

# A rare case of bilateral lower extremity edema due to low dose gabapentin therapy in a young male patient

## Abstract

46 year old male with past medical history of schizoaffective disorder and chronic lower back pain, was admitted for management of worsening depression and anxiety. He was started on gabapentin, 300mg twice daily for his back pain and anxiety symptoms. His only other medication was hydrocodone. Over next few days, he started developing worsening bilateral lower extremity edema. He did not have any cardiovascular related symptoms. Physical exam was only significant for 3+ pitting edema with all laboratory values and imaging being unremarkable. Gabapentin was discontinued and his lower extremity swelling improved over subsequent days. Incidence of pedal edema with gabapentin use is approximately 7 to 7.5% with all studies being in elderly patients receiving doses above 1200 mg/day. This case illustrates that lower doses of gabapentin can also cause this adverse effect. It is important to recognize this adverse effect because gabapentin is used in conditions like diabetic neuropathy, which is associated with multiple co-morbidities that can give rise to bilateral leg swelling. Presence of gabapentin induced leg swelling can thus confound the clinical picture.

### Key words:

*Edema, gabapentin, lower extremity*

## Introduction

Gabapentin was originally developed as a muscle relaxant/anti-spastic agent. It was later approved by the Food and Drug Administration for epilepsy and postherpetic neuralgia. Since then, it has found its use in fibromyalgia, bipolar disorder, trigeminal neuralgia, diabetic neuropathy, postoperative analgesia, migraine headaches, social phobia, depression, panic disorder, insomnia, restless leg syndrome, and many other off-label uses.<sup>[1]</sup> One of its uncommon adverse effects is bilateral pitting edema. This adverse effect has been reported at doses higher than 1800 mg/day<sup>[2,3]</sup> and mostly in the geriatric population.<sup>[2,3]</sup> This report is a classic presentation of bilateral pitting edema due to gabapentin use at a significantly lower dose than previously reported.

## Case Report

A 46-year-old male with a past medical history of the schizoaffective disorder and chronic lower back pain secondary to disc herniation was admitted to the psychiatry

ward for the management of his worsening depression and anxiety. Patient's back pain, described as a shooting pain radiating down from his lower back to his legs bilaterally was poorly controlled. His pain at the time was managed with hydrocodone. This was the only medication he was on. He was put on gabapentin 300 mg twice daily to relieve his pain and anxiety. Over next few days, he started developing worsening lower extremity edema causing discomfort on ambulation [Figure 1]. He denied dyspnea, orthopnea, paroxysmal nocturnal dyspnea, dysuria, and any other cardiovascular or

**Arunpreet Kahlon, Naveen Gnanabakthan,  
Amrita Dhillon, Dinesh Subedi**

Department of Medicine, State University of New York Upstate Medical University, Syracuse, New York, USA

### Address for correspondence:

Dr. Dinesh Subedi,  
Department of Medicine, 750 East Adams Street,  
Syracuse 13210, New York, USA.  
E-mail: subedid@upstate.edu

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**Figure 1:** Bilateral pitting edema due to gabapentin

genitourinary symptoms. Physical exam was significant for 3+ pitting edema up to his knees bilaterally. Serum sodium, potassium, chloride, and bicarbonate levels were 141 mmol/L, 4.2 mmol/L, 101 mmol/L, and 24 mmol/L respectively, all of which were within normal limits. The thyroid function test was also normal with thyroid-stimulating hormone level of 2.1 milli-international units/ml. His serum creatinine and albumin levels were 0.8 mg/dl and 4.2 g/dl respectively, which were unchanged from his previous levels. Urinalysis was negative for any bacteria, nitrite, leukocytes, casts, or protein. He denied use of any over the counter medications. Echocardiogram and ultrasound Doppler of his lower extremities were also unremarkable. Gabapentin was discontinued, and his lower extremity swelling dramatically improved over next few days.

## Discussion

Gabapentin is frequently used in conditions such as fibromyalgia, anxiety disorders, neuralgias, migraine headaches, restless leg syndrome, diabetic neuropathy, and many other off-label uses.<sup>[1]</sup> The exact mechanism of action of gabapentin remains unknown, but the most predominant theory involves inhibition of alpha 2 delta voltage-dependent calcium channel subunit leading to reduced neurotransmitter release and decreased postsynaptic excitability.<sup>[4]</sup> How gabapentin causes, pedal edema is unclear and the data published on gabapentin induced pedal edema is very scarce. We hypothesized that the mechanism of causing pedal edema could be similar to that of other calcium channel blockers, such as amlodipine, which also causes peripheral edema.<sup>[5]</sup>

Almost all cases of gabapentin induced pedal edema have been reported in elderly patients receiving doses >1200 mg/day.<sup>[2,3]</sup> In a pooled analysis of three clinical trials of gabapentin used in postherpetic neuralgia, Parsons *et al.* found the incidence of pedal edema to be 7.5% in geriatric patients receiving doses above 1800 mg/daily.<sup>[2]</sup> In another study, Moore *et al.* found the incidence to be 7% at doses 1200 mg/day or more.<sup>[3]</sup> There has been one reported case of gabapentin induced pitting edema in a 76-year-old male at a dose of 300 mg daily.<sup>[6]</sup> Thus, the case discussed above describes a classic presentation of a patient developing bilateral pedal edema on a low dose of gabapentin and resolving upon its discontinuation. The clinical presentation was rare because the dose of gabapentin used was much lower than that was reported in previous studies. Also, since previously reported cases have all been in elderly patients who are more prone to developing lower extremity edema, the relatively young age of this patient makes the presentation more unusual.<sup>[7]</sup> This is clinically important as gabapentin is a very commonly prescribed medication to patients with neuropathies, especially in diabetic neuropathy who may also have other co-morbid condition such as heart failure, malnutrition, nephropathy, that can give rise to bilateral leg swelling.

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## Conflicts of interest

There are no conflicts of interest.

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