

Listeria Rhombencephalitis: Tale of a Survivor

Sir,

A 47-year-old professional photographer, with no co-morbidities, developed holocranial headache associated with vomiting one week before his presentation to us. On the next day, he developed fever, neck pain and became confused, forgetting an assignment he had on that day. He also developed double vision, unsteadiness of gait and hiccoughs with which he was brought to our hospital. In Emergency room, he was febrile (100°F) and confused, with stable vitals. His fundus examination, extraocular movements and rest of the cranial nerve examination were normal. He had mild gait ataxia, and neck stiffness with positive Kernig's and Brudzinski's sign. Total leucocyte count in the peripheral blood was 14,400 with 74% polymorphs, ESR was 85 mm/hour and platelet count was 1 lakh/mm³. MRI brain with contrast showed FLAIR hyperintensity in the sulcal spaces with mild enhancement [Figure 1a]. CSF showed 131 cells with 90% lymphocytes, protein of 300 mg/dl and sugar of 3 mg/dl with corresponding blood sugar 154 mg/dl. He was provisionally diagnosed to have pyogenic meningitis and was started on Ceftriaxone 2 g bd and Vancomycin 1 g bd. CSF gram stain, India ink stain and TB NAAT were negative. Serum antibodies against Leptospira, Dengue, Salmonella and Scrub typhus were negative. His HIV Eliza test was negative.

After two days of antibiotics, he remained confused and responded minimally to questions. There was horizontal gaze evoked nystagmus and bilateral restricted abduction, with the development of left LMN facial palsy, left palatal palsy and right sternomastoid weakness [Video 1]. Dorsiflexion and plantar flexion of the left ankle were weak with normal power in the rest of the muscle groups, with left extensor plantar and left-sided cerebellar signs. Meanwhile, the CSF culture grew gram-positive organism, confirmed as *Listeria monocytogenes*. He was started on Inj. Ampicillin (200 mg/kg/day in 4 doses) and Gentamicin (5 mg/kg/day). Repeat CSF study done showed 373 cells, 88% lymphocytes, sugar 54 mg/dl (blood sugar 130 mg/dl) and protein 700 mg/dl. Repeat MRI brain showed T2/FLAIR hyperintensities in the dorsal pons [Figure 1b]. Over the next

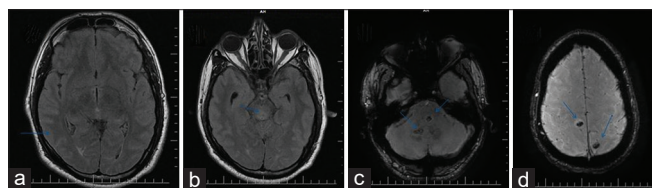


Figure 1: (a) MRI brain with contrast- FLAIR sequence showing hyperintensity in the sulcal spaces with mild enhancement; (b) MRI brain FLAIR sequence showing hyperintensities in the dorsal pons; (c and d) Susceptibility weighted images showing blooming involving dorsal pons and bilateral cerebellum (c) bilateral posterior parietal (d) areas

4 days he developed asymmetric ptosis, impaired right eye adduction and bilateral supraduction. He also developed left UMN facial palsy with worsening of weakness in his left foot (MRC 1/5) and weakness of proximal lower limb (MRC 3/5) and upper limb (distal MRC 1/5, Proximal 4/5). Repeat MRI brain showed multiple foci of blooming on Susceptibility weighted images involving bilateral posterior parietal, left anterior frontal juxtacortical, right centrum semiovale, dorsal pons and bilateral cerebellum suggesting acute hemorrhages [Figure 1c and d]. Repeat CSF study showed 460 cells, 98% lymphocytes with sugar 64 mg/dl and protein 283 mg/dl. Considering resistance to the treatment, Gentamicin was stopped. Levofloxacin 500 mg bd IV was added.

Two days later he developed shallow breathing, with PaCO₂ of 56, for which he was intubated and ventilated. From day 11 onwards he showed improvement in his limb weakness, extraocular movements and in sensorium. By day 17 he was extubated. Injection Levofloxacin was stopped after three weeks and ampicillin was continued for six weeks. At the time of discharge, he was fully conscious and oriented, with residual ophthalmoplegia and able to walk independently.

Listeria has emerged as the third most common cause of meningitis in adults, typically occurring in neonates, elderly, pregnant women, and immunocompromised states.^[1] *Listeria rhombencephalitis*, in particular, has been noted to occur more frequently in immunocompetent young individuals.^[2] *Listeria* usually is transmitted via contaminated food (unpasteurized milk and dairy products, coleslaw, soft cheese, undercooked chicken, sausages, etc.), apart from vertical transmission in new-borns.^[3] In our patients, no specific food products were identified that may have caused the infection. While meningeal involvement may occur in as much as 48% of all *Listeria* infection, rhombencephalitis is rare, accounting for approximately 10% of those with neurolisteriosis.^[2] Our patient had bilateral ptosis, bilateral lateral rectus palsy, left medial rectus palsy, right peripheral facial palsy, right palatal palsy and bilateral gaze-evoked nystagmus, unsteadiness of gait and hiccups suggesting involvement of the midbrain, pons, dorsal medulla and cerebellum. Mrowka *et al.* reported a 48-year-old immunocompetent lady with *Listeria rhombencephalitis* who presented with a facial palsy, one and half syndrome, hemiparesis and cerebellar features.^[4] Stroke-like features with hemiparesis is not uncommon in listeriosis.^[4] One of 30 patients in the prospective Dutch study had an infarct.^[5] Our patient developed respiratory failure that may occur in as much as 40% of patients with rhombencephalitis.

CSF pleocytosis seen with *Listeria* may be either lymphocytic or neutrophilic.^[5,6] Listeriosis has significantly fewer WBCs and lowers protein concentrations in CSF and less

hypoglycorrhachia than patients with infections caused by other bacterial pathogens.^[7] Our patient had lymphocytic pleocytosis in CSF along with peripheral blood neutrophilic leucocytosis. Although CSF sugar may be low in listeria meningitis, very low sugars such as seen in this case has not been reported to the best of our knowledge. The most common manifestation of MRI in neurolisteriosis is a mild meningeal enhancement. Rhombencephalitis is characterized by cerebellar and brainstem lesions that may be nodular and ring enhancing, abscess like^[8] ischemic or hemorrhagic. Intracranial hemorrhage has been observed more frequently in infants and young children. The mortality associated with neurolisteriosis varies from 15% to 26%.^[9] Mortality is higher at 35% for patients with rhombencephalitis, with neurological sequelae in 55% of survivors.^[10] Lavetter *et al.* observed that initial cerebrospinal fluid glucose level more than 30 mg/dl correlated with good recovery.^[7]

The treatment of listeriosis has not been standardised. The most commonly used treatment regime includes a combination of Ampicillin with Gentamicin in high doses, to which our patient didn't respond. Other antibiotics reported effective include cotrimoxazole, rifampicin, meropenem, linezolid, moxifloxacin and levofloxacin, tetracyclines. We used combination therapy with Ampicillin and Levofloxacin for 3 weeks followed by continuation of monotherapy with ampicillin for a total of 6 weeks.

Other etiologies also should be looked into in a patient with rhombencephalitis. Other infectious causes include Epstein-Barr virus, tuberculosis and *Streptococcus pneumoniae*. Non-infectious causes include multiple sclerosis, Behçet's disease and paraneoplastic syndromes associated with anti-Yo, anti-Tr, anti-Hu, anti-Ri, anti-Ma and anti-amphiphysin antibodies.

Our patient had many unusual clinical features including development of multiple cranial nerve palsies, intractable hiccups, respiratory failure, the development of multifocal brain parenchymal hemorrhages and extremely low CSF sugars despite a lymphocytic pleocytosis. He survived despite having many poor prognostic factors including low CSF sugar, presence of hemorrhage, extensive brain parenchymal involvement and need for ventilatory support.

This case highlights the key learning points. *Listeria* is an important cause of rhombencephalitis in immunocompetent individuals, with a high mortality and morbidity rate. However, it can be misdiagnosed at an early stage of the disease as the initial CSF study may be often normal and CSF cultures may be negative. *Listeria* should be considered in the differential diagnosis, especially in immunocompetent adult patients who develop fever, and focal neurological symptoms localized to the brainstem. Early diagnosis and prompt commencement

of appropriate antimicrobial therapy are essential to improve outcomes.

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Conflicts of interest

There are no conflicts of interest.

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