Spinal Cord (2012) 50, 472–473

www.nature.com/sc

CASE REPORT

Reversible post-pregabalin peripheral edema in a spinal cord injury patient

U Guzelkucuk, I Duman, B Yılmaz and AK Tan

Department of Physical Medicine and Rehabilitation, Gülhane Military Medical Academy, Turkish Armed Forces Rehabilitation Center, Ankara, Turkey

Study design: Case report.
Objectives: To report a case of paraplegia with limb edema caused by pregabalin.
Setting: Turkish Armed Forces Rehabilitation Center, Ankara, Turkey.
Case report: A 40-year-old male patient with T11 paraplegia had the complaint of swelling in both the lower limbs. He had been given pregabalin because of the neuropathic pain in both the lower limbs. At 10 months, the patient has experienced edema in lower limbs. There was severe edema in both legs, ankles and feet, more evident on the left. Venous Doppler ultrasound was normal on both sides. Blood tests for possible etiologies were normal. No other etiology could be found. The edema was considered to be caused by pregabalin and the medicine was ceased gradually. The edema resolved completely in 2 weeks.
Conclusion: Pregabalin, which is one of medications used for neuropathic pain, might cause limb edema, that is, a condition needs differential diagnosis. This is particularly important for patients with spinal cord injuries (SCIs). Such adverse effect of pregabalin should be kept in mind as an etiology of limb edema in SCI management.
Spinal Cord (2012) **50,** 472–473; doi:10.1038/sc.2011.79; published online 12 July 2011

Keywords: pregabalin; limb edema; deep venous thrombosis; paraplegia; spinal cord injury

Introduction

Pregabalin is one of the medications used for the treatment of neuropathic pain.[1–5] Although peripheral edema is one of the adverse effects, it was reported to be less common.[1,3,4] As deep venous thrombosis (DVT) is a life threatening complication, swelling in a limb is an important condition to be differentiated in spinal cord injury (SCI) patients.

In search of the literature, we could reach only two case reports, regarding facial and feet edema in generalized anxiety disorder, and limb edema in posttraumatic stress disorder.[3,4] Limb edema caused by pregabalin in SCI patients has not been reported previously to our knowledge. Herein, we represent a case of a SCI who developed limb edema because of pregabalin.

Case report

A 40-year-old male patient with T11 paraplegia ASIA-B (American Spinal Injury Association-B) was admitted to our department with the complaint of swelling in both the lower limbs. He had experienced a surgery because of T10 vertebral fracture 2 years ago. Six months later, he had been administered pregabalin 300 mg per day because of the neuropathic pain in both the lower limbs. Ten months after the pregabalin was started, edema developed in both the feet and ankle. Through the following 8 months edema increased gradually, including the cruris.

In physical examination, there was severe edema in both legs, ankles and feet. Venous Doppler ultrasound was normal on both sides. Blood tests for liver and renal functions were normal. Blood glucose, electrolytes, albumin, erythrocyte sedimentation rate and C-reactive protein were normal. The patient was under no other medicine except for baclofen and pregabalin. His blood pressure was normal and has no medical history regarding the conditions that can potentially cause peripheral edema.

As all of the laboratory and radiological evaluations were normal and the DVT was excluded, the edema was considered to be caused by pregabalin and the medicine was ceased gradually. The edema resolved completely in 2 weeks. Circumference decreased by 3 cm on each leg.

Discussion

Edema in a limb can be caused by various conditions, such as venous problems, malnutrition, protein deficiency, liver,

Correspondence: Dr U Guzelkucuk, Department of Physical Medicine and Rehabilitation, Gülhane Military Medical Academy, Turkish Armed Forces Rehabilitation center, Bilkent, Ankara 06533, Turkey.
E-mail: druguzelkucuk@yahoo.com
Received 9 May 2011; revised 24 May 2011; accepted 10 June 2011; published online 12 July 2011

kidney heart diseases, malignancy, inflammatory process or can occur as an adverse effect of some medications such as non-steroidal anti-inflammatory drugs, calcium channel blockers, steroids, cyclosporin, immune modulators and lithium.[3]

Pregabalin has been reported to be tolerated well and its most common side effects are vertigo, dizziness, balance disorder, ataxia, tremor, diplopia, amblyopia, euphoria, disturbance in attention, somnolence, confusional state, asthenia and fatigue, and its less common side effects are constipation, dry mouth, edema and peripheral edema.[1,2]

Limb edema is particularly important in patients with SCI as it may be caused by some life threatening conditions. DVT is the one that must be thought first in this regard. We performed venous Doppler ultrasound and excluded DVT in our patient. Other reasons for edema were also excluded by blood testing and detailed medical history. Our patient was under only two medications, pregabalin (300 mg per day) and baclofen (60 mg per day). Baclofen is not known to cause edema. Thus, we considered edema was secondary to pregabalin and ceased the medicine gradually. Although baclofen was continued to be used, the complete recovery of edema within 2 weeks after the pregabalin was ceased, supported our opinion. Our case considers that pregabalin might cause limb edema. Such adverse effects experienced in use of pregabalin are usually mild.[1,4] In contrast, the edema in our patient was severe enough to make us consider DVT.

Wustmann[4] proposed a mechanism for the development of edema through K^+ channels in smooth muscle cells. However, exact mechanism is still unclear and should be elucidated in future studies. As patients with SCI are already prone to develop edema in lower limbs because of immobilization and loss of muscle strength, it might be hypothesized that SCI patients are more at risk of leg edema while using pregabalin. Side effects of medications are usually expected to present near after they are started. In our case, edema occurred approximately at the 10th month of medication use. We do not have an explanation for its late occurrence, but we think that this might be valuable because of two points. First, edema might develop even long after pregabalin is started. Second, because the edema that occurred long after pregabalin was started might not be considered to be secondary to pregabalin; being aware of such a side effect might prevent a delay in diagnosis and some unnecessary tests.

In conclusion, edema is one of common problems that needs differential diagnosis. Pregabalin should be kept in mind as an etiology of limb edema in SCI management.

Conflict of interest

The authors declare no conflict of interest.

References

1 Zaccara G, Gangemi P, Perucca P, Specchio L. The adverse event profile of pregabalin: a systematic review and meta-analysis of randomized controlled trials. *Epilepsia* 2011; **52**: 826–836.
2 Semel D, Murphy TK, Zlateva G, Cheung R, Emir B. Evaluation of the safety and efficacy of pregabalin in older patients with neuropathic pain: results from a pooled analysis of 11 clinical studies. *BMC Fam Pract* 2010; **11**: 85.
3 Krüger S, Lindstaedt M. Pregabalin and edema in young women suffering from premenstrual syndrome. *Pharmacopsychiatry* 2010; **43**: 202–203.
4 Wustmann T, Piro J, Gutmann P. Metabolic considerations in a case of pregabalin-induced edema. *Pharmacopsychiatry* 2009; **42**: 75–76.
5 Siddall PJ. Management of neuropathic pain following spinal cord injury: now and in the future. *Spinal Cord* 2009; **47**: 352–359.