A case of Listeria monocytogenes Meningitis Complicated with Acute Hydrocephalus in an Immunosuppressed Patient

İmmünsüprese Hastada Akut Hidrosefali ile Komplike Listeria Monocytogenes Menenjiti Olgusu

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ABSTRACT

Listeria monocytogenes meningitis is seen in elderly or immunosuppressed patients and may cause high mortality. Hydrocephalus is a serious complication of *L.monocytogenes* meningoencephalitis. Inappropriate empirical antimicrobial therapy and the development of hydrocephalus are the main independent prognostic factors associated with mortality. *L.monocytogenes* may be a causative agent of meningitis and bacteremia, especially in immunosuppressed patients. It may cause acute hydrocephalus and should be considered because of its high mortality risk.

The presented case is a 58-year-old female patient, who was previously using steroids with a diagnosis of autoimmune hepatitis, and was admitted to the hospital with blurred consciousness and fever for two days. She was diagnosed with meningitis due to *L. monocytogenes*, which was complicated by acute hydrocephalus. The patient died on the 21st day of intensive care follow-up and the 16th day of mechanical ventilator support.

L.monocytogenes may be a causative agent of meningitis and bacteremia, especially in immunosuppressive patients. *Listeria* should be kept in mind in elderly or immunosuppressed patients, and effective empirical treatments for Listeria should be started. Acute hydrocephalus should be kept in mind in patients with clinical worsening despite treatment.

Keywords: Hydrocephalus, *Listeria monocytogenes*, Meningitis

ÖZET

Listeria monocytogenes menenjiti, yaşlı veya bağışıklığı baskılanmış hastalarda görülür ve yüksek mortaliteye neden olabilir. Hidrosefali, L.monocytogenes meningoensefalitinin ciddi bir komplikasyonudur. Uygunsuz ampirik antimikrobiyal tedavi ve hidrosefali gelişimi, mortalite ile ilişkili ana bağımsız prognostik faktörlerdir. L.monocytogenes, özellikle bağışıklığı baskılanmış hastalarda menenjit ve bakteriyemi etkeni olabilir. *L.monocytogenes*'in akut hidrosefali ve yüksek mortaliteye sebep olabileceği unutulmamalıdır.

Olgumuz; 58 yaşında kadın hastaydı ve otoimmün hepatit tanısı ile öncesinde kortikosteroid kullanmaktaydı. İki gündür bilinç bulanıklığı ve ateş şikayeti ile hastaneye başvurdu. Akut hidrosefali ile komplike olan *L. monocytogenes*'e bağlı menenjit tanısıyla yoğun bakımda izlemi yapıldı. Hasta yoğun bakım takibinin 21. gününde ve mekanik ventilatör desteğinin 16. gününde kaybedildi.

L.monocytogenes, özellikle immünosupresif hastalarda menenjit ve bakteriyemi etkeni olabilir. Yaşlı veya bağışıklığı baskılanmış hastalarda Listeria akılda tutulmalı ve *Listeria* için etkin ampirik tedavilere başlanmalıdır. Tedaviye rağmen kliniği kötüleşen hastalarda akut hidrosefali akılda tutulmalıdır.

Anahtar kelimeler: Hidrosefali, Listeria monocytogenes, Menenjit

INTRODUCTION

Listeria monocytogenes is a Gram-positive bacillus, which is common in nature and is usually a zoonotic infection agent. Although it is rarely seen in healthy individuals, it is more common in newborns, the elderly, and in conditions such as lymphoma, pregnancy, acquired immunodeficiency syndrome (AIDS), and corticosteroid use, where cellular immunity is insufficient, and may cause life-threatening infections (1,2). L. monocytogenes can cause serious infections such as bacteremia, meningitis, encephalitis, endocarditis or local infections (gastroenteritis, cholecystitis, osteomyelitis, arthritis, pleuropulmonary infection, endophthalmitis, etc.) in humans (3,4).

Central nervous system (CNS) infections due to L. monocytogenes can cause various clinical presentations, ranging from mental status changes accompanied by mild fever to mortality. Bacteria reach the central nervous system frequently secondary to bacteremia (1). Although meningoencephalitis is the most common, ventriculitis, rhomboencephalitis, intracerebral hemorrhage, or hydrocephalus may also develop rarely. CNS infections caused by L. monocytogenes have been reported to represent 5-10% of listeriosis cases. Listeria meningitis is seen in elderly or immunosuppressed patients and may cause high mortality (1,5).

Hydrocephalus is a serious complication of L. monocytogenes meningoencephalitis. In the etiology of hydrocephalus, defective CSF reabsorption due to arachnoid granulation caused by severe inflammation together with impaired CSF

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absorption secondary to the obliteration of the subarachnoid space due to elevated cerebrospinal fluid (CSF) protein and increased meningeal exudate is thought to play a role in L. monocytogenes, after Streptococcus pneumoniae (6,7). It is the second most prevalent pathogen (8). Pelegrin et al. (9) reported that the mortality rate of Listeria meningitis cases with hydrocephalus was 75%.

This case is presented to emphasize that L. monocytogenes may be a causative agent of meningitis and bacteremia, especially in immunosuppressive patients. It may cause acute hydrocephalus and should be considered because of its high mortality risk.

CASE REPORT

A 58-year-old female patient was brought to the emergency room by her relatives with complaints of altered consciousness and fever for two days. She had no other complaints. She had a history of hypertension, autoimmune hepatitis, which he was diagnosed with 3 months ago, and overlap syndrome. She was using methylprednisolone tablets, 40 mg/day for 3 months.

On the physical examination of the patient, her general condition was moderate, she was confused and disoriented, and her cooperation was limited. Her examination details were as follows; axillary fever: 38º C, pulse: 80/min, blood pressure: 140/70 mmHg, respiratory rate per minute: 14/min, rhythmic. There was no nuchal rigidity, and no signs of meningeal irritation were detected. No focal neurological deficit was detected in her neurological examination. She had no abnormalities on other systemic examinations.

At her first admission, she had leukocytosis [26000/mm3 and polymorphonuclear leukocytes (90%) predominance]. No anemia (hemoglobin was 12.3 g/dl). The C-Reactive Protein (CRP) level was 62 mg/L, the Erythrocyte sedimentation rate (ESR) was 39 mm/hour, and the procalcitonin level was 0.18 ng/ml. In biochemical examination results were as follows; alanine transaminase (ALT) 62 U/L, gamma-glutamyl transferase (GGT): 313 U/L, glucose: 151 mg/dL, and other biochemical laboratory parameters were all within normal limits. There were no abnormal findings in the complete urinalysis. In thorax computed tomography (CT), there was no metastatic, infiltrative, infective lesional appearance, and no pathological finding was detected in the cerebral CT (Figure 1). No pathology was detected in cerebral magnetic resonance Imaging (MRI), cerebral diffusion MRI and MRI angiography at the first admission.

The patient was hospitalized in the intensive care unit (ICU) with a preliminary diagnosis of meningitis and a lumbar puncture (LP) was performed. In the cerebrospinal fluid (CSF) examination the results were as follows; the appearance of CSF was opalescent, pressure increased, 500 leukocytes/mm3 (60% lymphocytes, 40% neutrophils), glucose 37 mg/dL (simultaneous blood glucose of 220 mg/dL), and protein 229 mg/dL. In the Gram stain examination of the CSF sample, 2 leukocytes were seen in each area, but no microorganisms were seen. Vancomycin 2×1 g IV intravenous (IV) and ceftriaxone 2×2 g IV empirical treatments were started. On the 2nd day of the treatment, the patient developed limited gaze, ptosis, and pupil dilation in the left eye. In the control cerebral CT scan, there was acute hydrocephalus that was not present in the previous scan (Figure 2).

She was unconscious, had no light reflex in her left eye, and was found to have bilaterally middilated pupils. Multiple cranial nerve palsies, including the oculomotor (3rd cranial nerve) nerve, developed under empirical treatment during her hospitalization. Upon the clinical deterioration of the patient, Ampicillin 6×2 g IV treatments were added to her treatment with the preliminary diagnosis of Listeria meningitis. Emergency external ventricular drainage (EVD) catheterization was performed due to acute hydrocephalus (Figure 3). On the 5th day of her hospitalization, the patient lost consciousness and her breathing worsened, and she was intubated. Blood and CSF cultures taken at the time of hospitalization were reported on the 5th day of hospitalization. L. monocytogenes grew in both blood cultures. There was diphtheroid bacillus growth in the preliminary evaluation of the CSF culture. However, the current results were re-examined when the patient's clinical information and the growth of L. monocytogenes in the blood culture and it was defined as L. monocytogenes. In the susceptibility test performed with the disc diffusion method, it was observed to be sensitive to all antibiotics that were included such as meropenem, ampicillin, penicillin, trimethoprim- sulfamethoxazole, vancomycin.

No leukocytes were observed in the control CSF sample taken on the 7th day of hospitalization, and there was no growth in the control CSF culture. Ehrlich Ziehl Nielsen Stain staining and tuberculosis PCR results of CSF negative were negative. Followed up with a diagnosis of Listeria meningitis and bacteremia patient died on the 21st day of intensive care follow-up and the 16th day of mechanical ventilator support.

DISCUSSION

Listeria monocytogenes can cause bacteremia and life-threatening serious infections such as meningitis, encephalitis, endocarditis, hepatitis in humans, and local infections such as gastroenteritis and arthritis (1,2). CNS involvement often develops secondary to bacteremia and is most seen as meningitis (1).

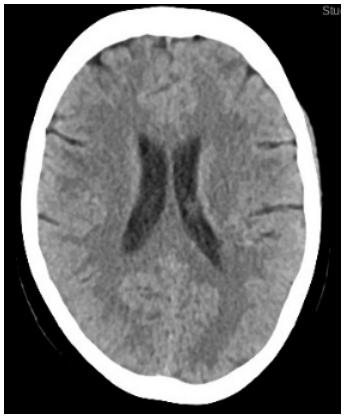

Figure 1. Cerebral CT without contrast

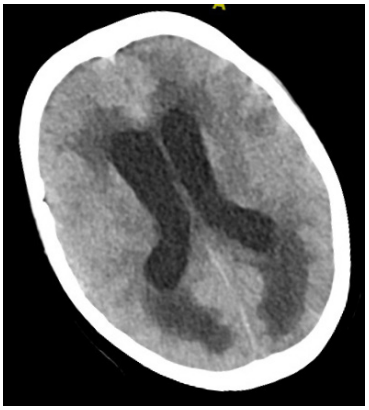

Figure 2. Non-contrast cerebral CT on the 5th day of hospitalization.
*Diffuse edema of periventricular white matter

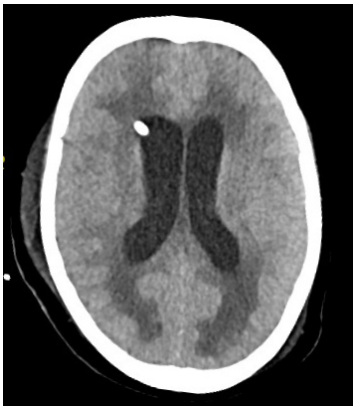

Figure 3. Cerebral CT without contrast
* External ventricular drainage (EVD) catheter extending to the right lateral ventricular horn is seen.

CNS infections caused by L. monocytogenes have been reported to represent 5-10% of listeriosis cases. It is seen that 66% of 32 listeriosis cases reported from Turkey between 1987 and 2001 are meningitis (5). L. monocytogenes is the third most common cause of meningitis in adults and is usually associated with old age and an immunocompromised condition (10). Our case was using 40 mg/day of methylprednisolone for 3 months with the diagnosis of autoimmune hepatitis. Taking 40 mg of prednisolone for 3 months causes immunosuppression and it was one of the predisposing factors for Listeria. Listeria should not be forgotten in empirical treatment in such patients who use corticosteroids at doses and durations that may cause cellular insufficiency. In a previous study, it was reported that arterial hypertension may impair the integrity and function of the blood/brain barrier and cause L. monocytogenes to invade the subarachnoid space and/or brain tissue (11). Arterial hypertension was thought to be one of the predisposing factors of our patient.

While there is growth in blood cultures in the early period in 60–75% of patients with Listeria meningitis, growth mostly occurs in CSF cultures in the late period (1). The protein level in CSF is usually high, and glucose can be at low or normal levels. It should not be forgotten that there may be neutrophil dominance in direct microscopy as well as monocytic cell dominance. In CSF gram staining, the causative agent cannot be shown most of the time (9,11). Gram staining revealed the causative agent in ~25 % (17/73) of the cases according to a study from our country (12). In the CSF examination of our patient, the amount of protein increased, glucose values were low, monocytic cell predominance was present, and similar to the literature, no microorganism could be detected in the CSF gram staining. There was diphtheroid bacillus growth in the preliminary evaluation of the CSF culture. However, the current results were re-examined when the patient's clinical information and the growth of L. monocytogenes in the blood culture and it was defined as L. monocytogenes. Similar to our case, Akçam et al (13). Reported a case in which diphtheroid was initially reported in CSF culture, but was reported as Listeria after clinical information. L. monocytogenes should be considered in the differential diagnosis when clinically suspected, diphtheroid, streptococcus or enterococci are reported in CSF or blood culture (1,2,5). We think that the identification of gram-positive bacillus grown in CSF culture may be beneficial.

Diker et al (14). detected petechial hemorrhages in the brain parenchyma using unconventional magnetic resonance imaging techniques in 3 patients with neurolisteriosis and stated that this finding could be a diagnostic clue. In our case, no pathological finding was detected in the MRI scans at the first admission. MRI could not be performed due to the worsening of the patient's condition in the following period.

Acute hydrocephalus was observed in the early period of the follow-up of our case. L. monocytogenes is the second most common pathogen causing hydrocephalus after Streptococcus pneumoniae (8). While hydrocephalus is estimated to be 5% as a complication of bacterial meningitis, there is a higher incidence of Listeria (15). The incidence of hydrocephalus in neurolisteriosis cases has been reported to be between 10% and 30% (7,9,16). In addition, CSF reabsorption may be impaired due to arachnoid granulation caused by severe inflammation. These conditions are thought to play a role in the pathogenesis of hydrocephalus (6,7). In the initial CT scans, it can often go undetected, and the initial CT scan may seem to be normal. Studies have reported that the risk of developing hydrocephalus increases if the symptoms last longer than four days (9). Similar to those reported in the literature, while the first CT was normal in our case, acute hydrocephalus was detected in the cerebral CT performed on the fifth day. When the literature was reviewed, it was reported that hydrocephalus

developed a few days after admission, especially in patients who did not adequately cover L. monocytogenes in empirical treatment (17). Hydrocephalus should be suspected in patients with neurological deterioration within a few days of initial admission, particularly when empirical therapy has not been tailored to be effective against L. monocytogenes.

Charlier et al (18). reported neurological sequelae in 44% of the cases accompanied by hydrocephalus, while they stated that the 3-month mortality was around 30%. Pelegrin et al (9). reported that while mortality was 43% in Listeria meningitis, 75% of hydrocephalus cases were mortal. Our case was followed up with the clinic of meningitis secondary to bacteremia and had a mortal course. In another study, the mortality rate of 92 Listeria cases, 75% of whom had Listeria meningitis, was reported as 17.4% (16/92 cases), and it was reported that 93.8% of deaths (15/16 deaths) were cases with meningitis (19). Our case was followed up with the diagnosis of Listeria meningitis and bacteremia and had a mortal outcome.

While Pelegrin et al (9). considers appropriate empirical antimicrobial therapy and neurosurgery consultation regarding hydrocephalus management the most important points in patient follow-up, they reported that inappropriate empirical antimicrobial therapy and the development of hydrocephalus were the main independent prognostic factors associated with mortality.

The current meningitis guidelines recommend treatment to include Listeria in all patients over the age of 50 with suspected meningitis (17). In addition, in the presence of diabetes mellitus, cancer or immunosuppression regardless of age, it has been suggested that empirical therapy should be arranged to include Listeria. The standard treatment for L. monocytogenes meningitis is amoxicillin, ampicillin, or penicillin G (2,6,8). The addition of aminoglycoside to the treatment is left to the discretion of the patient's clinic and physician, but close follow-up in terms of renal failure is recommended for those who are planning to start treatment (9,11). Pelegrin et al (9). reported that there was no difference in mortality between ampicillin monotherapy and combination therapy with an aminoglycoside.

In another study, it was reported that rifampicin, which is effective against intracellular Listeria and penetrates the CSF, together with ampicillin, may be a good alternative regimen to minimize the risk of treatment failure, especially in the immunocompromised host (6). Although the optimal duration of treatment in Listeria meningitis is not clear, it is recommended to give treatment for at least 21 days (9,11).

CONCLUSION

It is noteworthy that Listeria meningitis is associated with hydrocephalus, which is one of the rare complications, and diphtheroid is reported in the CSF culture at the diagnosis stage. As a result, Listeria should not be forgotten in elderly or immunosuppressed patients, and effective empirical treatments for Listeria should be started. Acute hydrocephalus should be kept in mind in patients with clinical worsening despite treatment.

Conflict of Interest: The authors declare that they have no conflicts of interest.

Patient's Consent: Obtained from the patient's first-degree relatives.

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