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Letter

Refractory central supratentorial hiccup partially relieved with vagus nerve stimulation

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Case description

A 69-year-old male, with a 7-year history of persistent hiccups, came to our department after several unsuccessful traditional as well as alternative medical treatments. The symptoms began in January 1999, when the patient suffered a left insular ischaemic stroke with right hemiplegia and motor aphasia. Prompt medical management achieved full recovery of neurological functions; however, the hiccups emerged after a few days. The unwavering symptoms motivated the patient to visit our department 7 years later. The hiccups that began after the ischaemic stroke in 1999 were persistent: they lasted up to 20 successive days during awake states and sleep, each hiccup reappearing every 5–6 s. In addition, the hiccups were intense: within symptomatic periods, the hiccups progressively became disabling (9 on a 10-point scale according to the patient), and the patient lost 10 kg in weight. The hiccups often reached peaks with breath repercussions associated with glottic spasms and a choking sensation, resulting in profound anxiety and exhaustion. Within 7 years, the patient received several medical evaluations as well as aggressive medical treatment. Non-conventional therapies including acupuncture and shiatsu massages were also utilised. Furthermore, only transoesophageal stimulation resulted in temporary relief. In 2006, he was advised to undergo a neurosurgical examination. After imaging his brain and reviewing the literature, we recommended vagus nerve stimulation, which was then implanted in January 2007. He was discharged from the hospital 2 days after the procedure, and the stimulator was activated in February 2007. The automatic current settings were 1.50 mA, 15 Hz and 500 s pulse width, delivered for 30 s every 5 min. Good partial relief was maintained for 30 days with an increased daily hiccups-free ratio. The patient and his relatives recorded the following parameters: (1) date; (2) occurrence of hiccups (yes or no); (3) duration of symptoms (days with or without hiccups); (4) intensity of symptoms (0–10 scale); (5) other significant observations. We noticed prolonged periods free of hiccups (figure 1A). In addition, the patient reported a gradual reduction in symptom's intensity to a mean of 5.5, as defined by a 10-point scale (figure 1B). The respiratory symptoms were effectively controlled while the glottic spasm spikes

were completely obliterated. After 1 month, the patient returned to the outpatient clinic for a progressive increased frequency of hiccups; stimulation settings were increased to 1.60 mA, 15 Hz and 500 s pulse width, delivered for 30 s every 3 min. After 4 months, the patient referred another slight worsening with increased hiccups frequency; stimulation was then set to 1.70 mA, 20 Hz and 500 s pulse width, delivered for 30 s every 2 min. In spite of the partial yet satisfactory results, the vagus nerve stimulation (VNS) pacer was turned off (automatic settings were 1.75 mA, 20 Hz and 500 s pulse width delivered for 30 s every 1.8 min) after a year due to undesirable side effects such as bitonal voice, intense pain radiation to the omolateral ear, a cold sensation (quivering) in the omolateral shoulder and an uncomfortable visceral sensation in the throat. After a relatively non-symptomatic period, symptoms that preceded the VNS implantation eventually returned.

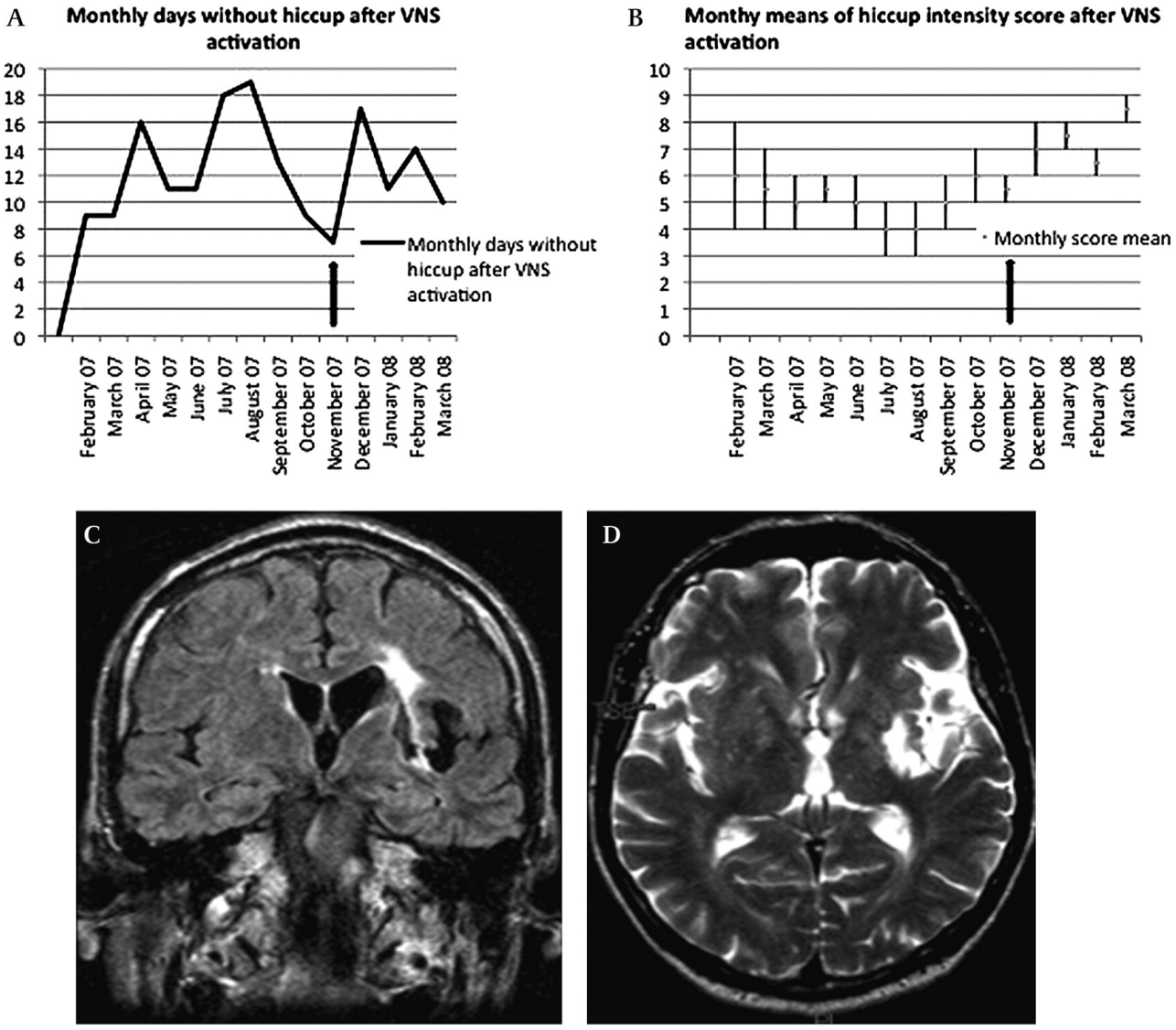

Figure 1

(A) Graphics depicting the 12-month time course of monthly hiccups-free days ratio (days with hiccups/days with no hiccups), the arrow underline the turning-off of the vagus nerve stimulation (VNS) pacer and consequently decrease in the ratio of hiccups-free days per month. (B) Graphics depicting the mean of scores (1–10) daily assigned by the patient over a month to the intensity of hiccups, the arrow underline the turning-off of the VNS

pacer and consequently increase in the intensity of symptoms. (C) T2 coronal fluid-attenuated inversion recovery MRI showing the radiological outcome 3 months after the left insular stroke. (D) T2 axial MRI showing the radiological outcome 3 months after the left insular stroke.

Discussion

The hiccups consist of spasmodic and forceful contractions of the inspiratory muscles. It is considered a primitive respiratory reflex with the phrenic or vagal nerves or the sympathetic ganglia as afferent pathways, and the phrenic, cervical, intercostal and recurrent laryngeal nerves as efferent pathways.[1] The central connection is unknown, but it is thought to involve the brainstem including the respiratory centre of the medulla, reticular formation and phrenic nerve nuclei as well as the hypothalamus.[1] In addition, supratentorial areas may be involved in normal inhibition of the hiccup reflex.[2] Chronic hiccups, defined as lasting over 48 h, are rare but can be exceptionally distressing. Furthermore, prolonged or recurring spells may cause depression, weight loss, insomnia and exhaustion.

For these pathological cases, the first step is medical therapy. If unsuccessful, many alternative treatments are available, but those of neurosurgical interest are the inhibition or pacing of the phrenic nerve,[3] or the stimulation of the vagus nerve.[4] Intractable hiccups of central origin are associated with a bilateral diaphragm contraction; therefore, a unilateral block of the phrenic nerve is ineffective to relieve hiccups. Furthermore, a bilateral block of the phrenic nerve may compromise pulmonary function. Although the phrenic nerve is believed to be the only motor nerve innervating the diaphragm, a blockade of the phrenic nerve may not paralyse the diaphragm due to an accessory phrenic nerve. We report a case of disabling hiccups, resistant to medical therapy. Satisfactory but not curative results were obtained from implanting a vagus nerve stimulator. Most cases of chronic hiccups due to disorders of the central nervous system are caused by brainstem lesions. The rare supratentorial lesions that have been associated with chronic hiccups were all, as in our case, located in one of the mesial temporal lobes.[2 5] This finding suggests that mesial temporal areas are involved in the control of hiccups. In this case, VNS for chronic hiccups induced by supratentorial lesions failed to resolve the symptoms completely and was terminated roughly 1 year after implantation due to undesirable side effects. On the other hand, the treatment temporarily reduced episodes of hiccups, eliminated hiccup spasm spikes and diminished the mean score of symptom intensity to a difference of 40%. Further research will determine the role of VNS in the treatment of chronic hiccups. At this point, we can infer that when triggered by a supratentorial lesion, the hiccups can be treated by identifying targets for deep brain stimulation, including the insula.

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