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Vagal nerve stimulation is beneficial in postural orthostatic tachycardia syndrome and epilepsy

Zeljka Petelin Gadze[a], Andreja Bujan Kovac[a,*], Ivan Adamec[b], Nina Milekic[c], Vlatko Sulentic[a]

[a] Department of Neurology, University Hospital Centre Zagreb, School of Medicine, University of Zagreb, Referral Centre of the Ministry of Health of the Republic of Croatia for Epilepsy, Zagreb, Croatia
[b] Department of Neurology, University Hospital Center Zagreb, School of Medicine, University of Zagreb, Referral Centre of the Ministry of Health of the Republic of Croatia for Autonomic Nervous System Disorders, Zagreb, Croatia
[c] Department of Neurology, Sibenik-Knin County General Hospital, Sibenik, Croatia

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POTS (Postural Orthostatic Tachycardia Syndrome) is a condition caused by cerebral hypoperfusion which results in general weakness, dizziness, lightheadedness, fatigue upon standing and visual blurring or fogging of the visual fields. Syncope occurs in 40% of patients. Other predominantly orthostatic symptoms include palpitations, tremulousness and anxiety. Gastrointestinal symptoms, such as nausea, cramps, bloating, constipation, diarrhea and acrocyanosis, as well as edema due to low venous pooling, can also appear in some cases. This syndrome was first described in 1871 by physician Jacob Mendes Da Costa. Hallmark of this disorder is an exaggerated heart rate increase in response to postural change [1].

A 29-year-old female patient was admitted to our hospital in December 2011 due to pharmacoresistant epilepsy from the age of 9. Clinically, according to the 2017 ILAE (International League Against Epilepsy) operational classification of seizure types, her seizures initially clinically presented as focal motor onset seizures to bilateral tonic-clonic seizures (central lobe seizures, prior referred as Jacksonian seizures of the left side of the body). Several years later, seizures of different origin also appeared and presented as focal impaired awareness seizures of motor onset with gestural automatisms and motor dysphasia, followed by sense of fear and panic attacks, with short-term postictal confusion, corresponding to left temporal lobe seizures. Brain MRI (Magnetic resonance imaging) showed bilateral frontoparietal polymicrogyria and right subependymal nodular grey matter heterotopia (Fig. 1). At the age of 27, she also noticed palpitations and dizziness in standing upright that were relieved by sitting or lying flat.

Due to complex malformation of cortical development patient was not considered as a candidate for resective neurosurgery. We decided to perform minimal invasive neurosurgical treatment – implantation of vagal nerve stimulator (VNS) [2]. During the preoperative work-up head-up tilt test (HUTT) was performed that revealed POTS refractory to lifestyle modification measures. Cardiovascular ultrasound and holter-ECG were normal. One week after implantation, VNS was initiated at 0.25 mA (duty cycle set to 30-Hz signal frequency, 500-ms pulse width, 30 s ON-time and 3 min OFF-time). HUTT done at one month and three months after implantation was normal. VNS was gradually increased to 1 mA, which led to significant reduction in seizure rate and disappearance of orthostatic intolerance symptoms (Fig. 2).

POTS is defined by a heart rate increment of 30 beats/min or more within 10 min of standing on HUTT, in the absence of orthostatic hypotension. As a form of orthostatic intolerance, it particularly occurs in younger adults and children in response to postural stressors, with a female to male ratio of 4–5:1 [1]. The reason for this is not known, however, observed gender differences in muscle sympathetic nerve discharge characteristics in healthy

* Corresponding author.
E-mail addresses: andreja.bujan.kovac@kbc-zagreb.hr (A. Bujan Kovac), ivan.adamec@kbc-zagreb.hr (I. Adamec), nina.milekic@bolnica-sibenik.hr (N. Milekic), vlatko.sulentic@kbc-zagreb.hr (V. Sulentic).

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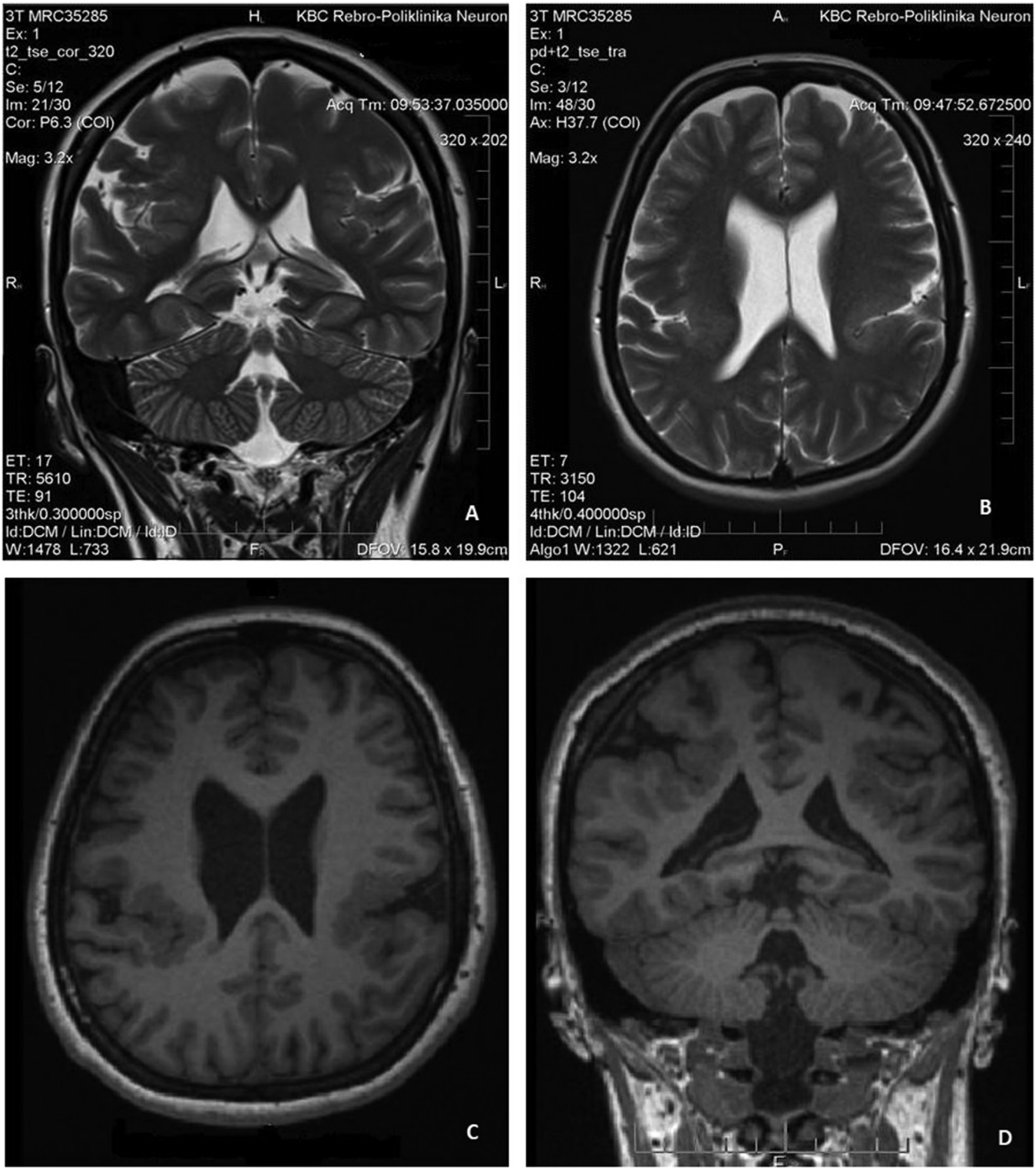

Fig. 1. (A–D) Brain MRI showing bilateral frontoparietal polymicrogyria and right subependymal nodular grey matter heterotopia.

patients may explain why women are more likely to develop POTS. The orthostatic nature of the symptoms is the primary clue to diagnosis. Pathophysiologically, POTS may involve sympathetic denervation in the lower limbs, a hyperadrenergic state and/or abnormalities in the noradrenaline transporter.

VNS is a safe and effective adjunctive treatment for drug-resistant epilepsy when surgery is inadvisable. In VNS therapy, the left vagal nerve is stimulated at the level of the neck by an electrode connected to a subcutaneous device. The left nerve is chosen to minimize the effect on heart rhythm, because most of the cardiovagal fibers course through the right vagal nerve. Efferent fibers of the vagal nerve originate from two separate nuclei in the brainstem, the dorsal motor nucleus and the nucleus ambiguus. They supply parasympathetic fibers to all internal organs except the suprarenal glands. Afferent fibers originate in the end organs and project to the nucleus tractus solitarius, from where axons project throughout the brain. These

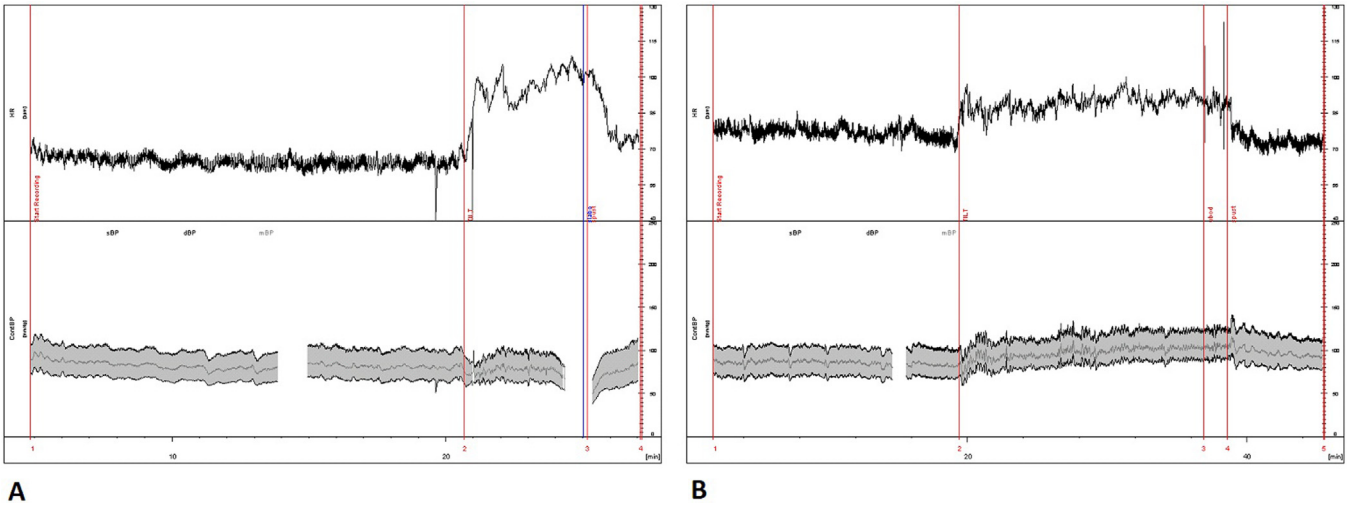

Fig. 2. (A) Preoperative HUTT showing POTS with vasodepressor syncope. (B) Postoperative HUTT showing normal response.

afferent axons and synapses are thought to be responsible for the therapeutic effect of VNS, since it reduces sympathetic nervous system and increases parasympathetic nervous system activity [3]. Increasing parasympathetic input to the heart via VNS is thought to be cardioprotective. Limited data suggest that long-term VNS therapy improves cardiac autonomic control and significantly attenuates heart failure (HF) development in the canine high-rate ventricular pacing model. VNS is a novel and potentially useful therapy for treating HF [4]. Therapeutic effects of POTS are further being explored, currently there is ongoing clinical trial addressing the effects of transdermal vagal nerve stimulation and POTS. Optimal therapy of POTS remains uncertain. No intervention has been systematically studied. To our knowledge, this is the first reported case of the positive effect of VNS in a patient with POTS and epilepsy. Further studies with a larger number of patients are needed.

Declarations of interest

None.

Ethical approval

This article does not contain research including human participants or animals performed by any of the authors.

Informed consent

Informed consent was obtained from the patient included in the study.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.seizure.2018.03.001.

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