Case report

A CASE OF LISTERIA MONOCYTOGENES MENINGITIS IN AN ELDERLY FEMALE COMPLICATED BY INTRACEREBRAL HEMORRHAGE AND HYDROCEPHALUS

ABSTRACT:

Listeria monocytogenes is an important foodborne bacterial pathogen inan immunosuppressed patients, pregnant women, and individuals at the extremes of age, including neonates and older adults. Invasion of the central nervous system (CNS) and bacteremia are the principal clinical manifestations of infection in these hosts. In contrast, normal hosts who ingest high numbers of Listeria may develop self-limited febrile gastroenteritis.

Hydrocephalus and intracerebral hemorrhage (ICH) are very rare and severe complications of L. monocytogenes infection. ICH associated with L. monocytogenes has been reported even less frequently.

L. monocytogenes was cited as the fifth most common cause of meningitis after H. influenzae, S. pneumoniae, N. meningitidis, and group B streptococcus; however, L. monocytogenes meningitis had the highest associated mortality rate (22%). The mortality rate is low (0-13%) for adults with listerial meningitis who do not have serious underlying disease or are not receiving immunosuppressive treatment.

In this paper, we present a case of L. monocytogenes bacteremia in a 74-year-old female, complicated by intracerebral hemorrhage. He presented at first with nonspecific symptoms of fever and vomiting for 10 days and ASOC for 2 days and on later admission presented with sudden deterioration of consciousness which prompted further investigations that revealed the presence of ICH.

Keywords: Listeria meningitis, intracerebral hemorrhage, hydrocephalus, gram positive rods, elderly patients.

INTRODUCTION:

Listeria monocytogenes is a gram-positive facultative intracellular bacillus. It is an important cause of foodborne illness, and in most cases, the illness manifests as acute, self-limited, febrile gastroenteritis in healthy individuals. However, it can also present as systemic (invasive) listeriosis in immunosuppressed patients, with more severe symptoms and high hospitalization and case fatality [1].. It has the ability to grow at refrigeration temperatures (at 4°C). It is generally transmitted to humans through ingestion of contaminated food (ready-to-eat food, deli meats and soft cheeses). The primary bacteraemia, after ingestion, is followed by dissemination in the central nervous system (CNS), endocardium and for pregnant women, invasion of the placenta and foetus. It principally affects specific groups of patients: pregnant women, neonates, the immunocompromised (especially if cell-mediated immunity is impaired), and the elderly, potentially causing life-threatening infections such as bacteriaemia and meningoencephalitis. Case reports of LM meningitis in healthy individuals occur very rarely.[2]L. monocytogenes invades the host cells using various protein and can escape to the human T-cell immune system by cell-to-cell spreading. If the infection is not controlled at the stage in which the bacterium is in the liver, for instance, due to a severe immunodepression, a secondary bacteraemia can be developed and L. monocytogenes reaches the preferred sites transgressing the blood-brain barrier or the placental barrier.[3] The symptoms most frequently reported are fever (in 60%–100% of patients), diarrhea (in 33%–88%), arthromyalgia (in 20%–100%), and headache (in 15%–88%). In most outbreaks, >70% of patients had at least 1 gastrointestinal symptom (e.g., diarrhea, vomiting, nausea,

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and/or abdominal pain) [4]CNS manifestations can range from a mild febrile illness with mental status changes to more severe manifestations including coma and death. Meningoencephalitis is the most common CNS Listeria infection, with less common complications including ventriculitis, rhomboencephalitis, hemorrhage, and hydrocephalus. The etiology of hydrocephalus is likely multifactorial andrelated to factors such as a high level of CSF protein and impaired CSF absorption due to the obliteration of the subarachnoid space by meningeal exudates or defective CSF reabsorption through arachnoid granulations because of severe inflammatory reaction. [5]

CASE PRESENTATION:

A 74 years old female was admitted to the Hospital with 10 days history of intermittent fever upto 101F, vomiting and loose stools and altered sensorium for 2 days and also gave history of 1 episode of generalized tonic clonic seizureduring this period. Her past medical history included type 2 diabetes mellitus, essential hypertension and right breast cancer with bony mets. Before admission in our facility patient remained admitted in another hospital for 1 week where lumber puncture was performed that was in favor of bacterial meningitis.She was treated there with empirical antibiotics.

On physical examination her Glassgow Coma Scale (GCS) was 8/15, doll's eye movements were present, pupils were reactive to light bilaterally, nuchal rigidity present and positive brudzinski sign. She was maintaining oxygen saturation at room air.

The blood laboratory findings showed raised white blood cells(WBCs) and erythrocyte sedimentation rate (ESR), while red blood cells, hemoglobin, urea, creatinine, liver function test, coagulation profile, C reactive protein (CRP), urine complete examination and serum electrolytes were normal. The lumber puncture on admission revealed turbid cerebrospinal fluid (CSF), with 867cells/microliter leukocytes (98% polymorphs and 2% lymphocytes), 800mg/dl proteins , sugar 76mg/dl, CSF gram stain showed gram positive rods and was negative for fungi and acid fast bacilli. On 3rd day urine culture and sensitivity showed candida spp. CSF culture showed no growth and on 8th day blood culture was positive for listeria monocytogens. Listeria meningitis was working diagnosis. So ampicillin 2gram 4 hourly was started for total of 21 days. Patient then discharged home after 5 days of initiating ampicillin. She completed remaining course of intravenous antibiotics at home.CT Brain was unremarkable. Patient kept in follow up every week after that.

Almost after 3 weeks , patient again presented with sudden deterioration of consciousness. Her GCS was 9/15, pupils were reacting to light, maintaining oxygen saturation at 2 liters. Other examination was unremarkable. All baseline laboratory investigations complete blood count, urea, creatinine, CRP and serum electrolytes were within normal limits. Blood culture showed no growth. In imaging, non contrast CT scan of brain was done that showed intracerebral hemorrhage as in figure 1. On 3rd day of repeat CT brain, there was right parietal lobe intracerebral bleed with interventricularipsilateral extension as shown in figure 2. So, extraventricular drain was placed and burr hole craniotomy done by neurosurgeon. Patient was put on ventilator after the procedure. Her conscious level did not improve and kept on deteriorating. And patient died on day 20th of admission.

The current empirical antibiotic treatment guidelines for community-acquired bacterial meningitis does not cover the treatment for LM in immunocompetent patients between 18 and 50 years of age, therefore the appropriate antibiotic treatment for LM meningitis in this case was a bit delayed. This could suggest that LM should be considered in the differential diagnosis of patients presenting with atypical neurological symptoms or those that do not improve on the classical treatment, regardless of age group or past medical history, especially in countries with a higher risk of infection with LM. Furthermore, LM should not be suspected only in immunocompromised patients, as this was also reported in patients with no specific risk factors.

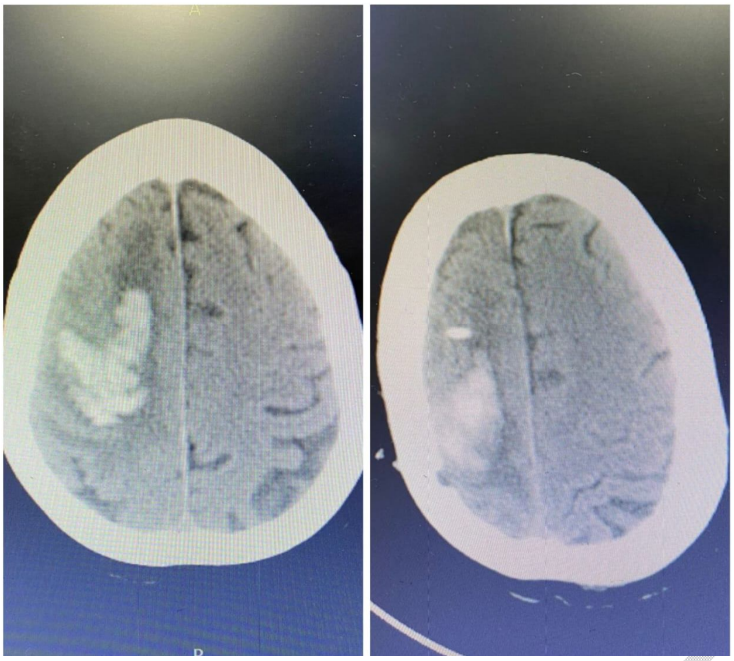

Figure 1 **: Intracerebral hemorrhage shown in Non contrast CT scan of brain (on right side) while Right parietal lobe intracerebral bleed with interventricularipsilateral extension in CT scan of brain(on left side)**

DISCUSSION:

L. monocytogenes is transmitted to the consumer mainly via contaminated ready-to-eat foods .The presence and potential persistence of *Listeria* spp. in food processing facilities are often caused by environmental recontamination at the farm or plant level. [6]

Several authors have concluded that it is virtually impossible to permanently eradicate *L. monocytogenes* from food environments because of its ubiquitous presence in the environment and many potential avenues for entry into the facility. Therefore, elimination and exclusion of the organism must be actively managed, for example by adequate hygienic design of a food premise and equipment, effective cleaning and sanitation, personnel practices and movement of people and materials into areas where food products are exposed. [7]

A rare complication of Listeria meningitis is intracranial hemorrhage, which is also one of the determinants of unfavorable outcomes. The underlying pathophysiology of intraventricular hemorrhage in L. monocytogenes infection is still unknown and may be related to dysregulation of both the coagulation and fibrinolytic pathways and to vascular endothelial cell swelling and activation[8] Intracranial hemorrhages are a severe complication of bacterial meningitis, occurring in about 3% of adults.[9]Listeria is reported as the second most common pathogen causing hydrocephalus, which develops in up to 14% of adult patients with Listeria meningitis.[10]A study from the Netherlands reviewed 26 hydrocephalus cases in 577 bacterial meningitis patients (4.5%), including four cases of L. monocytogenes (15%), all of whom underwent placement of an external ventricular drain catheter. None of these patients improved clinically after catheter placement, and all had poor outcomes for hydrocephalus, with three deaths (75%) and one case of serious sequela (25%), thus indicating that patients with hydrocephalus were at a high risk for unfavorable outcomes and that hydrocephalus was an independent risk factor for death.[11]CSF and blood cultures are the most specific for diagnosis. Early diagnosis of neurolisteriosis is difficult not only because the

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presentation of CSF is similar to the manifestations of other bacterial encephalitis and meningitis but also because approximately 50% of CSF Gram stains are negative.[11] .

Our patient was on immunosuppressive drugs (Pembrolizumab), which are linked to developing Listeria infections in multiple case reports. She is also older than 65 years and has type II diabetes mellitus, both of which place her at risk for developing listeriosis.

CONCLUSION:

Listeria monocytogenes is an important cause of systemic infection in immunosuppressed patients, and it can present with nonspecific symptoms in these hosts, such as fever, malaise, and mental status changes. Diagnosis is usually challenging, as it is often not possible to clinically distinguish L. monocytogenes infection from infections with other entities that manifest with fever and constitutional symptoms. Intracranial hemorrhage is one of the most severe and very rare complications of L. monocytogenes infection, and it is associated with a high mortality rate. Timely diagnosis and proper antibiotics administration are essential for a favorable outcome.

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