



Vertebral artery dissection induced lateral medullary syndrome characterized with severe bradycardia: a case report and review of the literature

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Background: Lateral medullary syndrome is the most common type of brainstem infarction. Lateral medullary syndrome results in damage to the corresponding cranial nerve nuclei and the nucleus tractus solitarius, with vertigo, ipsilateral ataxia, crossed sensory disturbances, Horner's sign, bulbar palsy, and other underlying symptoms or signs. However, cases with cardiac arrhythmia and other autonomic dysfunctions as the primary manifestations are less common. Clinically, sudden death occasionally occurs in patients with lateral medullary syndrome, which may be associated with severe cardiac arrhythmia. These patients may suffer in life-threatening arrhythmia and even cardiac arrest, and vital signs should be closely monitored to prevent sudden death. In younger patients, vertebral artery dissection is the most common cause.

Case Description: Here, we present a case of lateral medullary syndrome caused by vertebral artery dissection with severe bradycardia. The patient was a 49-year-old man who was admitted with “*sudden onset of numbness in the left limbs and right side of the face for 1 hour*”. Electrocardiogram (ECG) monitoring showed a repeated heart rate decrease to as low as 23 beats/min, followed by a gradual increase in heart rate to 35–55 beats/min after 2–3 seconds. Head magnetic resonance imaging (MRI) examination revealed right dorsolateral cerebral infarction of the medulla oblongata. Digital subtraction angiography (DSA) revealed a right vertebral artery dissecting aneurysm. We performed an emergency placement of a temporary pacemaker, followed by conservative treatment with platelet aggregation inhibitors, vascular softening agents and improved collateral circulation. Elective spring coil embolization of the vertebral artery dissecting aneurysm and stent implantation were performed. At outpatient follow-up, the patient had a good prognosis.

Conclusions: Clinical management of patients with lateral medullary syndrome should be prioritized, with close cardiac monitoring at the early stages of observation and pacemaker placement and tracheal intubation as required to prevent adverse events.

Keywords: Lateral medullary syndrome; bradycardia; vertebral artery dissection; cerebral angiography; case report

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Introduction

Lateral medullary syndrome is a common brainstem infarction of the dorsolateral region of the superior part of the medulla oblongata, due primarily to thrombosis of the posterior inferior cerebellar artery or vertebral artery. Infarction in this region damages the corresponding cranial nerve nuclei and solitary nuclei, with vertigo, ipsilateral ataxia, contralateral sensory deficits, Horner's syndrome, bulbar palsy, and other potential signs or symptoms (1,2). Since the regulatory center of the arterial baroreceptor reflex is located in the dorsal medulla, when elevated arterial pressure stretches the carotid sinus and aortic arch and excites the baroreceptors, the excitation is transmitted through the carotid sinus nerve and aortic nerve to the solitary nuclei on both sides of the dorsal medulla. From here, fibers project to the cardiovagal center in the medulla, which excites the cardiac vagus preganglionic neurons, slowing the heart rate and decreasing blood pressure through the cardiac vagus nerve (3,4). Thus, patients with lateral medullary syndrome may sometimes also present with clinical manifestations associated with autonomic dysregulation, including arrhythmia, hypotension, syncope, and even cardiac arrest. In the present case, lateral medullary syndrome caused by vertebral artery dissection with severe bradycardia as the primary manifestations was rare. Such patients may suffer in sudden death, and vital signs should be closely monitored to prevent sudden death. We present the following article in accordance with the CARE reporting checklist (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-1098/rc>).

Case presentation

The patient was an employed, 49-year-old male with a chief complaint of "hypertension" for 3 months. The patient's blood pressure reached a maximum of 160/95 mmHg, and the patient was on 0.15 g irbesartan q.d. per os. Blood pressure was not being monitored. The patient had smoked one pack of cigarettes per day for over 20 years and denied any history of other diseases or history of poisoning. The patient's father had hypertension, but the patient denied a family history of cardiovascular disease. He was admitted to the hospital for a "*sudden onset of numbness in the left limbs and right side of the face for 1 hour*". The initial symptoms were sudden onset of numbness of the left limbs and right side of the face with no obvious cause 1 hour prior (2020-06-12 11:30 a.m.) while meals, lack of flexibility of the left

lower limb while walking, and chest tightness. At 12:42 p.m., he arrived at the neurological emergency department of our hospital with a blood pressure of 160/80 mmHg and was conscious with clear speech, pupils equal and round, normal eye movements, and no nystagmus. The nasolabial folds were symmetrical, and the pharyngeal reflex was normal. The patient was able to extend his tongue. The heart rate was 80 beats/min, with regular rhythm and no pathological murmurs. Bilateral finger-to-nose tests were normal. The muscle strength of the left lower leg was level 5, and the muscle strengths of the remaining extremities were all level 5. The patient's right face and left limb suffer from hypoalgesia, with no elicited bilateral pathological signs. Head magnetic resonance imaging (MRI), magnetic resonance angiography (MRA), and diffusion-weighted imaging (DWI) examination at 13:35 p.m. indicated no significant abnormalities. DWI-negative cerebral infarction was considered, and intravenous alteplase thrombolytic therapy was advised, but the patient refused after discussion. The patient was immediately given enteric-coated aspirin tablets 0.2 g, clopidogrel tablets 300 mg, and atorvastatin calcium tablets 40 mg. An electrocardiogram (ECG) revealed a heart rate of 68 beats/min, sinus rhythm, atrioventricular conduction delay, and T wave changes. ECG monitoring showed a repeated heart rate decrease to as low as 23 beats/min with prolonged R-R intervals, followed by a gradual increase in heart rate to 35–55 beats/min after 2–3 seconds, which lasted about 1 min before returning to normal. The patient exhibited obvious dizziness, nausea and vomiting, chest tightness, palpitations, and profuse sweating during episodes of bradycardia. His finger-stick blood glucose level was 8.2 mmol/L, potassium was 3.6 mmol/L, sodium was 143 mmol/L, and creatinine was 71 μ mol/L. The troponin test, coagulation tests, and blood gas analysis indicated no abnormalities. A cardiac B-scan ultrasound indicated no significant abnormalities. An arteriovenous B-scan ultrasound of the lower limbs did not indicate thrombosis. Computed tomography angiography (CTA) of the aorta indicated no significant abnormalities. We consulted the cardiology department on an emergency basis, and sick sinus syndrome or acute coronary syndrome was considered. A temporary pacemaker was placed on an emergency basis, and coronary angiography indicated approximately 50% stenosis of the middle segment of the left anterior descending artery, with no significant stenosis elsewhere. At 2:50 p.m. on June 13, the patient exhibited dysarthria and anhidrosis on the right side of the face, reduced right palpebral fissure, a constricted right

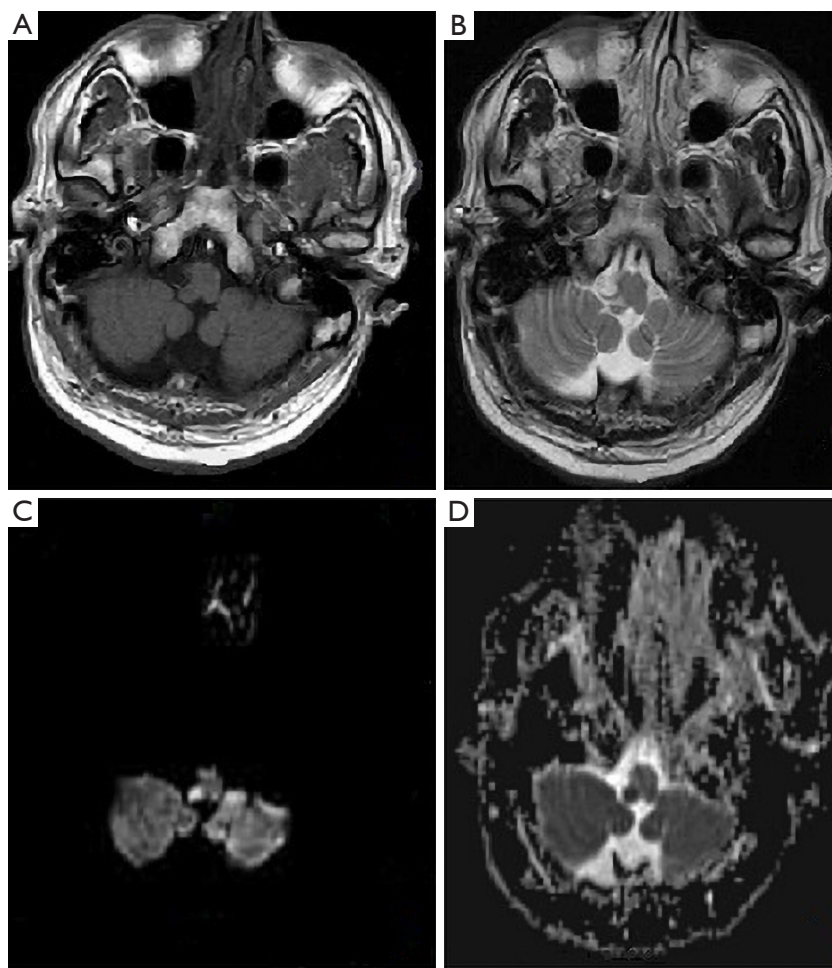


Figure 1 Patchy regions of abnormal signal in the dorsolateral aspect of the right medulla oblongata. (A) Slightly low signal on T1WI; (B) slightly high signal on T2WI; (C) high signal on diffusion-weighted imaging sequence; (D) low signal on apparent diffusion coefficient of the corresponding region. T1WI, T1-weighted imaging; T2WI, T2-weighted imaging.

pupil, and right finger-to-nose test failure. Head MRI and DWI re-examination revealed right dorsolateral cerebral infarction of the medulla oblongata (*Figure 1*). A head and neck CTA (June 13) showed bulging in the right side of the intracranial segment of the vertebral artery and possible arterial dissection (*Figure 2A*). Digital subtraction angiography (DSA) was recommended, and the patient indicated that he would decide whether to undergo DSA after discussion. On June 16, the pacemaker rate was adjusted to 40 beats/min, and ECG monitoring indicated a generally spontaneous rhythm. On June 17, the temporary pacemaker was removed, and the spontaneous heart rate ranged from 55 to 70 beats/min. Results of an ambulatory ECG on June 18 (total recording time: 21 hours and 32 min) revealed sinus rhythm, a minimum heart rate of

48 beats/min, a maximum heart rate of 77 beats/min, a mean heart rate of 63 beats/min, and 151 premature ventricular contractions/min. On June 26, the patient agreed to undergo DSA, which revealed a right vertebral artery dissecting aneurysm in the patient's posterior inferior cerebellar artery (*Figure 2B*). The patient had dizziness, nausea, and vomiting (damage to the vestibular nuclei), contralateral sensory deficits (damage to the spinal trigeminal nuclei and lateral spinothalamic tract), right Horner's syndrome (damage to the right inferior fibers of the sympathetic trunk), and right ataxia (damage to the restiform body). MRI indicated a right dorsolateral medullary lesion whose site corresponded with the symptoms, and the lesion was localized in the right dorsolateral medulla. Qualitatively, the patient had an acute onset with risk factors for cerebrovascular disease,

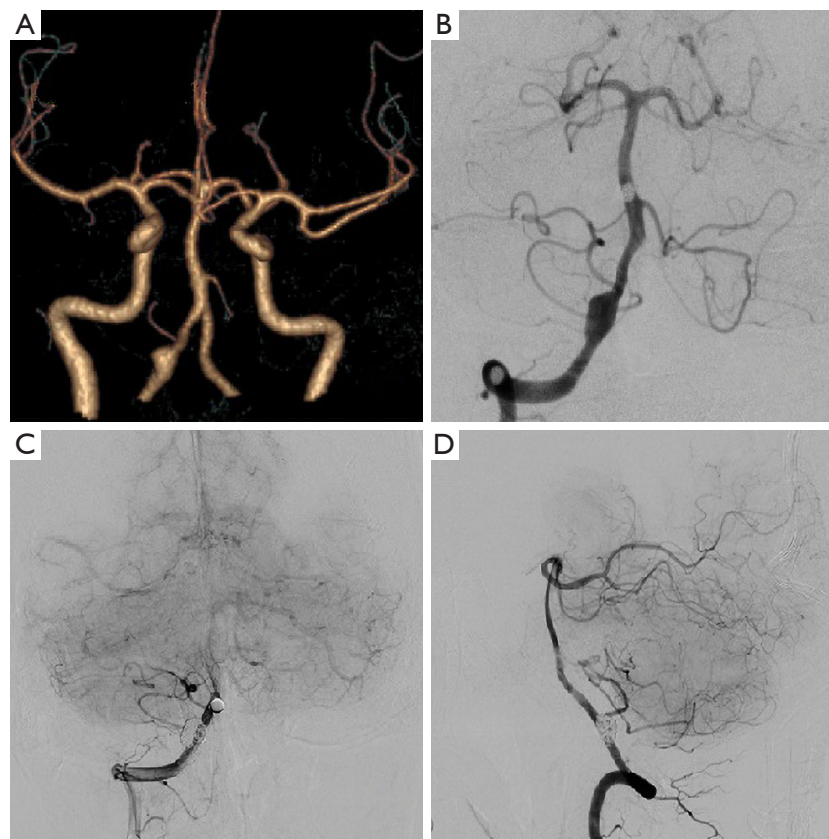


Figure 2 Vascular imaging of V4 segment aneurysm of right vertebral artery before and after endovascular intervention. (A) CTA showing localized enlargement of the V4 segment of the right vertebral artery; (B) preoperative DSA showing a right vertebral artery dissection aneurysm (approximately 5.7 mm × 7.5 mm in size) in the V4 segment; (C) postoperative DSA frontal view showing dense filling after spring coil embolization of the right vertebral artery aneurysm, good stent apposition, and smooth distal blood flow; (D) postoperative DSA lateral view showing dense filling after spring coil embolization, good stent apposition, and smooth distal blood flow in the basilar artery and small posterior cerebellar arteries. CTA, computed tomography angiography; DSA, digital subtraction angiography.

such as a history of hypertension and smoking, a high-signal DWI and a low-signal apparent diffusion coefficient (ADC) at the lesion site, and DSA indicating a dissecting aneurysm in the corresponding supply artery, so ischemic vascular disease was considered first. The treatment included enteric-coated aspirin tablets, atorvastatin calcium tablets, irbesartan tablets, n-butylphthalide injection, and hydroxyethyl starch in sodium chloride. No significant improvement in symptoms was observed. Subsequently, spring coil embolization and stent placement were performed (*Figure 2C,2D*); the procedure was uneventful. On August 26, the patient was followed up at our outpatient clinic, and his symptoms had generally resolved. On January 4, 2021, an ECG re-examination indicated sinus rhythm and a heart rate of 70 beats/min. On July 8, 2021, a head

computed tomography (CT) re-examination indicated nodular and punctiform dense opacities in the right brainstem with local metallic artifacts (right vertebral artery aneurysm intervention). A DSA re-examination indicated dense filling of the right vertebral artery aneurysm, good apposition of the stent to the vascular wall, and no significant abnormalities in other vessels. At the outpatient examination in July 15, 2022, the patient's general condition was satisfactory, with National Institute of Health Stroke Scale (NIHSS) score of 0 and Modified Rankin Scale (mRS) score of 0 (*Figure 3*).

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent

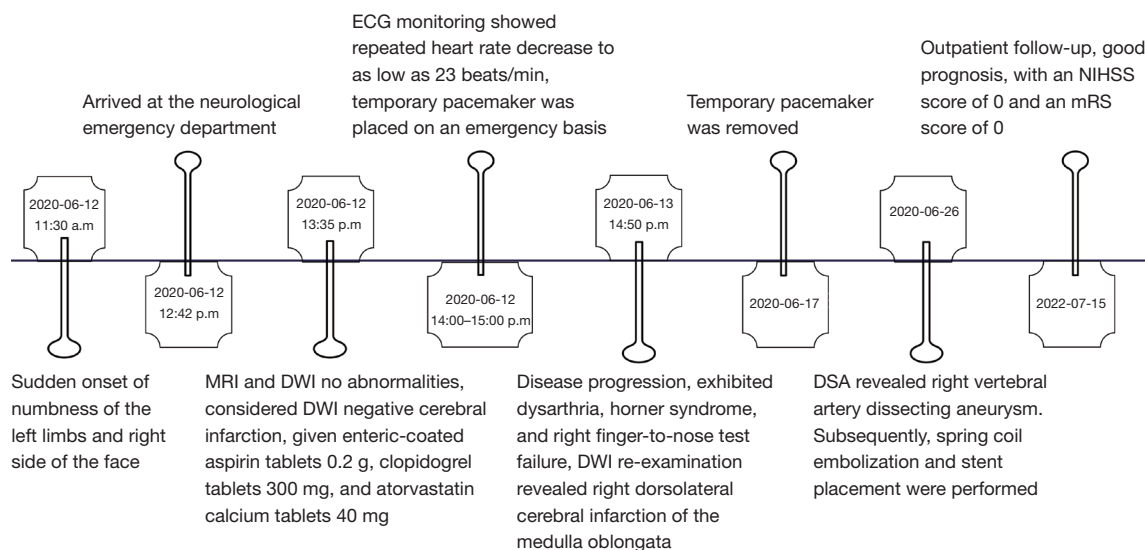


Figure 3 Timeline chart of the patient's clinical symptoms, diagnosis, treatment, and outcomes. MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging; ECG, electrocardiogram; DSA, digital subtraction angiography; NIHSS, National Institute of Health stroke scale; mRS, Modified Rankin Scale.

was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

The distinctive feature of the present case was the onset of transient and severe bradycardia with intensified chest tightness, palpitations, and dizziness when the heart rate dropped. Recurrent and severe bradycardia was found on ECG monitoring (lead II), with each episode of bradycardia lasting about 1 min. The episode began with the disappearance of P waves, morphological variation of the QRS wave groups, and a markedly prolonged R-R interval, followed by a reversion to sinus rhythm. It is presumed that the loss of ventricular beats may have occurred due to impaired excitation or delayed conduction at higher-order pacemaker nodes, such as the sinus node and atrioventricular node. Several cases of lateral medullary syndrome combined with sinoatrial arrest have been reported recently (5,6). Gofton *et al.* (7) reported a case of medullary dorsolateral syndrome combined with severe bradycardia and ataxia that has similarities to the present case. In addition, lateral medullary syndrome can also present with autonomic respiratory arrest due to damage to the decussating medullary and spinal pathways

and consequent central hypoventilation syndrome or “Ondine’s curse” (8). In the clinic, close ECG monitoring of patients with lateral medullary syndrome should be conducted for early detection of severe arrhythmias, cardiac arrest, respiratory arrest, and other adverse events, and early intervention should be practiced to reduce the possibility of sudden death. In the present case, ECG monitoring revealed severe arrhythmia immediately, and effective intervention at the first opportunity prevented the development of adverse events.

The patient in the present case was a middle-aged male with no previous history of cardiac disease and no chest tightness, palpitations, or other general discomforts. A cardiac B-scan ultrasound indicated a typical cardiac structure, and coronary DSA confirmed good coronary artery vascular structure. In the acute phase of cerebral infarction, the patient had recurrent, transient, severe bradycardia, chest tightness, palpitations, dizziness, nausea, and vomiting during episodes of bradycardia. However, after stabilization of the cerebral infarction, these symptoms did not recur. An ambulatory ECG did not indicate severe bradycardia or arrest, and no further arrhythmias, such as chest tightness or palpitations, occurred over the 1-year follow-up period. ECG re-examination indicated sinus rhythm, indirectly indicating satisfactory electrophysiology of the patient’s heart. Severe bradycardia developed during the acute phase of cerebral infarction, and there

was no evidence of bradycardia before infarction or after its stabilization. The structure, vasculature, and electrophysiology of the heart itself were not sufficient to cause severe bradycardia.

Theoretically, cerebral infarction can be visualized at 30 min on DWI, but in the present case, no lesion was detected on cranial MRI + DWI 2 hours after onset. This may be because the lesion area was in a state of critical hypoperfusion, and the decreased cerebral blood flow affected neuroelectrical activity but not to the level of neuronal membrane pump failure (9). It is also possible that the infarcts were not scanned by MRI due to their relatively small size at the beginning of the disease, but as the disease progressed and the infarcts expanded, the right dorsolateral medullary infarcts became clearly detectable on subsequent cranial MRI + DWI re-examination. Ohira *et al.* (10) found that thin-layer coronal DWI scanning in patients with negative standard axial DWI increased the positive detection rate of cerebral infarction by 50%. In clinical cases where acute cerebral infarction is highly suspected but DWI is negative, the condition should be carefully analyzed. The detection rate can be improved by a combination of high-resolution MRI + thin-layer scan + coronal and sagittal scans to avoid missing a diagnosis to the greatest extent possible.

In the present case, cerebral angiography indicated a vertebral artery dissecting aneurysm with many peripheral branches and a wide aneurysm dome. The risk of rupture of the dissecting aneurysm was considered, and stent placement + spring coil embolization was eventually selected, with the patient achieving a good outcome. Gofton *et al.* (7) reported a case of Wallenberg syndrome presenting with bradycardia and ataxia with vertebral artery stenosis found on cranial MRA without evidence of arterial dissection. The vertebral artery does not supply the autonomic nervous system, and bradycardia is not inherently related to dissecting aneurysms. Malignant arrhythmias should be associated with the center of the dorsolateral infarct in the medulla oblongata.

The medulla oblongata is the primary center for regulating cardiac activity and is one of the regulatory regions for autonomic nervous system input and output. The solitary nuclei on either side of the dorsal medulla oblongata inhibit sympathetic preganglionic neurons through inhibitory projections and excite vagal preganglionic neurons through excitatory projections, ultimately slowing the heart rate (11). We hypothesize that the compensatory increase in blood pressure after the acute

cerebral infarction in this patient led to sustained excitation of the arterial baroreceptor reflex, while the damaged solitary nuclei could not conduct the baroreceptor reflex normally. Persistently elevated arterial pressure leads to abnormal activity in the undamaged solitary nucleus, as well as in the dorsal nucleus of the vagus nerve, the nucleus ambiguus, and its surrounding reticular structure. The activity of the vagus nerve is abnormally increased, while the sympathetic tone and vasoconstriction of the heart are abnormally decreased, eventually leading to malignant arrhythmia, hypotension, and even cardiac arrest.

In conclusion, lateral medullary syndrome may result in life-threatening arrhythmia and even respiratory and cardiac arrest, and treating such patients should be highly prioritized in the clinic. Close cardiac monitoring should be performed in the early stages of observation, and pacemaker placement and tracheal intubation should be performed to reduce the risk of sudden death.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://apm.amegroups.com/article/view/10.21037/apm-22-1098/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-1098/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the

patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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