The Infectious Disease of the Immunocompromised Host and the Elderly: Listeriosis

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Abstract

Listeria monocytogenes is an uncommon cause of illness in the general population. However, this bacterium is an important cause of severe infections in neonates, pregnant women, the elderly, transplant recipients, and other patients with impaired cell-mediated immunity. Various clinical features due to L. monocytogenes have been described such as sepsis, central nervous system infections, endocarditis, gastroenteritis and localized infections. A review of the clinical aspects of listeriosis with emphasis on the elderly with underlying diseases and immunosuppressive therapy, is given in this paper.

Introduction

Clinical features of human listeriosis include self-limiting gastroenteritis in outbreak cases, spontaneous abortion in pregnant women, and severe infections (sepsis and meningitis) in immunocompromised persons and the elderly. In the latter, the case-fatality rate is 20%-30%. The incidence of nonpregnancy-associated listeriosis has increased recently in Europe despite strict food regulations. In Centers for Disease Control and Prevention (CDC)’s recent nationwide surveillance report, most listeriosis cases occurred among adults aged ≥ 65 years [1-3].

Listeriosis, usually a mild disease in pregnant women, but it can cause severe outcomes for the fetus or newborn infant. There is a growing interest for the investigation of food-borne listeriosis outbreaks [1]. Listeria monocytogenes, being the only human pathogen among Listeria species [4,5], has the potential for life-threatening invasive infections in elderly persons, immunosuppressed transplant recipients, and others with impaired cell-mediated immunity [1,4-6]. It is important that practicing immunologists and geriatricians are to be familiar with the non-specific and differing clinical aspects of this uncommon disease.

Clinical Aspects of Listeriosis

The predisposing factors of listeriosis

Listeriosis is mainly a food-borne zoonotic infection. The elderly is at high risk for listeriosis, but symptoms are non-specific and diagnosis is difficult. The intracellular life-cycle of Listeria protects the bacterium from host innate and adaptive immune responses [6,7]. Antibiotic treatment requires agents able to penetrate, distribute, and remain stable within host cells. Listeria activates T-cell mediated immunity which under the influence of cytokines, attracts macrophages that produce inflammatory granulomata where bacteria are destroyed. Memory T-cells provide an acquired resistance to Listeria infection, and this might explain why listeriosis is linked with malignancy, immunosuppressive therapy, AIDS, pregnancy and the neonate [7].

For most high-risk conditions, the risk for infection was higher among older patients. The epidemiology of listeriosis in England and Wales changed during 2001-2008; more patients ≥ 60 years of age had bacteremia than in previous years. For serious infection with L. monocytogenes malignancies accounted for more than one third of conditions and cancer patients had a 5-fold increased risk for development of listeriosis. Cancers of the blood seemed to have the greatest ratio. Other high-risk conditions included diabetes mellitus; alcoholism; certain diseases of the circulatory system and the musculoskeletal system and connective tissue; noninfective enteritis and colitis; and diseases of the liver and kidney. Authors have pointed out that physicians should consider a diagnosis of listeriosis when treating patients who have concurrent conditions [8].

Apart from the immune status of the host, other factors which influence whether or not invasive disease occurs include the virulence of the infecting strain and the size of the inoculum. The infective dose is unknown, but is estimated to be between 10^5-10^6 organisms/g of ingested product, although this estimate might be lower in groups at risk [7], and a high inoculum of ~10^9 is required to produce disease in healthy mammals [6,9]. Most often, Listeria are transmitted via the ingestion of contaminated food. unpasteurized dairy products, such as raw milk and soft cheeses, and preprocessed foods are reported to be especially associated with listerial infection. Iron is an additional virulence factor for L. monocytogenes, and clinically, iron-overload states are risk factors for listerial infection [6,8].

Clinical approach to listeriosis

The duration of the incubation period of listeriosis is unknown, but is likely to be about 31 (11-70) days [6]. Some studies demonstrate that the listeriosis incubation period is shorter than generally assumed and varies according to the clinical form of the disease. Not surprisingly the shortest incubation period is observed for listeria...
bacteremia can lead to the development of peritonitis, cholecystitis, hepatitis, pleuritis, splenic abscesses, pericarditis, osteomyelitis, and endophthalmitis. These localized infections can be seen as the result of septic emboli with listerial endocarditis. Patients having localized listerial infections usually suffer from underlying diseases [4,6,13].

Complications of invasive disease including disseminated intravascular coagulation, adult respiratory distress syndrome, and rhabdomyolysis with acute renal failure have been documented. Rare episodes of reinfection have occurred [6].

Diagnosis requires isolation of \textit{L. monocytogenes} from normally sterile clinical specimens (CSF, blood, joint fluid, and so forth) and identification through standard microbiologic techniques. In clinical specimens, the organisms may be gram-variable and look like diphtheroids, cocci, or diplococci. Laboratory misidentification as diphtheroids, streptococci, or enterococci is not uncommon, and the isolation of a “diphtheroid” from blood or CSF always should alert one to the possibility that the organism is really \textit{L. monocytogenes} [6].

Management of listeriosis

There have been no controlled trials to establish a drug of choice or the duration of therapy for listerial infection. Most of the experience of treating \textit{L. monocytogenes} is with the use of ampicillin, penicillin and amoxicillin and to date, no bacterial resistance to penicillin has been detected. Ampicillin is generally considered the preferred agent, although its superiority to penicillin is questionable. Carbapenems demonstrate delayed in vitro bactericidal activity (48 hours) at levels that are obtainable in the CSF as with ampicillin [6,7].

For those intolerant to penicillins, trimethoprim-sulfamethoxazole as a single agent, is thought to be the best alternative. \textit{In vitro, L. monocytogenes} has a wide range of antibiotic sensitivities but is resistant to cephalosporins, clindamycin, and chloramphenicol. Cephalosporins are ineffective against \textit{Listeria} because they do not bind to bacterial penicillin-bound protein-3 (PBP3). Gentamicin and tobramycin have been reported to have greater in vitro activity than the other aminoglycosides. There is limited experience with quinolones and rifampicin although they show in vitro activity. Listerial resistance to vancomycin is rare, and its use (though limited) has been employed in endocarditis, as well as in listerial meningitis (in which cerebral intraventricular injections were administered) [6,7].

Treatment of listeriosis requires collaboration with an infectious diseases specialist. Meningitis doses should be used for all patients, even in the absence of CNS or CSF abnormalities, because of the high affinity of this organism for the CNS. Relapses and treatment failures are reported in those with meningitis treated for less than 2 weeks; therefore, treatment for 3 weeks is recommended for all cases of meningitis. Bacteremic patients without CSF abnormalities can be treated for 2 weeks. Patients with rhombencephalitis or brain abscess should be treated for at least 6 weeks and followed with serial magnetic resonance imaging studies (or computed tomography scans). Endocarditis should be treated for 4 to 6 weeks. No data exist concerning antimicrobial efficacy in listerial gastroenteritis; the illness is self-limited, and treatment is not warranted [6].

Clinical experience with listeriosis

Authors presented three listeriosis cases with various clinical manifestations which the diagnosis was difficult [18]. Those three cases (Table 1) which appeared in two consecutive months (second case two days after the first case and the third one 40 days after), could have not been diagnosed as listeriosis, if \textit{L. monocytogenes} growths from blood cultures had not been reported from clinical microbiology laboratory of the hospital [18]. The bacteria was confirmed as \textit{Listeria monocytogenes} serotype 4b by the Institute of National Enteric Pathogens Laboratory, Ankara.

Conclusion

Listeriosis is a rare disease with increasing incidence occurring mainly in elderly people and patients suffering from underlying
diseases and immunosuppressive therapy, and it should be considered an emerging health problem.

References