

Listeria Meningitis in an Immunocompetent Adolescent

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L*isteria monocytogenes* is an aerobic and facultative anaerobic Gram-positive rod. In healthy individuals, *L. monocytogenes* usually manifests with self-limited febrile gastroenteritis with a typical duration of symptoms of 2 days or less [1]. Invasive *Listeria* infection is relatively rare, and in its severe form primarily affects neonates, elderly, and immunocompromised patients. Infection occurs mainly via ingestion of large inoculum of bacteria from contaminated foods such as cheese, unpasteurized milk, and raw meat. Invasive diseases such as bacteremia and central nervous system infection are rare. The most common central nervous system manifestation is meningoencephalitis. The most common symptoms include fever and mental status changes. A multicenter survey of bacterial meningitis in the United States showed that only 4% of the reported *Listeria* meningitis cases occurred in patients between the ages of 2–60 years. *Listeria* meningitis in immunocompetent children older than 3 months of age was scarcely reported.

PATIENT DESCRIPTION

A 17-year-old adolescent male of Bedouin ethnicity was treated in the emergency department with complaints of headache, diarrhea, and vomiting that began 2 days prior to hospital admission. His body temperature on presentation was 36.8°C and all other vital signs were normal. On physical examination, the patient appeared lethargic

and nuchal rigidity was observed. The rest of the physical examination was normal. He had no significant past medical history and was immunized according to schedule. Laboratory workup revealed a complete blood count with hemoglobin 13.9 g/dl, white blood cells (WBC) $14 \times 10^9/L$ (80% neutrophils), and a platelet count of $132 \times 10^9/L$. C-reactive protein was 120 mg/dl (normal range 0–5 mg/dl).

As the patient presented with diarrhea and vomiting without fever, our initial working diagnosis was of gastroenteritis and dehydration. Intravenous rehydration and normal urine output resulted in only mild improvement in his general condition, and the patient was admitted for further workup and treatment. A computerized tomographic examination of the head did not reveal any abnormal findings. A lumbar puncture revealed a WBC count of 1109 cells/ μ l, with 52% lymphocytes, 30% mononuclear cells, and 18% segmented cells. Protein and glucose concentration were normal. Following the lumbar puncture and after the body temperature peaked to 39.3°C, the patient started receiving high dose ceftriaxone (100 mg/day), acyclovir (80 mg/kg four times per day), and doxycycline (100 mg/kg/day). A cerebrospinal fluid (CSF) Gram stain was negative for organisms.

The clinical condition of the patient improved considerably after 24 hours of treatment. On the second day of admission, the CSF culture yielded *L. monocytogenes* according to morphology, positive catalase test, negative oxidase, and bile esculin test (Hylabs, Israel). Confirmation of bacterial identification was conducted by a Matrix Assisted Laser Desorption/Ionization Time of Flight Mass Spectrometry technique (Vitek MS, bioMerieux SA, Marcy-l’Etoile, France). Treatment was modified accord-

ing to the antibiotic susceptibility tests to ampicillin (100 mg/kg/day) and gentamicin (5 mg/kg/day). The polymerase chain reaction was negative for Herpes simplex virus.

Further questioning regarding eating habits and possible exposure revealed that on the day of his admission, the patient drank milk that was probably stored in improper conditions. Furthermore, prior to his illness, the patient ate a serving of raw meat (shared by other family members without any adverse symptoms).

Since *Listeria* infection is uncommon in an immunocompetent host, an immune workup was completed, including testing for acquired immunodeficiency and human immunodeficiency virus infection, which was negative. The immune workup, including immunoglobulin levels and lymphocyte markers, was normal [Table 1].

The patient recovered quickly with complete resolution of symptoms after 10 days of treatment. Three weeks after presentation the patient underwent a magnetic resonance imaging scan that showed a single focus with abnormal enhancement in the left subarachnoid space, most probably secondary to the inflammatory process, with no other abnormal findings. Clinically, he was doing well and returned to all of his regular activities.

COMMENT

We present an unusual case of *Listeria* meningitis. Several features in this patient were unusual for such an etiology: unusual age at presentation, lack of immune compromise of any sort, presentation without fever, a gastrointestinal symptomatology (which could potentially mislead physicians), and the apparent improvement with treatment by doxycycline. This treatment was administered empirically against a

Table 1. The immunologic evaluation, including immunoglobulins levels and lymphocyte population markers of the patients

	Result	Normal range
IgG (mg/dl)	621	549–1584
IgA (mg/dl)	175	61–348
IgM (mg/dl)	118	23–259
Ig-E total (U/ml)	102	0.0–100.0
CD3 (Absolute count × 10 ³ /ul)	1.53	1.00–2.20
CD4 (Absolute count × 10 ³ /ul)	0.99	0.53–1.30
CD8 (Absolute count × 10 ³ /ul)	0.44	0.33–0.92
CD19 (Absolute count × 10 ³ /ul)	0.29	0.11–0.57
CD3-/CD56+ natural killer cells (Absolute count × 10 ³ /ul)	0.24	0.07–0.48

possible rickettsial infection, a common disease in our geographic area.

There are few *L. monocytogenes* outbreaks reported in the literature. A report from 2011 describes 147 cases of *Listeria* in a multistate outbreak in the United States. The source for this outbreak was cantaloupes inoculated with the pathogen [3]. Among the affected individuals, 127 (86%) were older than 60 years of age with a median age of 77 years, as well as 7 pregnant women and 3 neonates. There were no cases of men or non-pregnant women under the age of 40. A high mortality rate of 22% was observed during this outbreak. An epidemiologic report from Israel documented 328 cases of listeriosis between 2001–2011. Eighty-four cases were reported in pregnant women, 30 in children younger than 1 year, and 150 in people older than 60 years. Of these patients, 50% had at least one risk factor for listeriosis such as pregnancy, cancer, diabetes, or immune suppression due to prolonged steroid treatment [2].

The southern region of Israel (the Negev) has a heterogeneous population, consisting of approximately 80% Jews, who live mainly in urban centers and a few rural communities, and 20% Bedouin Arabs (approximately 50% of all births), who are in various stages of transition from semi-nomadism to settled modern day life. These two groups differ in many aspects, with the

Bedouin population characterized by a lower socioeconomic status.

In the years 2017–2018, 43 cases of *Listeria* infection were reported to the Southern District Health Office [4]. Thirty-three cases, including our case, belonged to the same cluster (validated by pulsed-field electrophoresis and complete genomic sequencing) and occurred over a period of 3 months. All cases were reported from the Bedouin community. The majority of the cases occurred in pregnant women (n=24) and people with background health conditions [4]. Our patient was the only immunocompetent, healthy adolescent. A thorough epidemiologic survey failed to discover the source of the infection in this outbreak. There was no immediate geographic or social connection among the cases, suggesting that the source could have been a food product distributed illegally without proper inspection.

The present case highlights the importance of considering *L. monocytogenes* in the differential diagnosis of meningitis in some specific groups of patients, since standard treatment regimen in this condition (such as third generation cephalosporins or vancomycin) are not suitable for *L. monocytogenes* and untreated cases may be severe and have a fatal outcome. The initial empiric treatment in the presented case included ceftriaxone, acyclovir, and doxy-

cycline. The patient's condition improved markedly before switching the treatment to a standard regimen for *L. monocytogenes* invasive infection; therefore, it was probably doxycycline, which was started due to the high prevalence of rickettsial diseases in our area, that was crucial in his treatment. Indeed, several articles described high percentage rates of doxycycline efficiency against *L. monocytogenes* [5]. Nonetheless, ampicillin is the first-line treatment for listeriosis. In vitro synergism between ampicillin and gentamicin against *L. monocytogenes* was demonstrated in a number of reports and it is the cornerstone for treatment invasive infections with this pathogen.

CONCLUSIONS

During outbreaks of *Listeria*, this pathogen should be considered in the differential diagnosis of meningitis and septicemia even in healthy children and teenagers, and treatment with ampicillin should be considered. A cautious management should be more relevant when the patient presents with a prodrome characterized by gastrointestinal symptoms.

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“Maturity is the ability to think, speak and act your feelings within the bounds of dignity”

Samuel Ullman (1840–1924), businessman, poet, humanitarian, and religious leader