A case of Listeria monocytogenes brain abscess with a clinical presentation mimicking stroke

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Abstract

Purpose: Kidney transplant recipients are at a high risk of both stroke and infection. We report this case to inform readers of the possibility of the occurrence of Listeria monocytogenes brain abscess despite treatment with low dose trimethoprim–sulfamethoxazole (TMP/SMX).

Case Report: A 62-year-old man presented to our hospital with right facial palsy, left arm and leg weakness, and mild fever; he was diagnosed with a stroke in the emergency room. The patient had a history of cadaveric renal transplantation 2 years prior, for which he was prescribed tacrolimus-based immunosuppressive drugs. Multiple myeloma was diagnosed 18 months after renal transplant. He was treated with bortezomib and steroids for the multiple myeloma, and low-dose TMP/SMX for pneumocystis prophylaxis. A listeria brain abscess was diagnosed based on a comprehensive medical history, magnetic resonance images, positive blood culture, and brain biopsy. He underwent ampicillin therapy and achieved full recovery after a 3-month follow-up period.

Conclusion: Physicians should monitor unusual stroke symptoms and consider Listeria brain abscess as a differential diagnosis. This case suggests that listeria brain abscesses can potentially cause temporary neurological deficits akin to a stroke, despite TMP/SMX prophylaxis, but these symptoms resolve without necessitating surgical intervention.

Keywords: **Listeria monocytogenes, Listeriosis, brain abscess, stroke**

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INTRODUCTION

Listeria monocytogenes rarely causes illness in immunocompetent individuals. Even though Listeria monocytogenes infections are rare, they are a significant cause of mortality in solid organ transplant recipients. Compared with patients < 65 years without underlying conditions, those with multiple myeloma, dialysis,

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brain, lung, esophageal, and pancreatic cancer, and organ transplantation had a thousand-fold higher risk of developing listeriosis [1]. The Center for Disease Control in the United States estimates that Listeria sp. are responsible for 1,591 episodes of infection and 255 deaths annually, with a 16% fatality rate [2]. Here, we present the case of a renal transplant recipient who later developed multiple myeloma under low doses of trimethoprim–sulfamethoxazole (TMP/SMX) prophylaxis, subsequently developing a *Listeria monocytogenes*-associated brain abscess that was misdiagnosed as stroke in the emergency room.

CASE ILLUSTRATION

A 62-year-old man presented to the emergency department with sudden onset right facial palsy, left arm and leg weakness, and a history of mild fever (37.7°C) for 2 days. He was diagnosed with primarily unilateral stroke in the emergency room. The patient had a past history of 1.) End-stage renal disease after living renal transplantation 2 years prior, for which he was being maintained on tacrolimus, Everolimus, mycophenolic acid, and prednisolone; 2) multiple myeloma for which he was treated with bortezomib, cyclophosphamide, dexamethasone and low-dose TMP/SMX prophylaxis to prevent Pneumocystis jirovecii infection. On physical examination, the patient was conscious with a Glasgow Coma Scale score of 15, intact pupillary light reflex, and a soft neck. The patient had no history of vomiting, tinnitus, or blurred vision. Neurological examination revealed that he was unable to lift his right brow and could not completely close his right eye. He further showed drooping of the right corner of the mouth compatible with right peripheral-type facial palsy grade 4 on the House-Brackman grading system, and left-sided muscle weakness with positive left Babinski sign. Laboratory tests revealed an elevated C-Reactive protein of 1.24 mg/dL (normal range, <1 mg/dL). Brain computed tomography (CT) was performed without contrast to assess stroke, revealing a hypodense area which involved the right basal ganglion and right frontal region (figure 1a). Brain magnetic resonance imaging (MRI) showed brain edema and local mass effect compression of the right lateral ventricle in

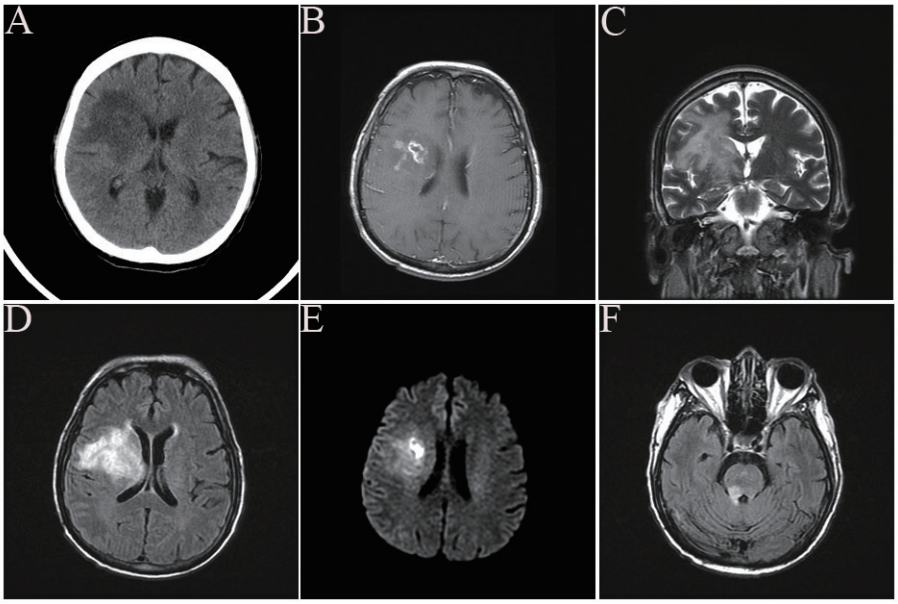

Fig. 1. Non-contrast computed tomography scans reveal low attenuation in the right frontal region (1a). Furthermore, brain magnetic resonance imaging (MRI) reveals: brain edema with local mass effect in the right frontotemporal, basal ganglion, and periventricular white matter region on post-contrast T1-weighted images in the axial position (1b) and T2-weighted images in the coronal position (1c). Fluid-attenuated inversion recovery (1d) and diffusion-weighted imaging sequences(1e) confirm the edema lesions. A brain edema lesion is also noted in the midbrain and pontine areas on T2-weighted and fluid-attenuated inversion recovery images (1f).

the frontotemporal, basal ganglion, and periventricular white matter region on post-contrast T1-weighted images in the axial position and T2-weighted images in the coronal position (figure 1b and 1c). Enhanced signals with low apparent diffusion coefficient were observed in the center of the lesion in fluid attenuated inversion recovery and diffusion-weighted imaging sequences (figure 1d and 1e, respectively). High signals were observed in the midbrain and pons areas on T2-weighted images and fluid attenuated inversion recovery images (figure 1f). Stereotactic biopsy was performed by a neurosurgeon, and brain abscess culture was positive for Listeria monocytogenes. Two of four sets of blood cultures were also positive for *Listeria monocytogenes*, and therapy with intravenous (IV) Ampicillin (2 g every 8 hours) was initiated. After receiving the culture report, we titrated the dose of IV ampicillin 2 g every 8 hours for 1 week to 2 g every 4 hours for 30 days. Forty days after the onset of antibiotic treatment, physical examination revealed that the patient was conscious and afebrile, with normal muscle power throughout. Right facial palsy and ptosis improved significantly as well. Therefore, we agreed to discharge the patient. Oral ampicillin was continued for 50 days to complete the treatment. Written informed consent was obtained from the patient for the publication of his images and clinical data.

DISCUSSION

Listeria monocytogenes is a gram-positive facultative intracellular food-borne pathogen that can cause serious infections in the elderly, neonates, and the immunocompromised populations. Listeria brain abscesses are rare, even among transplant patients. The diagnosis of brain abscesses developing after renal transplant is important. They may lead to temporary neurological deficits that resolve without requiring surgical intervention, in contrast to true strokes, which are associated with permanent neurological deficits.

Which population subset is more susceptible to Listeria infection with central nervous system involvement? Opportunistic infections and the reactivation of chronic listeriosis typically occur in immunocompromised populations. Listeria has been identified in a broad range of foods, including raw milk, cheese, raw meat products, and salads. Its typical route of transmission is the consumption of contaminated food. Listeria penetrates the intestinal epithelium via enterocytes and Peyer's patches. These organisms are well-adapted to the various microenvironments of the gastrointestinal tract, suggesting their ability to cause chronic infections [3]. Reactivation of listeriosis may occur in transplant recipients taking immunosuppressants. Renal transplant recipients often receive regular immunosuppressants to prevent graft rejection; poor compliance with immunosuppressant medication can lead to limited graft survival [4]. Current guidelines recommend that maintenance immunosuppression should consist of a calcineurin inhibitor and an anti-proliferative agent with or without corticosteroids [5]. Our patient was treated with tacrolimus, with everolimus as maintenance therapy for renal transplant, and bortezomib for multiple myeloma. Tacrolimus negatively affects infection-stimulated T cells [6], everolimus is associated with more frequent infections in patients with neuroendocrine diseases [7], and evidence has shown that bortezomib enhances the apoptosis of antibody-secreting cells such as plasma cells or memory B cells, and decreases the function of other immune cells, resulting in mild neutropenia, decreased T cell proliferation, decreased NK and CD8+T cell function, inhibition of dendritic cell function and viability, and alteration of cytokine secretion [8, 9]. Long-term immunosuppressant use poses a great risk for opportunistic infection and reactivation of chronic listeriosis because of a deficiency in antibody-related bacterial opsonization and dysfunctions of other immune cells.

What is the typical presentation of brain abscesses in transplant patients? Impaired inflammatory responses due to immunosuppressant use may obscure the clinical and radiological findings of microbial invasion. Consequently, patients are often minimally symptomatic, present late, and are diagnosed late [10], resulting in more severe infection in the central nervous system. Listeria penetrates the intestinal barrier through internalin A and internalin B by binding to the cellular receptors E-cadherin and a receptor tyrosine kinase for which the natural ligand is hepatocyte growth factor [11]. These receptors are also expressed on the surface of choroid plexus epithelial cells and brain endothelial cells [12], thereby allowing Listeria to invade the central nervous system.

Our case raises one important question; why did the patient develop a Listeria infection while being prophylactically treated with TMP/SMX? TMP/SMX prophylaxis is consistently included in the post-transplant regime for varying durations, from 3 months to a lifetime, according to the patient's comorbidities and physical conditions. This treatment prevents infections from a wide range of opportunistic agents such as *Pneumocystis pneumonia, Toxoplasma gondii, Isospora belli, Cyclospora cayetanensis*, and many *Nocardia* and *Listeria* species. Low-dose TMP/SMX is well tolerated and should be used unless the patient exhibits evidence of an allergy or interstitial nephritis [13]. Oral TMP/SMX therapy has excellent bioavailability, and is widely used in clinical practice. A low dose of trimethoprim (80 mg/kg/day) plus sulfamethoxazole (400 mg/kg/day) has comparable efficacy in Pneumocystis pneumonia. Our patient was administered low-dose TMP/SMX for Pneumocystis prophylaxis, but nevertheless experienced a breakthrough Listeria infection that caused their brain abscess. More evidence is required on the dosage of TMP/SMX required for prophylaxis during tacrolimus-based immunosuppressive medications and bortezomib treatments.

How do we distinguish stroke from brain abscess or other stroke mimics? Common characteristics for brain abscess including fever, headache, and changes in the level of consciousness, as well as elevated C-Reactive protein level, are often insufficient to precisely identify brain abscess and stroke [14, 15]. Despite a striking similarity in the clinical manifestation of stroke and brain abscess, several factors can aid their differentiation. First, anatomical localization based on neurological examination may suggest multiple lesions. For example, right peripheral-type facial palsy may suggest lesions over the right pons involving an infratentorial lesion, while left hemiparesis may suggest the involvement of the supratentorial lesion. MRI-confirmed brain abscesses can be located in a variety of regions, including right frontotemporal, basal ganglion, and periventricular white matter region, to the mid-posterior midbrain and pons, compatible with the clinical presentation described above. Lesions with these multifocal brain findings include cardioembolic stroke or infectious disorders, such as brain abscesses or congenital cytomegalovirus infection, and inflammatory disorders, such as multiple sclerosis [16]. Second, appropriate brain imaging studies should be selected. MRI or contrast CT should be performed, as these enable the visualization of unusual presentations, such as vessel territory distribution to detect the brain abscess. Cerebral abscesses with contrast enhancement such as ring signs may also be helpful [17].

CONCLUSION

Brain abscesses caused by Listeria monocytogenes are uncommon, but can develop despite low doses of TMP/SMX. CT and MRI are helpful in evaluating brain abscesses and further guiding stereotactic biopsy. Early and accurate diagnosis as well as proper treatment can effectively promote the recovery of neurological function, reduce morbidity and mortality, and improve prognosis.

AUTHORSHIP

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Acquisition, analysis, and interpretation of data:

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Ya-Chun Chu and Chien-Liang Chen

Study supervision:

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Consent for publication:

The patient provided written consent for their personal or clinical details along with any identifying images to be published in this study

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