Case Report

Brain Abscess Due to Listeria Monocytogenes: First Case Report in Thailand

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Brain abscess with bacteremia caused by Listeria monocytogenes in a young woman with immune thrombocytopenic purpura was reported. The clinical features included fever, headache, and left-side weakness. Computed tomography and magnetic resonance imaging of the brain showed a large single abscess at the right frontoparietal area. L. monocytogenes was isolated from a blood culture. The patient promptly received a surgical drainage. Because she had a history of penicillin allergy, and the organism was resistant to ampicillin, she was treated with trimethoprim-sulfamethoxazole (TMP-SMX) alone for 12 months. During a one-year follow-up period, the patient improved and her neurological deficit gradually recovered. This is the first case of listerial brain abscess in Thailand that was successfully treated with TMP-SMX monotherapy and surgical drainage.

Keywords: *Listeria monocytogenes, Brain abscess, Trimethoprim-sulfamethoxazole*

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Listeria monocytogenes, a facultative anaerobic Gram-positive bacillus, is an uncommon cause of food-borne diseases in the general population. However, it can cause a life-threatening infection in pregnant women, neonates, the elderly, and those receiving immunosuppressive therapy[1-3]. Infections caused by *L. monocytogenes* have wide varieties of clinical syndromes including sepsis, central nervous system (CNS) infections, endocarditis, gastroenteritis, and other focal infections in various organs[2]. Although *L. monocytogenes* possesses tropism to both the brain and meninges, meningitis is much more frequently observed in CNS listeriosis, whereas the other types of CNS listerial infection, such as rhombencephalitis and brain abscess, are extremely rare[1,2]. In many countries, *L. monocytogenes* is ranked the fifth most common cause of meningitis[1]. However, there are only three case reports of *L. monocytogenes* infection in Thailand and all of those were presented with meningitis[4,5]. This patient is the first report of brain abscess due to *L. monocytogenes* in Thailand who was successfully treated with trimethoprim-sulfamethoxazole (TMP-SMX) monotherapy and surgical drainage.

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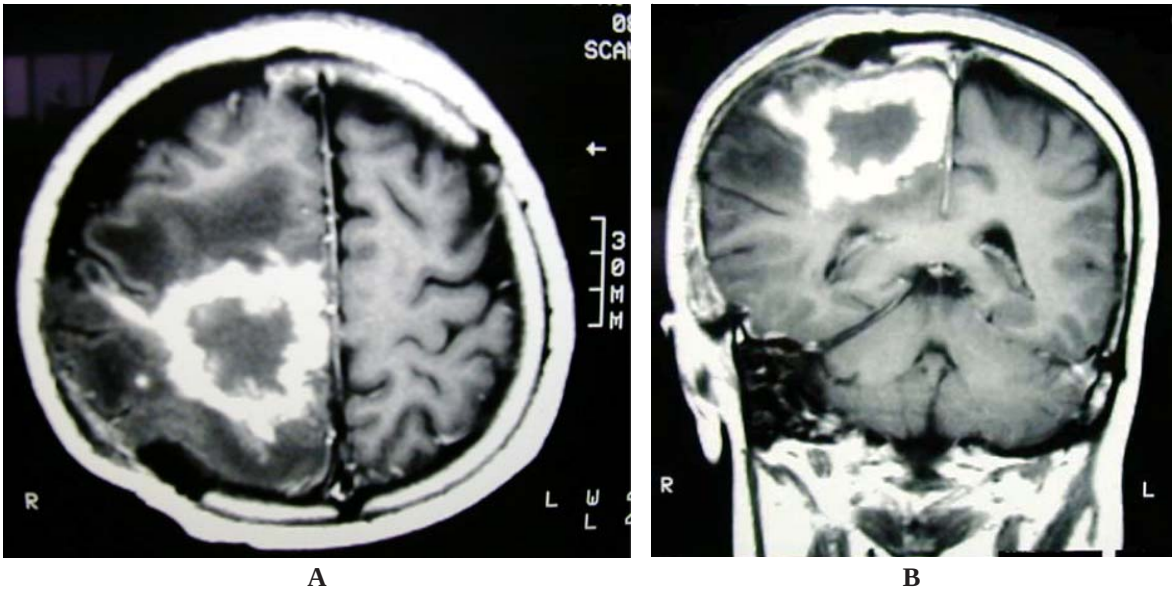
Case Report

A 23-year-old Thai woman with a history of immune thrombocytopenic purpura (ITP) who had been treated with prednisolone and cyclophosphamide for two months, was admitted with severe progressive headache, fever, and left-side weakness for two days. She was seen at the emergency room where she developed a left-side focal seizure with secondary generalized tonic-clonic seizures. The patient had been working in a shrimp export company, but did not have any history of having nonpasturized dairy products, raw or fermented meat products. Physical examination revealed a young obtunded woman with cushingoid appearance and a body temperature of 39 C. Neurological examination showed left-side hemiparesthesia,

hemiparesis, and hypereflexia with extensor response of the left plantar reflex. Complete blood count showed hemoglobin of 13.2 g/dl with a white blood cell count of 9,400 /mm^3 (neutrophil 68%, lymphocyte 26%, monocyte 6%), and thrombocytopenia (platelet count 60,000 /mm^3). Urinalysis revealed marked proteinuria (4+) and microscopic hematuria (red blood cells 50-100/HP) with dysmorphic red blood cells. A computed tomography (CT) brain scan was performed and revealed an ill-defined enhancing mass 5 cm in diameter at the right frontoparietal area with marked surrounding edema. T1-weighted magnetic resonance imaging with gadolinium of the brain disclosed an irregular ring-enhancing hyposignal intensity lesion, measuring 5 cm in diameter, at the right frontoparietal area with surrounding vasogenic edema and gyral enhancement of the adjacent meninges after gadolinium injection (Fig. 1). Lumbar puncture was carefully performed and revealed a high opening pressure of 330 mmH_2O. Cerebrospinal fluid (CSF) examination showed white blood cells of 25/mm^3, CSF protein of 20 mg/dl, and sugar of 98 mg/dl (blood sugar 175 mg/dl), and no organism was demonstrated on Gram, acid-fast bacilli and modified acid-fast bacilli stains. Aerobic culture of CSF on blood agar yielded no growth. A brain abscess was diagnosed and she was empirically treated with intravenous ceftriaxone, metronidazole, and TMP-SMX for coverage of common causative bacteria, including streptococci, Enterobacteriaceae, anaerobes, and *Nocardia* spp. Wide craniectomy and biopsies of the brain and meninges were performed 4 days after hospitalization and generalized brain swelling was noted without flank pus. Histopathological findings revealed acute inflammatory process. One of two blood cultures taken on the first day of admission and before initiation of antibiotics grew *L. monocytogenes*. The isolation and identification of this pathogen were performed by using the standard microbiological techniques described elsewhere[6,7]. The antimicrobial susceptibility test was performed by Kirby-Bauer disk diffusion method as described by National Committee for Clinical Laboratory Standards (NCCLS)[8]. *L. monocytogenes* isolated from this patient was sensitive to gentamycin, TMP-SMX, ampicillin/sulbactam, and imipenem. It was resistant to ampicillin, amoxicillin, ciprofloxacin, and all cephalosporins. All subsequent cultures were negative for any organism.

Ceftriaxone and metronidazole were discontinued after obtaining the blood culture results. The patient had a history of mild allergic reaction to penicillin, and the organism was resistant to ampicillin. Therefore, only TMP-SMX was continued intravenously and the patient gradually improved after six weeks of treatment. CT brain scan performed on the



A **B**

Fig. 1 Axial view (A) and coronal view (B) of the magnetic resonance imaging of the brain showed an irregular ring enhancing hyposignal intensity lesion in T1-weighted image with Gadolinium, 5 cm in diameter, with surrounding vasogenic edema at right frontoparietal area and gyral enhancement of the adjacent meninges

day 40 after hospitalization revealed persistent abscess with a slight decrease in size, reduced edema, and less gyral enhancement. Aspiration of brain abscess was repeatedly performed during the 6th and 7th week after hospitalization with approximately 7 ml of pus collected and all cultured specimens were negative. The patient was discharged from the hospital after eight weeks of hospitalization. She continued oral TMP-SMX and was monitored for response by serial brain CT scan every 3 months. CT scan of the brain at six months after treatment showed a significant decrease in abscess size. The antibiotic was continued for about 12 months resulting in resolution of the abscess. The patient had residual mild left hemiparesis after physical therapy. Dosage of her immunosuppressive drugs was also rapidly tapered after her thrombocytopenia was recovered. The patient was doing well one year after discontinuation of TMP-SMX.

Discussion

L. monocytogenes is an intracellular pathogen that capably survives in the host cells and spreads directly from cell to cell without exposure to the extracellular humoral immune system. However, because of the rarity of *L. monocytogenes*, it is not always included in the initial differential diagnosis as the causative pathogen of brain abscess, although the presented patient was recognized as immunocompromised host as her cell-mediated immunity was suppressed by corticosteroid and immunosuppressive therapy[1,9].

The most common form of CNS listeriosis is meningitis, but *L. monocytogenes* also causes a small number of brain abscesses, ranging from 1-10% of all CNS listeriosis reported. There are only 40 cases of listerial brain abscesses described in the literatures between 1968 and 2003[10]. Some features of listerial brain abscess are relatively uncommon in brain abscess caused by other bacteria. These include: 1) presence of bacteremia in most cases, 2) a quarter of cases having concomitant meningitis, and 3) subcortical abscesses located in thalamus, pons and medulla being common[1,11]. The presented patient did have a positive blood culture. However, the CSF findings were not characteristic for listeriosis and were consistent with aseptic meningitis that could be seen in any parameningeal infections. In addition, the abscess in the presented patient was located at the subcortical frontoparietal area, which is an usual site for a brain abscess caused by hematogenous spreading. The predisposing factor for acquiring listeriosis in the presented patient is not clear. The presented patient did not have any particular risk factors such as ingestion of dairy products or raw meat. However, she had been working in a shrimp company and this exposure could have been a possible mode of acquiring infection in this patient. In fact, there has been a report of listeriosis outbreak related to shrimp consumption[12] and also reports of *L. monocytogenes* as contaminants in seafood including shrimp[13,14]. In nature, *L. monocytogenes* is found primarily in soil and water, and therefore vegetables and animals can become contaminated with this bacterium from the soil. Furthermore, animals can carry *L. monocytogenes* without apparent infection and therefore *L. monocytogenes* can be found in a variety of raw foods as well as in processed foods that become contaminated after processing. However, there are currently no sufficient food surveillance data of *L. monocytogenes* contamination in Thailand and further studies in these issues are necessary.

Although there has been no randomized-controlled trial to address a drug of choice for treatment of listeriosis, ampicillin or penicillin G are considered the preferred drugs for any forms of listerial infection[15]. Gentamicin is usually added to achieve synergism in a serious infection. This regimen had been shown to be an effective antimicrobial therapy[1,11]. However, there is no zone diameter interpretive standard for disc diffusion susceptibility testing in *Listeria* spp. according to NCCLS and the zone diameter interpretive standards for *Staphylococcus* spp. are generally used to interpret disc susceptibility tests in *L. monocytogenes*. Ampicillin-resistant *L. monocyrogenes* was firstly reported in the United States in 1984[16]. Although ampicillin-resistant *L. monocyrogenes* has been considered a rare entity, a recent retrospective study of 84 clinical isolates of *L. monocyrogenes* in a cancer center revealed that 9.2% and 2.3% of those isolates were resistant to ampicillin and penicillin, respectively[17]. There are no epidemiological data of ampicillin-resistant *L. monocytogenes* in Thailand and, therefore, a close surveillance should be conducted. The presented patient was allergic to penicillin and the causative organism was resistant to ampicillin, thus she was treated with solely TMP-SMX. TMP-SMX is bactericidal against *L. monocytogenes*, can achieve adequate levels in serum and CSF, and has documented clinical efficacy in case reports[18-20]. It has also been recommended to be an alternative regimen for listeriosis. The presented patient received TMP-SMX on the first day of admission and this could explain the negative result of pus culture from the surgical specimen performed on the forth day of hospitalization. However, clinical

experience in treatment of listerial brain abscess with TMP-SMX is limited. In a current review of 40 cases of supratentorial listerial brain abscesses by Cone et al, most patients received ampicillin and/or gentamicin for the treatment. Although five cases received TMP-SMX in combination with other antibiotics, no case of successful treatment with TMP-SMX monotherapy has been observed[10]. However, Rossi et al have described a 58-year-old woman with a listerial spinal cord abscess that responded to TMP-SMX monotherapy[18]. The optimal duration of antibiotic therapy for listerial brain abscess varies with the patient's underlying disease, clinical severity, number, and size of abscess, and adequacy of surgical treatment. Immunocompromised patients with CNS infection should continue treatment for at least 6-8 weeks with antibiotics until the culture is negative and/or the imaging of the brain is improved. Decreased use of immunosuppressive agents must be considered especially in a patient with poor response. Listerial CNS infections in immunocompromised patients usually have a high mortality rate and the neurological sequelae are common among the survivors[1,11].

In conclusion, the authors report a case of a brain abscess in an immunocompromised ITP patient caused by a rare organism, *L. monocytogenes*. Fortunately, the patient was successfully treated with surgical interventions and a twelve-month course of TMP-SMX. The authors would like to emphasize that listeriosis should be considered in the differential diagnosis when an immunocompromised patient presents with a brain abscess from hematogenous spreading and is unresponsive to cephalosporins.

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ฝีในสมองจากเชื้อ ลิสทีเรีย โมโนซัยโตจีนีส รายงานผู้ป่วยรายแรกในประเทศไทย

พรพิศ ตรีบุพชาติสกุล, สมพร ศรีเฟื่องฟุ้ง, เมธี ชยะกุลคีรี

รายงานนี้เป็นรายงานการเกิดฝีในสมองร่วมกับการติดเชื้อในกระแสเลือดจากเชื้อแบคทีเรีย ลิสทีเรีย โมโนซัยโตจีนีส ในผู้ป่วยหญิงที่เป็นโรคเกล็ดเลือดต่ำจากภูมิคุ้มกัน ผู้ป่วยมีไข้ ปวดศีรษะ และแขนขาซีกซ้ายอ่อนแรง ภาพถ่ายคอมพิวเตอร์สมองพบมีฝีขนาดใหญ่ที่สมองซีกขวาส่วนฟรอนโตพาไรทัล การเพาะเชื้อจากเลือดผู้ป่วยขึ้นเชื้อลิสทีเรีย โมโนซัยโตจีนีส ผู้ป่วยได้รับการรักษาโดยการผ่าตัดระบายหนองทันที เนื่องจากผู้ป่วยมีประวัติแพ้ยาเพนนิซิลินและเชื้อที่เพาะขึ้นดื้อต่อยาแอมพิซิลิน จึงใช้ยาไตรเมโทปริม-ซัลฟาเมทอกซาโซลเป็นเวลา 12 เดือน ผลการรักษา 1 ปีต่อมาผู้ป่วยมีอาการดีขึ้นและการฟื้นตัวของระบบประสาทดีขึ้นตามลำดับ ผู้ป่วยรายนี้เป็นผู้ป่วยฝีในสมองจากเชื้อ ลิสทีเรีย โมโนซัยโตจีนีส รายแรกของประเทศไทย และตอบสนองดีต่อการรักษาด้วยยาไตรเมโทปริม-ซัลฟาเมทอกซาโซล เพียงชนิดเดียวร่วมกับการผ่าตัดระบายหนอง