Clinical Case Report

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# Bilateral sciatic neuropathy with severe rhabdomyolysis following venlafaxine overdose

## A case report

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**Abstract**

**Rationale:** Venlafaxine is an antidepressant and anxiolytic agent that functions by inhibiting central serotonin and norepinephrine reuptake, and it is a relatively recently introduced drug. In particular, overdose of venlafaxine has been reported to cause severe cardiac toxicity including ventricular tachycardia, prolongation of QT interval, and seizure or severe muscular injury. However, reports describing venlafaxine-induced rhabdomyolysis with neuropathy remain scarce. Accordingly, we report such a case involving a 49-year-old woman with bilateral sciatic neuropathy combined with rhabdomyolysis following venlafaxine overdose.

**Patient concerns:** The patient complained of severe pain and tenderness in both thighs, weakness in both ankle flexor and extensor muscles, and a tingling sensation in the toes of both feet.

**Diagnoses:** Bilateral sciatic neuropathy combined with rhabdomyolysis following venlafaxine overdose.

**Intervention:** Needle electromyography revealed fibrillation potentials and positive sharp waves, with absent recruitment in all the major muscles innervating the sciatic nerve bilaterally. Pelvic magnetic resonance imaging was performed after electromyography and revealed multifocal enhancement of signal intensity, suggesting muscle necrosis in the gluteus and thigh muscles, and swelling of both sciatic nerves on short tau inversion recovery (STIR) imaging sequences.

**Outcomes:** Two months later, the patient's ankle dorsiflexion strength, measured with manual muscle test, was grade 0/0, and ankle plantar flexion was grade 0/0. The patient reported little sensation at the lateral and posterior aspects of her lower leg, and dorsum and sole of the foot. A follow-up electromyography study revealed improvement in the long head of the right biceps femoris; polyphasic motor unit action potentials with diminished recruitment were observed, but otherwise unchanged.

**Lessons:** When encountering patients who have overdosed on venlafaxine, it is very important to detect and treat severe complications such as cardiac toxicity, seizure, and rhabdomyolysis, among others. However, if rhabdomyolysis has already materialized, it should not be forgotten that the secondary damage caused by it. Physicians should rapidly detect and be minimized to mitigate future complications.

**Abbreviations:** ALT = alanine aminotransferase, Amp = amplitude, AST = aspartate aminotransferase, CK = creatine kinase, Dur = duration, Fibs = fibrillation potential, Ins = insertional activity, N = normal, Poly = polyphasic activity, PSW = positive sharp waves, Recr = recruitment, WBC = white blood cell.

**Keywords:** rhabdomyolysis, sciatic neuropathy, venlafaxine hydrochloride

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## 1. Introduction

Venlafaxine is a relatively new antidepressant and anxiolytic agent that functions by inhibiting central serotonin and norepinephrine reuptake.[1] There are a few side effects, including tachycardia, fatigue, headache, dizziness, sexual dysfunction, and dry mouth.[1,2] Notably, overdose of venlafaxine has been reported to cause severe cardiac toxicity, including ventricular tachycardia, prolongation of QT interval, and seizure or severe muscular injury.[3,4] Rhabdomyolysis, especially following overdose of venlafaxine, has been repeatedly reported. However, reports describing venlafaxine-induced rhabdomyolysis with neuropathy remain scarce. Accordingly, we report such a case involving a 49-year-old woman with bilateral sciatic neuropathy combined with rhabdomyolysis following venlafaxine overdose.

## 2. Case report

A 49-year-old woman with depression, sleeplessness, and feelings of helplessness began taking venlafaxine (75 mg) daily 4 months prior to this encounter. She was admitted to hospital with stupor (Glasgow Coma Scale score = 8) 4 hours after ingestion of

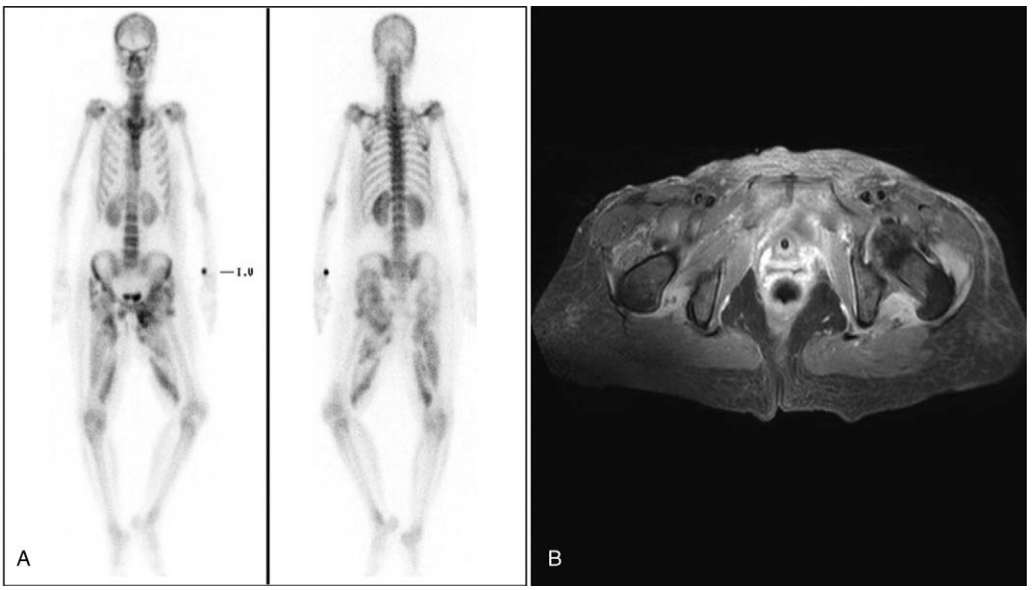


**Figure 1.** (A) Diffuse increased muscle uptake in the back, both buttocks, both thighs, and calf area. (B) Axial sort tau inversion recovery image revealing hyperintensity in both hamstrings, adductor muscles, and quadriceps femoris.

approximately 40 tablets (total of 3 g) without signs of trauma. She did not take any other medication in this attempted suicide.

Initial vital signs were as follows: arterial blood pressure 101/77 mmHg; heart rate 64 beats/min, respiratory rate 22 breaths/min; and core temperature 34 °C. Electrocardiography revealed QRS duration of 105 ms and prolonged QT interval (0.51 second). Neurological and physical examination revealed reactive mydriasis (5 mm), generalized muscle weakness, and normal tones. Dark urine was revealed upon Foley catheter insertion.

Laboratory findings revealed elevated levels of plasma creatine kinase (CK, 19,090 IU/L), alanine aminotransferase (ALT, 150 IU/L), aspartate aminotransferase (AST, 105 IU/L), a white blood cell count of 23,900/μL, serum calcium (7.0 mg/dL), serum creatinine (0.34 mg/dL), and urine myoglobin (1263 ng/mL). Initially, intravenous normal saline, infused at a rate of 150 mL/h, was started after 300 mL hydration, as was alkalization with bicarbonate infusion; a hot air fan was used to counteract low core temperature.

Six hours later, the patient's mental status improved to lethargic (Glasgow Coma Scale score = 13) and core temperature improved to 36.2 °C. However, arterial blood pressure was low (90/60 mmHg), CK levels were elevated (34,540 IU/L), and oliguria was evident. She was admitted to the intensive care unit with a diagnosis of rhabdomyolysis and underwent continuous renal replacement therapy for 3 days. Subsequently, her mental status fully recovered. Laboratory data were as follows: plasma CK 16,238 IU/L; ALT 242 IU/L; AST 192 IU/L; white blood cell counts 21,960/μL; and urine myoglobin (407 ng/mL). A bone imaging study was conducted with Technetium-99m methylene (Fig. 1A). Three weeks later, all abnormal laboratory findings were normalized.

The patient complained of severe pain and tenderness in both thighs, weakness in both ankle flexor and extensor muscles, and a tingling sensation in the toes of both feet. Although swelling was observed in both thighs and buttocks, it was not severe and there was no evidence of arterial insufficiency in both lower extremities in three-dimensional computed tomography angiography. Two weeks later, she was referred to the Department of Rehabilitation for lower leg weakness and gait disturbances. An electrodiagnostic study (Synergy 12.2, VIASYS Healthcare, Warwick, Warwickshire, UK) was performed and the patient was diagnosed with severe bilateral sciatic neuropathy. A nerve conduction study of the upper extremities was normal. The sural and superficial peroneal nerves were bilaterally inexcitable, and the saphenous nerves were unremarkable. Compound muscle action potential was not evoked in the bilateral common peroneal nerve at the tibialis anterior muscle and posterior tibial nerve at the gastrocnemius muscle. There was no response to somatosensory evoked potential in the posterior tibial nerve. Needle electromyography revealed fibrillation potentials and positive sharp waves, with absent recruitment in all the major muscles innervating the sciatic nerve bilaterally (Table 1). Pelvic magnetic resonance imaging was performed after electromyography and revealed multifocal enhancement of signal intensity, suggesting muscle necrosis in the gluteus and thigh muscles, and swelling of both sciatic nerves on short tau inversion recovery imaging sequences (Fig. 1B).

Two months later, the patient's ankle dorsiflexion strength, measured with manual muscle test, was grade 0/0, long toe extension was grade 0/0, and ankle plantar flexion was grade 0/0. The patient reported little sensation at the lateral and posterior aspects of her lower leg, and dorsum and sole of the foot. A follow-up electromyography study revealed improvement in the long head of the right biceps femoris; polyphasic motor unit action potentials with diminished recruitment were observed, but otherwise unchanged. Informed consent was obtained from the patient for the purpose of publication.

## 3. Discussion

In a case series study, patients with venlafaxine poisoning were divided into 2 groups based on the presence of seizures. Median and interquartile range were as follows: venlafaxine dose was 2800 (2006–4350) mg and the measured serum CK level was 317

**Table 1**

**Electromyography—lower extremities.**

| Side | Muscle | Ins | Fibs | PSW | Amp | Dur | Poly | Recr |
|---|---|---|---|---|---|---|---|---|
| Right | Psoas major | N | N | N | N | N | 0 | Complete |
| Right | Vastus medialis | N | N | N | N | N | 0 | Complete |
| Right | Tibialis anterior | N | 3+ | 3+ | - | - | 0 | No activity |
| Right | Peroneus longus | N | 3+ | 3+ | - | - | 0 | No activity |
| Right | Medial gastrocnemius | N | 3+ | 3+ | - | - | 0 | No activity |
| Right | Biceps femoris short head | N | 3+ | 3+ | - | - | 0 | No activity |
| Right | Biceps femoris long head | N | 2+ | 2+ | - | - | 0 | No activity |
| Right | Tensor fascia lata | N | N | N | N | N | 0 | Complete |
| Right | Gluteus maximus | N | N | N | N | N | 0 | Complete |
| Right | Lumbar paraspina muscles | N | N | N | | | 0 | |
| Left | Psoas major | N | N | N | N | N | 0 | Complete |
| Left | Vastus medialis | N | N | N | N | N | 0 | Complete |
| Left | Tibialis anterior | N | 3+ | 3+ | - | - | 0 | No activity |
| Left | Peroneus longus | N | 4+ | 4+ | - | - | 0 | No activity |
| Left | Medial gastrocnemius | N | 3+ | 3+ | - | - | 0 | No activity |
| Left | Biceps femoris short head | N | 2+ | 2+ | - | - | 0 | No activity |
| Left | Biceps femoris long head | N | 2+ | 2+ | - | - | 0 | No activity |
| Left | Tensor fascia lata | N | N | N | N | N | 0 | Complete |
| Left | Gluteus maximus | N | N | N | N | N | 0 | Complete |
| Left | Lumbar paraspinal muscles | N | N | N | | | 0 | |

Amp = amplitude, Dur = duration, Fibs = Fibrillation potential, Ins = insertional activity, N = normal, Poly = polyphasic activity, PSW = positive sharp waves, Recr = recruitment.

(109–588) U/L in the seizure group. Venlafaxine dose was 1500 (900–2700) mg and the measured serum CK level was 91 (61–150) U/L in the non-seizure group.[4] Venlafaxine overdose directly caused skeletal muscle toxicity and severe rhabdomyolysis. In the case of severe rhabdomyolysis, a CK level of 52,600 U/L was measured after the ingestion of 4.5 g of venlafaxine.[5]

It is also known that muscle necrosis, compartment syndrome, acute renal failure, and peripheral nerve damage occur as major adverse effects of rhabdomyolysis.[6,7] The patient in the present case was not taking any other accompanying medication, was in a drowsy state for a few hours, sustained no direct trauma, and exhibited no evidence of vascular insufficiency in both lower extremity arteries in three-dimensional computed tomography angiography.

Although pathogenesis in the present patient was unclear, the most likely diagnosis was compressive neuropathy due to increased tissue gluteal compartment pressure, with rhabdomyolysis and swelling of the gluteal muscles. In this patient, rhabdomyolysis occurred after taking venlafaxine, and it was assumed that additional muscular injury, including postural muscle compressions, may have occurred in the gluteal region while the patient was in an unconscious state and during her stay in the intensive care unit.[8] While the pressure of the gluteal compartment was not measured during the early days of hospitalization, this putative diagnosis was made with consideration of symptoms of pain, tenderness, and sensory depression of both thighs, as well as three-dimensional computed tomography and blood tests. The sciatic nerve does not pass through the fascial compartment, but is known to be vulnerable to swelling of the surrounding muscles as it passes under the gluteus maximus.[8,9]

Nevertheless, the possibility of hypoperfusion of the nerves and compromised circulation in the thighs due to increased tissue pressure cannot be completely excluded.[6] The possibility of direct nerve injury due to the drug is unlikely, considering the results of the nerve conduction studies on the upper extremities.

In this case, the diagnosis was compartment syndrome, and early diagnosis and proper decompression procedure, such as fasciotomy to lower tissue pressure, was performed; it was possible to lessen the severity of nerve injury and increase the probability of better neurological recovery.

There were some limitations in this case. First, the dose of venlafaxine was dependent on the patient's memory alone. We did not measure the serum concentration of venlafaxine; thus, it is difficult to determine the exact dose of venlafaxine. Nevertheless, it was determined that the patient ingested a sufficient dose to cause rhabdomyolysis. Secondly, a careful neurological examination was not performed at the time of admission to the emergency room. This was because medical treatment was prioritized, focusing on the patient's unconscious state and vital signs. Therefore, it is not known exactly when the patient's neurological symptoms began and how they progressed. Finally, because the pressure in the compartment was not measured, there was weak evidence for a putative diagnosis of compartment syndrome and therapeutic recommendations, including fasciotomy.

When encountering patients who have overdosed on venlafaxine, it is very important to detect and treat severe complications, such as cardiac toxicity, seizure, and rhabdomyolysis. However, if rhabdomyolysis has materialized, the secondary damage caused by it should be acknowledged. Physicians should rapidly detect and mitigate future complications.

## Author contributions

**Conceptualization:** Goo Joo Lee.
**Investigation:** Hyeunsuk Seo.
**Supervision:** Goo Joo Lee.
**Writing – original draft:** Jae Ung Ko.
**Writing – review & editing:** Goo Joo Lee, Donghwi Park.

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