Gabapentin-induced myositis in a patient with spinal cord injury – a case report
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ABSTRACT
Myositis and rhabdomyolysis are the same forms of myopathy, with rhabdomyolysis being a more severe form of myopathy. Gabapentin is frequently used in patients with spinal cord injury for neuropathic pain. We report a case of probable gabapentin-induced myositis in a patient with spinal cord injury who was on an increasing dose of gabapentin.

This paraplegic patient was receiving an increasing dose of gabapentin for neuropathic pain in the lower limbs. Gabapentin-induced myositis was diagnosed by a combination of new-onset generalized body pain with tenderness, an increase in creatine kinase, elevated myoglobin levels, and a score of 6 on the Naranjo adverse drug reaction probability scale. Withdrawal of the gabapentin resolved the symptoms completely. Blood parameters became normal within two weeks.

We suggest that myopathy, in the form of myositis, should be recognized as a potential side effect of gabapentin in the literature.

Keywords: neuropathic pain, gabapentin, myositis, spinal cord injury

INTRODUCTION
We report a case of probable gabapentin-induced myositis in a patient with spinal cord injury. Gabapentin is frequently used to treat neuropathic pain in patients with spinal cord injury. The patient was on an increasing dose of gabapentin because of neuropathic pain in his lower limbs. Gabapentin-induced myositis seems rare with few case reports. Rhabdomyolysis was reported in the FDA Neurontin (gabapentin) literature as postmarketing experience. Rhabdomyolysis is still not an adverse event because of insufficient data to support its estimated incidence or establish causation.
The objective of this case report is to confirm the suspicion of myositis in a patient with gabapentin who developed new-onset generalized muscle pain.

**CASE PRESENTATION**

Our patient was a 29-year-old Sri Lankan male, with no known previous comorbidities. On October 31, 2018, he presented to the emergency department of Hamad General Hospital. He had a history of a heavy object falling on his back. He complained of severe back pain and the inability to move his lower limbs. He was able to move both of his upper limbs; however, the power of his lower limbs was 0/5. His sensations were intact, the anal tone was weak, and bulbocavernous reflex was +ve. A CT scan and MRI were performed and showed a burst fracture of the L2 vertebral body with retropulsion, which compromised the spinal canal, causing severe spinal cord injury.

On October 31, 2018, he underwent urgent T12-L4 transpedicular screw fixation and a T12 and L1 laminectomy. He was kept postoperatively in the trauma ICU for observation. A follow-up X-ray of his spine showed satisfactory alignment and placement of the screws.

The patient was reviewed by the rehabilitation physician, who agreed to move the patient to the Qatar Rehabilitation Institute for an active rehabilitation program.

On November 8, 2018, the patient was transferred from the neurosurgery ward to QRI.

The patient underwent rehabilitation by a multidisciplinary team in a spinal cord injury rehabilitation unit.

On admission to QRI, the patient was paraplegic ASIA B level L2.[6] He had no power in both lower limbs but had intact sensations. He was dependent for activities of daily living with a functional independence measure (FIM) score of 69/126.[6]

He was on gabapentin 300 mg, three times a day, for neuropathic pain in his lower limbs. He was also taking dalteparin sodium, senna, and a multivitamin. His pain score was a numeric rating score (NRS) 6/10.[6] His pain was not relieved but was increasing.

On November 13, 2018 (day 13 postinjury), the dose of gabapentin was increased to 600 mg, three times a day. On the next day, (day 14 postinjury), he complained of increased lower limb and whole-body pain of NRS 9/10. On examination, he had severe muscle tenderness throughout his whole body, including his upper and lower limbs (NRS 9–10/10). He was observed for a few days presuming that the pain was due to exercise and the preexisting pain. When his pain had not improved, an internal medicine consultation was performed. A blood workup was sent on suspicion of myositis on 5th December 2019 and returned with the following results: serum creatine kinase (CK) was high– 747 U/L (reference range, 39–308 U/L), myoglobin was high– 152 ng/ml (reference range, 28–72 ng/ml), C-reactive protein (CRP) was high– 22.9 mg/L (reference range, 0–5 mg/L), ALT was high– 75 U/L (reference range, 0–41 U/L), AST was high– 46 U/L (reference range, 0–40 U/L), and the creatinine level was normal. Unfortunately, his CK and myoglobin levels before the increase of gabapentin dose were not available.

A diagnosis of gabapentin-induced myositis was made from the background of blood investigations (increase CK and myoglobin), clinical profile (new-onset generalized muscle pain and tenderness), and Adverse Drug Reaction Probability Scale (Naranjo algorithm) score of 6 of gabapentin. The Naranjo algorithm score of 6 indicated that gabapentin is the probable cause of myositis.[7,8] Other medications- senna, dalteparin sodium, and the multivitamin were excluded as causes of myositis by their negative Naranjo algorithm scores (senna –2, dalteparin sodium –2, and multivitamin -2). On December 12, 2018 (day 42 postinjury), gabapentin was discontinued. His severe muscle pain of the whole body reduced dramatically in the next three days after discontinuation of the gabapentin. His follow-up blood workup on December 19, 2018 (day 49 postinjury) showed a CK of 203 U/L (previously 747 459 U/L) and myoglobin 90 ng/ml (previously 152 ng/ml). After discontinuation of gabapentin, his pain was managed effectively with paracetamol 1000 mg, when necessary, three times daily (if pain NRS 4/10 or more).

On January 16, 2019 (day 77 postinjury), the patient was discharged from QRI. On discharge, the patient was ASIA C level L2. He was on self-intermittent catheterization and was wheelchair bound (self-propelled) for indoor and outdoor mobility. His FIM score was 111/126 (FIM on admission to QRI: 69/126). There were no adverse effects after discontinuing gabapentin. He was followed up in an outpatient rehabilitation program. Table 1 describes the timeline of important clinical developments of the case.
DISCUSSION

Myositis and rhabdomyolysis are the same forms of myopathy; however, rhabdomyolysis is the more severe form of myopathy with CK levels more than 11 times greater than normal in the blood. The CK level of our patient was 747 U/L, and so we used the term myositis instead of rhabdomyolysis.

It was difficult to diagnose gabapentin-induced myositis clinically because of preexisting neuropathic pain in both lower limbs. The suspicion occurred because of generalized muscle pain and tenderness. Blood tests provided the necessary evidence for myositis. The most important laboratory tests were the measurements of CK and myoglobin in the serum, which are sensitive and pathognomonic, respectively.

The dramatic relief of pain after discontinuation of gabapentin, and the gradual normalization of CK and myoglobin levels following discontinuation of gabapentin, indicated that gabapentin was the most probable cause of the symptoms. The probability of gabapentin as the causative agent of the myositis was determined by the Naranjo Adverse Drug Reaction Probability Scale, which showed a score of 8 (probable adverse drug reaction).

Gabapentin-induced myositis can be localized, generalized, or can exacerbate existing pain. In our case, it was generalized muscle pain and tenderness. Gabapentin is frequently used in rehabilitation for patients who have neuropathic pain. The exacerbation of existing pain, or the initiation of generalized pain, should call attention to possible gabapentin-induced myositis if the patient is on gabapentin. Table 2

The mechanism of myositis by gabapentin is not exactly known. The most probable primary cause of myositis, in our case, is medication-induced auto-immune reactions. Idiosyncratic rhabdomyolysis due to gabapentin was reported. In our case, the increase of gabapentin dose with increased generalized muscle pain indicates that it was also dose dependent.

Common side effects of gabapentin include sleepiness and dizziness. Serious side effects include acute renal failure, hepatitis, pancreatitis, Stevens-

| Dates            | Important history                                                                 | Pain scale (NRS)          | FIM      |
|------------------|----------------------------------------------------------------------------------|---------------------------|---------|
| October 31, 2018 | The patient presented to the emergency department of Hamad General Hospital with paraplegia. | Not available             | Not performed |
| October 31, 2018 | He underwent urgent T12-L4 transpedicular screw fixation and T12 and L1 laminectomy. | Not available             | Not performed |
| November 8, 2018 | He was transferred from the neurosurgery ward to QRI. Gabapentin was increased to 600 mg, 3 times a day from 300 mg, 3 times a day. | 3/10                      | 69/126   |
| November 13, 2018| The patient started having severe muscle tenderness in his whole body.          | 6/10                      | 72/126   |
| November 14, 2018| Gabapentin was discontinued after a diagnosis of gabapentin myositis.           | 8/10 lower limbs pain score 9-10/10 muscle tenderness pain score | 72/126   |
| December 12, 2018| His pain improved dramatically in three days after discontinuation of gabapentin. | 8-10/10                  | 101/126  |
| December 15, 2018| His blood workups showed normal levels within 2 weeks                            | 1/10                      | 101/126  |
| January 16, 2019 | He was discharged from QRI.                                                      | 0/10                      | 111/126  |

NRS: numeric rating score; FIM: Functional Independence Measure; QRI: Qatar Rehabilitation Institute
Johnson syndrome, suicidal ideation, and thrombocytopenia.\textsuperscript{14}

Gabapentin-induced rhabdomyolysis or myositis is rare. We could not find myopathy, myositis, or rhabdomyolysis as the side effects of gabapentin in the British national formulary BNF.\textsuperscript{70} Rhabdomyolysis is reported as postmarketing experience in the FDA Neurontin (gabapentin) literature. Rhabdomyolysis is not a well-established adverse effect of gabapentin because of the absence of sufficient evidence. We believe that additional similar case reports might help to include myositis as a potential adverse effect of gabapentin in the literature.

The similarity of the clinical presentation of myositis in patients with neuropathic pain might make the diagnosis of myositis difficult. We feel that rehabilitation specialists should be more aware of this condition, for early diagnosis and management of gabapentin-induced myositis.

There are some limitations to this study. Preexisting myositis could not be excluded because of the unavailability of CK and myoglobin levels of the patient. However, preexisting myositis can be excluded indirectly by observing CK levels becoming normal after the discontinuation of gabapentin. Another limitation is that myositis was not confirmed by biopsy or EMG studies. Myositis was diagnosed by new-onset generalized muscle pain and increased CK and myoglobin only.

CONCLUSION

Gabapentin-induced myopathy is rare. Any exacerbation of existing pain, or new generalized muscle pain in patients on gabapentin, should call attention to possible gabapentin-induced myopathy. Clinical findings of muscle tenderness increased CK and myoglobin levels, increased Naranjo Adverse Drug Reaction Probability Scale scores, could collectively confirm the diagnosis. Withdrawal of gabapentin relieves muscle pain rapidly and reduces the values of laboratory parameters.

ABBREVIATIONS

Alanine aminotransferase: ALT
American Spinal Injury Association: ASIA
Aspartate aminotransferase: AST
British national formulary: BNF70
Computed tomography: CT
C-reactive protein: CRP
Creatine kinase: CK
Functional independence measure: FIM
Intensive care unit: ICU
Lumbar: L
Magnetic resonance imaging: MRI
Milligrams Per Liter: mg/L
Nanograms per Milliliter: ng/ml
Numeric rating score: NRS
Thoracic: T
Units per Liter: U/L

DECLARATION

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Authors’ contributions
SG contributed in design, acquisition, analysis, interpretation, drafting, and revision of the article. SV
and WY contributed in analysis, interpretation, and revision of the article. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

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This case report was written in accordance with the recommendations of the Declaration of Helsinki. The patient is described anonymously and gave written informed consent for the publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Competing interests**

The authors declare that they have no competing interests.

**REFERENCES**

1. Kaya, YE. An evaluation of gabapentin and pregabalin usage in the treatment of neuropathic pain related to spinal cord injury. *Ann Med Res.* 2019;26(3):521 – 8.

2. Coupal TM, Chang DR, Pennyooke K, Ouellette HA, Munk PL. Radiologic findings in gabapentin-induced myositis. *J Radiol Case Rep.* 2017;11(4):30 – 7.

3. Qiu X, Tackett E, Zeid K. A case of gabapentin overdose induced rhabdomyolysis requiring renal replacement therapy. *Clin Case Rep.* 2019 Jul 11;7(8):1596 – 9.

4. American Spinal Injury Association. International Standards for Neurological Classifications of Spinal Cord Injury. revised ed. Chicago, Ill; American Spinal Injury Association. 2000;1 – 23.

5. Wright J. Functional independence measure. In: Kreutzer J.S., DeLuca J., Caplan B. (eds) Encyclopedia of Clinical Neuropsychology. Springer, New York, NY 2011.

6. Krebs EE, Carey TS, Weinberger M. Accuracy of the pain numeric rating scale as a screening test in primary care. *J Gen Intern Med.* 2007;22(10):1453 – 8.

7. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther.* 1981;30(2):239 – 45.

8. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012 [Internet]. Adverse Drug Reaction Probability Scale (Naranjo) in Drug Induced Liver Injury. [Updated 2019 May 4]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK548069/.

9. Pasternak RC, Smith SC Jr, Bairey-Merz CN, Grundy SM, Cleeman JI, Lenfant C, et al. ACC/AHA/NHLBI Clinical Advisory on the Use and Safety of Statins. *Stroke.* 2002;33(9):2337 – 41.

10. Keltz E, Khan FY, Mann G. Rhabdomyolysis: the role of diagnostic and prognostic factors. *Muscles Ligaments Tendons J.* 2013;3(4):303 – 12.

11. Tuccori M, Lombardo G, Lapi L, Vannacci A, Blandizzi C, Del Tacca M. Gabapentin-induced severe myopathy. *Ann Pharmacother.* 2007;41(7):1301 – 5.

12. Jones JD, Kirsch HL, Wortmann RL, Pillinger MH. The causes of drug-induced muscle toxicity. *Curr Opin Rheumatol.* 2014;26(6):697 – 703.

13. Goa KL, Sorkin EM. Gabapentin. A review of its pharmacological properties and clinical potential in epilepsy. *Drugs.* 1993;46(3):409 – 27.

14. Joint Formulary Committee. BNF 70 (British National Formulary September 2015–March 2016). London: BMJ Publishing and the Royal Pharmaceutical Society of Great Britain; 2016.