LISTERIA MENINGOENCEPHALITIS CONCURRENT WITH CMV HEPATITIS

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ABSTRACT

Listeria monocytogenes is not a common cause of infection. It may be a cause of life-threatening infections like bacteremia and central nervous system (CNS) infections. We report a 29-year-old man admitted to emergency room with headache, fever, nausea-vomitting, weakness of right upper and lower extremities and aphasia, who presented with listeria meningoencephalitis after steroid treatment due to polymyositis. The treatment with ampicillin and gentamicin, was changed because of side effects to trimethoprim-sulfamethoxazole and vancomycin. Under this treatment, transaminases of the patient increased. The reasons of acute hepatitis were investigated and Cytomegalovirus (CMV) DNA level was 2494 copy/ml, revealing CMV hepatitis. Gancyclovir treatment was started. The patient was discharged with cure after 42 days of antibacterial treatment and 23 days of antiviral therapy.

Key Words: *Listeria monocytogenes, Cytomegalovirus, meningoencephalitis, hepatitis* ***Nobel Med 2013; 9(3): 136-138***

CMV HEPATİTİ İLE SEYREDEN LİSTERİA MENİNGOENSEFALİTİ

ÖZET

Listeria monocytogenes infeksiyonların nadir rastlanan bir nedenidir. Bakteriyemi ve santral sinir sistemi (SSS) infeksiyonları gibi hayatı tehdit edici infeksiyonlara neden olabilir. Biz de acil servise baş ağrısı, ateş, bulantı, kusma, sağ üst ve alt ekstremitede güçsüzlük ve afazi şikayetleri ile başvuran ve polimiyozit nedeniyle steroid tedavisi alan 29 yaşında bir erkek hastayı *Listeria* meningoensefaliti nedeniyle sunmaktayız. Hastanın ampisilin ve gentamisin tedavisi sırasında yan etkiler nedeniyle tedavisi trimetoprim sulfametaksozol ve vankomisine değiştirildi. Bu tedavi altında transaminaz değerleri yükseldi. Akut hepatit nedenleri araştırıldı ve CMV DNA seviyesi 2494 kopya/ml saptanarak CMV hepatiti tanısı kondu. Gansiklovir tedavisi başlandı. Hasta 42 gün antibakteriyel ve 23 gün antiviral tedavi verilerek şifa ile taburcu edildi.

Anahtar Kelimeler: *Listeria monocytogenes,* Sitomegalovirus, meningoensefalit, hepatit **Nobel Med 2013; 9(3): 136-138**

INTRODUCTION

Listeria monocytogenes is not a common cause of infections among the general population. It can be isolated from water, soil and decaying vegetation. However, in some groups, including neonates, pregnant women, elderly people, immunosuppressed transplant recipients and others with impared cell-mediated immunity, it is an important cause of life-threatening infections like bacteremia and central nervous system (CNS) infections.[1] Clinical syndromes due to *L. monocytogenes* in CNS are mostly meningitis, meningoencephalitis and brain abscess.[1] Even with appropriate antibiotic therapy, listeriosis is fatal in about 1 out of 3 cases.[2] We report a case that presented with listeria meningoencephalitis concurrent with CMV hepatitis after steroid treatment due to polymyositis and treated successfully.

CASE REPORT

A 29-year-old man admitted to emergency room with headache, fever, nausea-vomitting, weakness of right upper and lower extremities and aphasia. He had been diagnosed with polymyositis one month earlier and corticosteroid treatment had been given.

At admission to hospital, physical examination revealed right hemiplegia, restricted lateral eye movement in the right eye and neck stiffness. White blood cell count was 8300/mm^3, glucose level was 224 mg/dl. Other biochemical results were normal. Lomber puncture (LP) was performed. Cerebrospinal fluid (CSF) leucocyte count was 80/mm^3, glucose 91 mg/dl, protein 139 mg/dl, LDH 86 IU/l and chloride 116 mEq/l. Vancomycin 500 mg every 6 hours, ceftriaxone 2 gr every 12 hours, acyclovir 750 mg every 8 hours and ampicillin 2 gr every 4 hours were started. Forty eight hours later control LP findings revealed 1340 cells/mm^3 (80% lymphocyte), high protein (136 mg/dl) and LDH (865 mg/dl) and low glucose (24 mg/dl) levels. No microorganism was seen on gram stain. Serum and CSF Wright agglutination tests were →

negative. The CSF examination for acid fast microorganism and CSF Tbc PCR were negative. Culture of blood and CSF samples grew *L. monocytogenes* on day 4 which was catalase positive, oxidase negative, beta hemolitic gram positive rod and CAMP test was positive (Figure 1). Ceftriaxon, vancomycin and acyclovir treatments were stopped and gentamicin 80 mg every 8 hours was added to ampicillin. Corticosteroid treatment decreased 4 mg every 3 days. Magnetic resonance imaging (MRI) of the brain revealed; hypointense areas on T1-weighted images and hyperintensities on T2-weighted images in pericallosal-frontoparietal subcortical white matter (centrum semiovale) and left parasagittal frontal subcortical white matter and also postcontrast enhancement in T2-weighted images and edema in cortical sulcus, all in association with encephalitis and Acute Demyelinating Encephalomyelitis (ADEM) (Figure 2). The MRI of the lesion was interpretted to the *Listeria* encephalitis by neurology specialist and control LP was not recommended. Gentamicin treatment was stopped on day 8 because of the nephrotoxicity. The patient had diplopia on day 14 and the control MRI revealed regression of the lesion. On the 17th day of the treatment, transaminases increased (AST:178, ALT:897). Viral markers for CMV, EBV, HAV, HBV and HCV were tested and only anti CMV and anti EBV IgG positivity were detected. Ampicillin therapy was stopped and vancomycin and trimethoprim-sulphametoxazole were started. Under this therapy transaminases decreased, however on the 29th day of the treatment transaminases re-elevated and viral markers were retested and anti CMV IgG titers were increased. CMV DNA load was reported as 2494 copy/ml and ganciclovir 5 mg/kg every 12 hours, was added to the therapy. During the treatment, his neurologic findings deteriorated slowly. He started talking, the right sided weakness of the patient regressed. After a negative result of CMV DNA, ganciclovir was stopped on the 23th day of the therapy. The patient was discharged with cure after 42 days of antibacterial treatment.

DISCUSSION

L. monocytogenes may cause a self-limited gastrointestinal tract illness or localized infection like septic arthritis, osteomyelitis, pneumonia or more severe infections like bacteremia, CNS infection and endocarditis.[1,2] There are several case reports of meningitis and sepsis due to *Listeria* from our country.[2-5]

Although listeriosis as a whole occured most often in patients with underlying risk factors (81%), Goulet et al reported that 80% of nonpregnant cases with listeria CNS infections were previously healthy patients.[6-8] In a review; 21% of all cases had immunosupression because of cancer, diabetes, alcoholism, chronic liver disease, 8% were given immunosuppressive therapy for cancer, transplantation or connective tissue diseases although 71% were middle-aged previously healthy adults.[9] Glucocorticoids suppress both cell-mediated immunity and humoral immunity and trigger opportunistic infections. Our patient was started steroid treatment about one month ago. Similar to our case; in patients with compromised T cell-dependent immunity, the life-time risk of *Listeria* infections is estimated to be 100-300 fold higher than the general population.[6,10] Our patient developed CNS infection due to listeria in the first month of his steroid treatment.

Listeria has a predilection for the brain parenchyma, especially the brainstem, and the meninges.[1,9] As in other causes of acute bacterial meningitis, fever was the most common presenting symptom. Approximately two-thirds of patients had an altered sensorium and hemiplegia might have occured. The incidence of meningeal irritation signs among patients with *Listeria* meningitis has been reported to be lower than that among cases of meningitis due to other bacterial pathogens.[9,11] Although nuchal rigidity is rarely seen, focal and generalized seizures occur in at least 25% of patients. Single or multiple asymmetric cranial nerve deficits and movement disorders including tremor, ataxia and myoclonus may develop.[9] Our patient had fever, altered sensorium, right hemiplegia, and abducens nerve paralysis. Three-Fourths of patients with *Listeria* meningitis have a CSF pleocytosis with a predominance of neutrophils frequently mixed with lymphocytes or monocytes. In the remaining cases, lymphocytes or monocytes predominate.[12] Raynaud et al. reported that 88% of cases with listerial brainstem encephalitis had low grade pleocytosis (mean, 392 cells/mm^3) with lymphocytic predominance, 89% had hyperproteinorrachia (mean, 99 mg/dl) and 21% had hypoglycorrhachia.[9] In our patient pleocytosis and lymphocytic predominance were seen. The protein level was 199 mg/dl, but the glucose level was very low (24 mg/dl). Hypoglycorrachia was variable and had been reported to be associated with a worse prognosis; however, the mean and median glucose levels were reported in the normal range in a review.[11] CSF gram stain results are positive in less than 50% of patients.

The rates of gram positivity from previous studies in listerial encephalitis, meningitis and other bacterial meningitides were; 14%, 28% and 60%, respectively. CSF cultures are reported to be positive in more than 80% of cases of meningitis and 42% of encephalitis.[9] Since blood cultures revealed *Listeria* earlier than CSF cultures and were positive in 60-83% of patients, it should be performed especially in cases presenting with CNS infection like symptoms.[9] In our patient, on the 5th day blood and CSF cultures grew *L. monocytogenes*.

MRI yielded positive findings in 87% of the patients. Postcontrast enhancement in T1-weighted images, patchy hyperintensity with hypointense areas in T2 weighted images, microabscesses have been reported in previous studies, although negative findings were also documented.[9] The brain MRI of our patient revealed positive findings that could be associated with neurolisteriosis.

Ampicillin is generally the treatment of choice. Gentamicin or tobramycin are added to ampicillin or penicillin →

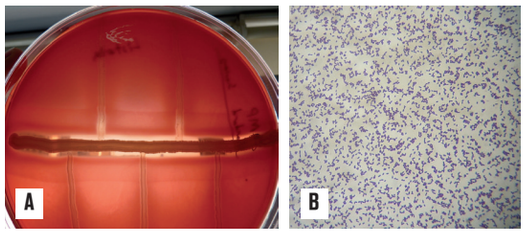

Figure 1. Listeria monocytogenes (A: CAMP test, B: gram staining)

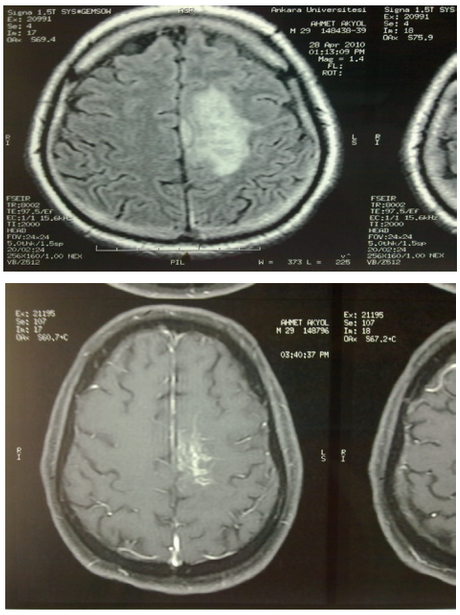

Figure 2. Magnetic resonance imaging

frequently for synergy. Vancomycin and trimethoprim-sulfamethoxazole could be alternative to ampicillin. Delayed treatment is associated with bad prognosis. The mortality and sequelae rates were reported as 35% and 55% in a review, respectively.[9] We started the treatment of the patient empirically in about 3 hours after admission to emergency department. Since the patient was immune suppressive because of steroid treatment, we added ampicillin to the empirical treatment. When the blood and CSF cultures yielded *L. monocytogenes*, gentamicin was added to the treatment. Because of the hepatotoxicity, the treatment was switched to vancomycin and trimethoprim-sulfamethoxazole. According to the guidelines, first choice of the treatment is ampicillin and gentamicin. The alternative treatment is trimethoprim-sulfamethoxazole or meropenem.[12] The therapy was continued for 6 weeks, and no sequelaes were observed.

Our patient had also a concurrent infection with CMV. Reactivation of human CMV infection appears to have a significant role in promoting the risk for secondary opportunistic infections, because CMV infection is associated with virus mediated suppression of T lymphocyte-dependent immune responses.[10,13] However; the association between CMV infection and subsequent *Listeria* infection was rarely reported. Safdar et al. assessed six patients with systemic *L. monocytogenes* infection at Bone Marrow Transplantation Unit and a concurrent primary opportunistic infection was present in five individuals (83.3%) and four (80%) were being treated for acute human CMV viremia.[10]

In summary, we report the case of *Listeria* meningoencephalitis and CMV hepatitis in a patient undergoing corticosteroid therapy without concomitant another immunosupressive therapy for polymyositis. To our knowledge, this is the first case of *Listeria* meningoencephalitis concurrent with CMV hepatitis reported from our country. High index of suspicion is necessary for more than one opportunistic infection in patients treated with corticosteroids and adverse drug reactions should be closely observed.

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