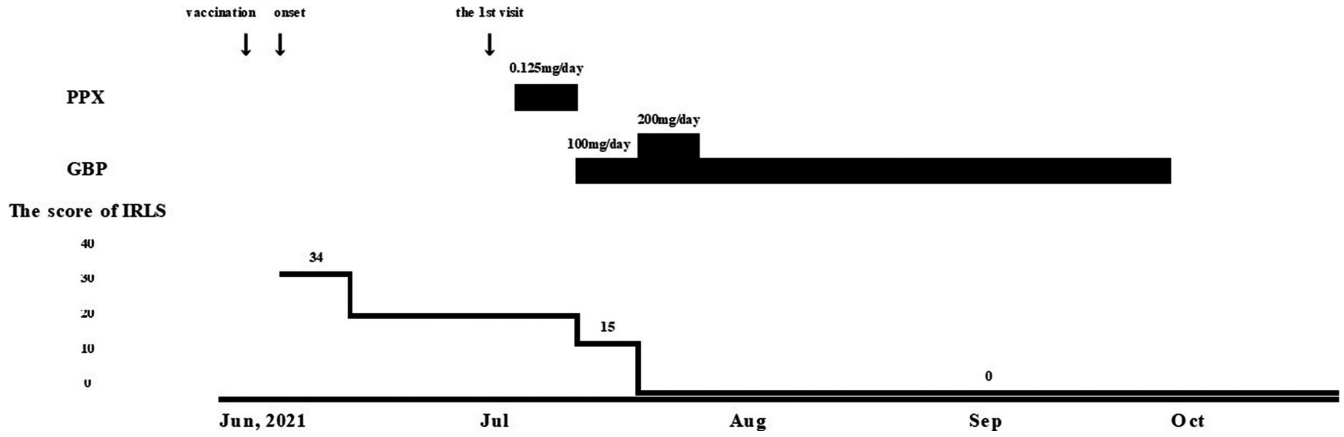

FIGURE 1 Clinical course. RLS developed 2 days after the vaccination and improved over time. The score of IRLS at the onset was assessed at the first visit. GBP, gabapentin; IRLS, International Restless Legs Syndrome Study Group rating scale for severity of restless legs syndrome, PPX, pramipexole

15.0 g/dL; Fe 104 μg/dL; Ferritin 89.6 ng/mL). Brain MRI showed old ischemic changes in bilateral deep white matter, and dopamine transporter single-photon emission computed tomography was normal (specific binding ratio = R: 5.29, L: 4.98, Ave: 5.14). Lumbar spinal MRI showed mild disc herniations. Sural nerve conduction was normal. She did not consent to the examination of cerebrospinal fluid. We administered 0.125 mg of pramipexole (PPX) at bedtime based on the diagnosis of RLS[5]; however, it showed no efficacy. According to her wishes, we switched from PPX to gabapentin (GBP). The symptoms disappeared with 200 mg of GBP at bedtime (total score of IRLS: 0). Thereafter, we reduced and eventually discontinued GBP, which did not induce the recurrence of RLS (Figure 1).

3 | DISCUSSION

Restless legs syndrome is categorized into primary (idiopathic) and secondary (symptomatic). The latter is associated with several conditions, such as iron-deficiency anemia, chronic renal failure, diabetes mellitus, pregnancy, polyneuropathy, and Parkinson's disease.

While the efficacy of the BNT162b2 mRNA COVID-19 vaccine is well-known, various neurological adverse events have been reported (Table 1).[1–3] The post-marketing surveillance of the BNT162b2 mRNA COVID-19 vaccine in Japan listed only one case of RLS.[6] To the best of our knowledge, this is the first detailed report of RLS occurring after vaccination of this novel vaccine. Since vaccine-associated RLS might have been overlooked in the past, we need to focus on it and investigate the frequency of its occurrence.

A limitation was that we could not clarify the pathogenesis of RLS in this patient. Nowadays, both dopaminergic system dysfunction and brain iron deficiency are recognized as main mechanisms in the development of RLS. In addition, the endogenous opioid system, glutamatergic system, and serotonergic system may also be involved in RLS pathophysiology.[7] Further investigations on the relationships between these conditions and this novel vaccine are necessary. Moreover, there is one more possibility. RLS as the phenotype of somatic symptom disorder (SSD) was reported[8] and vaccination could induce SSD.[9] The possibility of RLS of SSD origin is not excluded since GBP is reported to ameliorate SSD.[10] However, it is important to exclude SSD in the diagnosis of RLS after vaccination.

CONFLICT OF INTEREST

None.

DECLARATION OF CONSENT

The authors certify that appropriate patient consent for publication of this report was obtained.

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