Tramadol Induced Intracerebral Hemorrhage: A rare case report

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Case Report

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Abstract

Background: Tramadol is a centrally acting synthetic analgesic, chemically related to morphine and codeine. Tramadol abuse is being used by many people with different adverse effects; most likely seizures, and respiratory depression. Some men use tramadol for erectile dysfunction. We report a case of tramadol-induced intracerebral hemorrhage.

Case report: A 36-year-old male with no history of chronic diseases presented to the emergency department with a sudden onset of left-sided weakness. He had no other conventional vascular risk factors such as hypertension, diabetes, or dyslipidemia. A neurological examination showed right gaze preference and mild right facial droop with left-side hemiplegia, and the left Babinski sign was positive. He denied smoking cigars or consuming khat, and he had no family history of stroke. Routine vital signs were normal. The electrocardiogram was normal. And routine blood investigations were normal. NIH Stroke Scale = 22 when he came in. A CT head showed a 53x24 mm hemorrhage in the right basal ganglia region. He had an MRI angiogram, which showed normal intracranial and extracranial vessels. The patient confirmed that he had been using tramadol for two years due to erectile dysfunction.

Conclusion: A previously healthy middle-aged male with no vascular risk factors developed a hemorrhagic stroke. It was reported that he had been using tramadol for two years. So, the patient developed the right basal ganglia due to tramadol addiction. It is the first time in the literature that tramadol-induced intracerebral hemorrhage has been reported.

Introduction

Tramadol hydrochloride (Ultram; OrthoMcNeil Pharmaceutical, Inc., Raritan, NJ) is a centrally acting synthetic analgesic. Tramadol was authorized for sale as a secure analgesic in 1995 under the brand "Ultram®." Initially, Recent research has shown that the main contributor to its pharmacological efficacy is its opioid activity. Many doctors feel comfortable prescribing it to drug abusers who are in recovery from addiction and to those who are already abusing drugs because the product's labeling is inadequate and its misuse potential has not been shown. Because of this, there have been many cases of abuse and dependency [1] and [2].

The relationship between tramadol and sexual function might be thought of as dialectic. On the other hand, there is evidence to suggest that males who suffer from premature ejaculation (PE) may benefit from the unapproved use of tramadol [3]. Here we report a case of intracerebral hemorrhage due to tramadol addiction. This is the first time in the literature that tramadol has been said to cause a hemorrhagic stroke.

Case Report

A 36-year old male with no history of chronic diseases presented to the emergency department with a sudden onset of left-sided weakness. He had no speech or visual disturbance, no headache, no vomiting
or dizziness. No seizure had been witnessed. He had no other conventional vascular risk factors such as hypertension, diabetes, or dyslipidemia. On examination, normal observations were made. His pulse was regular, his chest was clear, and his heart sounds were normal. Blood glucose was 102 mg/dL and blood pressure was 130/81. His abdomen was soft and non-sensitive and his calves were neither swollen nor tender. A neurological examination showed that the cranial nerves were normal except for right gaze preference and mild right facial droop. Motor examination: 0/5 power in the proximal and distal parts of the left upper and lower limbs. He had an upgoing left plantar reflex (the Babinski sign is positive). His sensation was normal.

The patient had a normal ECG and a score of 22 on the National Institutes of Health Stroke Scale (NIH Stroke Scale = 22) when he came in. Routine blood examination: hemogram, renal and liver function tests were normal; electrolytes and coagulation profile also were normal.

A CT head (figures 1-2) showed a 53x24 mm hemorrhage in the right basal ganglia region. He had an MRI angiogram which showed normal intracranial and extracranial vessels.

The patient was diagnosed with a hemorrhagic stroke and admitted to the neurology department. Treatment of anti-brain edema was started with regular control of blood pressure. The patient started to develop agitation. After asking for a complete history of drug addiction, the patient confirmed that he had been using tremadol for two years due to erectile dysfunction. Throughout, he was hemodynamically stable, with a systolic blood pressure of between 110 mm Hg and 130 mm Hg and a heart rate of between 86 beats per minute and 95 beats per minute. For the agitation, we started haloperidol 5 mg injection twice a day intramuscularly with significant improvement from the agitation.

So we decided to discharge the patient after one week of stabilization and did control head CT (figures 3–4) before discharge and it showed slight resorption of the hematoma in the right basal ganglia with vasogenic edema. After twenty days, we repeated the CT head (figures 5-6) and showed significant resorption of the hematoma (12x24 mm) with improvement of the left side (power 2/5).

**Discussion**

The two enantiomers of tramadol, a centrally acting analgesic chemically related to morphine and codeine, each contribute to analgesic efficacy in a unique way. Both (+)- Tramadol and its byproduct (+)-O-desmethyl-Tramadol (M1) are opioid receptor agonists. Tramadol blocks the reuptake of norepinephrine and serotonin, which slows down the way the spinal cord, sends pain signals [5]. Results of the retrospective cohort analysis revealed that less than 1% of all tramadol users in the general population experienced a presumed incident seizure occurrence as indicated by claims data. [4].

Additionally, confusion, drowsiness, convulsions, and respiratory depression are negative consequences of tramadol misuse. Any of these bad effects makes it more likely that a driver, passenger, or pedestrian will be in an accident because it affects performance and good judgment. Numerous case reports have
been reported to cause seizures in non-epileptic people. Tramadol use increases mortality and the risk of major adverse cardiovascular events in rheumatoid arthritis patients [5].

It has been demonstrated that higher doses of tramadol (200 and 400 mg), but not lower doses (50 and 100 mg), also chronic oral tramadol intake, even in the therapeutic concentrations (100 to 300 ng/ml) for a dose of tramadol which is always prescribed in treatment of mild to moderate pain, may lead to physical dependence, boost its effects, and dose-dependent opioid like withdrawal symptoms. However, lower doses of tramadol (50 and 100 (16). Because of this, many nations throughout the world have placed tramadol on their lists of substances that are subject to controlled distribution [6] [7]. There is a theory that long-term tramadol addiction raises blood pressure and eventually causes small arteries in the brain to rupture, resulting in hemorrhagic stroke, but there isn't enough evidence to back it up. There have been a few rare case reports of strokes with different etiologies, such as stroke of unknown origin and abnormal behavior associated with hemorrhagic stroke [8] [9] [10].

Our case was a middle aged male who had been using tramadol for two years for erectile dysfunction. He used a dose of 200 to 300 mg per day, as he said he benefited from using it and took more time in bed as reported. So he became addicted and unable to hold it. He had no history of chronic diseases like hypertension, diabetes, and hyperlipidemia. He denied smoking or using khat (Catha edulis), which is a plant that is deeply rooted in the cultural life of East African and Southwestern Arabian populations. His blood pressure during the presentation and routine monitoring was normal. So, this is the first time to report for tramadol-induced intracerebral hemorrhage in the literate. There have been reports of seizures and addiction with tramadol, but no reports of strokes yet.

On MRI brain and angiogram, there were no intracranial and extracranial vessel abnormalities like aneurysms, cavernomas or masses. Only the CT head revealed a hematoma in the right basal ganglia. After few control of the CT head, there was significant resorption of the hematoma and with gradually recovering from the weakness in the left side, the patient started to walk with no assistance.

**Conclusion**

A previously healthy middle-aged male with no vascular risk factors developed a hemorrhagic stroke. He had been using tramadol due to erectile dysfunction for two years. So, the patient developed right basal ganglia due to tramadol addiction. There is a theory that long-term tramadol addiction raises blood pressure and eventually causes small arteries in the brain to rupture, resulting in hemorrhagic stroke, but there isn't enough evidence to back it up. It is the first time in the literature to report tramadol-induced intracerebral hemorrhage.

**Declarations**

**Ethical Consideration:** there is no need ethical approval for the case reports in our hospital.
Consent for publication: Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Guarantor: Nor Osman Sidow, the corresponding author

Conflict of interest: The authors declare no conflict of interest.

Author contribution: All the authors are involved this case report writing and publishing.

References


Figures

Figure 1 and 2.
CT head showing hematoma of 53x24 mm in the right basal ganglia.

Figure 3 and 4.
CT head showing slight hematoma resorption of 51x22 mm in the right basal ganglia after 5 days.

Figure 1
A CT head (figures 1-2) showed a 53x24 mm hemorrhage in the right basal ganglia region.
(figures 3–4) before discharge and it showed slight resorption of the hematoma in the right basal ganglia with vasogenic edema.

Figure 2

CT head (figures 5-6) and showed significant resorption of the hematoma (12x24 mm) after 20 days since admission.