Dear editor:

Vagus nerve stimulation (VNS) is a well-established neuromodulation approach for the treatment of intractable focal epilepsy, by affecting the thalamus and other limbic structures [1]. Typical adverse effects of VNS include hoarseness, cough and local paresthesia [2]. Here, we report a case of a focal epilepsy patient treated with VNS who developed aggravation of seizures and occurrence of status epilepticus, which is considered a rare post-VNS adverse effect (see Fig. 1).

A 48-year-old right-handed woman suffered from focal, impaired awareness epilepsy for past 46 years, characterized by head and eyes skewed to the right followed by right-upper tonic posturing. She had a history of head trauma and her cranial MRI showed left temporal lobe encephalomalacia. Her medical history was unremarkable, and she had no family history of epilepsy. The previous EEG exhibited bilateral slow, spike and sharp waves, more represented on the left-side, particularly in the occipital, parietal and central areas. The patient had failed a variety of anti-seizure medication (ASM) regimens and took levetiracetam (1000mg/day) and topiramate (150mg/day). During the 3-month baseline period prior to VNS implantation, she experienced approximately one seizure event per month.

A vagus nerve stimulator was implanted in April 2021, according to standard protocol. Subsequently, the current was gradually increased during regular visits, in order to evaluate its efficacy. The generator and lead were checked for faults upon each clinic visit, while ASM treatment remained unchanged. The possible shifts in seizure frequency and severity were assessed by the patient's calendar and observations of family members upon manifestations of seizure events. Three months post-implantation, with 'normal cycling' (30s on; 5 min off) stimulation at 1.25 mA, there were no effective improvements in the patient's seizure event frequency during this period (one event monthly). The current was subsequently increased to 1.5 mA. On the night of the last modification, the patient had three recurrent seizures within 30 minutes, so she was admitted to the Department of Neurology for video-electroencephalogram (VEEG) telemetry. Through VEEG monitoring, the patient's ictal presentation was recorded. Her head was twisted to the right-side, the right-upper limb was stiff and clonic, and occasionally, lower limbs clonus occurred. Each seizure was accompanied by an increase in heart rate, from approximately 108 beats/min to 140–170 beats/min. The corresponding ictal EEG

![Fig. 1a. Post-current increase to 1.5mA, the ictal EEG demonstrated approximately 16-Hz rhythmic sharp wave with left frontal predominance.](https://doi.org/10.1016/j.brs.2022.10.011)
revealed that 10–20s prior to onset of clinical manifestations, 15–17 Hz fast waves/multiple spike waves appeared in the left-frontal area and consequently evolved into 30–40 Hz low amplitude fast waves, followed by a left-frontal sharp wave rhythm of approximately 16 Hz, with electromyography (EMG) artifacts on the right. Slow waves were observed to be interspersed with spike waves within the left-frontal-temporal region, following seizure cessation, with consequent gradual recovery to background levels.

The patient was on ASMs as prescribed. She was sleeping normally and had not experienced a stressful event. She also had no recent history of trauma or infection. Both the generator and the lead had no malfunction. Midazolam and sodium valproate were micro-pumped, Topiramate was gradually administered orally up to 200 mg/day, and Perampanel was added up to 8 mg/day. During the four months of follow-up, the patient reported two episodes of absence seizures and did not experience any generalized tonic-clonic seizures.

To our knowledge, this is the first reported adult case with aggravation of status epilepticus, upon current output being increased to a relatively moderate level (1.5mA, ‘normal cycling’) without any other factors that could cause aggravation, including generator/lead failure. Koutroumanidis et al. reported an adult case with aggravation of pre-existing seizures and emergence of a novel seizure type post-current output increase (from 2.25 to 2.5mA) [3]. A novel seizure type emerging in another adult case was reported in 2011 following initiation of VNS and a current output of 0.5mA [4]. In addition, a pediatric case with the manifestation of status epilepticus due to an increase of current output (from 1.5mA to 2.0mA) was also reported in 2018 [5].

The degree of tolerance to VNS can vary across patients [6]. The emergence of status epilepticus and novel seizure types can be a specific manifestation of patients’ inability to tolerate VNS treatment, possibly since VNS has both a synchronizing and desynchronizing effect on EEG activity, and such synchronization allows the activation of specific structural networks that facilitate the propagation of potentially epileptogenic foci [4].

This report expands the knowledge-base of VNS-related adverse reactions and emphasizes the uncertainty of the effects of VNS therapy in patients with focal epilepsy, within certain rare instances.

Declaration of competing interest

The authors have no financial or personal relationships that inappropriately influence this work.

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