Lateral Medullary Syndrome in Patients with Vertebral Artery Dissection: Case Series Illustration and Review of the Neuroanatomical Correlates

Original Article

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Abstract— Introduction. Lateral medullary syndrome (LMS) is the most common of the crossed brainstem syndromes involving the posterior circulation. The typical clinical pattern (i.e., classical Wallenberg syndrome) includes ipsilateral Horner syndrome, hoarseness, nystagmus, dysphagia, dizziness, ataxia, and crossed pain and temperature sensory loss (i.e., ipsilateral face and contralateral body). There are several patterns of sensory dysfunction according to the site of lesion. Although some sources still cite cardioembolism or atherothrombotic occlusions as the main causes of lateral medullary infarctions, it is increasingly recognized vertebral artery dissection (VAD) as the chief etiology. **Patients and Methods.** We report on nine patients presenting with LMS due to confirmed VAD in predominantly young individuals (6 men, age range 23-54 years). **Results.** Most patients presented with sudden headache or neck pain, ataxia and nystagmus (n=7). On neurological examination the majority (n=7) had crossed sensory loss of the classical Wallenberg pattern and all but two had Horner syndrome. At 6-month follow-up no deaths or recurrences were observed: five patients were completely asymptomatic, three patients persisted with mild or moderate deficits and one was unable to walk without assistance. Seven patients had dysphagia that evolved unevenly within the 6-month follow-up period. We also discuss on the clinical and neuroanatomical correlates behind the LMS variants. **Conclusion.** VAD should be suspected in patients presenting with LMS and headache or neck pain. The functional and recurrence prognosis is fairly good. Given the intricacy of the medulla anatomy and the serendipitous nature of ischemia after VAD, a missing sign from the original Wallenberg's description is not incompatible with a lateral medullary infarction. **Ictus 2022;3(1):e17012203003**
Keywords—Artery dissection, lateral medullary syndrome, stroke, Wallenberg.

Resumen— Síndrome Bulbar Lateral en Pacientes con Disección de la Arteria Vertebral: Ilustración de Serie de Casos y Revisión de la Correlación Neuroanatómica.
Introducción. El síndrome medular lateral (SML) es el más común de los síndromes cruzados del tronco del encéfalo que afectan a la circulación posterior. El patrón clínico típico (es decir, síndrome de Wallenberg clásico) incluye AL síndrome de Horner ipsilateral, ronquera, nistagmo, disfagia, vértigo, ataxia y pérdida sensorial cruzada al dolor y temperatura (es decir, cara ipsilateral y cuerpo contralateral). Existen varios patrones de disfunción sensorial según el sitio de la lesión. Aunque algunas fuentes todavía citan el cardioembolismo o las oclusiones aterotrombóticas como las principales causas de infartos medulares laterales, se reconoce cada vez más la disección de la arteria vertebral (DAV) como la etiología principal. **Pacientes y Métodos.** Informamos sobre nueve pacientes que presentaron SML debido a DAV confirmado en individuos predominantemente jóvenes (6 hombres, rango de edad 23-54 años). **Resultados.** La mayoría de los pacientes presentaron cefalea o dolor de cuello repentinos, ataxia y nistagmo (n = 7). En el examen neurológico, la mayoría (n = 7) tenía pérdida sensorial cruzada del patrón clásico de Wallenberg y todos menos dos presentaron el síndrome de Horner. A los 6 meses de seguimiento no se observaron muertes ni recurrencias: cinco pacientes estaban completamente asintomáticos, tres pacientes persistieron con déficits leves o moderados y uno no podía caminar sin ayuda. Siete pacientes tenían disfagia que evolucionó de manera desigual dentro del período de seguimiento de 6 meses. También discutimos sobre los correlatos clínicos y neuroanatómicos detrás de las variantes de SML. **Conclusión.** Debe sospecharse DAV en pacientes que presentan SML y cefalea o dolor de cuello. El pronóstico funcional y de recurrencia es bastante bueno. Dada la complejidad de la anatomía de la médula y la naturaleza fortuita de la isquemia después de la DAV, un signo faltante en la descripción original de Wallenberg no es incompatible con un infarto medular lateral. **Ictus 2022;3(1):e17012203003**
Palabras clave—Disección arterial, ictus, síndrome medular lateral, Wallenberg.

INTRODUCTION

Up to 20% of ischemic strokes involve the posterior circulation.[1] Lateral medullary syndrome (LMS) is the most frequent of the so-called crossed brainstem syndromes.[2] The classical clinical pattern of LMS is known as Wallenberg syndrome after the 1895 clinical description and the 1901 postmortem confirmation of the disease caused by an infarction located within the left part of the medulla oblongata supplied by the posterior inferior cerebellar artery (PICA).[3,4] Gaspard Vieusseux provided the first description of the LMS in 1810 before the Medical and Chirurgical Society of London. Nonetheless, it is attributed to Adolf Wallenberg the clinical and anatomical correlation, which led to the inference of a lesion located within the lateral medulla supplied by PICA, only on clinical grounds.[4] Later it was recognized that LMS is mostly caused by spontaneous vertebral artery disease involving the PICA territory.5,6 Other etiologies include traumatic dissection, cardioembolism, vertebral artery atherothrombotic disease, artery-artery embolism, thrombophilia, cryptogenic, and more rarely inflammatory disease.[1,2,6]

The structures involved in the lateral medullary syndrome are the following: nuclei or fasciculi of cranial nerves V, VIII, IX and X, as well as the spinothalamic tract, descendent sympathetic tract, spinocerebellar or olivocerebellar fibers, the restiform body, and more rarely the gracillis and cuneiform nuclei (Figure 1).[7,10] The classical presentation is that described by Wallenberg and includes hypalgesia of ipsilateral face and contralateral body, dysarthria (i.e., hoarseness), ipsilateral Horner syndrome, lost throat reflex, dysphagia, ipsilateral ataxia, vertigo, ocular lateropulsion an occasionally vomiting or hiccups.[10] The Wallenberg syndrome comprises only about a third of cases with LMS.[7,8,10] Considering the rostral-caudal and lateral-medial extent of the lesion 6 variants have been consistently described based on the sensory pattern of presentation (Figure 2).[8,10] Type I pattern (the classical Wallenberg syndrome) presents with hypalgesia of the ipsilateral face and contralateral body, caused by involvement of the lateral spinothalamic tract (leading to contralateral body sensory deficit) and descending trigeminal spinal tract and trigeminal nucleus (leading to ipsilateral face sensory deficit). In type II the lesion extends posterolaterally and ventromedially, affecting the crossed trigeminothalamic pathway affecting the face bilaterally and the contralateral body. This contrasts with type III LMS in which pain and temperature sense is lost in the contralateral face and body due to trigeminothalamic and lateral spinothalamic tracts involvement. Type IV manifests by hypalgesia of the contralateral body, sparing the face. Type V LMS that involves only the trigeminothalamic tract spares the body and presents with hypalgesia of the ipsilateral face. Patients with the type VI pattern have no sensory deficit.[8,10] More subtle variants

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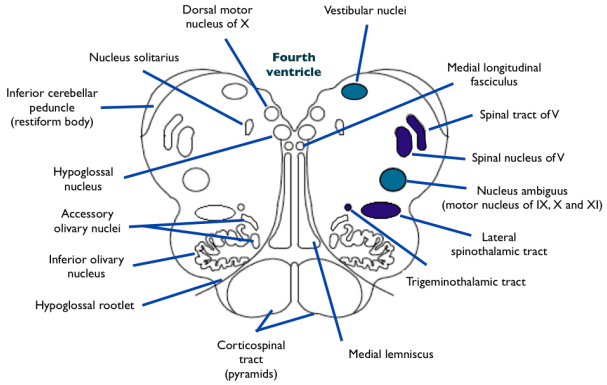

Figure 1: Midolivary cross-section diagram of the medulla oblongata showing the normal anatomy as a reference. The structures responsible for the sensory symptoms in the laterally medullary syndrome are colored in purple. The other two most commonly affected structures (i.e., the nucleus ambiguus and vestibular nuclei) are colored in aqua green. The restiform body is not consistently affected across the patterns of the laterally medullary syndrome.

are also taking into account based mainly on the implication of proprioceptive and vibration impairment, as well as the pattern of trigeminal territory involvement (i.e., "segmental" vs. "onion-skin" patterns, or incomplete implication of the 3 trigeminal branches).[8] A further LMS variant that includes ipsilateral hemiplegia (caused by caudal extension affecting the corticospinal fibers after the pyramidal decussation) added to the typical characteristics of the Wallenberg syndrome has been called Opalski syndrome.[11,12] Modern neuroimaging techniques (Figure 3) have facilitated the recognition of rare variants in vivo.10 Half of the patients did not fulfill all symptoms originally described by Wallenberg, or a significant proportion had additional clinical features of brain stem dysfunction.[2] Our objective was to provide a scholar neuroanatomical correlate discussion with graphical support on the clinical variants of the Wallenberg syndrome.

PATIENTS AND METHODS

Here we present a case series of the LMS caused by vertebral artery dissection in predominantly young individuals (Table 1). Due to the retrospective nature of the present report and the description of the usual care at our institutions, the Institutional Review Board of our centers exempted this study from the requirement to obtain informed consent. The first seven cases (case records 1-7) were diagnosed and treated in Departamento de Neurología, Hospital General Ignacio Zaragoza ISSSTE (hospitalized in years 2009 through 2013), while the last two cases (case records 8 and 9) were registered in Departamento de Neurología y Psiquiatría, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (hospitalized in years 2015 through 2019). These case records were selected among other acute ischemic stroke cases applying the following selection criteria: MRI-confirmed bulbar ischemic stroke leading to LMS (i.e., Wallenberg syndrome), age <55 years, complete clinical features detailed in the case records, and 30-day follow-up registered.

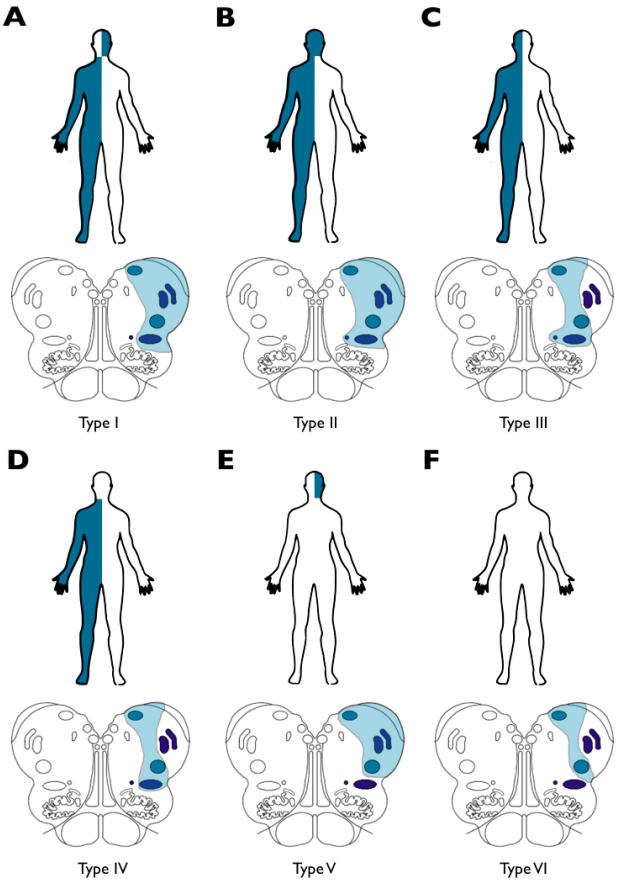

Figure 2: Midolivary cross-section of the medulla oblongata showing the anatomical structures and the corresponding anthropogram involved in each of the six variants of the Wallenberg syndrome (from A to F).

Results

Case 1. A 30-year-old man with a past medical history of cigarette smoking and hypertension was admitted with sudden onset occipital headache, vomiting, dysarthria, dysphagia, and right-sided clumsiness. Neurologic examination revealed right ptosis, right facial hypoesthesia, ipsilateral palatal weakness, as well as temperature and pain sensation decreased on the contralateral body. Right dysmetria and ipsilateral hemiataxia were also present. Cerebral magnetic resonance angiography (angio-MRI) revealed right vertebral artery dissection. Oral anticoagulation was started. Six months after the initial presentation, he showed no neurologic deficit.

Case 2. A 32-year-old man who practiced weightlifting felt sudden cervical and shoulder pain shortly after initiating his routine exercise. He developed right lateropulsion, vertigo, slurred speech, dysphagia, right face paresthesias and hiccups. Neurologic examination showed right ptosis, horizontal leftward-moving quick phase nystagmus, diminished gag reflex and ataxia. A first T2-weighted brain MRI showed a hyperintense signal on the right aspect of the medulla oblongata. Angio-MRI confirmed vertebral artery dissection. Anticoagulation was started, and at a 6-month follow-up, all the neurological symptoms had resolved completely.

Case 3. A 23-year-old otherwise healthy policeman suffered sudden neck pain while struggling with thieves. Minutes later, he had suddenly fallen ill with vertigo, dysphagia, nausea, and facial numbness. On neurologic examination, it was observed right ptosis, miosis, horizontal nystagmus, diminished gag reflex, right gait lateropulsion, and dissociative crossed loss of sensation for pain and temperature of the left body. A right vertebral artery dissection was suspected and confirmed later by angio-MRI. Anticoagulation was started, and at a 6-month follow-up, no neurologic deficit persisted.

Case 4. A previously healthy 33-year-old woman took a nap with an improper neck posture. The next morning, she perceived numbness on the left side of the face, ipsilateral axial lateropulsion, and dysphagia. On neurologic examination revealed vertical and horizontal spontaneous nystagmus, left palatal weakness with a diminished gag reflex, left facial hypoesthesia, and contralateral body involvement. A head MRI confirmed left lateral medullary infarction. Angio-MRI showed the pencil tip sign compatible with left vertebral artery dissection. She also received anticoagulation, and after a 6-month follow-up, she still had facial numbness.

Case 5. A 49-year-old man was admitted with a history of sudden-onset spontaneous cervical pain, left blurred vision, scanning speech, and left axial lateropulsion. On neurological examination, it was observed left quick phase nystagmus, left ptosis, left miosis with hemifacial anhydrosis, left soft palate paresis, right body hypoesthesia, and left appendicular hemiataxia. A laboratory thrombophilia investigation performed 3 months later showed a decreased C-protein activity. After 6 months on anticoagulation left ptosis, left palate paresis, diminished left gag reflex, right body hypoesthesia, and lateropulsion were still present.

Case 6. A 54-year-old woman with cigarette smoking as the only risk factor showed sudden cervical pain, vertigo, gait lateropulsion, and vomiting. The neurological examination revealed nystagmus characterized by a leftward-moving quick phase and abnormal gait with left lateropulsion. Anticoagulation with coumarin was started, and after 6 months of follow-up, she persisted with right hypalgesia and was unable to walk without assistance.

Case 7. A 41-year-old man with relevant medical history positive for hypertension woke-up one day with neck pain and vertigo. On neurological evaluation, it was identified rightward-moving quick phase nystagmus, right Horner syndrome, absent gag reflex, right gait lateropulsion, and crossed face-body sensory loss of pain and temperature. During hospitalization, it was diagnosed with type 2 diabetes mellitus. Vertebral artery dissection was confirmed on angio-MRI, and no clinical deficits remained on follow-up. Secondary prevention was established with aspirin. At 6-month follow-up the mRS scoring was 0.

Case 8. A 42-year-old man schoolteacher without a past history of hypertension, diabetes, hypercholesterolemia, or atherothrombotic events commenced during the morning while working with vertigo, vomiting, and nystagmus. No

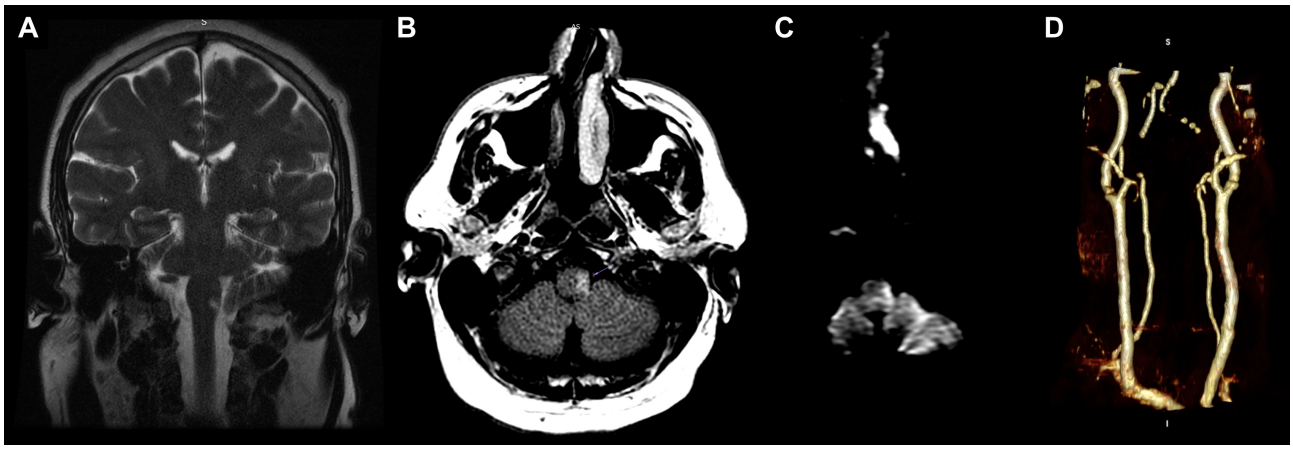

Figure 3: Angio-MRI neuroimaging of a patient with Wallenberg syndrome performed 5 days after symptoms onset (patient Nº 8). Coronal T2 sequence showing a left hyperintense signal consistent with a medullary infarction immediately above the left pyramid (A). Axial fluid-attenuated inversion recovery (FLAIR) sequence showing the left medullary infarction (B). DWI sequence showing a partially fainting restriction signal (the hyperacute phase had passed) within the same location (C). MRI angiography showing incomplete filling of the left vertebral artery consistent with vessel dissection (D).

headache or neck pain was reported. On neurological examination, it was evident nystagmus, left Horner syndrome, absent gag reflex, left gait lateropulsion, and crossed sensory loss in the left face and right body. Left vertebral artery dissection was confirmed on Doppler ultrasound of cervical arteries and angio-MRI. Mild dysphagia persisted up to a 6-month follow-up (mRS=1). No secondary prevention was established due to the cumulating evidence on the very low risk of recurrence in vertebral artery dissection.

Case 9. A 38-year-old woman diagnosed with primary hypothyroidism one year earlier and treated with levothyroxine arrived at the Emergency Room with a neurological syndrome that started 2 h before characterized by ataxia, vertigo, and nystagmus associated with sudden spontaneous neck pain. On neurological examination, it was evident a right face-body sensory loss of pain and temperature, as well as absent gag reflex and mild left gait lateropulsion. A left vertebral artery dissection (prevertebral segment) was identified by Doppler ultrasound, and minutes later confirmed with angio-MRI. Moderate dysphagia persisted up to a 6-month follow-up needing a gastrostomy tube for secure feeding and medications taking. No secondary prevention was established due to the cumulating evidence on the very low risk of recurrence in vertebral artery dissection.

Discussion

Stroke secondary to arterial dissection constitutes approximately 15-25 % of all strokes in young patients, compared with older adults in whom it represents only 2.5 % among the causes of acute cerebrovascular disease.[1,13–16] Vertebral artery dissections may be either extracranial or intracranial, according to the affected segment. The most affected arterial segment is V3, possibly due to its sinuous shape and surrounding bony structures.[15] Extracranial dissections can be classified as spontaneous or traumatic. Risk factors for vertebral artery dissection include fibromuscular dysplasia (about 15 % of cases), Ehlers-Danlos syndrome, osteogénesis imperfect,16 hypertension, infections, and atherosclerosis. Other uncommon risk factors are central venous catheter placement, percutaneous cranial nerve blockade, cancer, head and neck radiotherapy, and diagnostic angiography.[15–17] Vertebral artery dissection must be suspected in patients presenting with sudden onset neck pain or headache, especially if they are young and have concomitant brainstem symptoms.[18]

The clinical presentations of a vertebral artery dissection can be divided into three groups based on whether patients have symptoms and consistent neuroimaging findings[4,5] In the group 1, the patients have symptoms that are explained by ischemia findings on neuroimaging. Group 2 refers to patients with symptoms suggesting vertebral artery dissection but not consistent radiologic findings of ischemia or concluding symptoms. The last group represents those patients with incidental MRI findings for whom no clinical suspicion exists before neuroimaging due to the absence of critical neurological features.

In conclusion, vertebral artery dissection should be suspected in patients presenting with LMS accompanied by a sudden head or neck pain. A missing sign from the original Wallenberg's description is not necessarily incompatible with a lateral medullary lesion.

Declaration of Conflicting Interests

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Patient No	Sex/Age Infarct Side	Crossed Sensory Loss	Horner	Hoareseness	Abnormal gag reflex	Dysphagia	Vertigo Dizziness	Nystagmus	Nause Vomiting	Hiccups	LMS pattern	Neck pain headache	mRS 6-mo	
1	M/30y/R	+	+	+	-	+	-	-	+	+	-	Type I	+	0
2	M/32y/R	+	+	-	+	+	+	+	+	-	+	Type I	+	0
3	M/23y/R	+	+	-	+	+	+	+	+	+	-	Type I	+	0
4	F/33y/L	+	-	-	+	+	-	+	+	-	-	Type I	-	1
5	M/49y/L	+	+	-	-	+	-	+	+	-	-	Type I	+	2
6	F/54y/L	-	-	-	-	-	+	+	-	+	-	Type VI	+	3
7	M/41y/R	+	+	-	+	-	+	+	+	-	-	Type I	+	0
8	M/42y/L	+	+	+	+	+	+	+	+	+	+	Type I	-	1
9	F/38y/L	-	-	+	+	+	+	+	+	+	-	Type III	+	2

TABLE 1: MAIN CLINICAL CHARACTERISTICS OF THE PATIENTS PRESENTING WITH LATERAL MEDULLARY SYNDROME DUE TO VERTEBRAL ARTERY DISSECTION.
+ = PRESENT; - = ABSENT; F = FEMALE; L = LEFT; LMS = LATERAL MEDULLARY SYNDROME; M = MALE; MRS = MODIFIED RANKIN SCALE; R = RIGHT.

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