

## Case Report

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# Transient Positive Horizontal Head Impulse Test in Pregabalin Intoxication

Seong-Hae Jeong, Yong Soo Kim, Ju-Hoen Lee, Hyunjin Jo, Ae Young Lee, Jae-Moon Kim

Department of Neurology, Chungnam National University Hospital, Daejeon, Korea

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Corresponding author: Seong-Hae Jeong  
Department of Neurology, Chungnam  
National University Hospital, 282  
Munhwa-ro, Jung-gu, Daejeon 35015,  
Korea  
Tel. +82-42-280-8057  
Fax. +82-42-252-8654  
E-mail; mseaj@hanmail.net

Head impulse test (HIT) is helpful to understanding high-frequency vestibulo-ocular reflex in patients with dizziness and imbalance. There are some reports on abnormal HITs in cerebellar disorder. To our knowledge, there was no report of transient bilateral positive head impulse related to antiepileptic drugs. A 65-year-old woman developed dizziness and imbalance after treatment with pregabalin for pain control of radiation cystitis. Neurological examination exhibited positive bilateral HIT results, in addition to ataxia and gaze-evoked rebound nystagmus. Pregabalin intoxication can evoke transient positive horizontal head impulse test as another indicator of cerebellar dysfunction. (2015;5:101-103)

**Key words:** Pregabalin, Head impulse test, Cerebellum

## Introduction

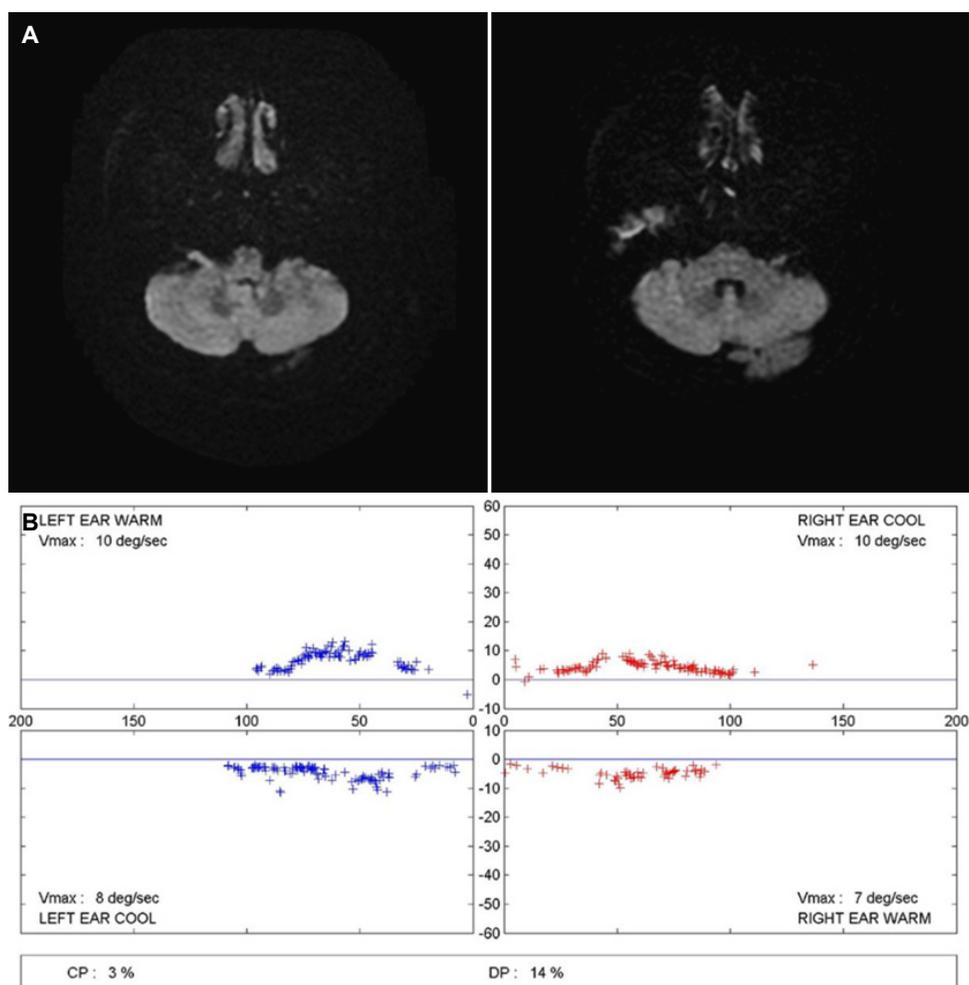
Even though pregabalin is commonly used in various diseases, it can cause dizziness and imbalance in many patients.<sup>1</sup> However, the change of high-frequency vestibulo-ocular reflex related to its intoxication has not been reported. The head impulse test (HIT) is helpful to understand the high-frequency vestibulo-ocular reflex (VOR) in patients with dizziness and imbalance.<sup>2</sup> To test the horizontal VOR, the examiner asks the patient to fixate upon a target in front of the eyes and then briskly turns the patient's head horizontally. Originally, the HIT was introduced by Halmagyi and Curthoys as a simple and reliable clinical sign of total unilateral loss of horizontal semicircular canal function.<sup>2</sup> Considering the lesions responsible for VOR, this condition may be influenced by the central vestibular system.<sup>3,4</sup> There are some reports on abnormal HIT results in cerebellar disorders.<sup>5-9</sup> To our knowledge, there is no report of the association between bilateral positive HIT and antiepileptic drugs. Here, we describe a case of transient bilateral positive HIT associated with pregabalin intoxication.

## Case

A 65-year-old woman was consulted to the neurology department for dizziness and imbalance. She had been treated with pregabalin 150 mg three times per day for the control of radiation cystitis pain four days before she visited our institution. Other medications in-

cluded cefixime (Suprax<sup>®</sup>, Ildong Pharmaceutical Co., Ltd., Seoul, Korea) and pentoxan polysulfate (Jelmiron<sup>®</sup>, Wave Bionomics, Zug, Switzerland) due to cystitis.

She denied previous dizziness, migraine or ear disease and symptoms. Her past medical history included a radical hysterectomy with pelvic lymphadenectomy for squamous carcinoma of the uterus twenty years prior to this incident. Her vital signs were stable. She looked somnolent. Head tilt was not noted. Ocular motor examination revealed some hypometric saccade and decreased gain of smooth pursuit. Spontaneous nystagmus was not observed; however, subtle gaze-evoked nystagmus with rebound nystagmus was noted in both horizontal gazes. Moreover, subtle upbeat nystagmus was evoked during upward gaze. Nystagmus was not evoked by a head-shaking and positioning manoeuvre. In addition, bilateral head impulse was positive on the horizontal plane. Limb ataxia was not definite; however, she could not walk in tandem. The laboratory findings were unremarkable except mild elevation of serum creatinine (1.36 mg/dL, normal range: 0.6-0.8 mg/dL). Brain diffusion-weighted image and T2-weighted magnetic resonance image were unremarkable (Fig. 1A). The bithermal caloric response was preserved (Fig. 1B). We recommended stopping pregabalin therapy based on a diagnosis of drug side-effects. Her symptoms and signs were resolved within five days of stopping pregabalin therapy. Overt saccades were not observed during a follow-up HIT five days after stopping the pregabalin.



**Figure 1.** A. Diffusion-weighted image shows no abnormality. B. The response of bithermal caloric test is preserved.

## Discussion

Our patient with imbalance exhibited gaze-evoked nystagmus and positive bilateral HIT. This presentation could be explained by pregabalin intoxication. It was based on the absence of structural brain lesions and the disappearance of the symptoms and signs mentioned above after stopping pregabalin therapy.

Many antiepileptic drugs have been reported to cause reversible or permanent dysfunction of the vestibulocerebellum, which may result in various neurological findings such as downbeat,<sup>10</sup> gaze-evoked nystagmus,<sup>11</sup> perverted head-shaking nystagmus and positional downbeat nystagmus.<sup>12-14</sup> Based on this scenario, the neurological findings observed in our patient may also have been related to cerebellar dysfunction, especially of the flocculus and/or nodulus. Recently, the dysfunction of the nodulus/uvula in pregabalin intoxication was also suggested in other patient with perverted head-shaking

nystagmus and positional downbeat nystagmus.<sup>13</sup>

There have been some evidences of cerebellar dysfunction in pregabalin intoxication. Similar to gabapentin, the main site of pregabalin action appears to be a specific subtype of the  $\alpha 2\text{-}\delta$  subunit of voltage-dependent calcium channels, which are widely distributed throughout the peripheral and central nervous systems.<sup>15</sup> The highest level of expression of these channels has been found in the cerebellum and in the hippocampus, and their dysfunction or decreased activity level has been linked to ataxia and cognitive impairment.<sup>6</sup> Similar to the case described here, reduced VOR gain at high-stimulus frequencies was observed in a previous animal study based on mice that carried mutations in genes that encode the ion pore of the P/Q calcium channel (Cacna 1a).<sup>16</sup>

In conclusion, our case demonstrates pregabalin intoxication could evoke transient positive horizontal HIT as another indicator of cerebellar dysfunction.

## Conflict of interest

The authors have no conflicts of interest to disclose regarding this manuscript.

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