Case Report

Listeria monocytogenes infection in a 56-year-old female cancer patient: a case report

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Introduction: Listeria monocytogenes, the aetiological agent of foodborne listeriosis, can cause a severe and potentially fatal foodborne infection. Listeriosis is associated with acquired immunodeficiency or the underlying immunosuppression found in pregnant women, cancer patients and the elderly. Listeriosis emerged in developed countries in the early 1980s with the emergence of human immunodeficiency virus/AIDS and the popularity of minimally processed foods; however, few cases have been reported from developing countries. Here, we present a successfully treated case of listeriosis in a patient undergoing chemotherapy.

Case presentation: An elderly female patient with thyroid carcinoma metastasized to the lungs became seriously ill following the initiation of chemotherapy. The patient was admitted with symptoms of generalized convulsion and an altered level of consciousness and was treated empirically with meropenem, amikacin and linezolid injection. Cultures of blood and cerebrospinal fluid revealed Listeria monocytogenes on day 5 post-admission. The patient was treated with ampicillin (2 g intravenously every 4 h), which resolved the bacterial infection by day 9. To the best of our knowledge, this is the first diagnosed and successfully treated case of listeriosis in a cancer patient to be reported from Bangladesh.

Conclusion: Early diagnosis is critical for successful treatment of listeriosis. We recommend raising awareness among healthcare professionals about the diagnosis and treatment of this potentially fatal disease. Patients undergoing immunosuppressive treatments that elevate the risk of listeriosis should be monitored, and the medical histories of patients presenting with possible listeriosis should be carefully reviewed for immunosuppression. The incidence of listeriosis should be established to identify susceptible populations and to implement food safety procedures in this rapidly developing country.

Keywords: Altered level of consciousness; antibiotics; Bangladesh; carcinoma; convulsion; elderly patient; ESBL; Listeria monocytogenes; listeriosis; meningitis.

Introduction

Listeria monocytogenes is an invasive foodborne pathogen of humans and the causative agent of listeriosis. In developed countries, listeriosis is the third greatest cause of death from foodborne disease after salmonellosis and toxoplasmosis (European Food Safety Authority, 2012; Scallan et al., 2011). L. monocytogenes are ubiquitous, Gram-positive, non-spore-forming, non-capsular, facultative anaerobic bacilli that occur in 13 known serotypes. Most outbreaks of L. monocytogenes associated with contaminated foods have been attributed to serotype 4b. Most sporadic cases of human listeriosis have been attributed to serogroups 1/2 (Cossart, 2002). Pathogenic L. monocytogenes induces entry into host intestinal cells and evades neutralization by translocating directly from cell to cell (Freitag et al., 2009). Severe listeriosis is characterized by sepsis, bacterial tropism to the central nervous system, meningitis and a case fatality rate of up to 30% (Gellin & Broome, 1989). L. monocytogenes micro-organisms are occasionally isolated from immunocompetent persons presenting with self-limiting febrile gastroenteritis, but pregnant women and immunocompromised persons are particularly vulnerable. Persons with diabetes, liver and kidney disease, organ transplants, untreated human immunodeficiency virus infection, drug dependencies, and corticosteroid and chemotherapy recipients have also...
been reported to demonstrate heightened susceptibility to this disease (Dieterich et al., 2006; Goulet et al., 2012; Louria et al., 1967; Mook et al., 2011; Schlech, 2000).

Antimicrobial therapy is the mainstay of treatment for listeriosis. However, the unusual growth characteristics of the organism and incorrect diagnoses often result in inappropriate and failed treatment with severe and potentially fatal consequences. It is important for healthcare professionals to be aware of the clinical features of this pathogen to be able to provide appropriate and timely treatment and to minimize the high risk of death from listeriosis. In this study, we present a case of infection by *L. monocytogenes* in an elderly female patient undergoing chemotherapy for thyroid carcinoma. To the best of our knowledge, epidemiological data for *L. monocytogenes* infection are not available from Bangladesh and here we present the first reported case and successful treatment of *L. monocytogenes* infection in a cancer patient in Bangladesh.

**Case report**

A 56-year-old female patient with diabetes and thyroid carcinoma with metastasis to the lungs was admitted to hospital after suffering a sudden altered level of consciousness. Her past medical history included a laparotomy followed by a left adrenalectomy with sample splenectomy in 2013. The patient also had a history of total thyroidectomy in 2008 and cholecystectomy with appendectomy in 1989. She received radiotherapy between July and September 2013 and a thyroxine tablet (15 μg, orally disintegrating), calcium plus vitamin D3 tablet, prednisolone tablet (20 mg, orally disintegrating) and intravenous (i.v.) insulin injection. On the last week of August 2014, her condition was stable and she went to Bangkok for surgery (excision of a group C. The patient was treated with intravenous antibiotics and discharged with the fever incompletely resolved. In the middle of September, the patient developed a very high temperature (105°F) and was readmitted to hospital. On examination, she was found to have generalized lymphenadopathy, revealed to be non-Hodgkin’s lymphoma on histopathological testing. The patient was discharged following treatment with steroids as the fever subsided (101°F) and there were no focal signs. In the second week of October 2014, the patient received the first cycle of chemotherapy using the cyclophosphamide, hydroxydaunomycin, vincristine (Oncovin®) and prednisolone (CHOP) schedule without complication. Four days later, the patient’s condition deteriorated. On the way to hospital, she developed an episode of generalized convulsion and was unconscious on reaching the emergency department. Repeated focal signs with secondary generalized convulsion resulted in immediate admission to the special care unit. Cerebrospinal fluid (CSF), obtained by lumbar puncture, appeared on examination to be slightly turbid with a white cell count of 250 μl⁻¹ with 80% neutrophils and 20% lymphocytes, protein of 219 mg dl⁻¹, glucose of 10.7 mmol l⁻¹, adenosine deaminase of 4.19 U l⁻¹ and a negative fungal stain. Initial treatment was empirical injection with meropenem (1 g i.v. every 8 h), amikacin (500 mg i.v. every 12 h) and linezolid (600 mg i.v. every 12 h), which continued for 9, 16 and 7 days, respectively. Ceftriaxone injection (2 g i.v. every 12 h) started on the next day and continued for 5 days. Injection of acyclovir and fluconzole started 1 week later and continued for 10 and 14 days, respectively. Two days after hospital admission, the patient’s white blood cell count was found to be 0.3 × 10³ μl⁻¹ and she received a transfusion of 1 U packed red blood cells, and filgrastim (Neupogen®) (5 μg kg⁻¹ day⁻¹) injection was started and continued for 2 weeks. For her convulsion, the patient was initially treated with midazolam and phenytoin injection plus sodium valproate and carbamazepine tablets. However, the convulsion was not controlled, so the drugs were rescheduled to parenteral phenytoin, phe nobarbitone and sodium valproate. She also received parenteral dexamethazone (Oraflexon®) and mannitol (Osmitrol®) for 14 and 3 days, respectively. On the fourth day of her hospital stay, her respiratory effort became poor and her overall condition deteriorated. She was shifted to the intensive care unit (ICU), where she was intubated and put on a mechanical ventilator. Parenteral thiopental sodium was started instead of the phenobarbitone injection. After 24 h in the ICU, convulsion occurred only very occasionally. On her fifth day in the ICU, parenteral levetiracetam was started instead of the sodium valproate injection, whilst parenteral thiopental sodium was stopped after 3 days. She developed hypotension, and a noradrenaline i.v. infusion was started.

On the fifth day of her hospital stay, her tracheal aspirate culture and sensitivity showed no growth and she was negative for *Mycobacterium tuberculosis*. However, her blood and CSF culture and sensitivity showed growth for a Gram-positive bacillus, which was later identified as *Listeria monocytogenes*. Antimicrobial susceptibility testing by disc diffusion showed that the strain was susceptible to amikacin (30 μg), ampicillin (10 μg), erythromycin (30 μg), gentamicin (10 μg), imipenem (10 μg), linezolid (30 μg), meropenem (10 μg), netilmicin (30 μg), penicillin G (10 μg), piperacillin + tazobactam (110 μg) and vancomycin (30 μg). However, it was resistant to ceftriaxone (30 μg), cefoxaxime (30 μg), ceftazidime (30 μg), ceftazidime (32 μg ml⁻¹), ceftazidime (32 μg ml⁻¹), ceftriaxone (4 μg ml⁻¹), gentamicin (0.064 μg ml⁻¹), imipenem (0.064 μg ml⁻¹), penicillin G (0.064 μg ml⁻¹) and vancomycin (0.75 μg ml⁻¹). She was treated with ampicillin (2 g i.v. every 4 h) and after 24 h she became afebrile. Ampicillin was continued for the next 3 weeks, and 4 days after ampicillin treatment, an Indian ink preparation of her CSF was negative. For the next month, she stayed at the hospital for rehabilitation purposes, and during that period her blood, tracheal aspirate and urine revealed sporadic infections with *Serratia*
rubidaea, Klebsiella pneumoniae, and Candida and Proteus spp., respectively. Her infection resolved after specific treatment. She was released in the first week of January 2015 whilst she was haemodynamically stable, afebrile and conscious but still disoriented from the side effects of her cancer treatment.

Diagnosis

The patient's blood and CSF samples were inoculated in BACTEC blood culture bottles and incubated in a BACTEC 9240 blood culture machine. The machine gave positive signals for culture after 48 h. Positive culture media of both samples were then subcultured onto blood, MacConkey and chocolate agar medium plates. After incubation in appropriate conditions, β-haemolytic colonies was detected on the blood agar plate. The colonies were subjected to a reverse CAMP (Christie–Atkins–Munch-Petersen) test for identification and an API profile index test to confirm the organism as L. monocytogenes (API index no. 0170164). An antibiogram was done by the disk diffusion method and MIC values were determined using E-test strips.

Discussion

L. monocytogenes is ubiquitous in the environment and is a normal member of the gut flora in many mammals. Cases of infection and disease (listeriosis) in humans are rare (estimated at 4.6 per million of the population). Elderly persons with defective immunity are at high risk of contracting this disease, with a case fatality rate of 24–62% (Pigrau et al., 1993). A few cases of L. monocytogenes infection have been reported from neighbouring south Asian countries (Adhikary & Joshi, 2011; Rahman et al., 2002; Soni et al., 2015). However, no epidemiological data exists on L. monocytogenes from Bangladesh, which makes our case particularly important.

The patient in this case was found sick 4 days after receiving the first round of chemotherapy for non-Hodgkin’s lymphoma. Although the early signs and symptoms matched listerial meningitis, infection with L. monocytogenes was not suspected until the pathogen was cultured from blood and CSF samples. The source of the infection was not determined. Ingestion of contaminated foods has been reported as the main source of infection by this pathogen. Foods such as ready-to-eat meats, seafood, soft cheeses, unpasteurized milks, hot dogs and ice cream have been linked to most cases of infection (Swaminathan & Gerner-Smidt, 2007). L. monocytogenes has the ability to survive and reproduce at low temperature, in a wide pH range (4.3–9.6) and at high salt concentrations, which gives it the ability to contaminate, persist and proliferate in a wide range of food items (Cossart, 2002; Low & Donachie, 1997). The infective dose of L. monocytogenes in healthy individuals is 10 to 100 million c.f.u., and is 0.1 to 10 million c.f.u. in immunocompromised persons (Farber et al., 1996). Infection with this pathogen in one of the hospitals that the patient visited for various treatments over a 6-week time period cannot be ruled out. There have been reports of nosocomial listeriosis with case fatality rates of nearly 50%, suggesting that a large proportion of hospitalized patients are in the high-risk group. A number of outbreaks in hospitals have lasted for several months or years (Graham et al., 2010). Hospital-associated outbreaks have typically been clustered and linked to contaminated foods or other environmental contacts. A recent worrisome development has been the increasing number of reported cases of sporadic non-clustered hospital-acquired listeriosis in different countries. Depending on the mode of transmission, dosage and other host factors, L. monocytogenes has an incubation period of 1–67 days (Goulet et al., 2013). The incubation period for gastroenteritis is very short (20–24 h). The incubation period of invasive illness is much longer, generally 20–30 days (Riedo et al., 1994). Therefore, in our study, the patient might have become infected during one of her hospital visits. The characteristic long incubation period of this organism makes it likely that the patient developed severe illness only after being immunosuppressed by her chemotherapy treatment.

The patient reached the hospital with signs of severe meningitis, but recent chemotherapy suggested toxic side effects including seizures or convulsions (Singh et al., 2007), and bacterial infection was not initially suspected. The initial treatment involved anticonvulsant drugs with other therapies targeted towards normalizing blood cell counts and physiological conditions. Although the L. monocytogenes strain in our study was sensitive to amikacin, meropenem and linezolid, the empirical treatment did not lead to an improvement in her condition. This may be due to the antagonistic effects in the combined empirical therapy, as reported previously between linezolid and aminoglycosides (Jaccodine et al., 2003). For meningitis patients with defective cellular immunity, it is recommended to target the treatment towards L. monocytogenes, Gram-negative bacilli or Streptococcus pneumoniae (Quagliarello & Scheld, 1997). The first choice of treatment for severe listeriosis is currently based on the synergistic effect of an aminopenicillin (ampicillin or amoxicillin) and gentamicin. Rifampicin, vancomycin, linezolid and carbapenems are alternatives, but trimethoprim is usually used in case of any complication with β-lactams (Hof, 2004; Temple & Nahata, 2000). L. monocytogenes shows natural resistance to expanded-spectrum cephalosporins, older quinolones and fosfomycin, but they are usually widely susceptible to clinically relevant antibiotics targeting Gram-positive bacteria (Troxler et al., 2000). L. monocytogenes strains with resistance to multiple antibiotics have also been reported, and it is suggested that they are capable of acquiring foreign antibiotic resistance genes (Charpentier & Courvalin, 1999).

Accurate diagnosis and microbiological confirmation are critical for the appropriate treatment for listeriosis. However, making a diagnosis of this pathogen is not always straightforward. The key point is suspicion of the presence of this organism. Good medical records of the
patient’s clinical symptoms and relevant host factors may provide indicative information for this purpose. As this organism shares some characteristics with other Gram-positive bacteria, especially streptococci, it is also necessary to establish some differential diagnosis. Additionally, the current lack of regular surveillance for this pathogen, especially in developing countries, makes it difficult to evaluate the changing epidemiology of this pathogen. However, we believe that proper awareness among healthcare professionals about the clinical features and severe consequences of listeriosis will help to implement proper measures to minimize the casualties associated with this infection.

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