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(Citation)

Neurology and Clinical Neuroscience, 8(4):183-185

(Issue Date)

2020-07

(Resource Type)

journal article

(Version)

Accepted Manuscript

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<https://hdl.handle.net/20.500.14094/90009401>



Letter to the Editor

A case of area postrema syndrome associated with sick sinus syndrome in an elderly patient with neuromyelitis optica spectrum disorder: case report

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23 **Keywords:** Area postrema syndrome, intractable hiccups, neuromyelitis optica, sick sinus syndrome

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Dear Editor,

Hiccups (singultus) are one of the most challenging symptoms to diagnose a cause. Causes range from the gastrointestinal and cardiovascular systems to the neurological system [1]. It is essential to remember that area postrema syndrome (APS), particularly in cases caused by neuromyelitis optica spectrum disorders (NMOSD), is an important differential diagnosis [2]. Persistent and intractable hiccups are a representative symptom in patients with NMOSD and associated with damage to areas abundant with the aquaporin protein [3-5]. However, intractable hiccups caused by APS with NMOSD rarely are associated with bradyarrhythmia [6,7].

A 77-year-old man presented with an acute onset of hiccups and reported vomiting 8 days prior to admission. Hiccups occurred about 10 times per minute and persisted over 48 hours. An electrocardiogram (ECG) did not show any abnormal findings. A gastrointestinal endoscope revealed an esophageal hiatal hernia and atrophic gastritis, but there was no clear cause of the hiccups. Intravenous administration of metoclopramide, haloperidol, diazepam, and chlorpromazine did not relieve the hiccups. At this point he was transferred to our hospital, where he lost consciousness because of sinus arrests lasting 13 seconds. He was diagnosed with SSS (Figure 1a) along with the persistent hiccups. Subsequently, a temporary pacemaker implantation was performed.

His past medical history included a coronary angina that required a drug eluting stent for his left coronary artery, 2 months prior to admission. He also had diabetes mellitus, hyperlipidemia, and a history of smoking. On examination, his vital signs showed a blood pressure of 92 / 52 mmHg and a pulse of 69 bpm with a normal sinus rhythm. He had no other abnormal findings in the lungs, heart, and abdomen. Neurological examination was normal, except for decreases in the bilateral deep tendon

reflexes.

Laboratory examination showed high levels of HbA1c (7.7%). Positive serology results included elevated anti-aquaporin 4 antibodies (enzyme-linked immunosorbent assay, 21.7 units/mL; normal, <3.0 units/mL). Cerebrospinal fluid analysis was 10 cellular/ μ L with normal total protein and glucose. ECG was normal, but coefficient of variation of R-R intervals (CVR-R) decreased to 1.12% at rest. Head-up tilt test and Valsalva maneuver revealed neither hypotension nor bradyarrhythmia. Cardiac ultrasounds and contrast-enhanced CT scan did not show any abnormalities, except for a fibroelastoma in the thyroid gland. Additionally, 18F-fludeoxyglucose positron emission tomography did not show any abnormalities. Although the bilateral lesions in the area postrema were obscure in the fluid-attenuated inversion-recovery (FLAIR) brain MRI on admission (Figure 1b), they became prominent by day 13 (Figure 1c). The patient was diagnosed with NMOSD accompanied with SSS following APS. His SSS resolved following the disappearance of the hiccups with intravenous administration of metoclopramide without any immunomodulative treatment.

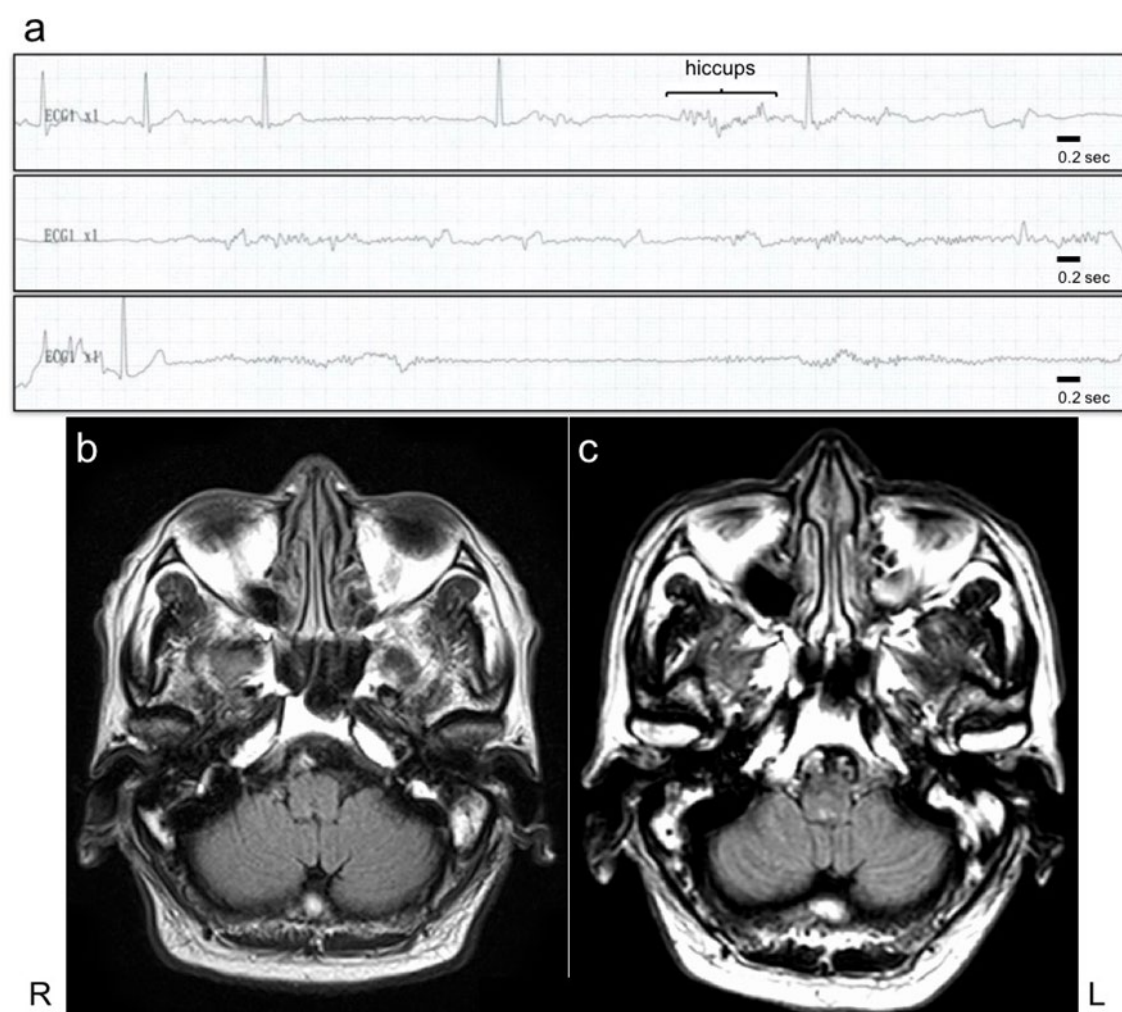


Figure 1. Sick sinus syndrome was subsequent to persistent hiccups (a). FLAIR imaging on admission did not show any hyperintensities in the area postrema (b), but it became prominent 13 days following admission (c).

Here, we described a patient with NMOSD causing bradyarrhythmia following intractable hiccups. Current theories of hiccups are: an aberrant neural network of reflex, including vagal nerves, and a “hiccup center” in the area postrema [1]. Physiologically, electrical stimulation in the area postrema results in a decrease in blood pressure and heart rate [8]. In general, patients with bradyarrhythmia linked with hiccups were relatively older in average age than those with NMOSD (from 40 to 47 year olds) [2,4,8,9]. Correlation of age, intractable hiccups, and

vomiting is not prominent in cases of NMOSD [10], but patients who suffer bradyarrhythmia following hiccups, including the present case, are usually elderly [78-year-old [6], 61-year-old [7], and 77-year-old]. Additionally, the present case had multiple cardiovascular risk factors though the previous two reports did not mention any apparent cardiovascular complications.

Although hiccups may be associated with bradyarrhythmia, because they result in increased intrapleural pressure, stimulating atrial mechanoreceptors and consequently parasympathetic hyperactivation [1], negative results of head-up tilt test and Valsalva maneuver further suggested an association between the patient's SSS and APS. We concluded the SSS was caused by area postrema stimulation due to NMOSD, with cardiovascular vulnerabilities from elderly age and multiple cardiovascular risk factors. Clinicians should be aware that severe bradyarrhythmia could be associated with APS, especially in NMOSD patients who are elderly and have cardiovascular complications.

Acknowledgements

We are grateful to, and thank, the patient and his family.

Declaration of Interest

None.

Funding

This work was supported by a Grant-in-Aid for Young Scientists from the Japan Society for the Promotion of Science (18K15453).

Informed Consent and Patient Details

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