

Clinical Reasoning: A 29-Year-Old Man With Fevers and Rapidly Progressive Cranial Neuropathies

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Section 1

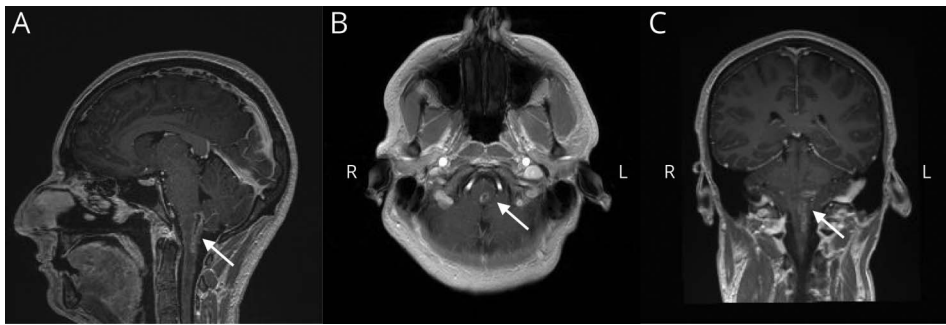
A 29-year-old man with no prior known medical diagnoses presented to the emergency department with 5 days of fevers, chills, vomiting, headache, and neck pain followed by voice changes, difficulty swallowing, and intractable hiccups. The patient denied vision changes, weakness, numbness, recent travel, new medications, or illicit drug use. He had no personal or family history of neurologic illness. On questioning concerning possible toxic exposure, he noted recent consumption of sushi and raw meat at a restaurant; a friend who had eaten with him also experienced gastrointestinal illness after that meal.

On examination, the patient was diaphoretic with a temperature of 39.4°C. He had nystagmus with left-beat in left gaze, right-beat in right gaze, and downbeat in the primary position. Ocular motility was full. Facial sensation was decreased in the left V2 and V3 distributions. There was subtle flattening of the right nasolabial fold. His speech was hoarse, dysphonic, and high-pitched. The uvula deviated to the right on palate elevation testing. There was subtle pronation in the left upper extremity. Sensation to light touch was decreased in the left extremities in a nondermatomal pattern. He leaned towards the right on Romberg testing. His gait was wide-based and unsteady.

Questions for Consideration:

1. How do the examination findings localize the lesion?
2. What is the differential diagnosis?
3. What are the next steps in evaluation?

GO TO SECTION 2



(A) Sagittal multiplanar reconstructed T1, gradient echo (MPR) demonstrating serpiginous medullary lesion extending into cervical cord (B). Axial T1 post-contrast demonstrating contrast enhancement in left medulla (C). Coronal MPR completing visual 3D depiction of longitudinal lesion.

Section 2

This constellation of multiple cranial nerve deficits, including trigeminal, facial, glossopharyngeal, and vagus impairment, with unilateral weakness and vestibulo-cerebellar involvement, localizes to the brainstem (lower midbrain to medulla, predominantly on the left side based on the cranial nerve palsies). The direction-changing nystagmus suggested involvement of tonic cells responsible for gaze-holding including the nucleus prepositus hypoglossi and medial vestibular nucleus in the medulla. The downbeat nystagmus localized to the cervicomedullary junction, resulting from imbalance of the semicircular canals favoring the anterior canal. Ipsilateral arm weakness suggested cruciate hemiplegia resulting from involvement of crossed lateral corticospinal fibers in the caudal medulla or injury to the anterior corticospinal tracts which travel ipsilateral. The differential diagnosis was broad, with initial emphasis on infectious etiologies, including common causes of bacterial meningoencephalitis in adults (e.g., *Streptococcus* and *Neisseria*), legionella, mycoplasma, Listeria, Lyme, syphilis, tuberculosis, and herpes simplex virus encephalitis.

Initial noncontrast head CT was normal. Neck CT with contrast suggested left vocal cord paralysis; ear, nose, and throat evaluation confirmed complete immobility of the left true vocal cord. Lumbar puncture initially revealed 460 nucleated cells with a lymphocytic predominance (79%), protein 68 mg/dL, and

glucose 72 mg/dL. The meningitis–encephalitis PCR panel was negative, as were bacterial and fungal cultures. MRI of the brain and cervical spine with and without contrast revealed an expansile, serpiginous, rim-enhancing lesion in the left dorsal medulla extending inferiorly to the level of C2–C3 (figure).

While undergoing evaluation, the patient’s symptoms progressed. Small angle esotropia was noted, suggesting a mild sixth nerve palsy. He reported new oblique binocular diplopia, which improved with left head tilt and a monocular patch. There was a left hypertropia worse in left gaze consistent with skew deviation in a pattern commonly observed with downbeat nystagmus and cervicomedullary lesions. Right facial weakness worsened to a complete lower motor neuron pattern, corresponding to extension of the lesion to the right facial colliculus on repeat imaging. His voice became notably more dysphonic. The left upper extremity had more pronounced drift and confrontation testing revealed 4/5 strength. There was left-sided dysmetria on finger to nose testing. The patient’s respiratory status subsequently deteriorated, requiring intubation for acute hypoxic respiratory failure. On subsequent examinations, he had preserved upgaze and downgaze, but now had impaired horizontal gaze in both directions.

Questions for Consideration:

1. How do the new findings modify the differential?
2. What further workup is required?
3. What are the most important next steps in management?

GO TO SECTION 3

Section 3

Rapid symptom progression over the course of days suggested neoplasm or pathogens such as *Coccidioides*, *Aspergillus*, and neurocysticercosis were less likely. With no identified pathogen and CSF studies indicating a lymphocytic process, the differential diagnosis was broadened to include autoimmune and inflammatory processes. Neuromyelitis optica or anti-myelin oligodendrocyte glycoprotein (MOG) disease were high on the differential given primary brainstem involvement, but aquaporin-4 receptor and MOG antibodies resulted negative. Other considerations included vasculitis (e.g., Behçet disease), neurosarcoidosis, or a paraneoplastic process.

Broad-spectrum antibiotics, vancomycin 15 mg/kg q8h and ceftriaxone 2 g q12h, had been started for empiric treatment of bacterial meningitis in the emergency department. Extensive workup was negative, including HIV antigen and antibody, immunoglobulin levels, titers for standard vaccinations, and complement levels. Additional serum laboratory studies were all negative, including blood cultures, Lyme disease, *Cryptococcus*, *Aspergillus*, syphilis, tuberculosis, histoplasma, β -D-glucan, antinuclear antibody, myeloperoxidase antibody, proteinase 3, angiotensin-converting enzyme, serum protein electrophoresis, and immunofixation.

Given the clinical deterioration, the decision was made to repeat a lumbar puncture on day 5. On this second set of CSF studies, *Listeria monocytogenes* was detected on the meningitis-encephalitis PCR panel. All empiric antibiotics and antifungals that had been initiated were discontinued with the exception of meropenem 2g q8h. Ampicillin 2g q4h and gentamicin 1.7 mg/kg q8h were started for synergistic treatment of *Listeria* rhombencephalitis. Notably, a single blood culture during this period returned positive for *Listeria*, suggestive of transient bacteremia. Serial MRI studies revealed T2/fluid-attenuated inversion recovery abnormalities consistent with worsening perilesional edema, prompting the addition of corticosteroids. Abscess drainage or surgical decompression were considered but ultimately not pursued after risk–benefit consideration. Meropenem was later changed to trimethoprim–sulfamethoxazole for a prolonged course. On follow-up examination 5 months after the initial presentation, the patient’s horizontal gaze deficits had improved but he was still esotropic. Nystagmus was also less prominent in right and left gaze. Weakness and sensory loss persisted on the left side. He ambulated with a walker. Extensive physical therapy during the next 3 months allowed him to walk independently, but the esotropia persisted, for which botulinum toxin was injected into both medial recti to prevent contracture.

Discussion

Our patient likely acquired *Listeria* as a foodborne illness. He presented with several key examination features that localized to the lesion in the left dorsal medulla seen on imaging, including downbeat nystagmus, skew deviation, and intractable hiccups. Notably, the ipsilateral arm weakness likely

represents cruciate hemiparesis, a rare neurologic manifestation that also localizes to the caudal medulla due to crossed lateral corticospinal tract fibers at that level or ipsilateral anterior corticospinal tracts.

Approaching the differential diagnosis from the perspective of neuroanatomic localization, a review of 34 cases of isolated medullary lesions from nonstroke causes identified neoplasms as the most common pathology observed (47%), whereas infections were among the least common (3%).¹ The remainder were largely attributable to vascular malformations (15%) and demyelinating or inflammatory lesions, including Sjögren, sarcoidosis, and Behçet (15%).¹ Interestingly, none of the patients with isolated medullary lesions were immunocompromised. *Listeria* is the most common cause of infectious rhombencephalitis and tends to affect immunocompetent individuals. Other common infectious etiologies for medullary lesions include tuberculomas and toxoplasmosis, particularly when ring enhancement or nodularity is present. *Listeria* rhombencephalitis appears to be an infrequent manifestation of neurolisteriosis overall, as brainstem involvement was identified in only 10% of cases in one imaging series.² More classically, *Listeria* meningoenzephalitis is observed in neonates or pregnant or elderly patients and arises either sporadically or from food outbreaks. When *Listeria* is suspected, ampicillin 2g IV q4h should be initiated empirically. Once the diagnosis is confirmed, preferred treatment includes ampicillin or penicillin, combined with gentamicin.

Our case demonstrates the typical biphasic pattern seen in *Listeria* rhombencephalitis, including a prodrome of 4–5 days followed by rapid evolution of neurologic symptoms. In a review of 62 cases of *Listeria* rhombencephalitis, isolated cranial nerve palsies were the initial presenting neurologic sign in almost half of the cases.³ However, with disease progression, up to 80% of cases involved hemiparesis, hemisensory loss, or cerebellar signs in addition to cranial nerve deficits. As in our patient, pontomedullary-localizing clinical signs and symptoms were frequent, including dysphagia, dysphonia, dysarthria, facial weakness, and vertigo. Asymmetry in the neurologic manifestations was also common, as in our case.

Listeria rhombencephalitis can be challenging to recognize, as the clinical and imaging characteristics may mimic other disease entities. The broad differential may engender initial misdiagnosis and treatment delay. Case reports commonly describe ring-enhancing abscesses with a serpiginous (“worm-like” or “tubular”) appearance with surrounding edema.^{4,5} Definitive diagnosis requires confirmation of the pathogen in CSF testing. However, initial CSF studies can be normal or nonspecific, as was the case in our patient. Among the 62 cases, lymphocytic predominance in the CSF was noted in only 58%. Initial cultures identified *Listeria* in 33% of cases, and repetition of cultures improved the yield to 41%.³ Therefore, even in the absence of compelling CSF studies or imaging, it is important to maintain a high index of suspicion based on the clinical scenario, particularly because early

treatment with antibiotics can mitigate the high morbidity and mortality associated with this disease. With appropriate initial treatment, the reported survival rate of patients with *Listeria rhombencephalitis* is greater than 70%.³ However, as in our case, long-term neurologic sequelae are common in patients who have survived treatment.

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Disclosure

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Appendix Authors

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Alexa Dessy, MD	NYU Langone Health, New York	Drafting and revising manuscript
Stephen Berger, MD, PhD	NYU Langone Health, New York	Drafting manuscript

Appendix (continued)

Name	Location	Contribution
Arooshi Kumar, MD	NYU Langone Health, New York	Drafting manuscript, figure design
Scott N. Grossman, MD	NYU Langone Health, New York	Drafting and revising manuscript
Myrna Cardiel, MD	NYU Langone Health, New York	Revising manuscript
Steven L. Galetta, MD	NYU Langone Health, New York	Revising manuscript

References

1. Prakkamakul S, Schaefer P, Gonzalez G, Rapalino O. MRI patterns of isolated lesions in the medulla oblongata. *J Neuroimaging*. 2017;27(1):135-143.
2. Charlier C, Poirée S, Delavaud C, et al. Imaging of human neurocysticercosis: a prospective study of 71 cases. *Clin Infect Dis*. 2018;67(9):1419-1426.
3. Armstrong RW, Fung PC. Brainstem encephalitis (rhombencephalitis) due to *Listeria monocytogenes*: case report and review. *Clin Infect Dis*. 1993;16(5):689-702.
4. O'Callaghan M, Mok T, Lefter S, Harrington H. Clues to diagnosing culture negative *Listeria rhombencephalitis*. *BMJ Case Rep*. 2012;2012:bcr2012006797.
5. Slezák S, Žižka J, Kvasnička T, et al. Worm-like appearance of *Listeria monocytogenes* brain abscess: presentation of three cases. *Neuroradiology*. 2020;62(9):1189-1193.

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