



CASE REPORT

A probable case of pregabalin - related reversible hearing loss

Pregabaline bağlı gelişen geçici işitme kaybı, beklenmedik bir olgu

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Summary

Pregabalin and gabapentin are similar compounds with analgesic, anticonvulsant, and anxiolytic characteristics. Due to these pharmacological features, they are commonly used throughout the world in neuropathic pain treatment and anxiety disorders. Mild to moderate side effects of the central nervous system, such as dizziness and somnolence, are important factors in deciding to terminate the use of pregabalin. Studies have also reported that the use of dose-dependent pregabalin resulted in peripheral edema and weight gain. Described in this case report is hearing loss occurring after an increase in the drug dose of a patient using pregabalin.

Keywords: Anticonvulsant drugs; hearing loss; neuropathic pain; pregabalin.

Özet

Pregabalin ve gabapentin, analjezik, antikonvülsan ve anksiyolitik özelliklere sahip benzer bileşiklerdendir. Bu tür farmakolojik özellikler nedeniyle, nöropatik ağrı tedavisinde ve anksiyete bozukluklarında genel olarak dünyada yaygın olarak kullanılmaktadır. Santral sinir sisteminde baş dönmesi ve uyuşukluk gibi hafif ila orta şiddette yan etkiler pregabalinin kullanımını sonlandırmada önemli faktörlerdir. Aynı zamanda, bazı çalışmalarda, doza bağlı pregabalin kullanımı, hastalarda periferik ödem ve kilo vermeye neden olmuştur. Bu olguda, önceden pregabalin kullanan hastanın ilaç dozunda bir artış yapıldıktan sonra oluşan işitme kaybını sunmak istedik.

Anahtar sözcükler: Antikonvülsan ilaçlar; işitme kaybı; nöropatik ağrı; pregabalin.

Introduction

Pregabalin and gabapentin are similar compounds with analgesic, anticonvulsant and anxiolytic characteristics. Owing to such pharmacological features, they are commonly used throughout the world in neuropathic pain treatment and anxiety disorders.^[1]

The greatest advantages of these drugs are listed as relative safety, ease of use, high tolerance and lack of adverse interaction with other drugs.^[1] Mild to moderate side effects such as dizziness and somnolence in the central nervous system are important factors in terminating the use of pregabalin. At the same time, in some studies, the use of dose-dependent pregabalin resulted in peripheral edema and weight gain in 5–20% and 4–12% of patients, respectively.^[2]

We are not aware of any case report about hearing loss and pregabalin in the literature. We want to emphasize that pregabalin treatment may be associated with dose dependent hearing loss with this case.

Case Report

A 68-year-old male patient came to our pain clinic with a complaint of low back pain. He had a history of diabetes mellitus and hypertension and was using oral antidiabetic and antihypertensive medication. When asked about his pain, he said that it was spreading from the right hip region to the tip of his toes and he described it as hot, pricking, and throbbing. The pain increased day by day and it was constant. On a scale of 1 to 10, he gave his pain intensity 7 points. His pain doesn't change according to the times of the day,

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it increases with movement and his sleep quality has decreased. The patient had been told to have a lumbar disc hernia on his brain surgeon's examination.

On the physical examination, leg lift test on the the right leg was positive at 45° and the laseque test was positive. There was no trigger points and nomuscle strength loss. MR imaging revealed a foraminal annular fissure at L3-4 level, a right resesial protrusion at L4-5 level anda midline supression of the tecal sac at the L5-S1 level.

The patient used non-steroidal anti-inflammatory drugs in treatments performed in different clinics and didn't benefit from them.

We started pregabalin 75 mg, only at nights, for 3 days and than 150 mg daily as two divided doses (BID) for his neuropathic pain. Because the analgesic efficacy was insufficient after 15 days, pregabalin was increased to 300 mg/day and then 450 mg/day. Five days after the increasement he came back with hearing loss. We referred the patient to the Ear-Nose-Throat (ENT) clinic. ENT evaluation revealed that he had normal examination findings, howeverthe hearing test showed mixed type hearing loss, severe in the right ear and mildin the left ear. Theyrecommended to repeat test five days later. Considering that the hearing lose might be related to the increased dosage of pregabalin, the dose was reduced to 300 mg/day. It was determined that hearing loss was reduced in the control tests performed five days later. Interventional treatment was planned and the patient underwent transforaminal steroid injection therapy.

The patient's treatment was continued with 300 mg (2x150 mg) daily dose and he did not develop any further problems.

Discussion

The mechanisms of action of pregabalin and gabapentin are not well known. Pregabalin Gamma is a lipophilic analogue of Amino Butyric Acid (GABA). It binds to the alpha-2 delta subunit of calcium channels, reducing the release of stimulatory neurotransmitters and enhancing neuronal GABA levels.^[3] Currently, the use of pregabalin for treatment of neuropathic pain, anxiety disorders and partial seizures is increasing rapidly.^[4]

The most frequent side effects of pregabalin treatment doses are; facial rash, dizziness, drowsiness, peripheral edema and weight gain.^[4-6] An increase in the incidence of hyponatremia and systolic dysfunction has been reported in elderly and mainly heart failure patients.^[7,8] There are also publications in the literature that report pregabalin-induced hepatotoxicity,^[9] visual hallucinations in a patient with Charles Bonnet syndrome,^[10] and heart failure in a patient without a cardiac problem.^[8] Dizziness and somnolence are frequent and important factors to terminate the use of pregabalin.^[2]

Pierce et al.^[11] reported a case of gabapentine-induced hearing loss in a patient with diabetes mellitus and acute renal failure, Top et al.^[12] have reported to detect sensorineural hearing loss due to gabapentin following gabapentin use in the presence of coronary artery disease, diabetes mellitus, and hypertension.

The fact that our patient did not receive any other treatment for 15 days after the dose increase and that his complaints improved only with reducing the treatment dose suggest that these effects are due to the dose increase of pregabalin.

This unexpected effect was recognized as a possible side effect by taking 6 points on the evaluation with the Naranjo algorithm.^[13] As far as the literature can be investigated, no information about hearing loss has been found, but some Pregabalin users have reported complaints about hearing-probably not serious-on the internet.

There are many reasons for loss of hearing. These causes can be divided into two main groups as conduction type hearing loss and sensorineural hearing loss. While conduction type hearing loss is caused by reasons that prevent the voice from shifting from the outer ear to the inner ear; the problem with sensorineural hearing loss is the vestibulocochlear nerve, the inner ear and the pathways between the inner ear and the brain or the brain itself. Sensorineural hearing loss is usually persistent and may occur suddenly or gradually, may be mild or severe, and sometimes improvement may be observed.^[14-17] In our patient, it was determined that he had mixed type hearing loss, severe in the right ear and mild in the

left ear, and it was observed that hearing loss was reduced in control tests.

Conclusion

In summary, clinicians should not forget that pregabalin, which is frequently preferred in the treatment of neuropathic pain, should be administered with caution due to potential side effects. Patients prescribed pregabalin should be informed in detail about possible and unexpected side effects.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report.

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References

1. Gilron I. Gabapentin and pregabalin for chronic neuropathic and early postsurgical pain: current evidence and future directions. *Curr Opin Anaesthesiol* 2007;20(5):456–72.
2. Page RL 2nd, Cantu M, Lindenfeld J, Hergott LJ, Lowes BD. Possible heart failure exacerbation associated with pregabalin: case discussion and literature review. *J Cardiovasc Med (Hagerstown)* 2008;9(9):922–5. [CrossRef]
3. Martinez JA, Kasamatsu M, Rosales-Hernandez A, Hanson LR, Frey WH, Toth CC. Comparison of central versus peripheral delivery of pregabalin in neuropathic pain states. *Mol Pain* 2012;8:3. [CrossRef]
4. Baidya DK, Agarwal A, Khanna P, Arora MK. Pregabalin in acute and chronic pain. *J Anaesthesiol Clin Pharmacol* 2011;27(3):307–14. [CrossRef]
5. Grosshans M, Mutschler J, Hermann D, Klein O, Dressing H, Kiefer F, et al. Pregabalin abuse, dependence, and withdrawal: a case report. *Am J Psychiatry* 2010;167(7):869.
6. Wood DM, Berry DJ, Glover G, Eastwood J, Dargan PI. Significant pregabalin toxicity managed with supportive care alone. *J Med Toxicol* 2010;6(4):435–7. [CrossRef]
7. Blum A, Simsolo C, Tatour I. Hyponatremia and confusion caused by pregabalin. *Isr Med Assoc J* 2009;11(11):699–700.
8. Erdoğan G, Ceyhan D, Güleç S. Possible heart failure associated with pregabalin use: case report. *Agri* 2011;23(2):80–3.
9. Sendra JM, Junyent TT, Pellicer MJ. Pregabalin-induced hepatotoxicity. *Ann Pharmacother* 2011;45(6):e32. [CrossRef]
10. Sawant NS, Bokdawala RA. Pregabalin in the treatment of Charles Bonnet syndrome. *J Pak Med Assoc* 2013;63(4):530–1.
11. Pierce DA, Holt SR, Reeves-Daniel A. A probable case of gabapentin-related reversible hearing loss in a patient with acute renal failure. *Clin Ther* 2008;30(9):1681–4. [CrossRef]
12. Top C, Terekci H. Gabapentin Kullanımına Bağlı Sensorinöral İşitme Kaybı. *Türkiye Klinikleri J Endocrin* 2008;3:23–5.
13. 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. [CrossRef]
14. Witsell DL, Hannley MT, Stinnet S, Tucci DL. Treatment of tinnitus with gabapentin: a pilot study. *Otol Neurotol* 2007;28(1):11–5. [CrossRef]
15. Bauer CA, Brozoski TJ. Assessing tinnitus and prospective tinnitus therapeutics using a psychophysical animal model. *J Assoc Res Otolaryngol* 2001;2(1):54–64. [CrossRef]
16. Walia KS, Khan EA, Ko DH, Raza SS, Khan YN. Side effects of antiepileptics--a review. *Pain Pract* 2004;4(3):194–203.
17. Dunner DL. Safety and tolerability of emerging pharmacological treatments for bipolar disorder. *Bipolar Disord* 2005;7(4):307–25. [CrossRef]