Case report

Cough syncope induced by post nasal drip successfully managed by Gabapentin

Hussein Algahtani a, *, Bader Shirah b

a King Abdulaziz Medical City/King Saud Bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia
b King Abdullah International Medical Research Center/King Saud Bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia

A R T I C L E   I N F O

Article history:
Received 10 June 2017
Received in revised form 15 June 2017
Accepted 18 June 2017

Keywords:
Cough syncope
Post nasal drip
Gabapentin

A B S T R A C T

Syncope is a common complaint in both neurology clinic and emergency department. It is defined as transient loss of consciousness with loss of postural tone, which is usually self-limited and followed by a spontaneous recovery. Our report describes a case of cough syncope resulting from chronic intractable cough caused by post nasal drip. Although his experience was debilitating, we were able to control his symptoms significantly using a small dose of Gabapentin. This dose is much lower when compared with the already established licensed indicated higher doses used for the treatment of neuropathic pain and epilepsy. Cough syncope is a demanding condition that results in comprehensive costly investigations. In addition, cough syncope could be misinterpreted as epilepsy by the treating team. Pulmonologists should be aware of the use of Gabapentin as the management of cough refractory to standard antitussive therapy. Further studies are needed to assess the effectiveness of low doses of Gabapentin in the management of chronic cough.

© 2017 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Syncope is a common complaint in both neurology clinic and emergency department. It is defined as transient loss of consciousness with loss of postural tone, which is usually self-limited and followed by a spontaneous recovery [1]. Although most causes of syncope are benign, this symptom may presage a life-threatening event in a small subset of patients. In addition, it may provoke substantial anxiety among patients and their families and may lead to extensive investigations by the treating physicians [2]. In this article, we describe a patient who developed recurrent cough syncope which was successfully treated with low dose Gabapentin. The patient was referred with the diagnosis of generalized tonic-clonic seizures and his episodes were misinterpreted as epileptic seizures.

2. Case report

A 47-year-old male presented to the emergency department with an episodic loss of consciousness following bouts of cough for two days. The fainting episodes occurred after seconds up to three minutes following the cough. Some of these episodes were followed by brief jerking of upper and lower extremities. Following each attack, he regained consciousness quickly with no postictal phenomena. During episodes, he was cyanosed and hypotonic. The cough started ten days prior to the presentation with a small amount of white sputum associated with streaks of blood and chest pain. He had no fever or shortness of breath but complained of nasal congestion and discharge. He had a history of Hodgkin’s lymphoma treated with chemotherapy and autologous bone marrow transplantation (relapsed). He was disease free for four years. He also had a history of diabetes mellitus, hypertension, hypothyroidism, ischemic heart disease, and pulmonary embolism. His medications include antidiabetic, antidyslipidemic, and antischismic heart disease medications including aspirin (81 mg). He was not on any medication known to cause cough including angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers. On examination, he was conscious, oriented, and alert. During examination, he had an episode of syncope for seconds following cough. He reported falling on his forehead during one of the episodes. His vital signs were all within normal limits with no postural drop of blood pressure or resting tachycardia. Cardiovascular and neurological examination were normal with no evidence of postural hypotension, autonomic, or length dependent...
peripheral neuropathy. Urgent computed tomography (CT) scan of the brain revealed no acute intracranial insult. The patient was admitted for evaluation of the cause of syncope. Investigations to evaluate syncope included brain CT scan and magnetic resonance imaging (MRI), electroencephalogram (EEG), echo-Doppler of the carotid arteries, electrocardiogram (ECG), 24 hour Holter monitoring, 24 hour blood pressure monitor, and Doppler echocardiogram. All investigations were normal which excludes cardiac and neurological causes. Investigations to evaluate the cough included chest X-ray, spirometry, bronchoprovocation test, pulmonary CT angiography, and upper gastrointestinal endoscopy. These investigations were normal, and the respirology team suggested that the most likely cause is post nasal drip. A detailed ear, nose, and throat examination with flexible nasolaryngoscopy was unremarkable apart from mild edema of the right vocal fold and moderate laryngopharynx acid reflux disease. The patient was given several trials of anticough medications including codeine, lidocaine, dextromethorphan, chlorpheniramine, levodropropizine, and morphine with no improvement. Following starting the patient on Gabapentin 300 mg daily, the patient responded well, and his cough episodes decreased in number until they disappeared completely. The patient was discharged home on Gabapentin 300 mg twice daily with complete resolution of his cough. In addition, post nasal drip was treated aggressively by the ear, nose, and throat team.

![Fig. 1. Schematic representation showing: (A) cough receptors involved in the normal cough mechanism, (B) structural model of GABA receptor, (C) α2β subunit of voltage-gated calcium channels.](image-url)
Cough is an important defense mechanism of the respiratory system and one of the most common complaints in the respirology clinics. Cough may be acute (less than 3 weeks), subacute (3–8 weeks), or chronic (more than 8 weeks). Cough reflex is mediated by the stimulation of several afferent nerves distributed along the nasal pathway and tracheobronchial tree. These include the vagus (mainly), glossopharyngeal, trigeminal, and phrenic nerves (Fig. 1 A). Thus, rapidly adapting receptors of these afferents are known to be evoked by mechanical stimuli and deformity in the airway epithelium, which results in cough. Causes of chronic cough are frequent and include persistent infection, cough-variant asthma, and gastroesophageal reflux disease [3]. Post nasal drip is one of the causes of chronic cough and refers to the sensation of nasal secretions at the back of the throat that usually results in the need to clear the throat. It is often associated with nasal stuffiness or nasal discharge [4].

Cough syncope is an uncommon condition that was first described in 1876 [5]. It requires extensive evaluation to explain the underlying etiology. The evaluation includes investigation of autonomic functions, anatomical brain abnormalities, structural and functional cardiac dysfunction, vascular carotid artery disorders, and sleep disturbance [5]. Several diseases have been linked to cough syncope and are summarized in Table 1.

Several pathophysiological mechanisms have been suggested as the underlying cause of cough syncope [5]. Epilepsy was thought to be the underlying mechanism of cough syncope in the early reports [6]. However, subsequent studies proposed that the increased intrathoracic and intra-abdominal pressures result in a decreased cardiac output with decreased cerebral perfusion leading to loss of consciousness [7]. Another theory suggests that the raised cerebrospinal fluid pressure increases extravascular pressure around the cranial arteries and veins causing the blood to be squeezed out of the cranium leading to hyperperfusion and eventually syncope [8].

The management of cough syncope is directed towards the elimination of the underlying triggering event (i.e. cough). Patients with cough due to upper respiratory tract infections are treated supportively since most of the infections are of viral etiology and self-limiting with resolution within three weeks. In patients with idiopathic cough syncope, direct suppression of the sensory cough reflexes is indicated. Such medications include codeine, lidocaine, dextromethorphan, chlorphenadin, levodropropizine, and morphine. However, these medications may not satisfactorily achieve the required effect [5].

Gabapentin, a lipophilic structural gamma-aminobutyric acid analog, is a medication used to treat neuropathic pain but recently has been suggested to effectively manage cough refractory to standard antitussive therapy [9]. It acts on gamma-aminobutyric acid B receptors and α2δ subunits of voltage-dependent calcium channels. Gamma-aminobutyric acid B receptors are expressed in the lungs and are involved in the prevention of bronchospasm, airway microvascular leakage, and cough (Fig. 1 B). α2δ subunits are mainly expressed in lung tissues (Fig. 1 C). Binding of Gabapentin to α2δ inhibits the release of neurotransmitters including those that have tussigenic properties (e.g. substance P). High doses of Gabapentin may lead to side effects such as nausea, fatigue, dizziness, and sedation [9]. Wu et al. [10] reported that a very low dose (200 mg) of Gabapentin was sufficient to treat and completely control cough syncope in their patient and avoiding the side effects of the high doses. They suggested starting with a dose of 100 mg daily and increasing by 100 mg daily every 2 weeks until a subjective improvement in cough is achieved.

4. Conclusion

Our report describes a case of cough syncope resulting from chronic intractable cough caused by post nasal drip. Although his experience was debilitating, we were able to control his symptoms significantly using a small dose of Gabapentin. This dose is much lower when compared with the already established licensed indicated higher doses used for the treatment of neuropathic pain and epilepsy. Cough syncope is a demanding condition that results in comprehensive costly investigations. In addition, cough syncope could be misinterpreted as epilepsy by the treating team. Pulmonologists should be aware of the use of Gabapentin as the management of cough refractory to standard antitussive therapy. Further studies are needed to assess the effectiveness of low doses of Gabapentin in the management of chronic cough.

Conflict of interest

The authors declare that they have no conflicts of interest.

References

[1] W.P. Cheshire, Syncope, Contin. (Minneap Minn) 23 (2017) 335–358 (2. Selected Topics in Outpatient Neurology).
[2] A. Moya, R. Sutton, F. Ammirati, et al., Guidelines for the diagnosis and management of syncope (version 2009), Eur. Heart J. 30 (21) (2009) 2631–2671.
[3] K.F. Chung, L.D. Pauw, Prevalence, pathogenesis, and causes of chronic cough, Lancet 371 (9621) (2008) 1364–1374.
[4] P. Macedo, H. Saleh, A. Torregro, et al., Postnasal drip and chronic cough: an open interventional study, Respir. Med. 103 (11) (2009) 1700–1705.
[5] P.V. Dicpinigaitis, L. Lim, C. Farmakidis, Cough syncope, Respir. Med. 108 (2) (2014) 244–251.
[6] D.S. O’doherty, Tussive syncope and its relation to epilepsy, Neurology 3 (1) (1953) 16–21.
[7] C.T. Kordiet, W. Wieling, P. Edward, Sharpey-Schafer was right: evidence for...
systemic vasodilatation as a mechanism of hypotension in cough syncope, Europace 10 (4) (2008) 486–488.

[8] H.D. McIntosh, E.H. Estes, J.V. Warren, The mechanism of cough syncope, Am. Heart J. 52 (1) (1956) 70–82.

[9] N.M. Ryan, S.S. Birring, P.G. Gibson, Gabapentin for refractory chronic cough: a randomised, double-blind, placebo-controlled trial, Lancet 380 (9853) (2012) 1583–1589.

[10] C.H. Wu, K. Gunasekara, J.H. Hull, A. Bikov, A.J. Morris, O.S. Usmani, Gabapentin as a potential treatment for cough syncope, Respir. Care 60 (2) (2015) e34–e37.