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Case Report

Sick Sinus Syndrome Combined with Wallenberg Syndrome: a Case Report

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HIGHLIGHTS

- First report of sick sinus syndrome with Wallenberg syndrome in South Korea.
- Clinicians could overlook sick sinus syndrome in Wallenberg syndrome.
- Sick sinus syndrome should be evaluated in Wallenberg syndrome.

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Conflict of Interest
The authors have no potential conflicts of interest to disclose.

ABSTRACT

Cardiac arrhythmia is a rare manifestation of the Wallenberg syndrome; lesions are located in the brainstem, especially the lower medulla, which regulates sympathetic and parasympathetic activity. A 55-year-old man was admitted to the university hospital with symptoms including ataxia, left ptosis, decreased sensation of pain and temperature on the right side, left facial numbness, and dizziness. Brain magnetic resonance imaging revealed an infarction in the left dorsolateral medulla. Therefore, he was diagnosed with Wallenberg syndrome. While he underwent conservative treatment for Wallenberg syndrome, he experienced several events of self-limiting heart pounding, which required an evaluation of cardiac function. The 24-hour Holter monitor showed an increased RR interval with bradycardia and prolonged sinus pause. As a result, the diagnosis of sick sinus syndrome combined with Wallenberg syndrome was made. Sick sinus syndrome is a rare cardiac complication of the Wallenberg syndrome, and clinicians could overlook it when the initial electrocardiography shows a normal sinus rhythm. Sick sinus syndrome can cause sudden death without appropriate medical intervention. Therefore, clinicians should consider further evaluation, including a 24-hour Holter monitor, to check for the potential presence of sick sinus syndrome in the acute phase of Wallenberg syndrome.

Keywords: Sick Sinus Syndrome; Lateral Medullary Syndrome; Solitary Nucleus

INTRODUCTION

Lateral medullary infarction causes Wallenberg syndrome with various symptoms, including ataxia, numbness of the ipsilateral face or contralateral body, dysphagia, and vertigo [1]. In addition, the nuclei of the medulla play an essential role in the autonomic regulation of cardiovascular functions. In particular, the nucleus of the solitary tract is involved in sympathetic and parasympathetic outflows [2,3]. Therefore, lesions in this area, such as in Wallenberg syndrome, can lead to cardiac dysfunction. Disinhibition of the solitary nucleus may lead to an increase in parasympathetic outflow, resulting in cardiac abnormalities [4].

Sick sinus syndrome is defined as sinus pause or arrest of 3 seconds or more without atrial activity. Atrial activity can be affected by various mechanisms, including cardiac structural

abnormalities, cardiac electrical dysfunctions, metabolic imbalance, and autonomic dysfunctions such as lesions in the nucleus tractus solitarii (NTS) [3].

Here, we report a rare case of a patient with sick sinus syndrome after a diagnosis of Wallenberg syndrome. To the best of our knowledge, this is the first case report of sick sinus syndrome combined with Wallenberg syndrome in South Korea.

CASE REPORT

A 55-year-old man was referred to the neurology department of our hospital for possible acute infarction presenting with dizziness, nausea, and vomiting. He reported that these symptoms abruptly began about 10 hours previously, and his mental status was alert. On physical examination, the patient had left-sided Horner syndrome and impaired pain and temperature sensation in the right arm, leg, and left face. The clinical pattern was consistent with Wallenberg syndrome.

The initial brain computed tomography scan did not reveal any hemorrhage or mass. However, brain magnetic resonance imaging (MRI) revealed an acute infarction in the left lower lateral medulla oblongata (**Fig. 1**). MR angiography showed weak flow with diffuse luminal narrowing and multifocal stenosis in the left V4 segment (**Fig. 2**). Therefore, he was admitted for further evaluation, and dual antiplatelet therapy, including aspirin and clopidogrel, was prescribed. After admission, he complained of 4 events of palpitations and lasting dizziness within 72 hours. Electrocardiography (ECG) was performed at every event and showed a normal sinus rhythm. Transthoracic echocardiography also showed no structural abnormalities, with an ejection fraction of 63%. Therefore, we performed an additional 24-hour Holter monitor to check for any missing cardiac arrhythmias. The results showed an increased RR interval with an average of 831 ms (**Fig. 3A**), 1,712 beats of bradycardia (≤ 60 bpm), and sick sinus syndrome with a maximal pause of 3.1 seconds (**Fig. 4**). When sick sinus syndrome was recorded by the Holter monitor, the patient experienced a pre-syncope type of dizziness and lightheadedness. The patient's blood pressure (BP) at that time was 104/47 mmHg. His mean arterial pressure was 66 mmHg, lower than his usual mean arterial pressure value of 80–100 mmHg. We

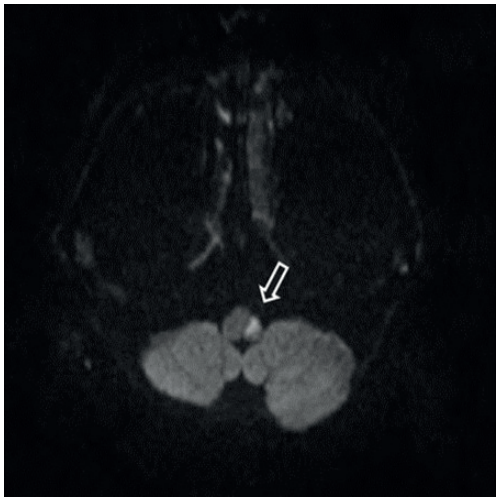

Fig. 1. Magnetic resonance imaging scan of the brainstem with an infarction on the left dorsolateral medulla (open arrow).

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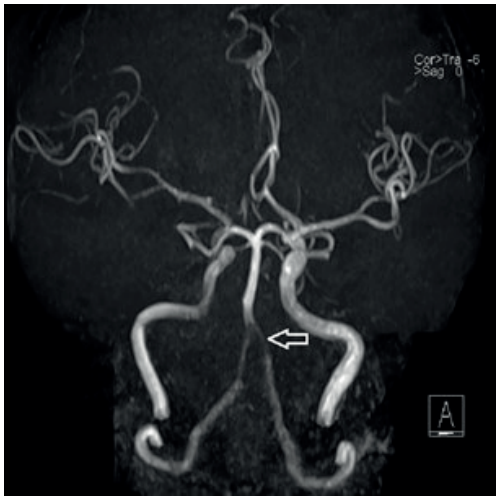

Fig. 2. Magnetic resonance angiography with diffuse luminal narrowing and multifocal stenosis in the left V4 segment (open arrow).

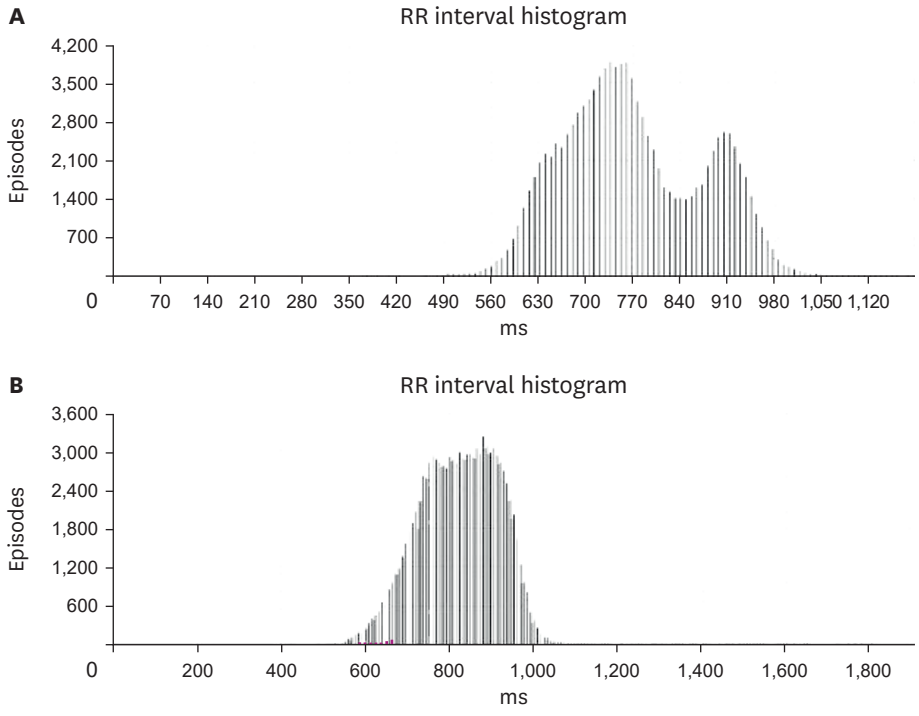

Fig. 3. (A) Increased initial RR interval with an average of 831 ms. (B) Decreased follow-up RR interval with an average of 771 ms.

consulted the cardiovascular department and considered implanting a pacemaker if the sinus pauses continued with symptom progression.

Fortunately, his symptoms spontaneously subsided. Two weeks later, a follow-up 24-hour Holter monitor showed a relatively decreased RR interval with an average of 771 ms (**Fig. 3B**), 745 beats of bradycardia (≤ 60 bpm), and no sick sinus syndrome with a maximal pause of 1.18 seconds. Therefore, the cardiologist recommended symptom observation without any medical intervention.

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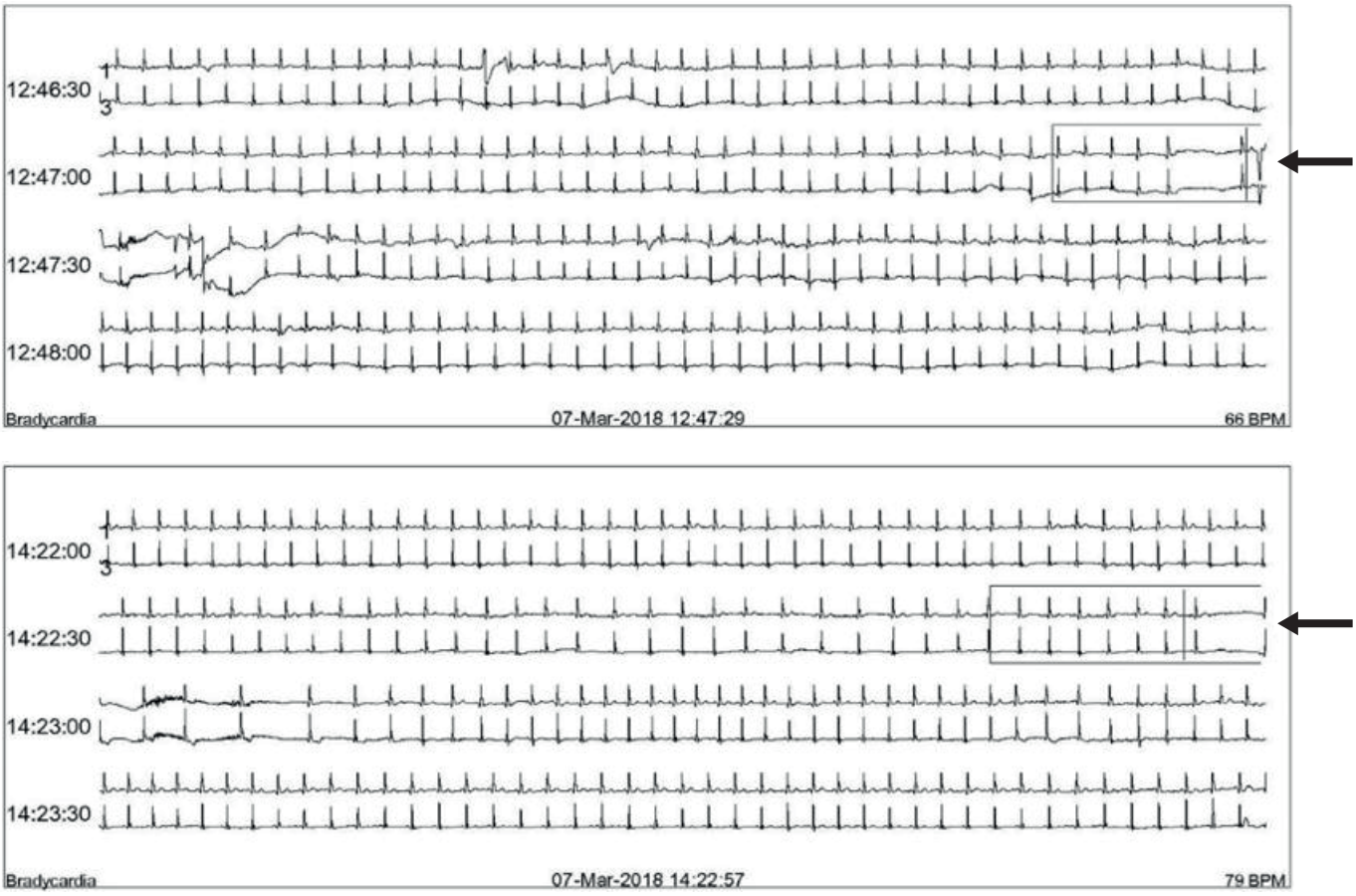

Fig. 4. Electrocardiography with sick sinus syndrome with a maximal sinus pause of 3.1 seconds (arrow).

DISCUSSION

As mentioned above, sick sinus syndrome can occur due to autonomic dysfunction, such as lesions in the NTS [3]. Previous studies have reported that the NTS controls the neurotransmission of cardiovascular reflexes. Stimulation of the NTS inhibits neurons in the rostral ventrolateral medulla, resulting in decreased sympathetic outflow, leading to low BP and bradycardia [3]. In contrast, acute lesions of the NTS cause sympathetic activation, neurogenic hypertension, and loss of baroreflex control of BP [5]. Stimulation of the P2X purinoceptors of the NTS causes rapid bradycardia by sympathetic withdrawal, parasympathetic activation, or a combination of both mechanisms [3]. Lesions in the commissural NTS block baroreceptor-mediated tachycardia, whereas lesions restricted to the subpostremal region of the NTS inhibit baroreceptor-mediated bradycardia [4]. In turn, the pathophysiology of cardiac dysfunction in the lateral medulla is diverse, and the cardiac manifestations can be determined by specific regions of the NTS in the medulla oblongata.

In addition, one study described another mechanism by which hypothalamic arcuate neurons stimulate the NTS and cause bradycardia [6]. Moreover, immunohistochemical analyses of the medullary sections of sudden infant death syndrome victims showed brain injury in the NTS, which might be responsible for cardiorespiratory dysfunction [7]. Even adults

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with hypoxic brain damage to the NTS after acute cardiac failure cannot recover cardiac and respiratory functions, despite appropriate medical interventions [8].

However, cardiac dysfunction following brainstem stroke is rare, and the overlap of cardiac and cerebrovascular diseases can be overlooked. Meglic et al. [9] evaluated the function of the autonomous nervous system in 6 patients with medullary brainstem infarcts and 8 patients without medullary brainstem infarcts by focusing on heart rate variability and catecholamine values. The authors suggested an apparent relationship between the transient autonomic nervous system dysfunction and acute medullary stroke, even though none of the patients experienced severe cardiac failure. Therefore, clinicians should pay attention to cardiac rhythmic changes even without severe cardiac failure that develop into cardiac arrest [4].

In this case report, the Horner syndrome seen at the primary visit suggests a lesion of the central sympathetic neurons caused by the dorsolateral medulla oblongata infarction. Therefore, we concluded that, in this case, failure of sympathetic outflow was responsible for the disinhibition of the NTS, increasing parasympathetic activity and decreasing sympathetic activity.

Several case reports have described patients with lateral medullary infarction who developed cardiovascular autonomic dysfunction or sinus arrest. Koay and Dewan [10] reported a 52-year-old patient with a left lateral medulla oblongata and left medial cerebellar hemisphere infarction. On 24-hour Holter monitor evaluation, he exhibited multiple bradycardic episodes and 56 asymptomatic episodes of sinus arrest with a maximal pause of 11.0 seconds. They inserted a permanent pacemaker. Takazawa et al. [11] reported a 78-year-old patient with infarction of the bilateral medial regions and the right tegmentum of the upper and middle medulla oblongata. She experienced post-hiccup cough syncope with 30–50 beats/minute sinus bradycardia and hypotension (systolic BP was 60–70 mmHg, and diastolic BP was 20–30 mmHg). In addition, a 24-hour Holter monitor detected 65 asymptomatic episodes of sinus arrest with a maximal pause of 8.3 seconds. Fortunately, the hiccups, cough syncope, and asymptomatic sinus arrest attenuated naturally from 1 month after clinical onset, and pacemaker insertion was not needed.

Compared to our case, the maximal pause on the Holter monitor in the above 2 cases was longer and showed more severe sick sinus syndrome. In addition, the second case report showed more prominent bradycardia and lower BP than those in our case, along with post-hiccup cough syncope. The size of the infarction observed on brain MRI in the above 2 case reports was more extensive than that of our case, resulting in more severe failure of the sympathetic outflow.

In addition, in our case, the sick sinus syndrome was self-limiting and showed rapid improvement compared to the above 2 case reports. It could be explained that since the size of infarction was relatively tiny, the edema around the lesion resolved quickly, or the central autonomic regulatory mechanism was easily reestablished [12]. Huynh et al. described a 67-year-old patient with right dorsolateral medullary infarction resulting in orthostatic hypotension and pre-syncope [13]. The brain MRI showed that the size of infarction was smaller than that in our case, and no sick sinus syndrome was observed. The previously mentioned cases showed only symptoms due to increased parasympathetic activity such as cough syncope, orthostatic hypotension, and presyncope, whereas in our case, the patient complained of palpitations 4 times, a symptom related to increased sympathetic activity. The commissural NTS contains pathways that mediate the cardiac sympathetic component,

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whereas the subpostremal region of the NTS mediates the cardiac parasympathetic component [4]. Therefore, various cardiovascular autonomic dysfunctions could be represented, depending on the size and location of the lateral medullary infarction.

This case report described a patient with Wallenberg syndrome who developed various symptoms, such as abnormalities in sympathetic and parasympathetic activity. In this case, sick sinus syndrome occurred in a patient with a relatively small lesion in the lateral medullary area compared with lesions described in previous case reports.

In conclusion, sick sinus syndrome is a rare cardiac complication of Wallenberg syndrome, and clinicians can overlook it when the initial ECG shows a normal sinus rhythm. Sick sinus syndrome can cause sudden death without appropriate medical intervention. Therefore, clinicians should consider further evaluation, including a 24-hour Holter monitor, to check for potential sick sinus syndrome in the acute phase of Wallenberg syndrome.

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