SEVERE INVASIVE LISTERIOSIS – CASE REPORT

Andra Teodor¹, D. Teodor²,³, Egidia Miftode²,³, D. Prisăcaru¹, Daniela Leca²,³, Cristina Petrovici²,³, Olivia Dorneanu⁵, Carmen-Mihaela Dorobăt²,³

1. Ph.D. student at University of Medicine and Pharmacy “Grigore T. Popa” - Iasi
   University of Medicine and Pharmacy “Grigore T. Popa” - Iasi
   School of Medicine
2. Discipline of Infectious Diseases
3. Clinical Hospital of Infectious Diseases “Sf. Parascheva”-Iasi

SEVERE INVASIVE LISTERIOSIS – CASE REPORT (Abstract): Listeriosis is a rare food borne infection which, in the invasive form, presents as bloodstream infection, central nervous system infection, materno-fetal infection, or focal infection. Certain immunosuppressive conditions have been identified as risk factors for severe invasive disease. The invasive forms of listeriosis are associated with a high case fatality rate. We present the case of a 62 year old male with an unremarkable medical history admitted to the Iasi Infectious Diseases Hospital for fever, headache, ataxia, and diplopia. Physical examination revealed high temperature, confusion, relative bradycardia, and signs of meningeal irritation. Laboratory test showed leukocytosis with neutrophilia, pathological CSF findings (high WBC count with predominance of neutrophils, low glucose and high protein levels), increased liver enzymes (ALAT, ASAT, AP, γGT), and important renal impairment (normal levels at presentation). No abnormalities at chest x-ray, cranial CT and abdominal ultrasound. CSF and blood cultures were positive for Listeria monocytogenes. Under antibiotics (ampicillin and ciprofloxacin), the course was marked by respiratory failure requiring mechanical ventilation, coma, hypotension, tachycardia, and death 12 days after admission. The particularity of this case consists in the association of the two classical forms of invasive listeriosis, meningitis and bacteriemia, with a focal infection, acute hepatitis, and a course marked by multiple organ dysfunction syndromes and exitus in a previously apparently healthy individual. Key words: LISTERIOSIS, MENINGITIS, BACTERIEMIA, MULTIPLE ORGAN DYSFUNCTION SYNDROME.

Listeriosis is a rare but potentially serious infection caused by Listeria monocytogenes. This agent has been recognized as a human pathogen for over 80 years. Epidemiological investigations during the past 30 years have shown that epidemic or sporadic listeriosis is mainly caused by consumption of contaminated food (1). Food borne listeriosis can occur in large or small outbreaks or as sporadic cases; however, the predominant form of disease is probably that of single sporadic and unrelated cases (2). The widespread distribution of Listeria monocytogenes provides numerous potential ways by which the disease may be transmitted to humans, although it is now generally accepted that the consumption of contaminated food is the main route of transmission (2). The infection has three major clinical presentations: bloodstream infection, CNS infection, materno-fetal listeriosis (3).
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Listeriosis is diagnosed by positive culture from a normally sterile site (clinical specimens such as blood, cerebrospinal fluid (CSF)) (1). When Listeria causes disease, it is usually severe with a high case fatality rate of 20-50% (4, 5).

CASE REPORT

In February 2012, a 62-year-old man presented to the Infectious Diseases Hospital for fever, chills, headache, vomiting, and cervical pain, symptoms that occurred four days earlier, associating after two days, ataxia and diplopia. His medical history was unremarkable except for hearing loss requiring auditory prosthesis. Physical examination revealed high temperature (39.5°C), confusion, relative bradycardia (74/min), signs of meningeal irritation, frequent vomiting, and diplopia.

On admission, laboratory findings were: white blood cell (WBC) count 10,850 per mm³ (88.7% neutrophils), hemoglobin level 12.2 g%, erythrocyte sedimentation rate 115 mm/h, urea 45 mg%, creatinine 1.39 mg%, alanine aminotransferase (SGPT) 37 UI/l, alkaline phosphatase (AP) 192 UI/l, gamma glutamyl transferase (γGT) 69 UI/l. CSF exam revealed WBC count 714 per mm³ (78% neutrophils), glucose level 0.20 g/l (blood level 1.25 g/l), protein level 4.62 g/l, chloride level 6.60 g/l. Chest radiography revealed no pulmonary abnormalities, cranial computed tomography showed no features suggestive for brain abscess, normal abdominal ultrasound. HIV test was negative. Cultures from blood and CSF were performed and empirical treatment with ampicillin associated with pathogenic therapy was initiated. Two days later, blood and CSF cultures showed a heavy growth of Listeria monocytogenes. An epidemiological history including food consumption was taken, and consumption of raw milk on a regular basis was found.

On day 4, the course was marked by a continuous alteration of mental status, leading to coma and requiring specific management in intensive care unit. Ampicillin was associated with ciprofloxacin. Biochemical exams revealed elevated liver enzymes and acute renal failure. The dynamic of laboratory parameters is detailed in the tab. I.

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>Evolution of laboratory parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>Day 1</td>
</tr>
<tr>
<td>WBC/mm³ (Neutrophils %)</td>
<td>10 850</td>
</tr>
<tr>
<td>Urea mg%</td>
<td>45</td>
</tr>
<tr>
<td>Creatinine mg%</td>
<td>1.39</td>
</tr>
<tr>
<td>ALAT UI/l</td>
<td>37</td>
</tr>
<tr>
<td>AP UI/l</td>
<td>192</td>
</tr>
<tr>
<td>γGT UI/l</td>
<td>69</td>
</tr>
<tr>
<td>CSF WBC/mm³</td>
<td>714</td>
</tr>
<tr>
<td>CSF glucose g/l</td>
<td>0.20</td>
</tr>
<tr>
<td>CSF protein g/l</td>
<td>4.62</td>
</tr>
</tbody>
</table>

On day 6, the patient developed respiratory failure requiring mechanical ventilation. On day 8, fever occurred again and ventilator-associated pneumonia was sus-
pected. Therefore, new blood and tracheal aspirate cultures were performed and an antiinfectious therapy with vancomycin, colistin and caspofungin replaced the initial antibiotic association. Despite adequate vasopressive therapy the patient presented persistent hypotension and died 12 days after admission.

**DISCUSSION**

*Listeria* is widespread in the environment. It can be found in soil, vegetation and animals. Considering the high exposure rate, the pathogenicity of this organism must be low. Listeriosis is a rare disease, with an annual incidence in most countries of <100,000 inhabitants (3, 5). Whereas much has now been learned about epidemic listeriosis, little is known about sporadic listeriosis which, in fact, represents the majority of cases (6).

*Listeria* is a facultative intracellular, Gram-positive, motile rod which causes both sporadic disease and outbreaks of food borne infection in humans. The genus *Listeria* comprises six species (*L. monocytogenes*, *L. ivanovii*, *L. innocua*, *L. welshimeri*, *L. seeligeri* and *L. grayi*). Almost all cases of human listeriosis are due to *Listeria monocytogenes* (2). This organism occurs ubiquitously in nature and, therefore, it is not possible to eliminate it totally from raw produce or ready-to-eat products prepared without a bacterial inactivation step (5). Consequently, humans are exposed regularly to *Listeria* (3). The main route of transmission is believed to be through consumption of contaminated food. *Listeria monocytogenes* is not a spore-producing bacterium and does not have unusual characteristics which allow survival in conditions commonly used in food processing (2). The bacterium is particularly successful in causing food-borne disease because it survives food-processing technologies and, unlike many pathogens, can continue to multiply slowly at low temperatures (7). Dietary risk factors (such as unpasteurized milk or other dairy products) for sporadic listeriosis have been assessed through case-control studies (1). The peak of human listeriosis occurs during late summer and autumn; the reasons for this being unknown (2).

The incubation period between consumption of contaminated foods and onset of clinical listeriosis is extremely variable and ranges from the first day to over 90 days (2). It is not known whether the differences in incubation period after oral ingestion are dose or strain dependent, or perhaps reflect unknown differences in host susceptibility (2). Certain conditions have been identified as risk-factors for severe invasive listeriosis, including the extremes of age, malignancies, diabetes mellitus, alcoholism, liver disease and other immunosuppressive diseases and treatments (3). The major host defense against listeriosis is cell-mediated immunity and, therefore, individuals with T-cell dysfunction seem to be particularly at risk for contracting the infection (8). Listeriosis also occurs in previously apparently healthy individuals without any of the above risk factors (2). Serious systemic listeriosis in previously healthy individuals has been reported, but is rare (9).

*Listeria monocytogenes* causes two forms of listeriosis: non-invasive gastrointestinal form and invasive form.

In immunocompetent individuals, non-invasive listeriosis develops as a typical febrile gastroenteritis; in immune-compromised adults, listeriosis can manifest as sepsis or meningoencephalitis. Invasive listeriosis can also be acquired by the fetus from its infected mother via the placenta (10). The onset of meningi-
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Encephalitis can be sudden, as in our patient, with fever, intense headache, vomiting, and signs of meningeal irritation. Rhomboencephalitis (with signs of ataxia, cranial nerve deficits), involving the brainstem, may be an unusual clinical form. *Listeria monocytogenes* can also produce a wide variety of focal infections: skin lesions, pleuropulmonary, eye or joint infection, lymphadenitis, liver impairment, brain or spleen abscess, cholecystitis, peritonitis, osteomyelitis, pericarditis or myocarditis, arteritis, necrotizing fasciitis. Focal non-meningeal infections are uncommon and very few cases affecting the liver have been reported (11). Two patterns of liver infection have been described: solitary or multiple liver abscesses and acute hepatitis with elevated liver enzymes (11). Recent observations that gastrointestinal disease and/or fever may be the only symptom in the majority of cases suggest that there may be a considerable number of undiagnosed subclinical cases of this infection (9).

Despite the high contamination rates of certain foods with *Listeria monocytogenes*, listeriosis is a relatively rare disease as compared with other common food borne illnesses, such as *Campylobacter* or *Salmonella* infection. However, because of its high case-fatality rate, listeriosis is, after salmonellosis, the second most frequent cause of food borne infection-related deaths in Europe (1). Clinicians may need to exercise more caution since the outcome involves increased morbidity and mortality.

The particularity of the reported case consists in the association of the two classical forms of invasive listeriosis, meningitis and bacteremia, with focal infection, acute hepatitis, with a course marked by multiple organ dysfunction syndromes and death, in a previously apparently healthy individual.

REFERENCES