The Body System

Case 4 PATH 417

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Case Summary

Carry, a 29-year-old woman, is 32 weeks pregnant with her first child. She recently ate a toasted pecan, strawberry, and mature goat cheese salad. A few days later, she develops mild diarrhea and night sweats and the following day she has a fever. Blood and stool cultures were collected and the blood cultures turn positive for ***Listeria monocytogenes***.

Presentation Summary

i. Signs, Symptoms, HPI, and Laboratory Samples
ii. Major Clinical Syndromes of *Listeria* infection
iii. Antibacterial Treatments
iv. ToRCH/SCoRCH infections and High Risk Groups for LM Invasive Disease

Signs, Symptoms, HPI, and Laboratory Samples

Retracing steps and providing evidence of infection

Listeria monocytogenes (LM) is the cause of Listeriosis, a life-threatening food-borne illness particularly found in dairy and leafy green products [1,2].

Signs & Symptoms

Signs	Symptoms
Case: fever	Case: fever, night sweats mild diarrhea

Other symptoms:

In pregnancy – flu, fatigue [3], amnionitis [4]

Invasive illness - stiff neck, confusion, loss of balance, and seizures [3]

Intestinal illness – vomiting [3]

Others – febrile gastroenteritis [5], nausea, cramps, constipation, headache, muscle ache, meningitis [1,2]

History of Presenting Illness

Location

No pain or discomfort reported; diarrhea implies gastrointestinal involvement; fever and night sweats suggest a systemic body reaction.

Quality

Symptoms reported are mild (diarrhea) but could indicate progression to severe symptoms.

Severity

Severity of symptoms is mild but may be on the path toward being more severe.

Timing

Symptoms developed a few days after food consumption. Diarrhea and night sweats presented first, while fever began one day after symptom onset. The timing is consistent lines up with the typical *Listeria* infection [6].

Context

Carry was likely infected upon eating raw or unpasteurized cheeses and leafy greens. Consumption of raw unpasteurized cheeses is not recommended in pregnancy as it carries between a 50-160-fold higher risk for LM infection. [7,8].

Modifying Factors

Patient is assumed to be immunocompetent but her pregnancy puts her at more of a risk for infection [9]. Antibiotic-resistant LM strains may resist penicillin and ampicillin treatment [10].

Associated manifestations

Any associated manifestations cannot be concluded until further testing is done. Some associated manifestations include meningitis and rhombencephalitis which only appear in immunocompromised patients [11].

Laboratory Samples

Blood

Cultures taken to detect the LM in the bloodstream, which can help diagnose invasive listeriosis, especially in pregnant people [3,12]

Stool

Can help identify LM in the feces, which may suggest gastrointestinal infection, but diagnosis of invasive *Listeria* infection should not made based on stool samples alone [3,13]

CSF

Only useful if the infection has spread to the nervous system like in rhombencephalitis syndrome [11]

Vaginal culture

During antibiotic therapy, samples are taken from nonsterile sites like stool or vaginal culture [11]

Major Clinical Syndromes of *Listeria* infection

How body systems are affected

Non-invasive *Listeria* infection leads to febrile gastroenteritis. It is a mild form of the disease affecting mainly healthy people. Symptoms include diarrhea, fever, headache and muscle pain. [14]

Clinical Syndrome #1
Non-Invasive Illness

LM first infects intestinal epithelial cells [15].

LM uses M cells of the intestine and intestinal villi cells as a point of entry [16].

Spread from infected intestinal cells to enterocytes causes enteritis and leads to gross intestinal lesions [16].

LM move from the gut to the mesenteric lymph nodes, targeting the liver and spleen [11].

If the immune response is unable to control the infection, LM move into the bloodstream and infect secondary target organs [11].

Invasive illness

Clinical Syndrome #2
Invasive Illness

Invasive illness results from the disseminated or systemic spread of LM (Figure 1) and may lead to various syndromes including meningitis, meningoencephalitis, encephalitis, rhombencephalitis, sepsis, endocarditis, peritonitis, myocarditis, pneumonia, pleuritis, sinusitis, conjunctivitis, ophthalmitis, septic arthritis, biliary tract disease, septicemia, hepatitis, liver abscess, endophthalmitis, febrile gastroenteritis, and osteomyelitis. [15]

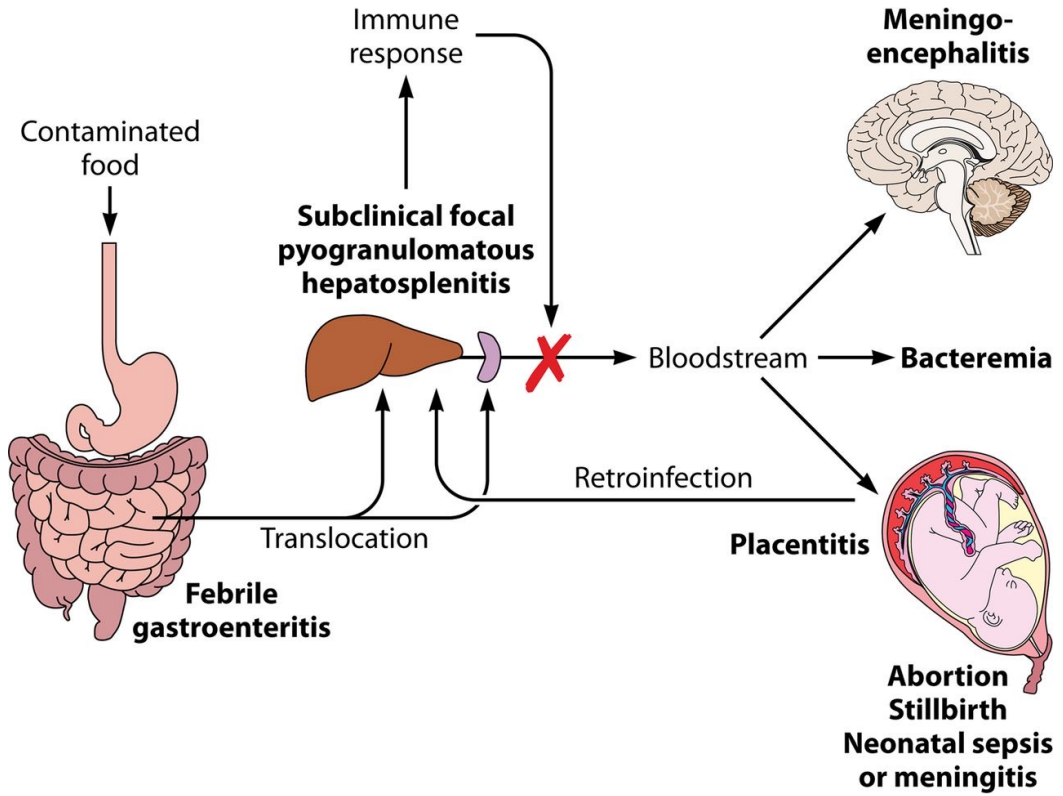

Figure 1. Introduction of LM to the host and its progression to invasive illness. [11]

Clinical Syndrome #2
Invasive Illness

Invasive illness impacts the brain, heart, abdomen, lungs, sinuses, eyes, joints, gallbladder, bone, liver, and intestine. [15]

Liver

Neutrophil recruitment to infected cells causes microabscess formation and destruction of infected hepatocytes [16].

Pregnancy

LM infects placenta causing inflammatory infiltration, necrosis, microabscesses, and focal necrotizing villitis. Infection may cause fetal death or premature birth and military pyogranulomatous lesions [16].

Brain – Meninges

LM causes meningitis with inflammatory infiltrates and infectious foci in the brain parenchyma, which may lead to focal necrosis, microabscesses, and macroscopic brain lesions. Brain lesions may cause unilateral cranial nerve paralysis [16].

Brain - Rhombencephalon

Rhombencephalitis is characterized by progressive brainstem dysfunction. Defects of the cranial nerve, hemiparesis, and brain stem lesions in the brainstem and cerebellum can occur [17,18].

Antibacterial Treatments

Fighting *Listeria* infection

Patients with invasive Listeria are usually treated with antibiotics. Intestinal illness does not usually require antibiotics and instead involves hydration with adequate fluids. [13]

The following are the antibiotics used for *Listeria* infection.

Antibacterial Drugs

Ampicillin and other β-lactam antibiotics

- Bind to penicillin-binding proteins (PBPs) in the bacterial cell wall resulting in inhibition of cell wall synthesis which interferes with autolysin resulting in lysis [19,20]
- Treatment may promote drug-resistance in LM [21]

Gentamicin

- Targets 30S ribosome to hinder protein translation which disrupts cell membrane integrity and activates macrophages to target LM [22,23]
- Mutations in the LM atpG2 gene may promote resistance to gentamicin [24]

Trimethoprim-Sulfamethoxazole (TMP-SMX)

- combination of sulfamethoxazole (blocks the synthesis of folic acid - essential for bacterial growth and reproduction) and trimethoprim (prevents conversion of dihydrofolic acid to tetrahydrofolic acid - interferes with DNA, RNA, and protein production [25]

A **combination treatment of ampicillin and gentamicin** is the current standard therapy [11,15].

Enumerated are the uses of each treatment and the reason why cephalosporin is ineffective against LM.

Antibacterial Treatments

Ampicillin + Gentamicin

- Used in invasive illness, persistent infection without meningitis (IV for 2 weeks), persistent infection with meningitis (IV for 3 weeks), and infection with rhombencephalitis or cerebritis (treatment for 4-6 weeks). [26,27]
- Primarily utilized in the treatment of high-risk patients like newborns or immunocompromised individuals [28]

Trimethoprim-Sulfamethoxazole (TMP-SMX)

- Prescribed to patients allergic to penicillin [26]

Cephalosporin

- Ineffectively binds to PBP3, the target of β-lactam antibiotics [15]
- Designed to target gram-negative bacteria, **NOT** gram-positive (LM) [15]

ToRCH/SCoRCH infections and High Risk Groups for Invasive Diseases

Characterizing and preventing *Listeria* infection

ToRCH / SCoRCH infections

ToRCH/SCoRCH is a group of diseases that **causes congenital conditions if a fetus is exposed to them in utero.** These are passed from an infected mother to a developing neonate through the placenta or perinatally during or after birth. [29]

ToRCH

Stands for **T**oxoplasmosis, **o**ther (including *Treponema pallidum*, varicella, human immunodeficiency virus, parvovirus B19, and ZIKV), **R**ubella, **C**ytomegalovirus, and **H**erpes simplex virus [30,31].

SCoRCH OR SCoRTCH

Stands for **S**yphilis, **C**ytomegalovirus (CMV), "**o**ther", **R**ubella, **T**oxoplasmosis, **C**hickenpox, **H**erpes simplex virus (HSV) and blood-borne viruses [32]

Though recognized as a pathogen that can cross the placenta, LM infection is **NOT** a ToRCH/SCoRCH infection because it is not typically transmitted vertically from mother to fetus, and it is not typically associated with congenital abnormalities in the fetus. [29,30,33]

High Risk Groups for LM Invasive Illness

Pregnant People

13 to 100 times greater risk of invasive infection [34] because immune systems are suppressed during pregnancy and changes in their gastrointestinal tract can make it easier for LM to colonize the gut [29,30]

Adults aged 65 years or older

4.4% more likely to be infected than the general population because of impairment of cell-mediated immunity and pre-existing liver dysfunction [2,35]

Newborns of infected mothers

More prone to severe complications of LM infection because of underdeveloped of cell-mediated immunity [35]

Patients undergoing treatment for cancer, AIDS, and organ transplants

Increased susceptibility due to immune suppression that predispose them to invasive infection [11]

Ensuring safety

Prevention of LM Infection

People who are immunocompromised **should avoid** unpasteurized soft cheese and milk products, unheated deli meat, premade salads, refrigerated meat spreads and smoked fish, raw sprouts, and certain melons. [36]

Ensure **foods are cooked thoroughly and properly**. Ensure that refrigerators are kept at or below 40°F (4°C) and freezers at 0°F (-18°C). [37]

Follow **general food safety and hygiene tips** and wash hands frequently [38].

Sterilize areas where there is direct food contact via alternating between biocides with different mechanisms of action in order to prevent drug resistance and ensuring that there is adequate biocide for disinfection. [39]

If one suspects that they got food poisoning from a restaurant, or if they notice unclean restaurants or grocery stores, they should **contact their local public health authority.** [38]

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