

# Serotonin syndrome in a patient with chronic pain taking analgesic drugs mistaken for psychogenic nonepileptic seizure: a case report

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Serotonin syndrome (SS) is a potentially life-threatening condition that is caused by the administration of drugs that increase serotonergic activity in the central nervous system. We report a case of serotonin syndrome in a patient with chronic pain who was taking analgesic drugs. A 36-year-old female with chronic pain in the lower back and right buttock area had been taking tramadol hydrochloride 187.5 mg, acetaminophen 325 mg, pregabalin 150 mg, duloxetine 60 mg, and triazolam 0.25 mg daily for several months. After amitriptyline 10 mg was added to achieve better pain control, the patient developed SS, which was mistaken for psychogenic nonepileptic seizure. However, her symptoms completely disappeared after discontinuation of the drugs that were thought to trigger SS and subsequent hydration with normal saline. Various drugs that can increase serotonergic activity are being widely prescribed for patients with chronic pain. Clinicians should be aware of the potential for the occurrence of SS when prescribing pain medications to patients with chronic pain.

**Keywords:** Chronic pain; Depression; Prescription drug; Seizure; Serotonin syndrome

## Introduction

Chronic pain reduces the quality of life, causes discomfort in daily living, and leads to a loss of labor [1]. Various mechanisms are involved in the development and amplification of chronic pain; consequently, multiple drugs are used in combination to control it effectively [2]. However, although it is generally accepted that analgesic drugs cause adverse effects on the liver, kidney, gastrointestinal, and cardiovascular systems, they can also result in serotonin syndrome (SS). It is a potentially life-threatening condition that is caused by the administration of drugs that increase serotonergic activity in the central nervous system [3,4]. Patients with SS present with a combination of various symptoms, including a change in mental status, neuromuscular hyperactivity, and autonomic in-

stability [3,4].

Here, we aimed to show that clinicians should consider the potential for the development of SS in patients taking analgesic drugs, by presenting the case of a patient with chronic pain who developed SS, which was initially mistaken for a psychogenic nonepileptic seizure.

## Case

A 36-year-old female visited the pain clinic in our university hospital for sudden onset agitation, abnormal movement, and hyperhidrosis (Supplementary Video 1). Three years previously, the patient had undergone surgical procedures (laminectomy and discectomy) owing to a herniated lumbar disc (HLD) on L4–5. After the

surgery, her pain due to HLD was almost relieved completely. However, 2 years after the surgery, she had a car accident; subsequently, she experienced lower back and right buttock pain (numeric rating scale, 8) that was not controlled despite receiving an epidural steroid injection in our pain clinic and taking various oral medications. She had been taking tramadol hydrochloride 187.5 mg, acetaminophen 325 mg, pregabalin 150 mg, duloxetine 60 mg, and triazolam 0.25 mg daily for several months. Five days prior to the visit to our pain clinic, to achieve better pain control, amitriptyline 10 mg was added at bedtime. Approximately 5 hours after taking amitriptyline 10 mg, the patient developed sudden agitation, abnormal movements, and hyperhidrosis.

One day before visiting our pain clinic, she visited the emergency room (ER) of our university hospital. The clinician in the ER diagnosed her with psychogenic nonepileptic seizure based on her history of visiting the psychology department for depression after the car accident and the agitation presented in the ER. Without performing further evaluation and treatment, the clinician discharged her to home. However, as the patient's symptoms continued the next day, she visited our pain clinic. She presented with agitation and nervousness, tremor and myoclonus of bilateral lower limbs, rigidity, hyperhidrosis, dyspnea, and tachycardia (110 beats/min). Her body temperature (36.7°C) and blood pressure (120/70 mmHg) were within normal ranges. Based on Radomski criteria, SS was diagnosed [3], and the patient was admitted to our hospital. Laboratory tests performed to exclude other possible etiologies did not show any abnormalities: white blood cells (WBC), 6,480/ $\mu$ L; hemoglobin, 11.6 g/dL; C-reactive protein, 0.075 mg/dL; aspartate aminotransferase, 23 IU/L; alanine aminotransferase, 15 IU/L; creatinine, 0.51 mg/dL; urine WBC, 0–1/high-power-field; blood culture, negative; and chest X-ray, negative. She was hydrated with normal saline, and pregabalin, duloxetine, and triazolam were discontinued. Approximately 48 hours after admission, her symptoms had completely disappeared.

## Discussion

We describe a case where the patient developed SS due to analgesic drugs. SS was diagnosed based on the Radomski criteria [3], which require the presence of at least four major symptoms or three major symptoms with two minor symptoms (major symptoms: confusion, elevated mood, coma or semi-coma, fever, hyperhidrosis, myoclonus, tremors, chills, rigidity, and hyperreflexia; minor symptoms: agitation, insomnia, tachycardia, tachypnea, diarrhea, low or high blood pressure, impaired coordination, mydriasis, and akathisia), and the historical coincidence of addition, or a recent increase in dosage of drugs that activate the serotonergic sys-

tem. Of the symptoms included in the Radomski criteria, our patient's symptoms fulfilled four major and two minor symptoms. In addition, the patient was administered several drugs that can activate the serotonergic system.

Nonepileptic seizures are characterized by sudden and time-limited disturbances of the motor, sensory, autonomic, emotional, and/or cognitive functions [5]. Symptoms of psychogenic nonepileptic seizures are similar to those of SS. However, unlike SS, the duration of nonepileptic seizures is usually brief, persisting 2 to 5 minutes [5].

Duloxetine and amitriptyline inhibit serotonin reuptake, which alleviates chronic pain through the attenuation of persistent pain mechanisms, such as central sensitization and hyperexcitability of the spinal and supraspinal pain-transmitting pathways [6]. The increased serotonergic activity caused by the action of duloxetine and amitriptyline can induce SS. In addition to the medications mentioned above, tramadol and opioids, popular choices for treating chronic pain, promote serotonin release and inhibit serotonin reuptake, and have been known to contribute to the development of SS [7]. Moreover, approximately 30% to 50% of patients with chronic pain have depression; many use antidepressants, which puts them at risk for the development of SS. As SS is a life-threatening condition, clinicians should be aware of the symptoms and, if patients taking pain medications exhibit these symptoms, drugs related to SS should be stopped immediately, and the patient should be hydrated. Clinicians also should be careful not to misdiagnose SS as psychogenic nonepileptic seizure.

## Supplementary materials

Supplementary Video 1 can be found via <https://doi.org/10.12701/yujm.2021.00948>.

## Notes

### Ethical statements

This study was approved by the Institutional Review Board (IRB) of the Yeungnam University Hospital (IRB No: 2021-01-021). Written informed consent was obtained for publication of this case report and accompanying video.

### Conflicts of interest

No potential conflict of interest relevant to this article was reported.

### Author contributions

Conceptualization, Visualization, Methodology: All authors; Data

curation, Formal analysis, Investigation, Supervision, Validation: MCC; Writing-original draft: All authors; Writing-review & editing: All authors.

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