**Listeria in Adults – Truly Rare or Rarely Diagnosed in India?**

Arjun Rajalakshmi¹, Ram Gopalakrishnan², P Senthur Nambi³, P Vishnu Rao⁴, V Ramasubramanian²

**Abstract**

*Listeria monocytogenes* is a facultative anaerobic intracellular Gram positive rod causing infection in pregnant women, extremes of age and immune-compromised hosts. In clinical specimens, the organisms may be gram-variable: laboratory misidentification of *L. monocytogenes* isolates as diphtheroids, streptococci, or enterococci is not uncommon and the isolation of a diphtheroid from blood or CSF should always alert the clinician to the possibility that the organism may be *L. monocytogenes*. The disease has rarely been reported in India in non-pregnant adults. We herein report four cases of *L. monocytogenes* infection in immune-compromised adults.

**Introduction**

*L. monocytogenes* infection is commonly reported in the Western literature as an important cause of bacteremia and meningitis in neonates, pregnant women, the elderly and patients with impaired cell mediated immunity.¹ The disease has rarely been reported in India in non-pregnant adults. We herein report four cases of *L. monocytogenes* infection in immune-compromised adults.

**Case 1**

A 62 year old lady presented with fever, headache, vomiting and altered mental status of 1 day duration. She had been diagnosed to have retroperitoneal fibrosis due to IgG4 related disease four years ago for which she was on mycophenolate mofetil (MMF) 360 mg twice daily and prednisolone 15 mg daily. On examination, she was confused, had neck stiffness and right lateral rectus palsy. General and other system examination was otherwise unremarkable. WBC count was 18,200 cells/cumm (89 % polymorphs). Contrast enhanced MRI revealed mild leptomeningeal enhancement. Cerebrospinal fluid (CSF) examination showed WBC of 425 cells/µL (lymphocytes- 92% neutrophils 8%), glucose of 26 mg/dl (corresponding blood glucose was 196 mg/dl), protein of 230 mg/dl and negative Xpert MTB, cryptococcal antigen and HSV PCR. Gram stain of CSF (Figure 1) and blood (Figure 2) revealed gram positive bacilli. CSF and blood cultures inoculated in blood agar (Figure 3) grew *L. monocytogenes*. Ampicillin 2 gm IV q4h and gentamicin 196 mg/dl (corresponding blood glucose was 160 mg/dl). She was started on ceftriaxone 2 gm IV q12h and ampicillin 2 gm IV q4h. Gram stain, AFB, fungal stain and Xpert MTB were negative. Blood culture did not reveal any growth. CSF culture grew *L. monocytogenes*. Gentamicin was added to the regime for initial 2 weeks. She improved rapidly and repeat CSF done at 12 days showed improvement and culture was negative. Ampicillin was continued for a total of 4 weeks.

**Case 2**

A 65 year old lady with well controlled diabetes presented with acute onset fever, headache, vomiting and altered sensorium of 1 day duration. She was not on any immune-suppressants. There was neck stiffness and remainder of the examination was unremarkable. Her WBC was 11,000 cells/cumm. (polymorphs 70%). Liver and renal parameters were normal. Chest x-ray and brain imaging were normal. CSF cell count was 240 cells/µL (polymorphs 60% lymphocytes 40%), protein was 120 mg/dl, sugar was 50 mg/dl (blood glucose was 160 mg/dl). She was started on ceftriaxone 2 gm IV q12h and ampicillin 2 gm IV q4h. Gram stain, AFB, fungal stain and Xpert MTB were negative. Blood culture did not reveal any growth. CSF culture grew *L. monocytogenes*. Gentamicin was added to the regime for initial 2 weeks. She improved rapidly and repeat CSF done at 12 days showed improvement and culture was negative. Ampicillin was continued for a total of 4 weeks.

**Case 3**

A 42 year old male from Syria with HCV related decompensated chronic liver disease presented to our center for liver transplant evaluation. He was admitted with fever, abdominal pain and distension after having diarrhea a week earlier. He denied consumption of raw milk, but used to consume raw salads. Ultrasound scan of the abdomen revealed features suggestive of cirrhosis with portal hypertension. Ascitic fluid analysis showed a WBC cell count of 5500 cells/mm³, polymorphs 50%, glucose of 103mg/dl, protein 1gm/dl. Ascitic fluid gram stain revealed gram positive bacilli. Culture of blood and ascitic fluid yielded *L. monocytogenes* (Figure 4). He was treated with ampicillin 2 gm IV q4h for initial 2 weeks and was switched to oral amoxicillin 1gm thrice daily for another 2 weeks, as he was...

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¹Fellow, ²Senior Consultant, ³Consultant, ⁴Fellow, Apollo Hospital, Chennai, Tamil Nadu  
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misidentification of L. may be gram-variable: laboratory has a low sensitivity, the organisms
symptoms. way to separate Listeria immunosuppressed patients, improved and was discharged.
3 weeks of parenteral ampicillin. She steroids were stopped. She received initiated on ampicillin 2gm IV q 4h and
culture grew L. monocytogenes granules were present in the peripheral unremarkable. WBC count was 19,890 vegetables. Physical examination was
vegetables, raw milk, cheese and meat are contaminated with L. Many foods such as raw vegetable, raw milk, cheese and meat (including fresh, frozen and processed) are contaminated with L. monocytogenes. In a susceptible host, consumption of uncooked food, unboiled milk, cheese and meat are the risk factors. Those who are colonised with L. monocytogenes in their gut are at increased risk of invasive infection following gastrointestinal infection with another pathogen and also following colonoscopy.
Being an intracellular pathogen, clearance of this infection is dependent mainly on cell mediated immunity as evidenced by the strong clinical association of listerial infections with conditions associated with impaired cellular immunity like pregnancy, HIV, lymphomas, transplant recipients and corticosteroid use. Tumor necrosis factor α used to treat rheumatoid arthritis and Crohn’s disease can be complicated by listeriosis. Elderly, alcoholism, cirrhosis and iron overload state are other risk factors. Listeriosis is not commonly encountered in HIV infection, possibly because of the use of trimethoprim-sulfamethoxazole prophylaxis for Pneumocystis.
Clinical syndromes caused by L. monocytogenes include infection in pregnancy, neonatal infection, bacteremia, CNS infection, endocarditis, localized infection and febrile gastroenteritis. Diagnosis is by isolating L. monocytogenes from normally sterile clinical specimens through standard microbiologic techniques. Pregnancy is usually associated with a decline in cell mediated immunity, especially in the third trimester and hence listerial infections are more common during this period. L. monocytogenes has a predilection for placenta, where it can multiply and cause fetal infection and abortions. In neonates it is among the three major microbial etiologies of meningitis.
Bacteremia without an overt focus is the most common manifestation of listeriosis after the neonatal period. It presents with non-specific fever and myalgia which may be preceded by a prodrome of diarrhea, thus mimicking other systemic febrile illnesses. Patient 3 in our case series presented with febrile illness and cough and had a positive blood culture.
CNS infection can present as meningitis, encephalitis, brainstem encephalitis, brain abscess and myelitis. Listeria is the commonest cause of bacterial meningitis in the immune-compromised host in adults older than 50 years and is second only to S. pneumoniae in the elderly. Patients 1 and 2 in our series had meningitis. Patient 1 had a typical history of consuming raw food and medication induced cell mediated immune compromise. Patient 2 was an elderly lady and age was apparently her only risk factor. CSF mononuclear cells predominate in one-third of patients with Listeria meningitis and can mimic tuberculous meningitis, as in our case. In contrast to organisms commonly causing bacterial meningitis, L. monocytogenes not only causes meningitis but has a tropism for brain parenchyma and causes brain abscess. Focal neurological findings are found in 35-40 % and movement disorders in 15-20 % of patients with listerial meningitis. L. monocytogenes has predilection from brainstem causing rhombencephalitis: 40 % of these patients develop respiratory failure and mortality is high.
Cirrhosis is usually not considered as a risk factor for listeriosis: however cirrhosis is associated with impaired cell mediated immunity and as in our second case, there are case reports of spontaneous bacterial peritonitis with bacteremia due to L. monocytogenes. L. monocytogenes causing spontaneous bacterial peritonitis (SBP) in cirrhotics, especially in alcoholics, is likely related to increased gut translocation and impaired cell mediated immunity. Listeria monocytogenes is an uncommon cause of peritonitis, with less than 50 cases reported in the medical literature.
Most cases were reported from Spain possibly related to consumption of diet rich in raw fruits, vegetables and dairy products. In Syria, where our patient 2 resides from, there are reports of higher rates of contamination of raw milk with *Listeria* spp, upto 10.96% in one study.

Due to inadequate food borne disease surveillance, very limited information is available on the prevalence of food borne listeriosis in India. On literature search, we found 42 case reports of human listeriosis from India all of which were in either pregnant women or neonates. There are very few reported cases in non-pregnant adults. It is unclear why human listeriosis is less commonly reported in India. Possible reasons include: refrigeration of food is not as widely practiced, salad and raw vegetable consumption is less common, widespread use of antibiotics for acute febrile illness may reduce diagnostic yield from cultures and laboratories may misidentify or discard *Listeria* as a contaminant.

All four of our patients had a good outcome with timely antibiotic therapy. The preferred agent is penicillin or ampicillin, while gentamicin is added for synergy for the initial 2 weeks in the treatment of bacteremia in those with severely impaired T-cell function and in all cases of meningitis, encephalitis, brain abscess and endocarditis. The best alternative agent is trimethoprim-sulfamethoxazole, especially for patients with anaphylactic beta-lactam allergy. Cephalosporins which are usually recommended for SBP, are bacteriostatic for *L. monocytogenes* while chloramphenicol is associated with failure and relapse and hence both are not recommended.

Treatment duration is 2 weeks for bacteremic patients, 3 weeks for meningitis, 6 weeks for brain abscess and rhombencephalitis and 4-6 weeks for endocarditis. Listerial gastroenteritis is self-limited and treatment is not warranted.

Preventing listeriosis requires proper food hygiene: thoroughly washing raw vegetables, cooking vegetables and meat and avoiding soft cheese and unpasteurised milk. In immune-compromised groups, trimethoprim-sulfamethoxazole given for pneumocystis prophylaxis will be effective in preventing listeriosis as well.

**Conclusion**

Listeriosis is not uncommon in India and is probably under-diagnosed. The disease should be considered in the differential diagnosis of meningitis and sepsis in cell mediated immune compromised hosts, especially those with impaired T cell mediated immune response. Cultures of blood and other involved fluids readily grow *Listeria*, and the laboratory should be alerted to this possibility. Ampicillin should be part of the empiric regimen for meningitis in these patients and outcome is generally very good with early and appropriate antibiotic therapy as in our patients.

**References**