Airway compromise secondary to vagus nerve stimulator: case report and implications for otolaryngologists

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Abstract

Introduction: Vagus nerve stimulators are devices used in the management of patients with drug-refractory epilepsy unsuitable for resective or disconnective surgery. Implanted usually by neurosurgeons, these devices are infrequently encountered by otolaryngologists. Despite significant anti-seizure efficacy, side effects related to laryngopharyngeal stimulation are not uncommon.

Case report: A 28-year-old man with a history of effective vagus nerve stimulator use presented with a cluster of seizures and respiratory distress associated with intermittent stridor. The duration of stridor corresponded to the period of vagus nerve stimulation. Endoscopy revealed forced adduction of the left vocal fold against a medialised right vocal fold. The device was switched off and the stridor immediately resolved.

Conclusion: Airway compromise is an under-recognised side effect of vagus nerve stimulation. We describe the first known case of stridor and contralateral vocal fold palsy in a vagus nerve stimulator user. We highlight the need for better understanding amongst otolaryngologists of the laryngopharyngeal side effects of this technology.

Key words: Vagus Nerve Stimulator; Vocal Cords; Airway Obstruction; Complications, Epilepsy

Introduction

Vagus nerve stimulation is a moderately effective treatment for patients with drug-resistant epilepsy for whom resection or disconnection surgery has either failed or is not an option.1 Its use has become increasingly commonplace over the past decade. Currently, the Vagus Nerve Stimulator Therapy System (Cyberonics, Houston, Texas, USA) remains the only such device approved by the US Food & Drug Administration. Since its licensing in 1997, more than 35 000 such devices have been implanted.

The vagus nerve stimulator is a surgically implanted device which delivers intermittent, pulsed currents from a subcutaneous generator located under the clavicle to the left cervical vagus nerve, through cuffed electrodes, without patient intervention. A typical program consists of cycles of 30 seconds of stimulation separated by 5 minute rest periods. Stimuli parameters can be varied to achieve optimal seizure control, via a programming ‘wand’. Additional stimuli can be achieved by magnet ‘swipes’ across the generator, and temporary device deactivation can be achieved by a more protracted magnet application.

Current hypotheses which seek to explain the device’s mode of action propose that stimulation of the central nervous system via the diffuse bilateral projections from the vagus nerve leads to increased cortical levels of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) which in turn reduces cortical hypersynchronous excitability.2 Others speculate that stimulation of the brainstem reticular activating system helps inhibits aberrant cortical activity.3

Stimulus-related side effects are not uncommon, and probably result from stimulation of laryngopharyngeal musculature via the superior and recurrent laryngeal branches of the vagus. Reported symptoms include dysphonia, dysphagia, dyspnoea and coughing, and tend to lessen with time.1 Endoscopic evaluation of the larynx during stimulation has shown that the most consistent laryngeal response is a reversible forced adduction of the left vocal fold.4–6

Most devices are implanted by neurosurgeons in regional centres, although in the USA up to 5 per cent have been implanted by otolaryngologists, with follow up and programming managed by neurologists.5 A US Food & Drug Administration approved expansion of candidacy criteria in 2005 to include drug-refractory chronic or recurrent uni- and bi-polar depression increases the likelihood that vagus nerve stimulator patients will present to otolaryngologists.

We present a case of vagus nerve stimulation causing intermittent stridor which resulted in an ENT referral, and we highlight the need for a basic understanding of the laryngeal side effects of these devices.

Case report

A 28-year-old man had developed seizures in early childhood following resection of a posterior fossa astrocytoma and adjuvant chemoradiotherapy. His seizures had become refractory to medical therapy, and he had thus undergone left vagus nerve stimulator implantation at the age of 20 years. Seizure frequency had improved post-implantation, and had stabilised at around two to three episodes per week. Medical therapy had been maintained at a lower dose, in the form of Tegretol® Retard 400 mg twice...
daily and clobazam 10 mg nightly. The patient had severe learning difficulties, with no verbal communication, but was able to indicate his needs to carers.

The most recent device reprogramming had been undertaken four months prior to presentation, and had consisted of a 0.25 mA increase in output to give settings of 1.5 mA output, 30 Hz frequency and a pulse width of 50 microseconds, with 30 seconds of stimulation followed by a 1.8 minute rest period.

The patient presented via the emergency department following a series of six to eight seizures over 24 hours. He remained in an uncharacteristically protracted postictal state, and developed intermittent stridor associated with respiration embarrassment and hypoxia. Intercurrent vomiting episodes, coupled with widespread pulmonary crepitations, led to a provisional diagnosis of aspiration with laryngospasm.

Treatment with continuous positive airway pressure ventilation, intravenous steroids and nebulised bronchodilators improved oxygen saturation, and normal consciousness returned. Treatment was weaned with no deterioration in vital signs; however, the stridor continued. This was noted to be intermittent and not associated with significant desaturations. The patient was also noted to be aspirating on feeding.

Flexible laryngoscopy at rest revealed both vocal folds to be lying in a paramedian position during quiet respiration. During stridulous episodes, the glottis was noted to narrow further, with adduction of the left vocal and vestibular fold. This lasted approximately 30 seconds and recurred every 2 minutes. It was suspected that vagus nerve stimulation was contributing to laryngeal dysfunction, and the device was switched off. Subsequent flexible laryngoscopy revealed a fully mobile left vocal fold but persistent right vocal fold palsy, in a paramedian position. Functional endoscopic evaluation of swallowing no longer showed signs of aspiration. Computed tomography of the brain, neck and chest revealed no obvious cause for this new right vocal fold palsy.

It was advised that the vagus nerve stimulator device remain switched off until functional recovery of the right vocal fold could be established. Alternative medical therapy was initiated for seizure control.

Discussion

Epilepsy has a UK prevalence of one in 130, with approximately one-third of patients having persistent seizures despite maximal medical therapy. In selected cases, resective and disconnective neurosurgery can give a 90 per cent reduction in seizure frequency. However, up to 40 per cent of patients with epilepsy refractory to medical therapy are not candidates for such procedures. In this group, and those unwilling to undergo intracranial surgery, vagus nerve stimulation is a valuable addition to patients’ treatment options. The use of such a device over an 18-month period has been shown to deliver a more modest 50 per cent reduction in seizure frequency in 50 per cent of patients studied.1

The vagus nerve forms from a condensation of rootlets emerging from the medulla oblongata between the inferior olive and the inferior cerebellar peduncle. It exits the skull base via the jugular foramen and then runs within the carotid sheath. The majority of fibres are afferent (80 per cent), synapsing bilaterally in the nucleus tractus solitarius. The nucleus ambiguous supplies the branchiomotor efferents to the laryngopharyngeal musculature.

The laryngopharyngeal sequelae of vagus nerve stimulator therapy may arise either as acute operative complications or more commonly as stimulus-related side effects. Surgical complications are infrequent, with early studies citing a rate of vocal fold palsy of less than 1 per cent. In one study, stimulus-related phenomena prompting consultation at three months post-operatively included periodic dysphonia (in 60 per cent of patients), cough (20 per cent), dyspnoea (16 per cent) and pain (15 per cent). Another study reported episodic dysphonia in as many as 95 per cent of patients. The intensity of such dysphonia appears to lessen with time; one study found that, five years after implantation, only 19 per cent of patients complained of dysphonia and fewer than 5 per cent complained of any other side effect. Reports of new onset dysphonia are inconsistent, but one study has demonstrated an increased risk of aspiration in patients with pre-existing dysphonia and learning difficulties. Indeed, vagus nerve stimulator induced coughing may represent salivary aspiration.

Airway compromise has rarely been discussed in the literature on vagus nerve stimulators. Safe management of such scenarios is helped by an appreciation of the laryngeal changes likely to result from electrical vagus stimulation. Studies have reported vocal fold responses ranging from ipsilateral adduction to the vocal fold assuming a paramedian position. Lundy et al. demonstrated that stimulus frequency altered vocal fold response, with 20 to 30 Hz correlating with abduction, 40 Hz with adduction and more than 40 Hz with a paramedial position. A few studies have described spasmodic contraction of all ipsilateral laryngeal musculature, producing a stif, bulging and adducted vocal fold on high intensity stimulation. Occasionally, this is accompanied by medial rotation of the arytenoids and pulling of the true vocal fold across the midline. The only prior description of vagus nerve stimulator associated stridor described laryngeal hemispasm periodically compromising the airway during laryngeal mask airway (LMA) assisted anaesthesia. In this case, the anaesthetic medication was believed to have unmasked a tendency to hemi-spasm; this suggests that a lower threshold for endotracheal intubation may be prudent when anaesthetising vagus nerve stimulator patients, or else consideration be given to deactivating the device when using the LMA. In our patient, persistent adduction of the left vocal fold against a pathologically medialised contralateral fold resulted in stridor. Whilst such a situation may be uncommon, a similar scenario might be brought about in the presence of any partially occlusive glottic or airway lesion. Indeed, vagus nerve stimulator use has been shown to worsen pre-existing obstructive sleep apnoea (OSA), and current guidance advises that clinically significant OSA be treated before vagus nerve stimulator implantation. Significantly, OSA is not an uncommon co-morbidity amongst patients with drug-refractory epilepsy.

Given that few patients receiving vagus nerve stimulators are seizure-free, treatment strategies aim to stimulate to the limits of tolerance, which necessarily results in most patients experiencing stimulation-induced side effects. Strategies to manage commonly occurring side effects are developed on an individual basis, given the heterogeneity of patients’ laryngeal responses. Such strategies include generator reprogramming, use of a magnet to temporarily suspend device function during relevant activities (e.g. feeding, singing or general anaesthesia), local botulinum toxin type A injections, and, lastly, switching off the device. Given the degree of airway compromise in our patient, and the uncertainty of contralateral vocal fold recovery, we elected to deactivate the stimulator.

The vagus nerve stimulator system is only licensed for use on the left vagus nerve, based on animal studies demonstrating right-sided dominance of cardiac innervation, in order to minimise potential cardiac side effects.
A recent case series describing right-sided implantation in patients who had previously benefited from an explanted left-sided vagus nerve stimulator (e.g. post-infection) reported no significant side effects.20 In our patient, a right-sided implant may prove to be an option if spontaneous recovery of right vocal fold function is not apparent after prolonged observation, and if seizures again become refractory to pharmacotherapy.

- Vagus nerve stimulators are currently indicated in the UK for use in the management of drug-refractory epilepsy
- Laryngeal side effects due to stimulation of the superior and recurrent laryngeal nerves are not uncommon
- Forced adduction of the ipsilateral vocal fold is the most consistently encountered laryngeal response to vagal nerve stimulation
- This is the first report describing the consequences of contralateral vocal fold palsy together with vagal nerve stimulation

This case highlights the importance of pre-operative laryngeal assessment prior to vagus nerve stimulator implantation, especially in patients unable to vocalise. Whilst the majority of stimulus-related side effects are well tolerated by patients and would not alter their decision to receive the vagus nerve stimulator again, a small but serious risk of airway compromise exists for certain patient groups.8 We advocate closer ties between the otolaryngologist and neurologist during vagus nerve stimulator program adjustment, in order to maximise the quality of life for the growing number of patients using this technology.

References
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