

Hyperkinesia after High-Dose Prednisolone Therapy in a Patient with West Syndrome

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West syndrome is the most common developmental and epileptic encephalopathy in infancy and is characterized by clinical spasms, hypsarrhythmia on electroencephalogram (EEG), and developmental regression. Despite the accumulation of discoveries of genetic causes, steroids and vigabatrin (VGB) remain as the first-line treatments because they are more effective than other available therapies [1]. Due to the risk of treatment failure with VGB or hormonal therapy alone and the grave consequences of delayed treatment, instead of choosing either VGB or hormonal therapy, the literature increasingly supports the combination of VGB and hormonal therapy as the initial treatment for West syndrome [2].

However, adverse effects of corticosteroids and VGB are important factors to take into consideration when treating patients with West syndrome. Potential serious adverse effects of hormonal therapies include immunosuppression, hypertension, hypokalemia, adrenal or pituitary insufficiency, and gastrointestinal bleeding [2]. Adverse effects of VGB include permanent defects of the bilateral concentric peripheral visual field and magnetic resonance imaging (MRI) toxicity presenting as a reversible high T2 signal and restricted diffusion in the thalamus, basal ganglia, brainstem tegmentum, and cerebellar

dentate nucleus which often occur in association with hyperkinetic movement disorders [2].

Here, we report the case of a patient receiving VGB and high-dose oral prednisolone combination therapy who presented with hyperkinetic dyskinesia, which was potentially attributed to the adverse effects of high-dose prednisolone rather than VGB. This study was approved by the Institutional Review Board of Pusan National University Yangsan Hospital (05-2020-403). Informed consent was obtained from the parent of the patient.

An 8-month-old girl who had been treated for West syndrome with VGB and high-dose prednisolone add-on therapy presented to the clinic with hyperkinesia that started 4 days earlier. The patient adhered to the following protocol for VGB and high-dose prednisolone add-on therapy: 50 mg/kg/day VGB on day 1, 100 mg/kg/day VGB on days 2–4, 150 mg/kg/day VGB on days 5–13, 150 mg/kg/day VGB+40 mg/day prednisolone on days 14–20, 150 mg/kg/day VGB+60 mg/day prednisolone on days 21–27. The dosages or increments were to be altered if the spasms or EEG hypsarrhythmia persisted. After the treatment protocol, the prednisolone dosage was to be tapered over the following 15 days, while the VGB dosage was to be maintained for 5 months and then tapered over 1

month [3]. The hyperkinetic movement started when the patient was on the 7th day of 60 mg prednisolone. It first started as intermittent shaking of the hands, which soon included occasional shaking of the head, followed by nearly continuous shaking of the whole body while conscious, making it difficult for her to drink milk from the bottle. The hyperkinetic movement showed oscillating large amplitude tremor-like appearance which appeared at rest or during movement. There were no identifiable triggering factors, but the hyperkinetic movements disappeared during sleep (Supplementary Video 1).

She had been diagnosed with West syndrome of an unknown etiology, with no brain MRI abnormalities and negative results for an epilepsy gene panel. She had shown normal development before the onset of West syndrome, and regressed since—she cannot contact her eyes, and can barely control her head. She had been seizure free since the administration of 60 mg of prednisolone, despite constant drowsiness. The physical examination results including pupil reflexes and deep tendon reflexes, as well as routine laboratory results including blood chemistry, glucose, and electrolytes were normal. Her EEG did not show any changes since her last exam, which was 4 days earlier. The hyperkinetic movement did not accompany any ictal changes, and her brain MRI was normal without any signs of VGB-related toxicity. Because prednisolone treatment exhibited a potential temporal causal relationship and was therefore more likely the source of the adverse effects, we tapered off the prednisolone while providing nutritional support via a nasogastric tube. The abnormal movement started to improve 2 days after discontinuation of prednisolone and completely disappeared after 5 days. The patient also gained alertness at this time.

It is well known that patients receiving VGB can show reversible MRI lesions, as described above [4]. However, whether those lesions are the true cause of abnormal movements, such as those observed in West syndrome patients receiving treatment, remains unclear. MRI changes associated with VGB are not specifically related to movement disorders, and patients often show improvement without a dose reduction of VGB or no improvement after discontinuation of VGB [4]. Also, in clinical trials evaluating VGB and corticosteroid combination therapy, the incidence rates of abnormal movements and drowsiness have been as high as 8% and 24%, respectively, suggesting that corticosteroids may partially contribute to the dyskinesia and drowsiness or increase the susceptibility to VGB toxicity [2].

Our patient showed hyperkinesia during combination therapy, which soon stopped after the discontinuation of prednisolone. She continued with 150 mg/kg/day of VGB over the following 5 months without any signs of hyperkinesia. To the authors' knowledge, there is only one report on a series of patients showing dyski-

nesia after hormonal treatment [5]. However, movement disorders are inconsistently related to VGB toxicity, and there is an increased incidence of movement disorders in patients receiving combination therapy than those receiving monotherapy [2,4]. Therefore, prednisolone may directly or indirectly attribute to movement disorders. However, the pathological mechanism of this phenomenon warrants further investigation.

Supplementary Material

Supplementary materials related to this article can be found online at <https://doi.org/10.26815/acn.2020.00248>.

Conflicts of interest

Ara Ko, Sang Ook Nam are the editorial board member of the journal, but They was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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