

HIV pozitif olguda *Listeria*. *monocytogenes* infeksiyonu

Doç. Dr. Elif Tükenmez Tigen

Sene 1997-2000

- 41 yaş, ♂
- 1997→ HIV tanısı (20 yaş)
- HIV RNA: 140.000 kopy/mL, CD4: 100 (%10.7)
- 2000→ Pulmoner ve ekstrapulmoner TBC
- 20 ay anti-TBC
- ART→Epivir (lamivudin), retrovir (zidovudin), crixivan(indinavir),

Sene 2002-2006

- 2002→ Combivir+viramune
- 2006→ HT (170-180/105-117 mmHg)
- Renal doppler N
- Kreatinin: 1.21 TİT proteinüri var. HT'e sekonder
- Kinetra (karvedilol), exforge (amlodipin valsartan)

Sene 2013....

- 2013 → Kreatinin 1.54
- Takip HIV RNA: 67-200 kopy/mL
- Kreatin yüksekliği ve HIV RNA parsiyel supresyon → NRTI' siz rejim
- 2013 → Prezista 2x600, norvir 2x100, ısentress 2x400
- Takipte HIV RNA:125 → 3TC (epivir ile güçlendirme (300 mg/gün)

Kasım 2015

- Görme bulanıklığı baş ağrısı, karın ağrısı
- Kelimeleri söylemekte zorluk, davranış bozukluğu, (kazağını ters giyinme, inatlaşma), ellerde uyuşma ağızda yamulma, unutkanlık yakınmaları
- İnfeks. Hast. Ve Klin. Mikr. Klin →Yatış
 - Bilinç uykuya meyilli
 - Gözdibi N
 - BOS açılış basıncı 19 cm su, berrak, 376 RBC, 23 WBC (%89 lenfosit) gram boyamada nadir lökosit mo yok

Laboratuvar

- WBC: 10.500/ μ L
- Hbg: 13.7 g/dL
- MCV: 100 fL
- PLT: 242.000
- BUN: 26 mg/dL, kreatinin: 1.32 mg/dL
- AST:21 U/L, ALT:26 U/L, ALP: 67 U/L
- CD4:%15 CD4:450
- HIV RNA: Negatif.

Kasım 2015

- EEG normal
- Kanda TPHA negatif
- BOS enterovirus, CMV negatif
- VZV ensefaliti ???→VZV Ig G pozitif asiklovir 3x10 mg/kg başlandı
- HIV'e sekonder vaskülopati??
 - Kraniyal ve servikal MR ve MR anjiyografi planlandı.
- Kraniyal MR patoloji Ø
 - MR anjiyoda→Bilateral internal karotid arterlerde belirgin daralma!!!

Asıl Neden Neydi???



- Takipte bilinci tamamen düzeldi
- Ekolali ve hareket bozuklukları geriledi
- Hastanın sonradan hatırladığı bir madde kullanımı olduğu ortaya çıktı
- Amsterdam poppers
- Son 4-5 aydır almakta imiş hatta miktarını da giderek arttırmış.
- Klinik kötüleşmeden 1 gün önce de yüksek düzeyde aldığı öğrenildi
- Amsterdam poppers indüklediği stroke ???

Amsterdam Poppers

- Amsterdam poppers etkileri →
 - Vaskülaopati
 - Beyin parankim hasarı
 - Geçici hareket bozuklukları
 - Amnezi
- Konvansiyonel serebral anjiyo →
 - Her iki servikal segmentinde petroz kemiğe girdiği düzeye kadar
 - en belirgin yerinde sağ İCA 'da % 70 sol İCA'da % 65 darlık .
 - **Vaskülit** ??? dışlanamadı.
 - Pulse prednol 3 gün 1 gram
 - 1 mg/kg idameye geçildi
 - CD4 : 1104 HIV RNA 42 bulundu
 - Genel durum düzelerek taburcu edildi.



Ocak 2016

- 2 ay sonra
- Ateş ,üşüme, titreme, halsizlik, ishal (4 kez /gün)
- Lab→WBC : **11400**,
 - Neut: 10400,
 - **Hgb:9.4**,
 - Plt: **76.000**,
 - AST 42, ALT: 56,
 - **CRP: 283**, prokals: 1.2,
 - Alb: 2.18,
 - **BUN: 48**, kreat: 1.25
 - pH: **7.17**, Laktat: 4.6
 - **TİT: Hgb +, glukoz ++, protein+**

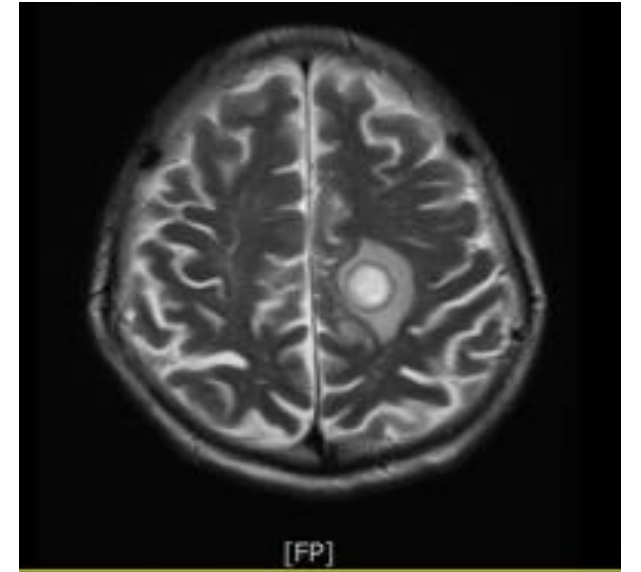
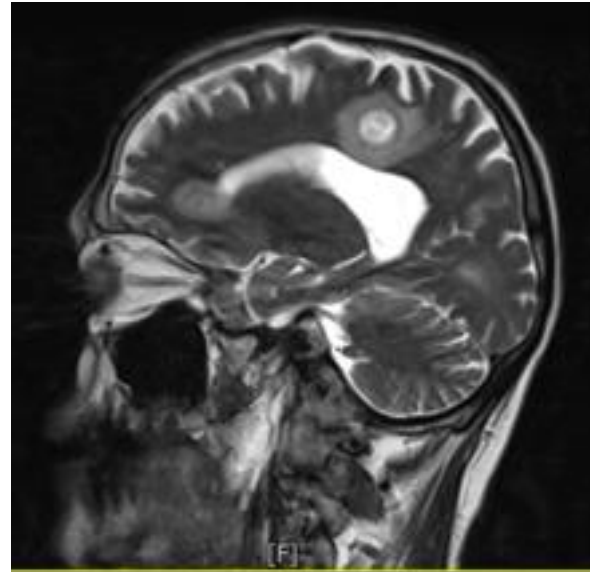
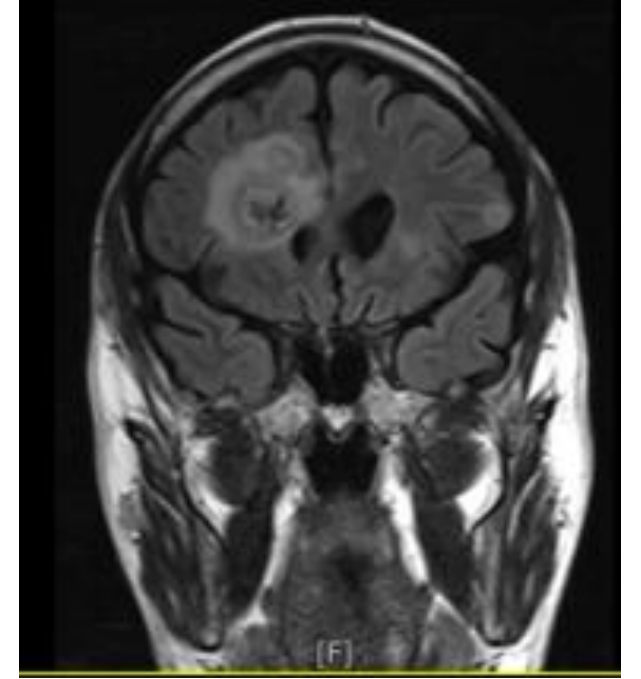
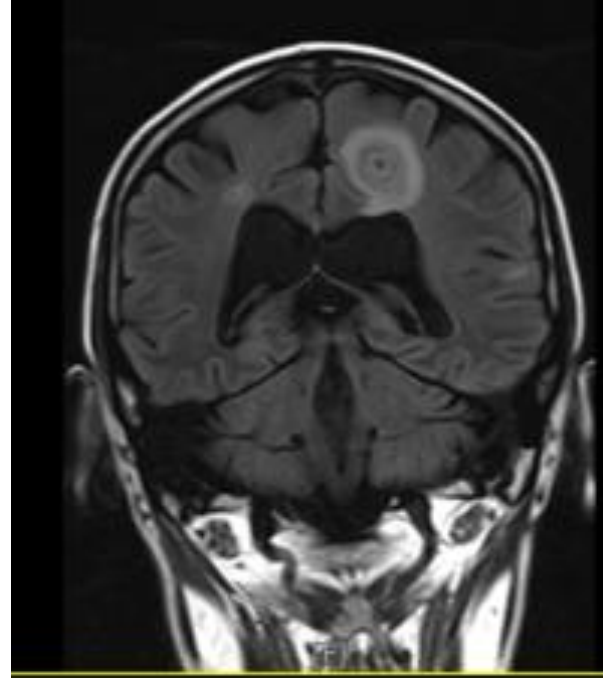
Ocak 2016

- Sepsis !!!→ Sefepim
 - Kan kx→ Gr (+) pozitif basil
 - *Listeria monocytogenesis*
 - Tedavi→Ampisilin 12 gr
 - Prednisolon 1x8 mg'a düşüldü.
 - Plt:66.000, Hgb: 8.4 gr/dL
 - AST/ALT: 57/149
 - prokals : 1.24
 - Tedavi sonrası düzelme
- } İnfeksiyona sekonder

- Ateş, solunum sıkıntısı, bilinç bulanıklığı
- TBC reakt?? Listeria absesi??
- Kraniyal MR
- Toraks BT

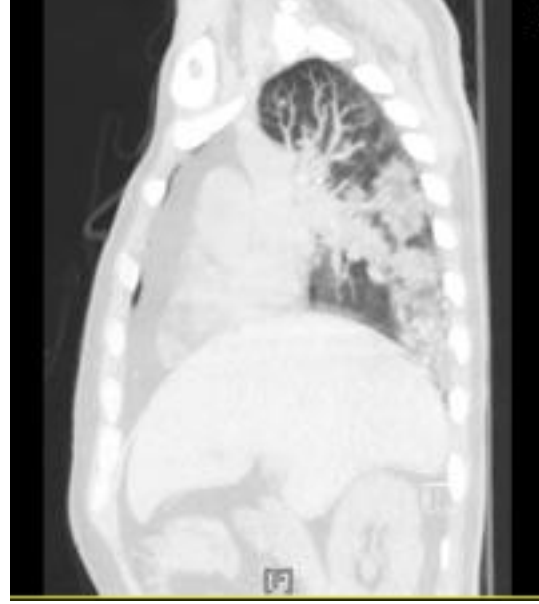
Kraniyal MR

- Bilateral tüm beyin parankiminde
- sağ serebellumda
- en büyüğü sağda frontal lobda aksiyal kesitte 28x25 mm kontrast tutan difüzyonda kısıtlanma gösteren lezyonlar
- ön planda toxo? Abse?



Akciğer BT

- Sağ akc üst lob posterior segmentte
- Bilateral akciğer alt lob superior segmentte
- sağ akc bazalde buzlu camın eşlik ettiği nodüler konsalide alanlar.



- Genta 3x80 mg başlandı
- Uyku hali derinleşti
- Ağrılı ve sesli uyarana cevap vermedi.
- Ta: 104/60 mmHg, SO2:75, SS:30, Nbz:134, GKS:8'e geriledi.
- 10 lt/dak O2
- →YBÜ→Exitus



**NATIONAL INSTITUTE FOR
COMMUNICABLE DISEASES**

Division of the National Health Laboratory Service

5 DECEMBER 2017

OUTBREAK RESPONSE,

DIVISION OF PUBLIC HEALTH SURVEILLANCE AND RESPONSE

CENTRE FOR ENTERIC DISEASES

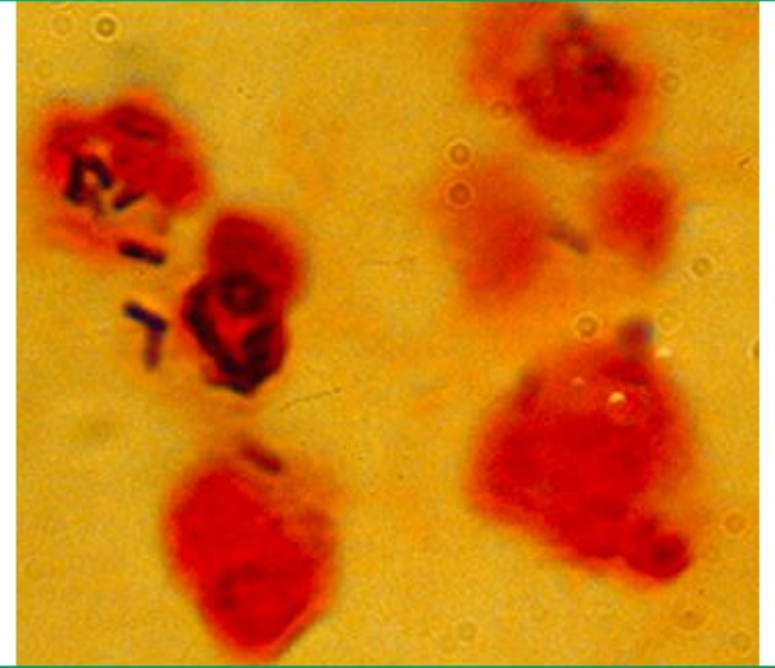
CONTRIBUTING PHYSICIANS

Listeriosis:

**Clinical recommendations for
diagnosis and treatment**

Listeria monocytogenes

- Gram (+) basil
- Fakültatif intraselüler bakteri
- Kontamine gıdalardan bulaş
- Klinik;
 - Febril gastroenterit
 - SSS infeksiyonu (~inkübasyon 10 gün)
 - Bakteriyemi/Sepsis
 - Gebelik ve infeksiyon
- Yenidoğanlar, immunkompramize hastalar, yaşlılar, ve gebeler





- Güney Afrika'da 2. en sık akut bakteriyel menenjit etkeni
- Kültür pozitif olguların %33'den azında, BOS'da gr(+) basil görülmüştür.
- Bu nedenle gram boyama dışlamak için yeterli değildir.
- Beyin sapı ve kafa çiftleri tutulumu ile seyreden rombensefalit olgularında BOS kültürü negatif olabilir.
- PCR Listeria tanısında sensitif ve spesifik

Tanı

- Klinisyen şüphe ettiğinde lab ile iletişime geçmeli
- Kan kültürü,
- Gram boyamada yakalama olasılığı düşüktür.
- 10 üzeri 3 organizma/mL eşik değeri ile PCR çalışmaktadır

Diagnosis of *Listeria monocytogenes* Meningoencephalitis by Real-Time PCR for the *hly* Gene^{▽§}

Alban Le Monnier,^{1,2†*} Eric Abachin,¹ Jean-Luc Beretti,¹ Patrick Berche,¹ and Samer Kayal^{1‡}

Listeria monocytogenes is a bacterial pathogen that can invade the central nervous system (CNS), causing meningoencephalitis and brain abscesses. The diagnosis of CNS listeriosis is often difficult based on the isolation of the bacteria in the cerebrospinal fluid (CSF) because of the low number of bacteria in the CSF. To improve the diagnosis, we have developed a real-time PCR assay for detecting and quantifying *L. monocytogenes* in CSF. The designed primers specifically amplify the *L. monocytogenes* *hly* gene, which encodes a pore-forming cytolysin. The PCR assay for the *hly* gene (PCR-*hly*) was evaluated for its sensitivity over a wide dynamic range of concentrations and was highly sensitive for the detection of *L. monocytogenes* in CSF. By assaying a large panel of bacterial species, including species that are not known to cause CNS infection, we determined the specificity of the PCR-*hly*, which exclusively detects *L. monocytogenes*. We analyzed 214 CSF samples from patients suspected of having CNS listeriosis. The results showed that 10 patients in which *L. monocytogenes* was isolated by culture. Positive PCR-*hly* results were obtained for all 10 patients. In addition, 10 patients of CNS listeriosis for which bacterial cultures were negative presumably due to previous treatment with antibiotics. As a complement to classical bacteriological CSF culture, our designed real-time PCR-*hly* assay proved to be valuable by enhancing the rapidity and the accuracy of the diagnosis of CNS infection by *L. monocytogenes*. In addition, the quantitative results provided may, in some instances, be useful for the follow-up of patients under treatment.

- Kx pozitif olan tüm olgularda PCR pozitif.
- Klinik şüpheli olgularda da (+)

Gastroenterit

- Asemptomatik taşıyıcılık
- İnk periyodu 1-10 gün arasında
- Semptomlar 1-3 gün → 1 haftaya kadar değişir.
- Yaşlı ve çocuklarda gastroenterit kliniği ile yatış sıklığı.
- Salgın durumlarında GIS semptomu olmadan flue like illness kliniği ile de başvurabilir hastalar
- Kolonizasyon veya geçici taşıyıcılık sağlıklı bireylerde %1-5 arasında

1.Grif K, Hein I, Wagner M, et al. Wiener klinische Wochenschrift. 2001

2.Grif K, Eur J Clin Microbiol Infect Dis. 2003

Bakteriyemi

- Bakteriyemi sıklıkla gastroenteriti takiben meydana gelir
- İzole bakteriyemi; HIV pozitif bireylerde steroid kullanımı, malignite, KT ve >65 yaş olma ile ilişkilendirilmiştir.

SSS tutulumu

- SSS de tutulum → menenjit, ensefalit, rombensefalit, beyin absesi şeklinde olur
- SSS tutulumlu listeri inkübasyon peryodu 0-21 gün, ortalama 10 gündür.

Targeting of the central nervous system by *Listeria monocytogenes*

Olivier Disson^{1,2} and Marc Lecuit^{1,2,3,*}

- Menenjit %70-97
- Meningoensefalit %70-97
- Rombensefalit
- Beyin absesi %10
- Patogenez→
 - Retrograt nöral yolla oral epitelden
 - Bakteriyemi sonrası Kan beyin bariyerinden
- Inkübasyon periyodu 0-21 gün

Case report

Two cases of listeria rhombencephalitis

Christopher Thomas Mansbridge^{a,*}, Irina Grecu^a, Jimmy SW Li Voon Chong^a, Clive Vandervelde^a, Kordo Saeed^{a,b}

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A B S T R A C T

Listeria rhombencephalitis (LRE) is a rare encephalitis of the hindbrain that can present with a variety of neurological symptoms. It is a diagnostic challenge, but prompt antimicrobial therapy is important to prevent high rates of mortality and morbidity. We report two cases of LRE, with several contrasting clinical features and different disease courses. Despite being rare, it is important to consider listeria in patients with possible meningoencephalitis, even if cultures are negative. Empirical treatment of meningoencephalitis should provide coverage for listeria, especially if the patient is at risk of listeriosis or there is a potential history of listeria exposure.

Tedavi

- İntrinsik olarak PBP olmaması nedeni ile *L. monocytogenes* sefalosporinlere dirençlidir.
- Penisilin, ampisilin, imipenem, gentamisin makrolid, kotrimaksozol ve cipro ya invitro duyarlılık vardır.
- Klinik tecrübeler çoğunlukla ampisilin ile olmuştur.
- Kılavuzlar HIV ile infekte olmanın ampisilin başlanması için endikasyon olmadığını söylemektedir.

Table 3. In vitro activity and CSF penetration of selected antibiotics active against *Listeria*^{33,39}

Antibiotic	MIC range	Comments	CSF penetration (CSF: blood ratio, %) ³⁹
Ampicillin	0.06-0.5 (susceptible)	Bacteriostatic <i>in vitro</i>	13-14%
Gentamicin	0.06-4 (susceptible)	Bactericidal <i>in vitro</i>	0-30%
Rifampicin	0.04-0.25 (susceptible)	Bacteriostatic <i>in vitro</i>	7-56%
Co-trimoxazole	0.06-0.5 (susceptible)	Bactericidal <i>in vitro</i>	<41%

Tedavi

- 1. seçenek→Ampisilin
- Gentamisin sinerji için eklenebilir
- Penisilin alerjisi halinde TMP-SMX
- Dekzametazon kullanımını destekleyen veri yok

- Ampisilin aslında→

- Ampisilin bakteriyostatik
- BOS penetrasyonu da düşük <%15
- Düşük intraselüler konsantrasyon
- İn vitro olarak ampisilin listerolizin ve beta-galaktozidaz denen önemli bir virülans faktörü inhibe etmektedir. Bu yolla organizmanın hücre aracılı yıkımı sağlanmakta ve kür kolaylaşmaktadır.

Prognoz

- SSS tutulumu varsa tedavisiz mortal seyreder
- > %70 erken tedavi ile iyi seyir
- %61 kalıcı nörolojik sekel

Listeria monocytogenes Infection and Serotype Distribution Among HIV-Infected Persons in Los Angeles County, 1985-1992

*Donnell P. Ewert, †Loren Lieb, ‡Peggy S. Hayes, ‡Michael W. Reeves, and
*Laurene Mascola

- Genelde listeria enfeksiyonları asemptomatik seyrederek
- Hücresel immunitesi zayıf olan bireylerde SSS enfeksiyonu, sepsis, bakteriyemi yapar
- 1985-1992 AIDS ve tüm HIV pozitif bireyler arasında Los Angeles listeria vakaları 95.8 ve 8.8 olgu/100.000 hasta yılı iken total popülasyona bakıldığında 1 olgu/100.000 hasta yılı

TABLE 2. *Rates of listeriosis among persons with acquired immune deficiency syndrome (AIDS), all human immunodeficiency virus (HIV)-infected persons, and in the total population, Los Angeles County, 1985–1992*

Group	Person-years of observation	No. of listeriosis cases	Rate ^a
Persons with AIDS	26,102	25	95.8
All HIV-infected persons			
Lowest plausible estimate	371,459	34	9.2
Best plausible estimate	384,849	34	8.8
Highest plausible estimate	404,806	34	8.4
Total population	63,320,656	652	1.0

^a Per 100,000 person-years.

Tedavi

- Gentamisin ve ampisilin sinerjik etkili
- Mortalite üzerine etkisi net değil!!!
- Gentamisin BOS geçişi zayıf ve toksik
- İntraselüler konsantrasyon yüksek ama lizozom içindeki pH'da inaktif forma dönüşür.

Tedavi

- 4 çalışma; 3 retrospektif 1 prospektif ampisilin mono terapive kombinasyon tedavilerini karşılaştırmışlar
 - Mitja et al. 102 vaka amp. tek/kombine (%4.3-11.8 p: 0.003)
 - Genta komb erken mortaliteyi OR: 3.9 artırmakta
 - Thonnings et al. 229 hasta Danimarka komb daha iyi. Fakat yaşlı genç ve yenidoğan ayrımı yok
 - Arslan et al. 100 hasta fark yok
 - Charlier et al. MONALISA prospektif çalışmada 3 aylık mortalite üzerine komb tedavisi koruyucu etkili.

Tedavi

- Gentamisin eklenmesi hasta bireyinde değerlendirilmeli
- Yaş, renal faktörler
- Bakteriyemi ve menenjit olgularında tedavi süresi 21 gün olmalı
- Beyin absesi, rhombensefalit 4-6 hafta

Targeting of the central nervous system by *Listeria monocytogenes*

Olivier Disson^{1,2} and Marc Lecuit^{1,2,3,*}

- Avrupa 2009 1645 vaka, 4 vaka/milyon mortalite %16.6
- Amerika 2500 vaka/her yıl, mortalite %30 uygun tedaviye rağmen

Listeria monocytogenes-associated respiratory infections: a study of 38 consecutive cases.

Morgand M¹, Leclercq A², Maury MM², Bracq-Dieye H², Thouvenot P², Vales G², Lecuit M³, Charlier C⁴.

OBJECTIVES: *Listeria monocytogenes* (*Lm*) causes various infections including meningitis, encephalitis, neurolisteriosis, maternal-fetal and focal infections.

METHODS: Retrospective study of culture-confirmed *Lm* infections at the French Reference Center for *Listeria* from January 1993 to December 2016.

RESULTS: Thirty-eight consecutive patients were included. Median age was 72 (range 29-90). Two patients had an immunosuppressive condition (97 %), with 15 patients on immunosuppressive therapy and 50% (19/38) had a pre-existing pulmonary disease. Antibiotic therapy was initiated in all patients. Thoracic drainage was performed in 7/19 (37%) patients. In-hospital mortality reached 35%. At 2-year follow-up, recurrence of empyema (time interval of 1 week to 1 month after treatment completion) was observed in 4 patients. In total, only 10 patients diagnosed with *Lm*-respiratory infection (42%) experienced uneventful outcome at 2-year follow-up.

CONCLUSION: *Lm* is a rare but severe cause of pneumonia and pleural infection in older immunocompromised patients, requiring prompt diagnosis, adequate management and follow-up.

- 1993-2016 38 vaka listeria pnömoni
- 2 vaka nörolisteriosis
- %97 immunsupresif kullanımı
- %75 inceden pulmoner infeksi var
- Hastane içi mortalite %35

Listeria monocytogenes meningitis: an uncommon opportunistic infection in HIV/AIDS.

Patil AB¹, Nadiger S, Chandrasekhar MR, Halesh LH, Kumar M.

⊕ Author information

Abstract

OBJECTIVE: To report an interesting case of meningitis caused by *Listeria monocytogenes* in an HIV seropositive individual.

MATERIALS & METHODS: A previously healthy 45 years old HIV seropositive man, presented with atypical clinical features of meningitis. Blood and Cerebrospinal fluid (CSF) were obtained for biochemical and microbiological investigations.

RESULTS: CSF analysis showed pleocytosis with lymphocytic predominance. Gram stain of CSF was negative; however culture yielded growth of gram positive bacilli with tumbling motility. Based on relevant biochemical tests the isolate was identified as *Listeria monocytogenes*. Patient was treated with i.v. ampicillin and recovered completely.

CONCLUSION: Listeriosis is relatively rare in HIV/AIDS among the immunodeficient populations. Atypical clinical and laboratory findings make the diagnosis difficult and these infections may go undiagnosed. Since it is easily treated with readily available antibiotics, it is important to diagnose them at the earliest and thereby prevent treatment failure.

HIV/AIDS
olgularında *Listeria*
infeksiyonu nadirdir

CASE REPORT

Listeria monocytogenes Bacteremia and Meningitis
in HIV-Infected Patients

Report of 2 Cases and Review of Literature

Valentyna Goloborodko, MD, Anca Georgescu, MD,*† George Psevdos, Jr, MD,†‡
Darren Buonocore, MD,§ and Victoria Sharp, MD‡*

Abstract: *Listeria monocytogenes* is the causative agent of listeriosis, a potentially fatal food-borne infection in humans. Listeriosis is an infrequent disease in HIV-infected patients. In the pre–highly active antiretroviral therapy era, however, patients with AIDS had a 145 times increased risk for invasive listeriosis compared with the general population. Cases of listeriosis continue to be reported in HIV-infected patients. We report a case of an African man living in New York who presented with febrile illness and *L. monocytogenes* bacteremia. The Gram stain from blood cultures showed diphtheroid-like organisms, which were considered contaminants. He received vancomycin and quickly defervesced. The blood culture isolates were finalized as *L. monocytogenes*. The second report is of an African American woman. She was not in medical care and had a very low CD4⁺ T-cell count. She presented with *L. monocytogenes* bacteremia and meningitis and died despite appropriate therapy.

Pre ART döneminde
AIDS olgularında 145
kat listeriyosis riski
varken ART ile bu risk
azalmıştır.

Bacterial Meningitis in HIV-1–Infected Patients in the Highly Active Antiretroviral

Era of

Background: The burden that spontaneous bacterial meningitis (SBM) currently represents among HIV-1–infected patients is poorly known.

Methods: We prospectively evaluated 32 episodes of SBM in HIV-1–infected patients from the VACH (VIH-Aplicación de Control Hospitalario) Cohort and compared findings with those of 267 episodes in uninfected persons, matched by age and year of infection. A group of 13,187 HIV-1–infected patients from the VACH Cohort were used to identify predictors for acquiring SBM.

Results: Between 1997 and 2006, we found 32 episodes of SBM among HIV-1–infected patients for an annual incidence rate of 62.0 cases per 100,000 population compared with 3.2 (3.0 to 3.4) per 100,000 population for uninfected patients ($P < 0.001$). The last CD4 $\geq 200/\text{mm}^3$ count was the only predictor for developing SBM. Compared with uninfected, HIV-1–infected patients with SBM had a greater prevalence of primary extrameningeal infection, especially pneumonia ($P = 0.02$), bacteremia ($P = 0.02$), focal neurologic signs ($P = 0.005$), seizures ($P = 0.06$), a lower cerebrospinal fluid to blood glucose ratio ($P = 0.02$), and a lower prevalence of nuchal rigidity ($P = 0.005$). *Streptococcus pneumoniae* was the most frequent etiologic agent among HIV-1–infected patients. HIV-1–infected patients had neurologic complications more frequently ($P = 0.02$), a higher overall case fatality rate ($P = 0.004$), and greater incidence of neurologic sequelae ($P = 0.001$).

1997-2006
300 SBM olgusu 32 HIV pozitif .
Listeria menenjitisi %9 sıklıkla
görülmiüş.

Causative microorganisms (%)		
<i>Streptococcus pneumoniae</i>	15 (46.9)	48 (18.0)
<i>Neisseria meningitidis</i>	2 (6.2)	146 (54.7)
<i>Listeria monocytogenes</i>	3 (9.4)	9 (3.4)
<i>Staphylococcus aureus</i>	2 (6.2)	2 (0.7)
<i>Escherichia coli</i>	1 (3.1)	0 (0)
<i>Pseudomonas aeruginosa</i>	1 (3.1)	1 (0.3)
<i>Haemophilus influenzae</i>	1 (3.1)	6 (2.2)

Bu Hasta Bize Ne Anlattı??

- HIV ve Listeria İnfeksiyonu sık değil ama...
- Ateş ve ishali olan immunsupresif bir hastada mutlaka düşünülmeli
- Nadir olmakla beraber pulmoner tutulum yapar
- Sadece menenjit değil, rombensefalit ve beyin abseleri yapar
- BOS kx ve gr boyama tanıda geri planda
- PCR istenebilir
- SSS tutulumu prognozu kötüdür

Teşekkürler