

Kronik MSS İnfeksiyonlarının Tanısında Neredeyiz?

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İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği

11.03.2022

Merkezi Sinir Sistemi İnfeksiyonları

Bakteriler

Virüsler

Mantarlar

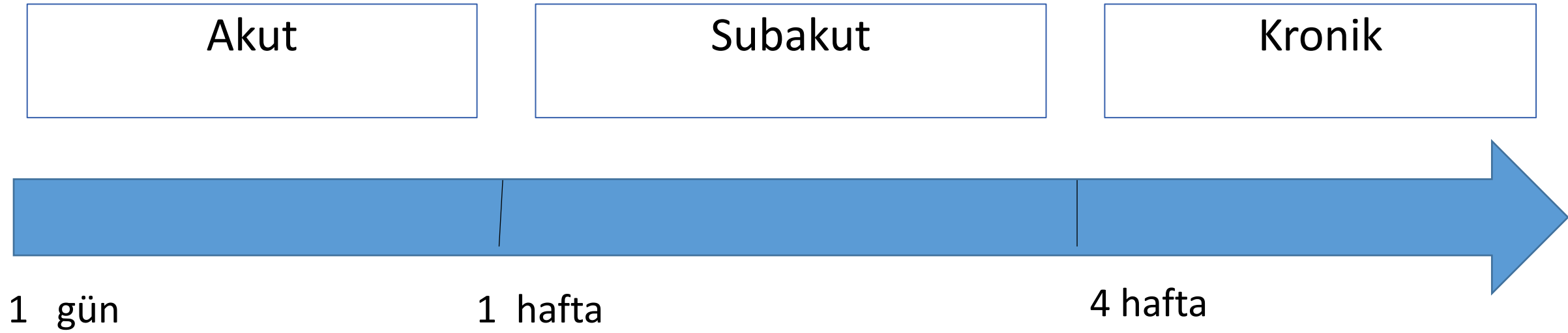


Helmintler

Protozoalar

Beyin omurilik sıvısındaki (BOS) inflamasyon aynı anda beyni, kranial sinirleri, spinal kordu ve sinir köklerini etkileyebilir.

Kronik menenjit, klinik semptomlar ile birlikte en az bir aydır devam eden BOS'ta inflamasyon



Öncelikle detaylı anamnez !

- ❖ Şikayetlerinin süresi
- ❖ Sistemik semptomların eşlik edip etmediği
- ❖ Seyahat öyküsü
- ❖ Maruziyet (Hayvan, toksin, riskli gıda)
- ❖ İntravenöz ilaç kullanımı
- ❖ Tüberkülozlu hasta ile temas, tüberküloz geçirmiş olma
- ❖ Kullandığı ilaçlar (Non steroid anti-inflamatuvarlar, IVIG ?)
- ❖ Hastanın immunitesi, immunizasyon öyküsü

Şikayetleri

- Sürekli devam eden ve giderek artan baş ağrısı
- Letarji, mental durum değişikliği
- Ateş yüksekliği
- İşitmede azalma
- Görme bozukluğu
- Konvülziyon
- Kognitif bozulma, hızla ilerleyen demans tablosu



Fizik muayene

- Uzak veya yakın hafıza kaybı
- Konfüzyon
- Apati
- Kraniyel sinir felçleri

- Ense sertliği
- Üst motor nöron bulguları
- ✓ Derin tendon reflekslerinde artış
- ✓ Ayak bileği klonusu
- ✓ Babinski pozitifliği

Fizik muayene normal olabilir

❖ Üveit, lenfadenopati, akciğer tutulumu

❖ Sarkoidoz

❖ Üveit, vitiligo, alopesi, sağırılık

❖ Vogt-Koyanaga-Harada

❖ Tekrarlayan genital / oral ülser
veya retinal lezyonlar

❖ Behçet hastalığı

❖ Sterid enjeksiyonları, sırt ağrısı

❖ Fungal menenjit

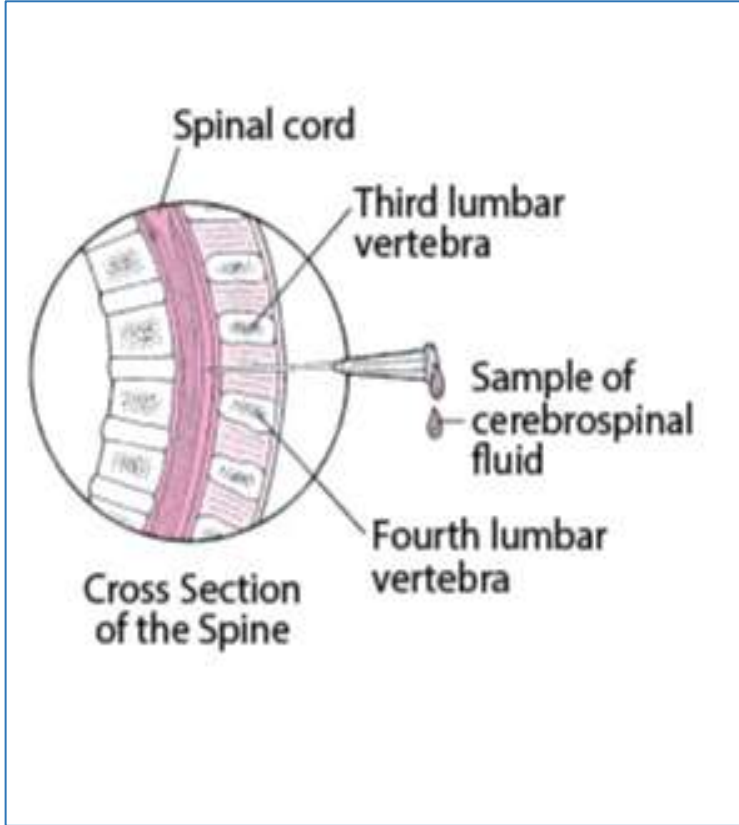
Kronik menenjit yapan nedenler

<u>İmmünkompeten hasta</u>	<u>Nötropeni</u>	<u>B lenfosit fonksiyonunda bozulma</u>	<u>T lenfosit fonksiyonunda bozulma</u>
<i>T. pallidum</i> <i>B. burgdorferi</i> <i>M. tuberculosis</i> <i>Bartonella</i> <i>C. neoformans</i> <i>C. gatii</i> <i>H. capsulatum</i> <i>C. immitis</i> <i>B. dermatitidis</i> <i>C. albicans</i> HIV VZV HSV-2 (Mollaret) <u>Batı Nil virüsü</u>	<i>A. fumigatus</i> <i>C. albicans</i> Mucorales CMV HSV VZV HHV 6,7 <u>Astrovirüs</u> <u>Batı Nil virüsü</u>	<u>Leptospiroz</u> <u>C. albicans</u> CMV HSV VZV JC virüs EBV HHV 6,7 <u>Astrovirüs</u>	<i>L. monocytogenes</i> <i>N. asteroides</i> <i>T. pallidum</i> <i>M. tuberculosis</i> Mucorales <i>C. neoformans</i> <i>H. capsulatum</i> <i>C. immitis</i> <i>B. dermatitidis</i> <i>A. fumigatus</i> CMV HSV, VZV JC virüs EBV HHV 6,7 <u>Astrovirüs</u> Neoplasm <u>Lenfoma</u>
<u>İnfeksiyon dışı nedenler</u> Lenfoma Leptomeningeal <u>karsinomatosis</u> <u>Paraneoplastik tutulum</u> <u>Sarkoidoz</u> <u>Sjogren sendromu</u> <u>Sistemik lupus eritematozus</u> <u>Behçet hastalığı</u> <u>Primer angitis</u>			

TANI

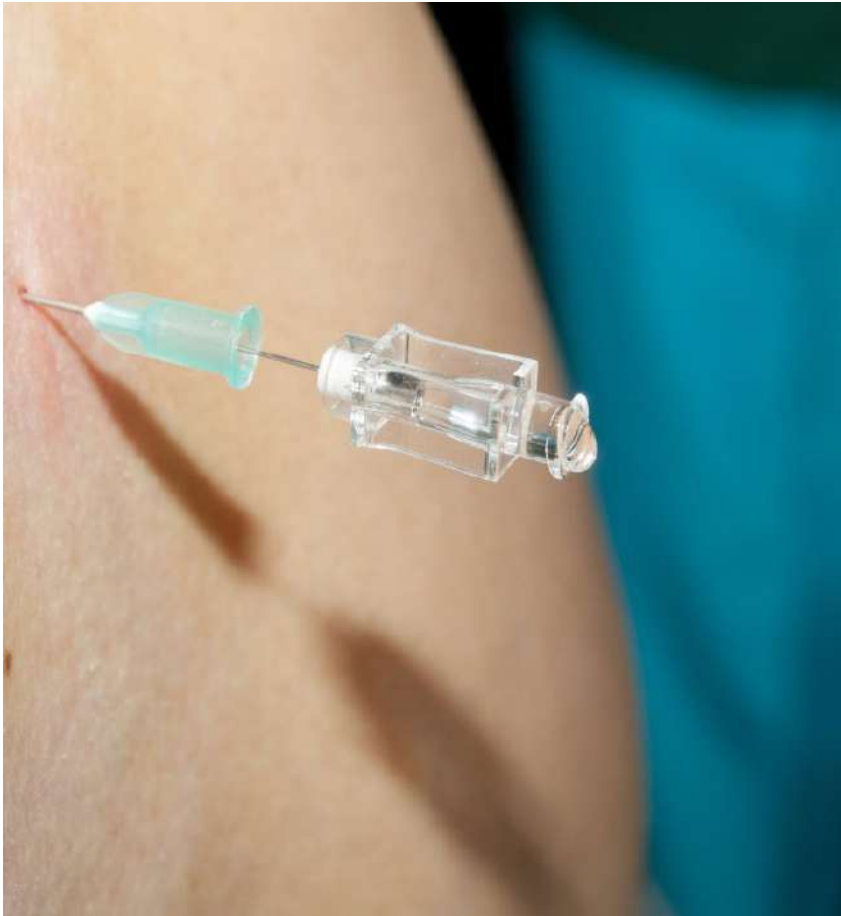
- BOS ve kanda incelemeler
 - ✓Kültür
 - ✓Serolojik testler
 - ✓Moleküler testler
- Görüntüleme yöntemleri
- Deri veya lenf nodu biyopsisi, patolojik incelemeler

BOS incelemesi



- ❖ Hücre sayısı ve tipi (eozinofil?), protein, glukoz
- ❖ Gram boyama
- ❖ ARB, VDRL, FTA-ABS
- ❖ Brusella aglütinasyonu
- ❖ Çini mürekkebi incelemesi, kriptokok antijen testi
- ❖ Serolojik testler (lyme, mantar)
- ❖ Lyme için antikor indeksi

BOS incelemesi



- ❖ PCR (*M.tuberculosis*, *T. whipplei* , enterovirus, aspergillus)
- ❖ Beta-D-Glukan (kandida), galaktomannan
- ❖ Kültür (Bakteriyel, fungal, tüberküloz)
- ❖ Metagenomik analiz
- ❖ Sitolojik inceleme

BOS incelemesinde genelde beklenen lenfosit hakimiyeti

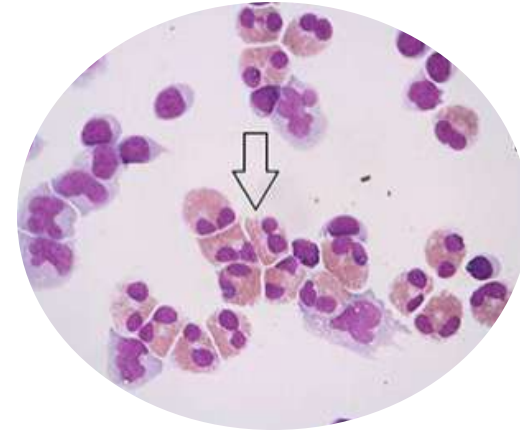
BOS'ta ntrofilik pleositoz

- Tberkloz, bruselloz
- Nokardiyoz, aktinomies
- Zigomies, kandidiyaz
- Koksidioidomikoz, aspergilloz
- SLE
- Kimyasal veya ilalarla ilikili menenjit



BOS'ta eozinofilik pleositoz

- Koksidioidomikoz
- *A. cantonensis*
- Sistiserkoz
- Şistozomiyaz
- Lenfoma
- İlaçlar (NSAİ, siprofloksasin, trimetoprim-sulfametoksazol, intraventriküler gentamisin, vankomisin uygulaması)



Serum

- VDRL/TPHA
- Anti-HIV
- Brusella aglütinasyonu
- Brusella ELISA
- *B. burgdorferi* ELISA
- Toxoplasma ELISA
- Galaktomannan
- ENA, ANCA, CCP antikoru



- Kan kültürü





Akciğer görüntülemesi

- ❖ Lenfadenopati
- ❖ Kavitasyon
- ❖ Neoplazm

- ❖ Tüm vücut PET incelemesi
- ❖ PPD deri testi
- ❖ IGRA

Tomografi

- Hidrosefali
- Lomber ponksiyon öncesi kitle lezyonu

saptayabilir

*Kronik menenjit yapan etkeni belirlemede yetersiz

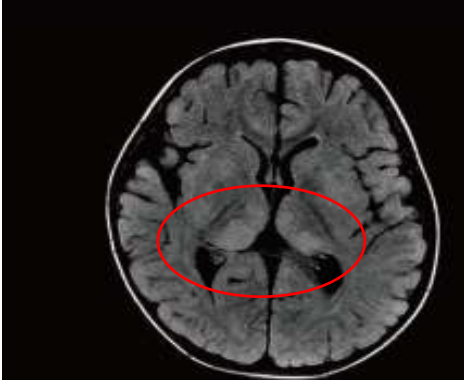


Kontrastlı BT'de kriptokokkoma

Beyaz cevherde tutulum

MRI

Viral (CMV, EBV, VZV, PML)

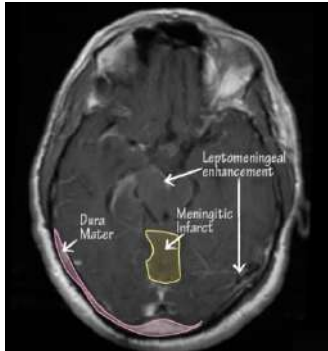


Epstein-Barr virus ensefaliti

Jang YY et al. Korean J Pediatr 2011 54(9): 389–393.

Meningeal tutulum

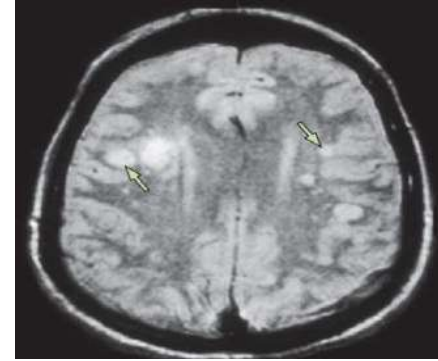
Bakteriyel, fungal, otoimmün, neoplastik



<https://www.drawittoknowit.com/course/neuroanatomy/glossary/immunology-microbiology/meningitis-cryptococcal>

İnme ve vasküler bulgular

Mantar (Aspergillus, Cryptococcus, Mucor)
Varicella zoster



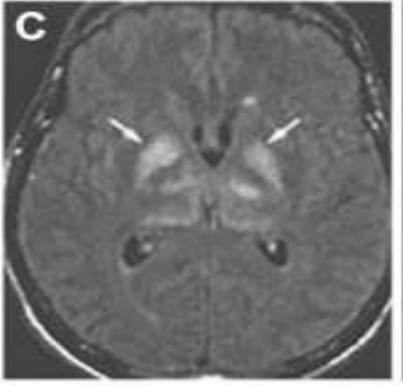
VZV vaskülopatisi

Gilden D et al. Lancet Neurol. 2009 August ; 8(8): 731.

Thakur KT et al. Continuum (Minneap Minn). 2018 ; 1298–132

Beyin sapi tutulum

Listeria, varicella, PML, WNV



WNL ensefaliti

Bailet C et al. Radiology Case Reports .15(11):2422-2426

Kitle lezyon

Bakteri (nocardia, tüberküloz), kriptokokkoma
Tokso plazmoz, lenfoma

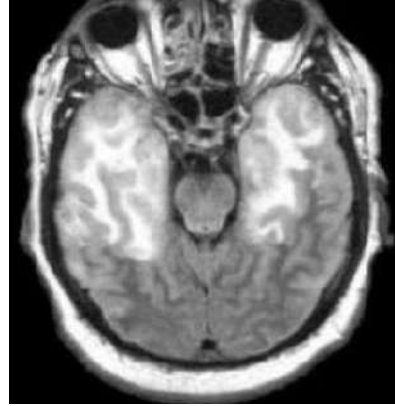


Nocardia farcinica

Kim S. et al. Infect Chemother 2014 Mar; 46(1):45-49

Bitemporal tutulum

HSV, paraneoplastik



HSV ensefaliti

<https://case.edu/med/neurology/NR/hsvsummary3.htm>

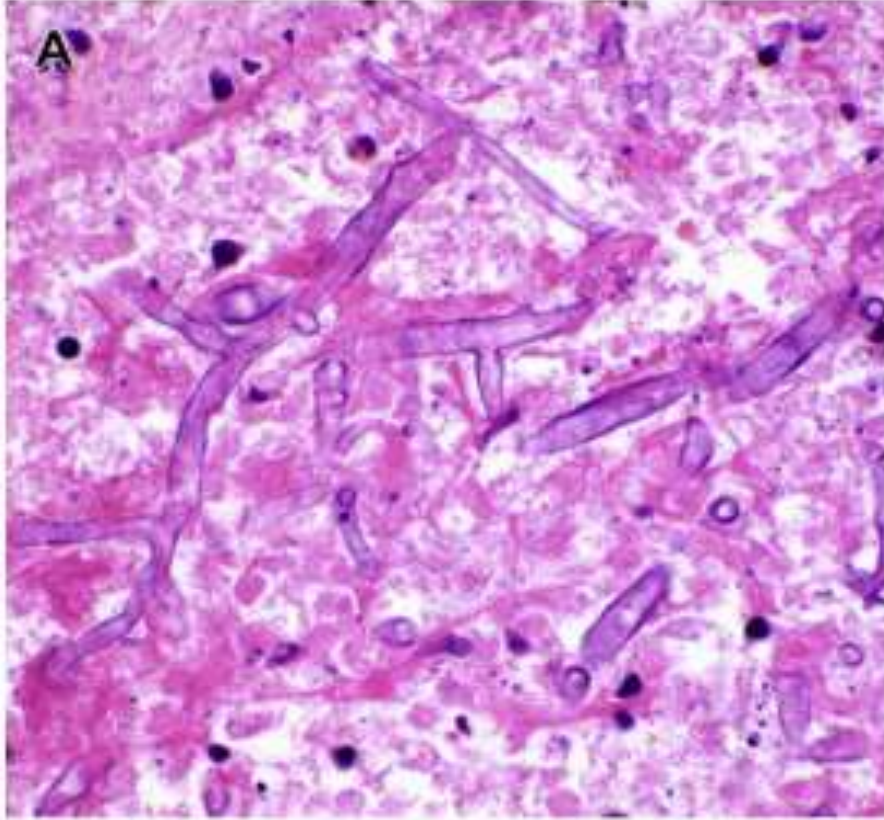
Thakur KT et al. Continuum (Minneap Minn). 2018 ; 1298–1326

Beyin biyopsisi

- Nörolojik tabloda kötüye gidiş
- Sistemik ve BOS değerlendirme sonuçları ile tanı konulamaması

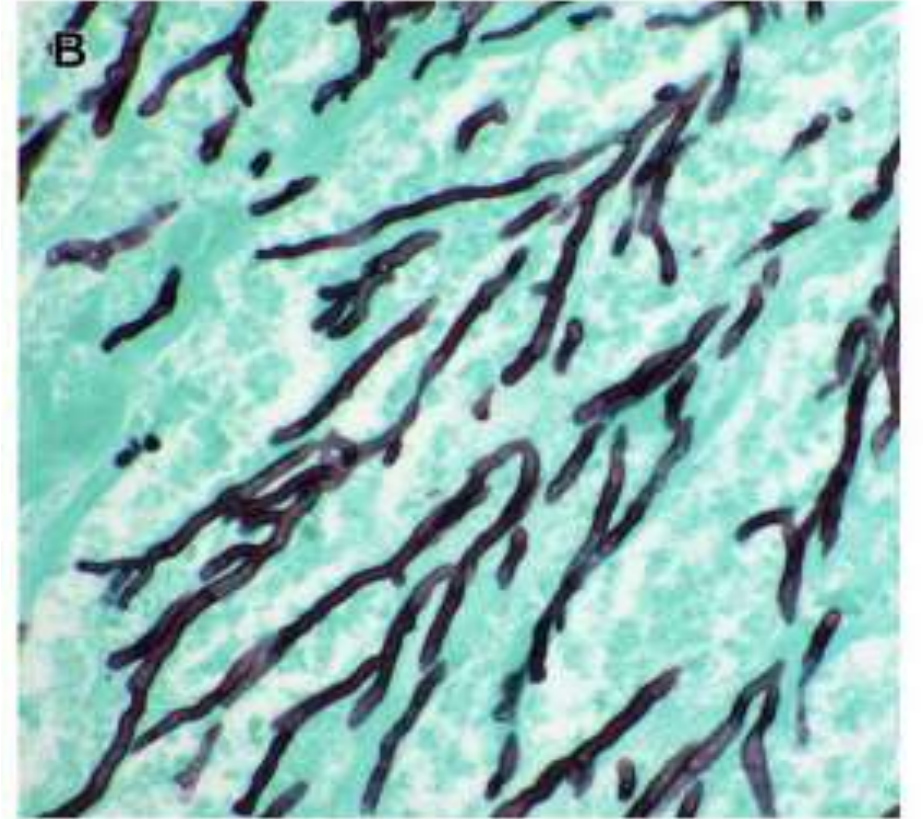


Oksipital lob kitle lezyon



Mucorales (*Lichtheimia corymbifera*)

Temporal lob lokalizasyonunda abse



Aspergillus spp (*A. fumigatus*)

FFPE: Formalinde tespit edilmiş, parafine gömülü patoloji arşiv materyalinin kantitatif gen ekspresyon analizi

Solomon IH. Surg Pathol Clin. 2020 Jun;13(2):277-289.

Moleküler ve histolojik yöntemler

Table 1
Overview of histologic features and broad-spectrum molecular assays for diagnosis of CNS infections

Organism	H&E	Special Stains	Immunohistochemistry	Molecular Assays
Bacteria	Cocci and bacilli variably visible	Gram, Warthin-Starry, Steiner, PAS (<i>Tropheryma whipplei</i>)	<i>Treponema</i>	16S rRNA
Mycobacteria	Rarely detectable	Ziehl-Neelsen, Fite-Faraco	Not widely used	16S rRNA, <i>hsp65</i> , <i>rpoB</i> , IS6110 (<i>Mycobacterium tuberculosis</i>)
Fungi	Yeast and hyphae often visible as eosinophilic or negatively staining structures	GMS, PAS, Gram (<i>Candida</i>), Mucicarmine/Fontana-Masson (<i>Cryptococcus</i>)	Not widely used	28S rRNA, D1/D2, ITS
Viruses	Characteristic cytoplasmic or nuclear inclusions present for some viruses	Luxol fast blue (PML)	HSV, VZV, EBV (ISH), CMV, adenovirus, polyomavirus	mNGS
Parasites	Diagnosis based predominantly on morphologic features	Giemsa, acid fast (cestode hooklets), GMS/PAS (ameba cyst walls)	<i>Toxoplasma</i>	mNGS

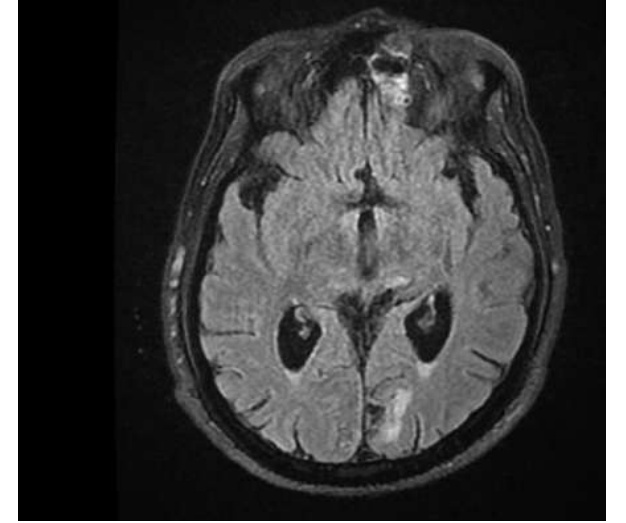
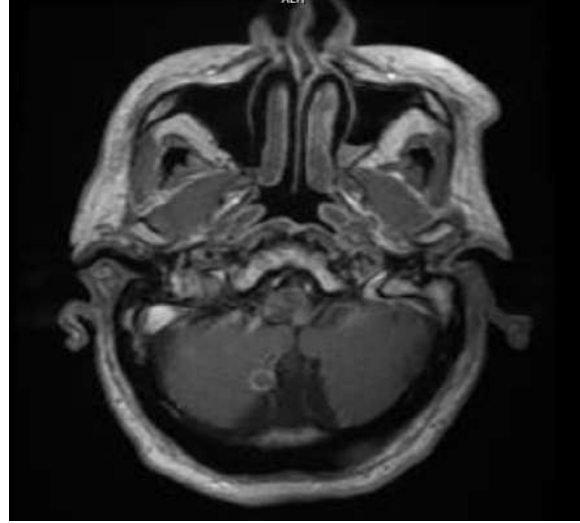
OLGU

- SŞ, erkek, 55 yaşında, İstanbul'da yaşıyor.
- İki aydır devam eden ateş yüksekliği
- Bir aydır süren baş ağrısı
- 15 gündür işitme azlığı
- Konvulziyon, kognitif fonksiyonda bozulma, halsizlik
- Tekrarlayan acil servis başvurularında hiponatremi tedavisi
- Karın ağrısı

❖ Genel durumu kötü, vital bulguları stabil

BOS incelemesi

- Hücre sayısı: 124 hücre/mm³
- Protein: 131 mg/dl
- Glukoz: 31 mg/dl
- BOS ARB negatif
- PPD anerjik



Beyin MR: Sağ parietal lob, mezensefalon, sol orta pedikülde, sol temporooksipital ve bilateral serebellar hemisferde noduler lezyonlar



- Toraks BT: Mediatinal milimetrik lenf nodları, bronkovasküler dansitede artış

Başka bir hastanenin dahiliye kliniğinden, kliniğimize tedavisinin 3. gününde nakil olarak alındı.

Hasta kliniğimize yatırıldıktan 8 saat sonra YBÜ endikasyonu konularak, özel bir üniversitenin YBÜ'ne nakledildi.

YBÜ yatışının 3. günü hastanın kaybedildiği öğrenildi.

Balgamda *M. tuberculosis* PCR pozitif

Merkezi sinir sistemi tüberkülozu

MSS tüberkülozu tüberküloz menenjit, intrakranial tüberkülom ve spinal araknoiditi kapsar.

Ateş yüksekliği

Baş ağrısı

Halsizlik

Fokal nörolojik bulgular

Konvulziyon

Bilinç değişiklikleri

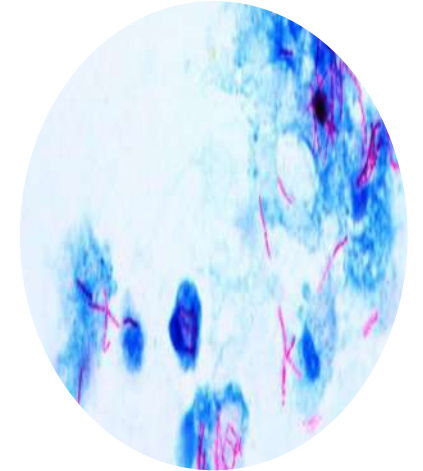
Koma

Table 8.1 The CSF findings in the patients with tuberculous meningitis

Reference no	No of patients	CSF glucose (mmol/L)	CSF protein (mg/dl)	CSF WBC (/mm ³)
Verdon et al. [117] ^a	47	1.9 ± 1.3	345 ± 286	273 ± 722
Roca et al. [85] ^b	29	1.33(0.94–1.77)	125 (98–246)	148 (65–388)
Hsu et al. [48] ^a	46	2.35 ± 1.90	346.3 ± 548.1	221.8 ± 306.5
He et al. [44] ^a	161	2.11 ± 1.53	138.7 ± 70.4	198 ± 198

	Total	Positive	Sensitivity (%)
Use of diagnostic tests			
IGRA	41	37	90.2
CSF-ACS	192	157	81.8
CSF L-j culture	439	319	72.7
CSF-PCR	206	118	57.3
CSF-ADA	137	41	29.9
CSF EZNs	469	128	27.3
Concordant use of diagnostic tests			
L-j, ACS, IGRA, and EZNs,	2	2	NA
L-j, ACS, and IGRA	2	2	NA
ACS, EZNs, and IGRA	2	2	NA
ACS and IGRA	2	2	NA
EZNs, PCR, and IGRA	34	34	100
ACS, L-j, and EZNs	152	146	96.1
ACS and PCR	88	84	95.5
ACS and L-j	154	146	94.8
ACS, L-j, and PCR	70	66	94.3
L-j, EZNs, and IGRA	34	34	100
ACS and EZNs	188	163	86.7
L-j and PCR	166	138	83.1
L-j and IGRA	41	41	100
EZNs and IGRA	41	41	100
EZNs and PCR	192	119	62

CSF, cerebrospinal fluid; L-j, Löwenstein-jensen medium; ACS, automated culture system; EZNs, Ehrlich-Ziehl-Neelsen staining; IGRA, interferon- γ release assay; ADA, adenosine deaminase; NA, not applicable.



BOS incelemesinde EZN %10-60, löwenstein-jensen kültüründe pozitiflik %25-75

Erdem H et al. Clin Microbiol Infect 2014;20(10):0600-8.
Springer Nature. <https://www.springer.com/us/book/9783030047436>

Bir meta-analize göre
Nükleik asit testlerinde duyarlılık %82, özgüllük %99

Pormohammad A et al. J Clin Microbiol 2019; 24;57(6):e01113-18

Table 3. Distribution of the Cases According to Set Criteria and CSF ADA Levels

Group	Number of cases	ADA levels in U/L		Mean SD	t cal	P-value
Tuberculous	19	ADA $\geq$ 10	18	27.1684	4.0173	0.0007 (p<.01)*
		ADA < 10	01	22.7660		
Non-tuberculous	21	ADA $\geq$ 10	02	6.0619	4.0173	0.0007 (p<.01)*
		ADA < 10	19	2.5714		
Total	40		40			

*(p < 0.01) shows a highly significant difference between the tuberculous and non-tuberculous groups

Kesin tanılı 284 MSS tüberkülozu

%53.5 meningeal tutulum

%27.4 bazal tutulum

%38.3 parankimal tutulum (%38.3'ü tüberkülom,

%5.2'si serebrit, %5.2'si apse)

%28.1 hidrocefali

%20 ödem

%19.3 vaskülit

%1.7 spinal tüberküloz

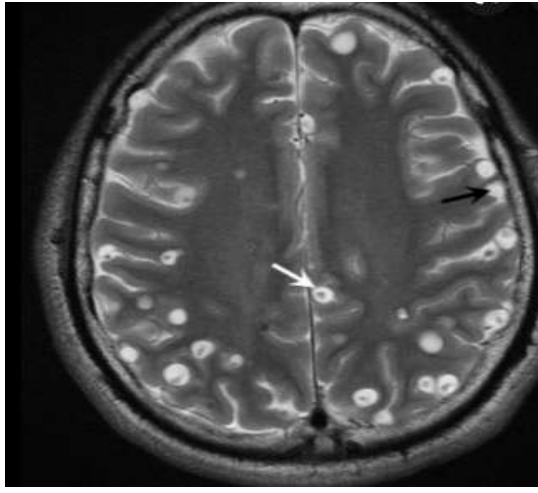
Table 1

Localization of lesions of tuberculous meningitis

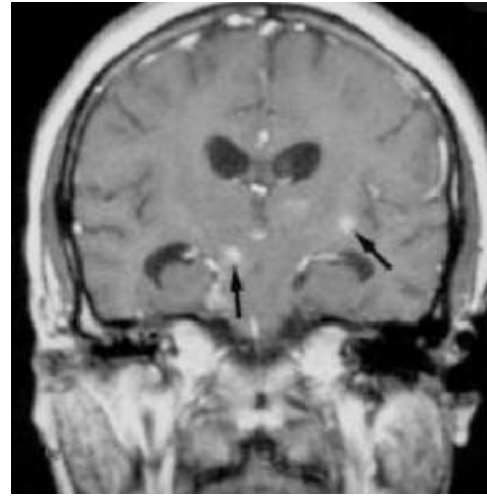
Localization	n	%
Localization of abscesses (n = 10)		
Cerebellum	7	70
Cerebral hemispheres	6	60
Basal ganglia	2	20
Brainstem	1	10
Multiple sites	7	70
Localization of tuberculomas (n = 91)		
Cerebral hemispheres	49	53.8
Cerebellum	29	31.8
Basal ganglia	17	18.6
Brainstem	13	14.2
Deep white matter	5	5.4
Multiple sites	62	68.1
Localization of vasculitis (n = 52)		
Basal ganglia	14	26.9
Middle cerebral artery zone	10	19.2
Deep white matter	2	3.8
Cerebellum	1	1.9
Posterior cerebral artery zone	1	1.9
Brainstem	1	1.9
Anterior cerebral artery zone	1	1.9
Venous infarctions	3	5.7
Lacunae	4	7.6
Multiple vasculitic lesions	17	32.6

TB menenjit

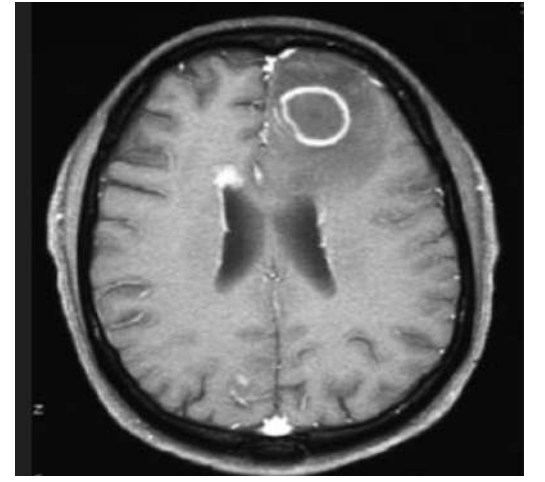
Ayırıcı tanı



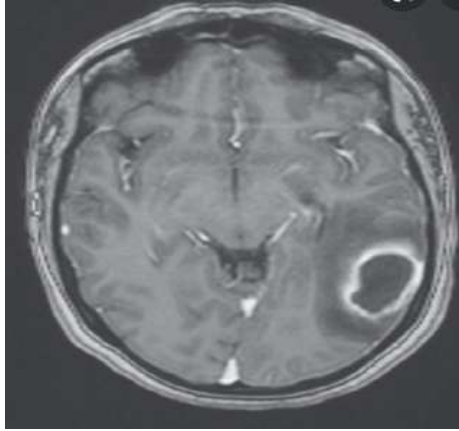
Nörosisterkosis



Kriptokokkoma



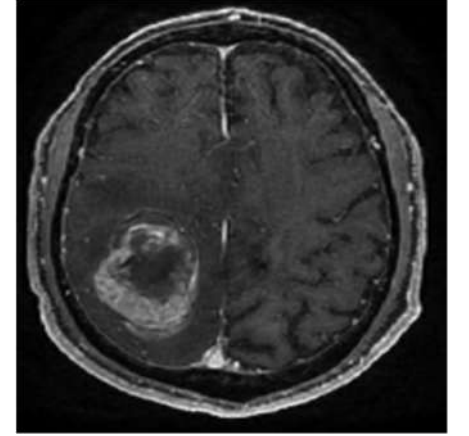
Toxoplasma



Beyin apsesi



Beyin lenfoması



Beyin tümörü

Nörosifiliz

- Sifilizin herhangi bir döneminde nörosifiliz gelişebilir

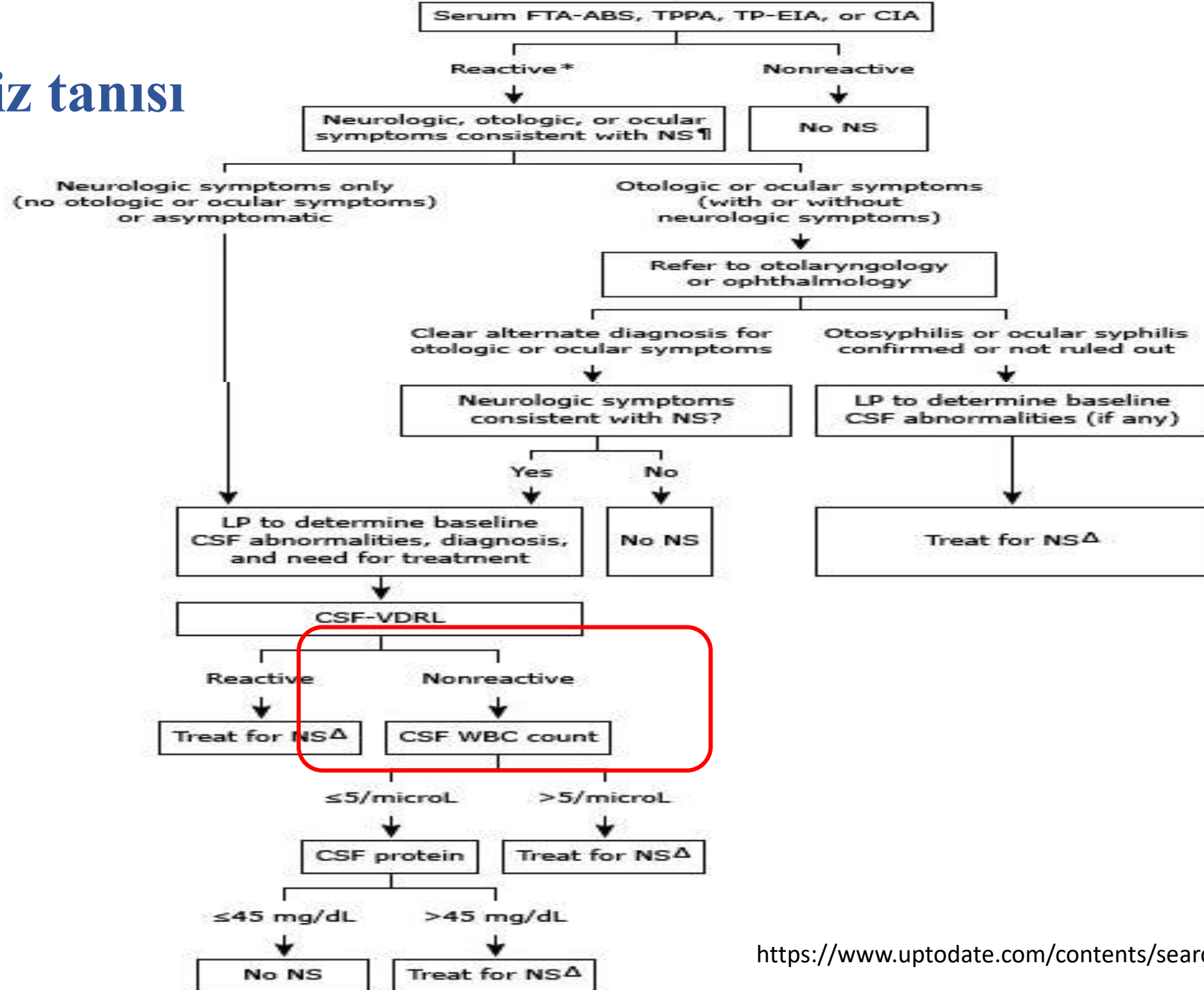
- ❖ Ateş, baş ağrısı
- ❖ Bulantı-kusma
- ❖ Kilo kaybı, halsizlik
- ❖ Atralji, çift görme
- ❖ Konvulziyon
- ❖ Tabetik semptomlar
- ❖ Paretik semptomlar
- ❖ Vasküler semptomlar
- ❖ Meninks iritasyon bulguları

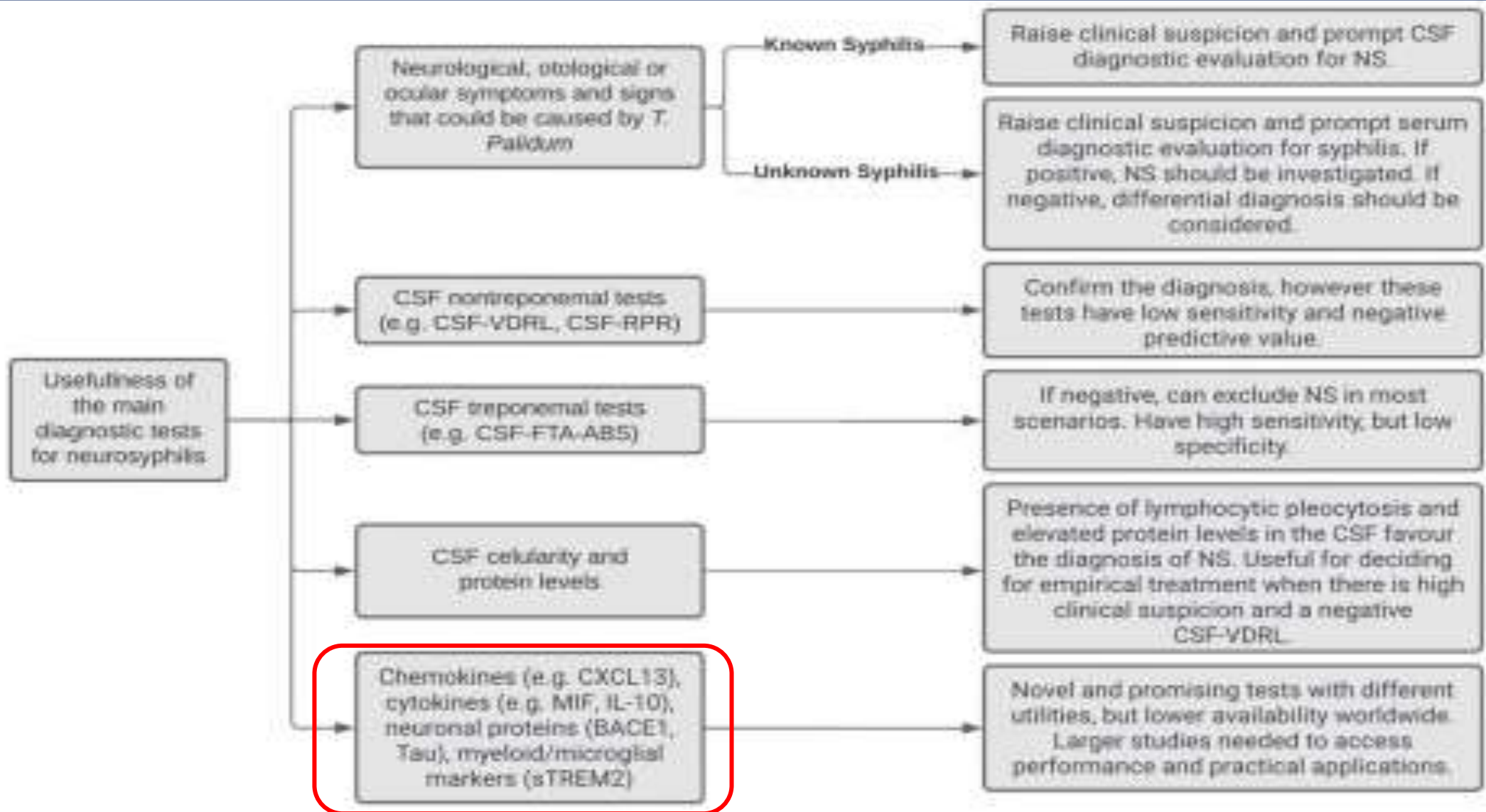
Factor N	Total n = 141	Favorable n = 76	Unfavorable n = 65	p value
Stage of neurosyphilis				0.032
Asymptomatic NS	22 (16%)	7 (9%)	15 (23%)	
Syphilitic meningitis	67 (48%)	41 (54%)	26 (40%)	
Meningovascular NS	13 (9%)	8 (11%)	5 (8%)	
Parenchymal NS	16 (11%)	5 (7%)	11 (17%)	
General paresis	13 (9%)	10 (13%)	3 (5%)	
Tabes dorsalis	10 (7%)	5 (7%)	5 (8%)	
HIV infection				0.16
No	98 (70%)	49 (64%)	49 (75%)	
Yes	43 (30%)	27 (36%)	16 (25%)	

Nörosifiliz

Nörosifiliz	Kesin (1,2 ve 3,4)	1-NTT pozitifliği (VDRL, RPR veya eşit değerde serolojik yöntem)
		2- TT pozitifliği (TP-PA, EIA, CIA veya eşit değerde serolojik yöntem)
		3- Kanla kontamine olmayan BOS'ta VDRL pozitifliği
		4- Diğer sebepler ile açıklanamayan nörosifiliz ile uyumlu klinik bulgular
	Olası (1, 2 ve 3 ve 4)	1-NTT pozitifliği (VDRL, RPR veya eşit değerde serolojik yöntem)
		2- TT pozitifliği (TP-PA, EIA, CIA veya eşit değerde serolojik yöntem)
		3- Diğer sebepler ile açıklanamayan nörosifiliz ile uyumlu klinik bulgular
		4- Bu değerleri açıklayacak bir nedenin olmadığı durumda BOS proteini > 50 mg/dl, hücre sayımı >5 mm ³ olması
	Muhtemel (1,2,3)	1-NTT pozitifliği (VDRL, RPR veya eşit değerde serolojik yöntem)
		2- TT pozitifliği (TP-PA, EIA, CIA veya eşit değerde serolojik yöntem)
		4- Diğer sebepler ile açıklanamayan nörosifiliz ile uyumlu klinik bulgular

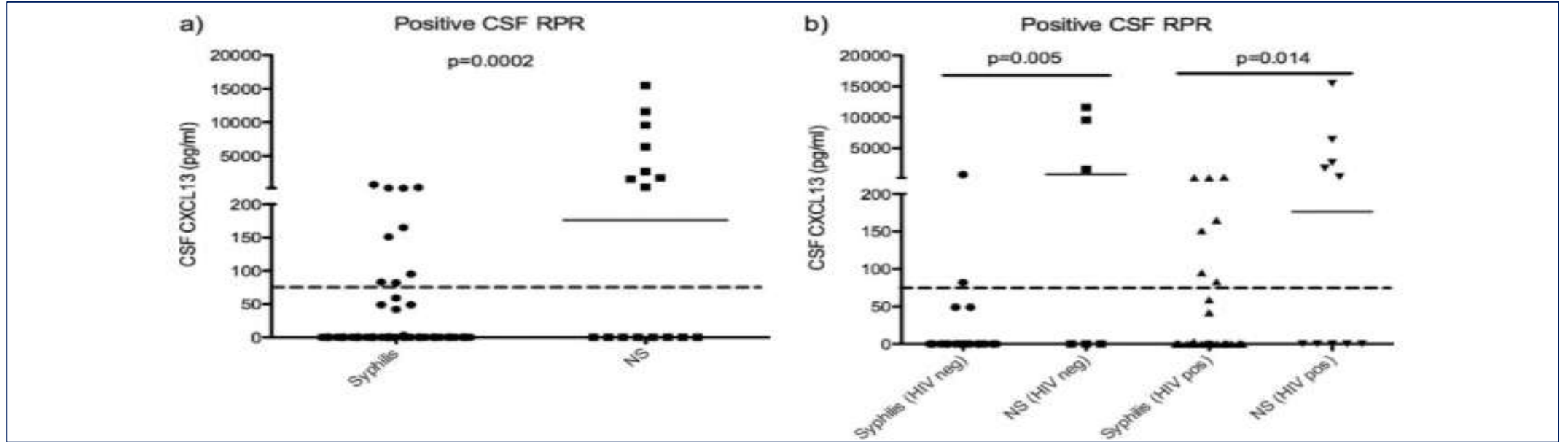
Nörosifiliz tanısı





Has CXCL13 an Added Value in Diagnosis of Neurosyphilis?

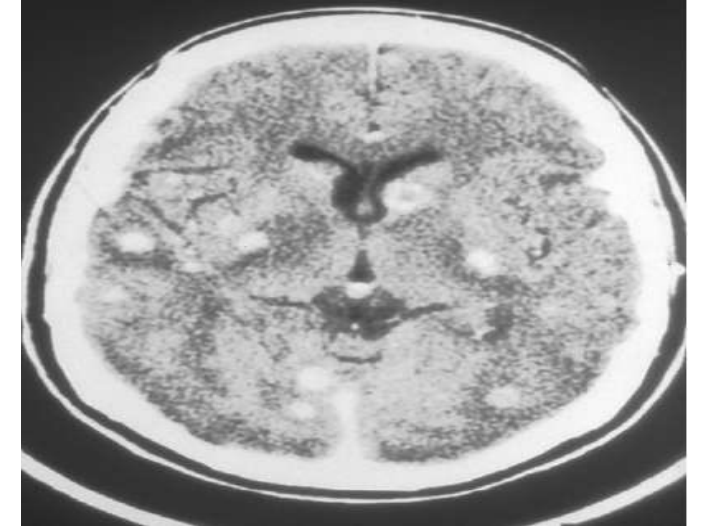
Khutso M. Mothapo^a, Marcel M. Verbeek^c, Lieven B. van der Velden^{b,d}, C. Wim Ang^e, Peter P. Koopmans^a, Andre van der Ven^a, and Foekje Stelma^b



Nörosifilizli olgularda BOS CXCL13 için duyarlılık %50, özgüllük %90

Kriptokok

Merkezi Sinir Sistemi Tutulumu



- ❖ Baş ağrısı
- ❖ Ateş (%50- bazı serilerde)
- ❖ Kraniyel sinir tutulumu
- ❖ Letarji
- ❖ Hafıza kaybı
- ❖ Koma

- Akut, subakut, kronik menenjit
- Kriptokokkoma
- Spinal kord granulomu
- Kronik demans

BOS incelemesi

- BOS basıncı yüksek özellikle HIV infekte olgularda
- HIV infekte hastaların %70'inde $>200 \text{ mmH}_2\text{O}$
- Hücre sayısı HIV infekte değilse $20-200 \text{ hücre/mm}^3$, HIV infekte olgularda $0-50 \text{ hücre/mm}^3$
- Glukoz düşük, protein yüksek. Hücre tipi lenfosit hakimiyetinde
- İmmünsüprese hastalarda hücre sayımı ve protein normal olabilir.
- Çini mürekkebi ile boyamada pozitiflik HIV infekte olmayanlarda %50, HIV olgularında %75

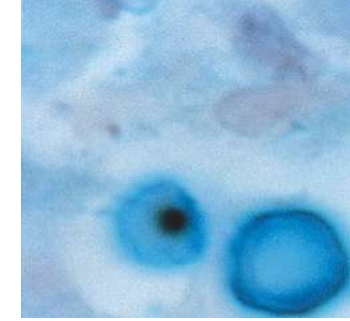


TABLE 2. False-positive and -negative results, sensitivity, and specificity by kit^a

Kit (n)	% Sensitivity	% Specificity	No. of FP (%)	No. of FN (%)
IBL LCAT				
Serum (88)	83	98	1 (1)	5 (6)
CSF (179)	100	98	4 (3)	0
MicroScan LCAT				
Serum (90)	83	100	0	5 (6)
CSF (181)	100	97	5 (3)	0
Immy LCAT				
Serum (88)	97	93	4 (5)	1 (1)
CSF (177)	93	93	12 (7)	1 (5)
Meridian LCAT				
Serum (90)	97	95	3 (3)	1 (1)
CSF (182)	100	96	7 (4)	0
Meridian EIA				
Serum (85)	93	96	2 (2)	2 (2)
CSF (173)	100	98	3 (2)	0

^a FP, false positives; FN, false negatives.



Kültür pozitif 19 BOS, 30 serum örneği
Antijen testlerinin duyarlılık ve özgüllüğü yüksek

Lateks aglütinasyon yöntemi ile kriptokok antijeninde yalancı pozitiflikler bildirilmiş

❖ *Stomatococcus mucilaginosus*

❖ *Trichosporon beigelii*

Chanock et al. *Lancet*. 1993; 342:1119-1120

EJ McManus EJ et al. *J Clin Microbiol*. 1985; 21:681-685

SHORT REPORT

Difficulty in diagnosing chronic meningitis caused by capsule-deficient *Cryptococcus neoformans*

Y Sugiura, M Homma, T Yamamoto

J Neurol Neurosurg Psychiatry 2005;76:1460-1461. doi: 10.1136/jnnp.2004.052662

We report a case of chronic meningitis due to capsule-deficient *Cryptococcus neoformans* which could not be diagnosed by routine morphological and immunological cerebrospinal fluid (CSF) examination. Repeated CSF examination and culture did not disclose the fungal body, and the cryptococcal antigen tests were always negative. Culture of ventricular fluid showed non-encapsulated cultured cells which were stained positively by indirect immunofluorescence using diluted sera from another patient diagnosed with cryptococcal meningitis. Inoculation of dispersed colonies into mice resulted in encapsulated *C. neoformans*. It is important to suspect capsule-deficient *C. neoformans* when the conventional diagnostic approaches fail to identify the organism or antigens.

throughout and the planter response was bilaterally extensor. The forced grasping and sucking reflexes were seen. Sense of position was diminished in his bilateral lower extremities. The cranial nerves were normal. His muscle power was not fully tested but showed no apparent weakness. Neither stiff neck nor the Kernig's sign were observed.

A lumbar puncture yielded clear, colourless fluid with an opening pressure of 140 mm CSF, an increased cell count (69/mm³, 78% monocytes), elevated protein (221 mg/dl), and low sugar (8 mg/dl, CSF/blood glucose ratio 8.2%). Gram staining, Indian ink preparations, CSF cytology with Ziehl-Neelsen staining, cultures for fungi, and cryptococcal antigen were all negative, and CSF examinations for *Mycobacterium tuberculosis* by culture and the polymerase chain reaction method were also negative. Full blood count showed RBC 4.10 million/mm³, platelets 75 000/mm³, WBC 6100/mm³.

Table 2 Clinical diagnostic performance of NASBA, PCR and colloidal gold

Parameter	NASBA	PCR	Colloidal gold
Sensitivity [% (95% CI)]	92.00 (72.50–98.60)	64.00 (42.62–81.29)*	100.00 (83.42–100.00)
Specificity [% (95% CI)]	95.00 (81.79–99.13)	80.00 (63.86–90.39)	82.50 (66.64–92.11)
Accuracy [%]	93.85	73.85	89.23
Positive likelihood ratio	18.40 (4.74–71.39)	3.20 (1.61–6.35)	5.71 (2.92–11.20)
Negative likelihood ratio	0.08 (0.02–0.32)	0.45 (0.26–0.77)	0.00 (0.00–NaN)
Positive predictive value [% (95% CI)]	92.00 (72.50–98.60)	66.67 (44.69–83.57)	78.13 (59.56–90.06)
Negative predictive value [% (95% CI)]	95.00 (81.79–99.13)	78.05 (61.97–88.89)	100.00 (87.02–100.00)
Youden index	0.87	0.44	0.83
Kappa	0.87	0.44	0.78

Best performance values are highlighted in bold, *P < 0.05 versus NASBA, colloidal gold

- Multipleks PCR duyarlılık >%90
- HIV negatif hastalarda ve daha düşük BOS mantar sayısında duyarlılık daha az.

RESEARCH ARTICLE

Open Access



Comparison of clinical features and prognostic factors in HIV-negative adults with cryptococcal meningitis and tuberculous meningitis: a retrospective study

Junyan Qu, Taoyou Zhou, Cejun Zhong, Rong Deng and Xiaoju Lü*

Results: A total of 126 CM and 105 TBM patients were included. CM patients were more likely to present with headache, abnormal vision and hearing, and they might be less prone to fever and cough than TBM patients ($P < 0.05$). Higher percentage of CM patients presented with cerebral ischemia/infarction and demyelination in brain MRI than TBM patients ($P < 0.05$). CM patients had lower counts of WBC in CSF, lower total protein in CSF and serum CD4/CD8 ratio than TBM patients ($P < 0.05$). After three months of treatment, CM group have worse outcome than TBM group ($P < 0.05$). Multivariate analysis showed that age more than 60y (OR = 4.981, 95% CI: 1.955–12.692, $P = 0.001$), altered mentation (OR = 5.054, 95% CI: 1.592–16.046, $P = 0.006$), CD4/CD8 ratios < 1 (OR = 8.782, 95% CI: 2.436–31.661, $P = 0.001$) and CSF CrAg $\geq 1:1024$ (OR = 4.853, 95% CI: 1.377–17.098, $P = 0.014$) were independent risk factors for poor prognosis for CM patients. For TBM patients, hydrocephalus (OR = 7.290, 95% CI: 1.630–32.606, $P = 0.009$) and no less than three underlying diseases (OR = 6.899, 95% CI: 1.766–26.949, $P = 0.005$) were independent risk factors, headache was a protective factor of prognosis.

Tüberküloz menenjit

Öksürük, ateş yüksekliği daha fazla, BOS'ta lökosit sayısı ve protein düzeyi ve serumda CD4/CD8 oranı daha yüksek

Kriptokok menenjit

Baş ağrısı, görmede bozulma, işitme kaybı, serebral iskemi, demiyelinizasyon daha fazla

Nörobruselloz

- ❖ Baş ağrısı, ateş
- ❖ Kilo kaybı, terleme
- ❖ Eklem ağrıları
- ❖ MIB (olguların üçte birinde)
- ❖ Konfüzyon

- Menenjit, ensefalit
- Radikülönöropati
- Serbellar tutulum
- Kraniyel sinir tutulumu
- Hidrosefali
- Miyelit

Nörobrusellozda serolojik tanı

TABLE 3 Serodiagnostic tests for human brucellosis and their recommended use

Serological test	Use(s)
Undiluted rose bengal test	Initial screening
Rose bengal test with serial serum dilutions	Confirmation of diagnosis
Standard agglutination test	Confirmation of diagnosis
2-Mercaptoethanol test	Follow-up and early detection of treatment failure
Complement fixation test	Confirmation of diagnosis
Coombs test	Diagnosis of relapses and chronic cases, detection of incomplete antibodies
ELISA	Diagnosis confirmation, diagnosis of <i>B. canis</i> infection and neurobrucellosis
IgG avidity ELISA	Differentiation between recent disease and past infection
Immunocapture agglutination test	Diagnosis confirmation
D-TEC CB test	Diagnosis of <i>B. canis</i> infection
Dipstick test	Rapid point-of-care diagnosis of acute cases
Lateral flow assay	Rapid point-of-care diagnosis
Fluorescent polarization immunoassay	Rapid diagnosis

TABLE 4 Causes of false-negative results of serodiagnostic tests and possible solutions

Cause of lack of demonstrable seroconversion	Possible solution
Too-early performance of the test	Retest after 2–3 wk
Prozone effect	Dilute the serum beyond 1:320
Blocking/incomplete antibodies	Perform a Coombs test
Low-affinity antibodies	Acidify diluent to pH 5.0
<i>Brucella canis</i> infection	Perform a species-specific test

Tanı

- Dört haftadan uzun süren menenjit veya meningoensefalit uyumlu klinik bulgular ve alternatif tanının olmaması
- BOS 'ta; $10/ \text{ hücre/mm}^3$, protein $>50 \text{ mg/dL}$, BOS/serum glukoz oranı <0.5
- Kan kültürü pozitifliği **veya** kanda serolojik test pozitifliği (Rose Bengal ve STA 1/160) **veya** BOS 'ta Rose-Bengal pozitifliği **veya** herhangi bir titrede STA pozitifliği **veya** kemik iliği kültür pozitifliği
- BT veya MRI bulgularının olması

TABLE 1. The sensitivities of the microbiological tests in chronic neurobrucellosis

	Total	Positive	Sensitivity %
Serum STA	172	162	94.2
CSF STA	144	113	78.5
Serum RBT	123	118	95.9
CSF RBT	106	75	70.8
Blood culture (Bactec, BacTAlert)	154	57	37
CSF culture (Bactec, BacTAlert)	87	22	25.3
CSF culture (conventional method)	52	5	9.5
CSF-Elia (IgM)	10	8	80
CSF-Elia (IgG)	10	8	80
Serum-Elia (IgM)	11	7	70
Serum-Elia (IgG)	11	10	91
BMI culture (Bactec, BacTAlert)	8	3	37

CSF, cerebrospinal fluid; RBT, Rose-Bengal test; STA, standard tube agglutination test; BMI, bone marrow.

TABLE 6 Performance of the different blood NAATs used in the diagnosis of human brucellosis^a

Authors (reference)	PCR method	Specimen ^b	No. of cases/ no. of controls	No. (%) of culture- confirmed cases	NAAT performance (%)			
					Sensitivity	Specificity	PPV	NPV
Matar et al. (219)	Conventional nested PCR	Buffy coat	20/39	1 (5.0)	100	100	100	100
Queipo-Ortuño et al. (242)	Conventional PCR	Whole blood	50/60	30 (60.0)	100	98.3	98.0	100
Zerva et al. (221)	Conventional PCR	Serum	31/45 ^c	13 (41.9)	94.0	100	100	95.7
Mitka et al. (205)	Conventional PCR	Buffy coat	200/100	148 (74.0)	100	100	100	100
Morata et al. (245)	PCR-EIA	Whole blood	59/113	40 (67.8)	94.9	96.5	93.3	94.7
Al-Nakkas et al. (241)	Nested PCR-EIA	Whole blood	195/250	89 (45.6)	98.9	100	100	99.2
Vrioni et al. (257)	PCR-EIA	Whole blood +	243/50 ^c	179 (73.7)	99.2	100	100	96.2
Queipo-Ortuño et al. (258)	Real-time PCR	Serum	62/65	40 (64.5)	91.5	99.4	95.0	92.5
Debeaumont et al. (259)	Real-time PCR	Serum	17/60	17 (100)	64.7	100	100	90.9
Surucoglu et al. (260)	Real-time PCR ^d	Serum	50/30 ^c	18 (36.0)	88.0	100	100	83.3
Hasanjani Roushan et al. (270)	Conventional nested PCR	Whole blood	50/30	5 (10.0)	100	100	100	100
Navarro et al. (271)	Q-RT-PCR	Whole blood	18/30 ^c	16 (88.9)	100	100	100	100
Vrioni et al. (137)	Q-RT-PCR	Whole blood	39/50 ^c	13 (33.3)	100	100	100	100
Queipo-Ortuño et al. (273)	Q-RT-PCR	Serum	46/64	32 (69.6)	95.7	92.2	89.8	96.7

^aAbbreviations: PPV, positive predictive value; NPV, negative predictive value; EIA, enzyme immunoassay; Q-RT-PCR, quantitative real-time PCR.

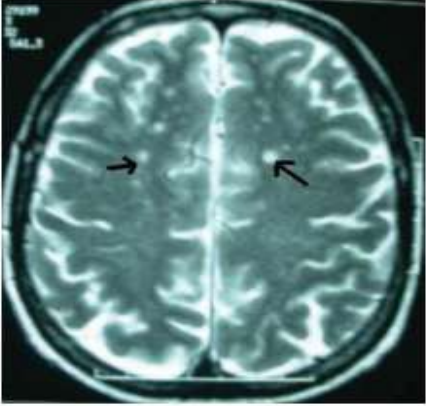
^bWhen multiple targets or specimen types were tested in the study, the data in the table refer to the target and sample that had the best diagnostic efficiency.

^cAll controls were healthy adults.

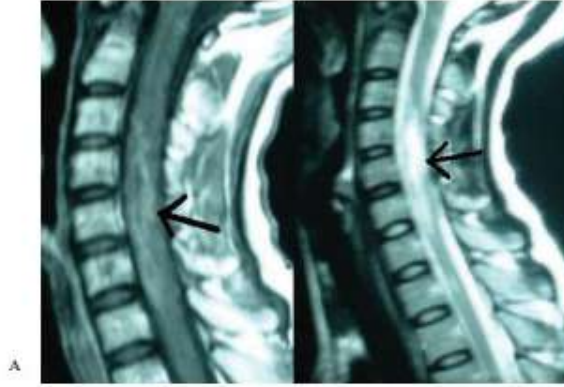
^dRoboGene *Brucella* detection kit (RoboScreen, GmbH, Leipzig, Germany).

PCR testleri maruziyetten 10. günden sonra pozitif bulunabilir

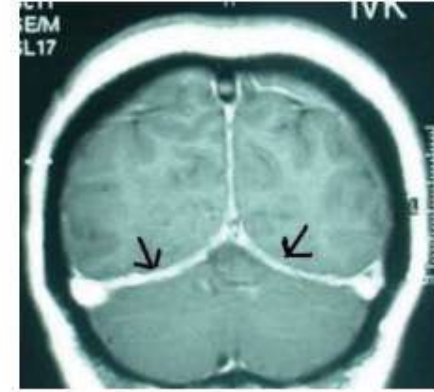
Radyolojik bulgular



T1-Beyaz cevherde lezyonlar



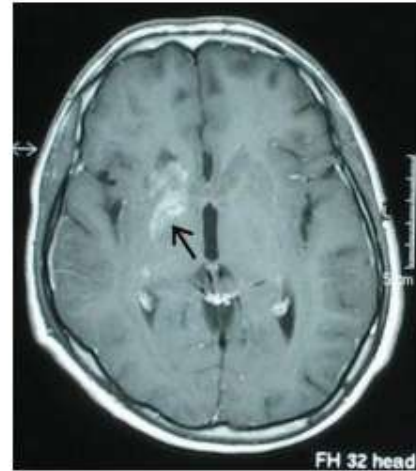
a. T1'de kontrast tutulumu
b. T2'de transfers miyelit



T1-Meningeal kontrast tutulumu



T1-Temporal lopta periferi kontrast tutan
granulomlar



T1-Vasküler deęişiklikler

Nöroborelyoz

Erken lokalize Günler, haftalar

- Eritema migrans
(%80-90)
- Atralji
- Miyalji
- Sub febril ateş
- Gece terlemesi

Erken yaygın Haftalar, aylar

- Eritema migrans
(%25-50)
- Eklem ve kalp tutulumu

Geç lyme Aylar, yıllar

- Sinir sistemi
- Deri
- Eklemler

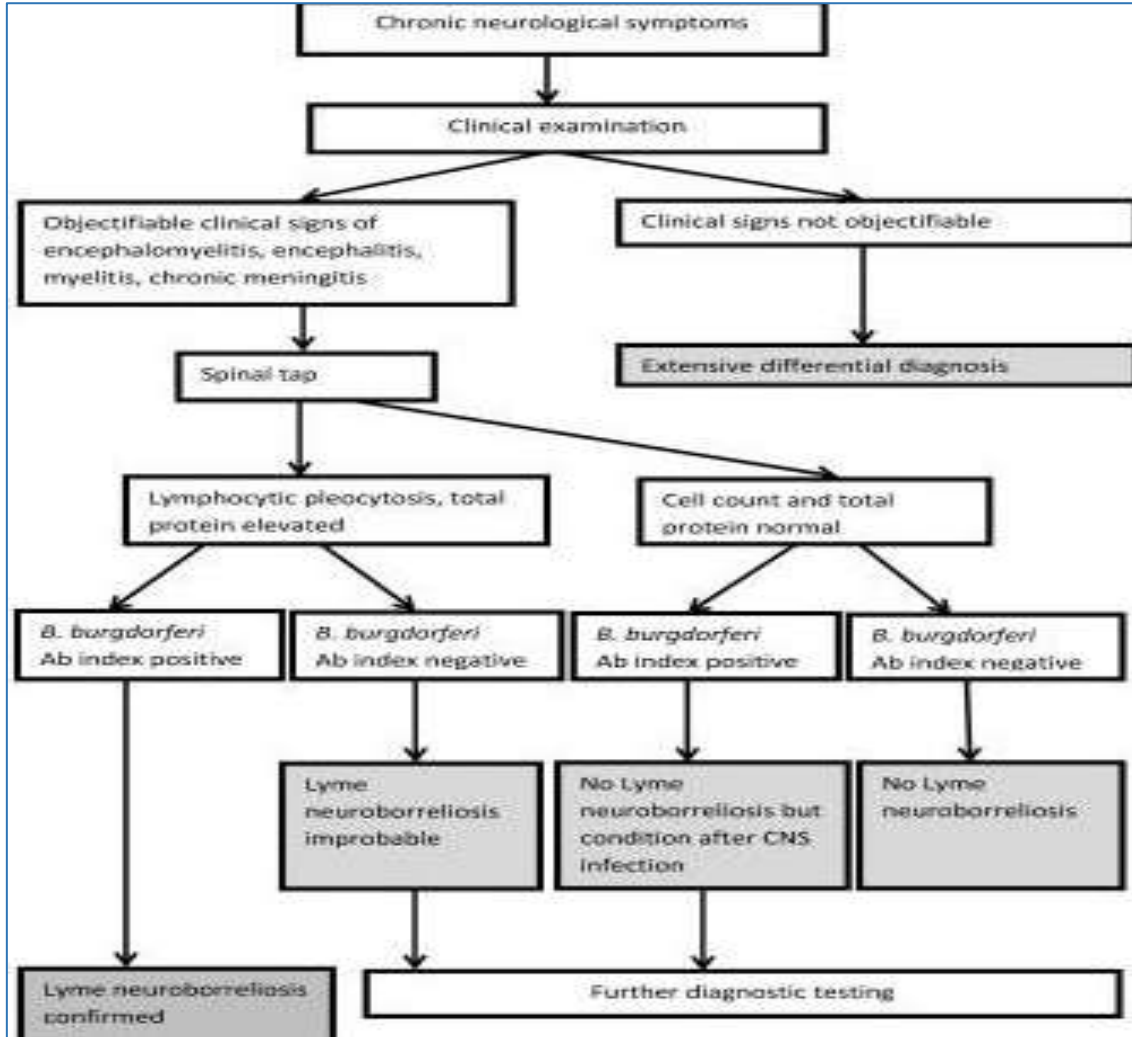
Nöroborelyoz

- Lenfositik menenjit
- Kraniyel nörit
- Radikülonöropati
- Vaskülit
- Miyozit
- Ensefalit
- Myelit

Bannwarth's sendromu



Anadure RK et al. Medical Journal Armed Forces India. 2021;77(1):101-104
Rauer S et. Al. Ger Med Sci. 2020; 18: Doc03.



- ❖ BOS antikor düzeyinin serum antikor düzeyine oranı anti-Borrelia antikor indeksi (AI)
- ❖ İntratekal antikor yapımını gösterir (≥ 1.5)

BOS spesifik IgG/ serum spesifik IgG

BOS IgG /serum IgG

Borrelia AI'nin sensitivitesi %75, spesifisitesi %97

Rauer S et. Al. Ger Med Sci. 2020; 18: Doc03.
Serindağ HC ve ark. Turk J Neurol 2018;24:334-336

CSF parameter	ELN N=118 (Djukic et al. 2012) [55]	Comparison of CFS results for ELN and LLN (Kaiser 1994) [50]	
		ELN N=37	LLN N=10
Cell count per µl	170.5 (57.0; 369)*	218 (6–757)**	95 (23–312)**
Total protein g/l	1.232 (697; 1926)*	N/A	N/A
Albumin ratio (x 10 ⁻³)	17.2 (9.7; 28.4)*	19.6 (8–58.4)**	45 (8–140)**
IgG synthesis rate**** conspicuous at	- N/A 19.5%	20% (17)*** 81%	50% (20)*** 100%
IgM synthesis rate**** conspicuous at	- N/A 70.2%	54% (32)*** 84%	9% (13)*** 40%
IgA synthesis rate**** conspicuous at	- N/A 9%	7% (17)*** 19%	39% (28)*** 80%
Lactate	2.0 (1.6; 2.6)*	N/A	N/A

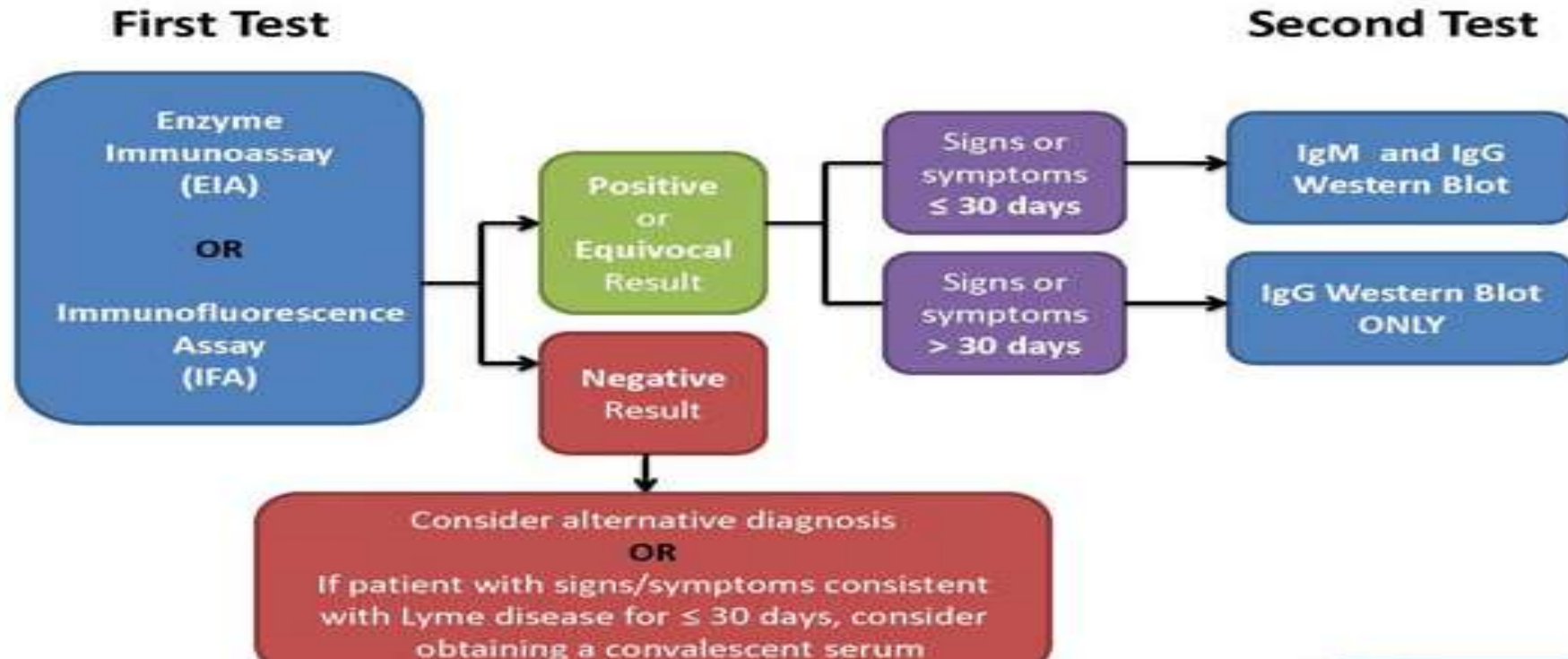
25% and 75% percentiles; **range; ***mean (standard deviation); ****according to Reiber [107]
ELN = early Lyme neuroborreliosis; LLN = late Lyme neuroborreliosis

Rauer S et. Al. Ger Med Sci. 2020; 18: Doc03

Erken nöroborelyoz olgularının %40'ında,
Geç nöroborelyoz olgularının %25'inde BOS Borrelia DNA PCR pozitif

Serindağ HC ve ark. Turk J Neurol 2018;24:334-336

Two-Tiered Testing for Lyme Disease



Criteria for Western blot diagnosis of Lyme disease

Type of infection	Isotype	Bands to be considered
First few weeks	IgM	Two of the following: ospC (24), 39, 41
After first few weeks	IgG	Five of the following: 18, 23, 28, 30, 39, 41, 45, 58,66, 93

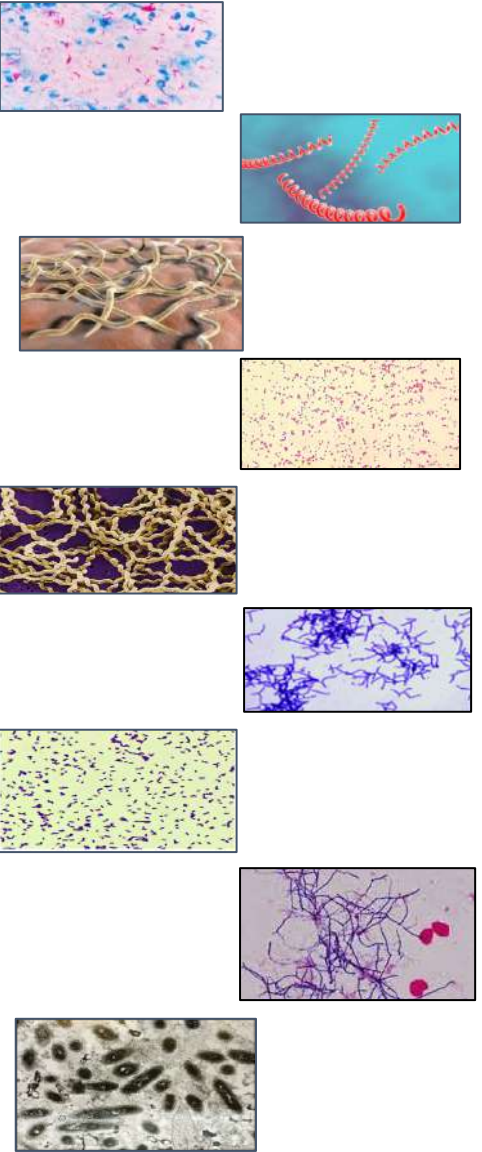
Criteria for positive Western blot (immunoblot) analysis in the serologic confirmation of infection with *Borrelia burgdorferi* (Lyme disease).

IgG WB hızlı değerlendirme



Şekil 2. WB IgM ve IgG sonuçları için hızlı değerlendirme şemaları.

* Yeni enfeksiyon için karakteristik değil.



Etken	Özellik / maruziyet	Tanı
<i>M. tuberculosis</i>	Bazal menenjit menenjit, serebral infarkt,immunosupresyon	PPD, IGRA test, BOS'ta ARB, Kültür, PCR
<i>T. pallidum</i>	Serebral infarktlar (meningovasküler)	CSF VDRL,FTA ABS
<i>B. burgdorferi</i>	Eritema migrans, meningoradikülit	Spesifik IgG indeks, PCR, kültür
<i>Brucella spp</i>	Pastorize olmayan süt ürünleri	Antikor testleri, kültür, PCR
<i>Leptospira spp.</i>	İnfekte sıvı, hayvan atıklarına maruziyet	Kültür, antikor testleri (MAT)
<i>Actinomyces spp.</i>	Sinuzit, otit, BOS'ta PNL	Kültür
<i>L. monocytogenes</i>	İmmunosüpresyon, ileri yaş, gebelik	Kültür, PCR
<i>Nocardia spp.</i>	Hücresel immunitede bozulma	Gram ve Modifiye Kinyon boyama, kültür, moleküler yöntemler, histolojik inceleme
<i>Tropheryma whipplei</i>	Kilo kaybı, ishal, atralji, karın ağrısı, kognitif bozukluk, ataksi	PCR, PAS, immunhistokimyasal yöntemler

Mantarlar	Özellik / maruziyet	Tanı
<i>C. neoformans</i>	İmmunosupresyon, kuş çıkartıları, papil ödem	Kültür, antijen, çini mürekkebi
<i>C. immitis</i>	Endemik bölgeler (Amerika), BOS eozinofili	Kültür, seroloji, histopatoloji
<i>H. capsulatum</i>	Ohio/Mississippi nehri vadisi, Nötrofilik menenjit	Kültür, seroloji
<i>B. dermatidis</i>	Endemik bölgeler (Missisipi vadisi), dış mekana maruz kalma	Kültür, seroloji, histopatoloji
<i>A. fumigatus</i>	Sinuzit, serebral infarkt, BOS'ta nötrofili	Kültür, biyopsi, BOS antikor
<i>C. albicans</i>	İmmunosupresyon, IV ilaç bağımlılığı, BOS'ta nötrofili	Kültür, 1-3 beta D glukan
<i>S. schenckii</i>	Bahçıvanlık, gül dikenleri	BOS'ta antikor, kültür

Virüsler	Özellik / maruziyet	Tanı
HIV-1	Serokonversiyonda semptomatik aseptik menenjit	BOS PCR
CMV	Fırsatçı infeksiyon, HIV-1, immunosupresyon	BOS PCR
Zoster	Karakteristik döküntü olmayabilir, infaktlar, lökoensefalopati	BOS PCR
HSV	Tekrarlayan genital herpes (HSV-2), sacral radikülit varsa ürner retansiyon, Bell's palsy, Mollaret's tekrarlayan menenjit (HSV-1, HSV-2), immunosupresyon (HSV-1,2)	BOS PCR
<i>Enterovirus</i>	Humoral immun sistemde baskılanma	Kültür, biyopsi, BOS antikoru
<i>Epstein-Barr virus</i>	Hepatit, immünosuprese konakta SSS lenfoma	BOS PCR

Parazitler	Özellik / maruziyet	Tanı
<i>T. solium</i>	Endemik bölge (Meksika, Orta ve Güney Amerika, Çin) kistik ve kalsifiye parankimal lezyonlar	Serolojik testler, PCR, histopatolojik inceleme
<i>A. cantonensis</i>	Endemik bölge (Güneydoğu Asya) salyangozlar, yengeçler, yumuşakçalar, kontamine sebzeler, eozinofilik menenjit	Serum antikor testi, PCR
<i>T. gondii</i>	Kediler, immünosupresyon; ensefalit menenjitten daha yaygın	Spesifik IgG indeksi, PCR
<i>Acanthameba</i> spp.	Granulomatoz meningoensefalit, primer deri ve akciğer enfeksiyonları	BOS incelemesi, PCR, biyopsi

İnfeksiyon dışı nedenler	Özellik / maruziyet	Tanı
Nörosarkoidoz	Meningeal granulomlar, pulmoner-hiler granulomlar, uveit, iritis, 7. sinir tutulumu, Diyabet insipidus MR'da hipotalamik, optik, piüter lezyonlar	Sistemik bulgular, meningeal biyopsi
<i>Behçet hastalığı</i>	Oral genital ülserler, iritis, beyin sapı lezyonları	Sistemik bulgular
<i>SLE</i>	İzole menenjit, nadiren lupusun kendisine bağlı	Sistemik bulgular, ANA (+)
<i>Wegener granülomatosis</i>	Sinus, hava yolları, böbrek tutulumu	ANCA (+)
<i>Neoplasm</i>	Karsinom, lenfoma, lösemi, eozinofiller	BOS sitoloji, meningeal biyopsi
<i>Primer beyin anjitis</i>	Serebral infarktlar, sistemik hastalık özelliklerinin olmaması	Anjiografi, biyopsi
<i>Voght- Koyanagi-Harada seniladromu</i>	Üveit, retinit, vitiligo, işitme kaybı, kulak çınlaması	Klinik bulgular
<i>İlaçlar</i>	Eozinofiller, maruziyet, nonsteroid antiinflamatuvar/ trimetoprim tedavisi	İlacın kesilmesine yanıt

The burden and epidemiology of community-acquired central nervous system infections: a multinational study

Table 2 The presentation of the patients according to etiological agents

	No.	Meningitis	Encephalitis	Meningoencephalitis	Brain abscess	Subdural empyema	Epidural abscess	Other abscesses	Other syndromes	Arachnoiditis	Chronic infections			Age (years)		
											Agents (n, %)	Patients* (%)		<65	>65	p-Value
<i>T. pallidum</i>	24	22	1	0	1	0	0	0	0	0	24	100	18	22	2	0.134
<i>Brucella</i> spp.	14	12	0	1	0	0	1	0	0	0	6	42.8	4.5	13	1	0.210
<i>M. tuberculosis</i>	152	84	4	59	1	0	2	0	3	1	37	24.3	28	129	23	0.011
<i>S. pneumoniae</i>	206	136	4	65	1	2	0	0	0	0	0			147	59	0.039
<i>Streptococcus</i> spp. (other)	55	22	0	14	16	3	4	0	0	0	0			45	10	0.0462
<i>S. aureus</i>	48	28	1	4	3	2	9	2	1	0	1	2.1	0.7	32	16	0.125
Co-NS	23	11	1	7	3	0	1	0	1	0	2	8.7	1.5	19	4	0.999
<i>Listeria</i> spp.	27	20	1	6	0	0	0	0	0	0	0			14	13	0.004
<i>Nocardia</i> spp.	4	0	0	0	4	0	0	0	0	0	1	25	0.7	0	4	
<i>Klebsiella</i> spp.	7	4	0	0	3	0	0	0	0	0	1	14.3	0.7	7	0	
<i>Haemophilus</i> spp.	10	8	0	1	1	0	0	0	0	0	0			9	1	
<i>Capnocytophaga</i> spp.	3	2	0	1	0	0	0	0	0	0	0			1	2	
<i>Neisseria</i> spp.	45	35	0	8	2	0	0	0	0	0						
<i>Fusobacterium</i> spp.	2	1	0	0	2	0	0	0	0	0						
<i>Borrelia</i> spp.	38	19	0	19	0	0	0	0	1	0						
<i>Enterococcus</i> spp.	5	3	0	2	1	0	0	0	1	0						
<i>Micrococcus</i> spp.	1	1	0	0	0	0	0	0	0	0						
<i>Gemella</i> spp.	1	0	0	0	1	0	0	0	0	0						
<i>Peptococcus</i> spp.	1	0	0	1	0	0	1	0	0	0						
<i>Peptostreptococcus</i> spp.	3	0	0	1	1	1	1	0	0	0						
<i>Lactobacillus</i> spp.	1	0	0	0	1	0	0	0	0	0						
<i>Corynebacteria</i>	1	1	0	0	0	0	0	0	0	0						
<i>Actinomyces</i> spp.	5	0	0	0	4	0	1	0	0	0						
<i>Escherichia coli</i>	9	6	0	0	0	0	3	0	0	0						
<i>Enterobacter</i> spp.	3	2	0	1	0	0	0	0	0	0						
<i>Proteus</i> spp.	2	1	0	0	1	0	0	0	0	0						
<i>Morganella</i> spp.	3	0	0	1	0	0	2	0	0	0						
<i>Campylobacter</i> spp.	1	0	0	0	0	0	1	0	0	0						
<i>Aggregatibacter</i> spp.	3	0	0	0	3	0	0	0	0	0						
<i>Pseudomonas</i> spp.	7	3	0	1	2	0	0	0	1	0						
<i>Acinetobacter</i> spp.	4	1	0	3	0	0	0	0	0	0						
<i>Moraxella</i> spp.	2	0	0	1	0	0	1	0	0	0						
<i>Sphingomonas</i> spp.	2	2	0	0	0	0	0	0	0	0						
<i>Prevotella</i> spp.	2	0	0	0	2	0	0	0	0	0						
<i>Bacteroides</i> spp.	1	0	0	0	0	0	1	0	0	0						
<i>Xanthomonas</i> spp.	1	0	0	1	0	0	0	0	0	0						
<i>Aerococcus</i> spp. <i>urinae</i>	1	0	0	0	1	0	0	0	0	0						
<i>Cryptococcus</i> spp.	27	23	0	4	0	0	0	0	0	0						
<i>Candida</i> spp.	5	4	0	1	0	0	0	0	0	0						

Eur J Clin Microbiol Infect Dis

Table 2 (continued)

	No.	Meningitis	Encephalitis	Meningoencephalitis	Brain abscess	Subdural empyema	Epidural abscess	Other abscesses	Other syndromes	Arachnoiditis	Chronic infections			Age (years)		
											Agents (n, %)	Patients* (%)		<65	>65	p-Value
<i>Saccharomyces cerevisiae</i>	1	0	0	0	0	1	0	0	0	0	0			1	0	
HSV-1	48	7	21	19	0	0	0	0	0	0	1	2.1	0.7	31	17	0.060
HSV-2	34	17	6	10	0	0	0	0	1	0	1	2.9	0.7	26	8	1.000
HSV-1/2	1	1	0	0	0	0	0	0	0	0	0			1	1	
EBV	16	9	3	3	10	0	0	0	0	0	3	18.8	2.2	12	4	0.772
CMV	5	3	0	0	2	0	0	0	0	0	1	20	0.7	3	2	
VZV	91	17	11	61	0	0	0	0	2	0	0			50	41	0.000
SFTV	1	0	0	1	0	0	0	0	0	0	0			1	0	
WNV	36	19	5	11	10	0	0	0	0	0	3	8.3	2.2	28	8	0.999
Parechovirus	1	0	1	0	0	0	0	0	0	0	0			1	0	
Mumps virus	6	1	0	5	0	0	0	0	0	0	0			6	0	
Measles virus	1	0	0	1	0	0	0	0	0	0	10	100	0.7	1	1	
Adenovirus	4	3	0	0	0	0	0	0	0	0	0			4	0	
PIV	2	1	0	1	0	0	0	0	0	0	0			2	0	
Enterovirus	91	74	3	15	0	0	0	0	0	0	1	1.1	0.7	89	2	0.000
HHV6	3	2	1	0	0	0	0	0	0	0	0			3	0	
HIV	12	2	4	5	10	0	0	0	0	0	6	50	4.5	10	2	0.693
JCV	5	0	4	1	0	0	0	0	0	0	2	40	1.5	5	0	
RSV	1	1	0	0	0	0	0	0	0	0	0			1	0	
TBEV	92	1	4	84	0	0	0	0	3	0	0			79	13	0.043
<i>Toxoplasma</i> spp.	8	0	0	1	7	0	0	0	0	0	4	50	3	6	2	
Specified	1079	546	64	388	48	7	23	2	15	1	96	8.9	73	829	250	
Unspecified	1504	746	144	500	49	7	8	0	54	1	36	2.4	27	1288	216	
Total patients	2583	1292	208	888	97	14	31	2	69	2	132	5.1	0	2117	466	

Etiyolojisi bilinen 1079 hastadan %8.9’u kronik MSS infeksiyonu

En sık etkenler *T. pallidum*, *Brucella* spp., *M. tuberculosis*

Erdem H et al. Eur J Clin Microbiol Infect Dis. 2017;36(9):1595-1611.

Chronic Meningitis without Predisposing Illness

TABLE 1. *Chronic meningitis – causes*

	<i>n</i>	<i>%</i>
Tuberculous	33	40
Cryptococcal	6	7
Malignant	7	8
Eosinophilic	4	5
Syphilitic	2	2
Sarcoid	1	1
Leptospiral	1	1
<i>Herpes zoster</i>	1	1
Idiopathic	28	34
Responsive to anti-Tb drugs	14	17
Responsive to steroids	9	11
No sustained treatment	4	5
Unresponsive to treatment	1	1
Total	83	



Outcome of Chronic Idiopathic Meningitis

- ❖ 49 kronik idiyopatik menenjit
- ❖ 39 hastada tanı konulamamış.
(10 olguya biyopsi veya otopsi ile tanı konmuş)
- ❖ 33 (%85) olguda prognoz iyi

toms, signs, laboratory values, results of imaging studies, findings on biopsies, results of any empiric treatment, and results of autopsy, if applicable, were assessed. Some of these findings were stratified on the basis of good versus poor outcome of the patients and were analyzed statistically.

• **Results:** Of the 49 patients who fulfilled the criteria for chronic idiopathic meningitis, 10 had a cause identified after repeated studies, brain biopsy, or autopsy (8 of these had a neoplasm). Of 21 brain biopsies, 5 (24%) yielded a diagnosis. Follow-up of the 39

showed that 33 (85%) had a good outcome after a often prolonged illness. Two patients had a meningeal process. Of the eight patients who responded empirically with antituberculous therapy, 5 responded. Corticosteroid therapy of the patients thus treated, but it

did not influence the outcome.

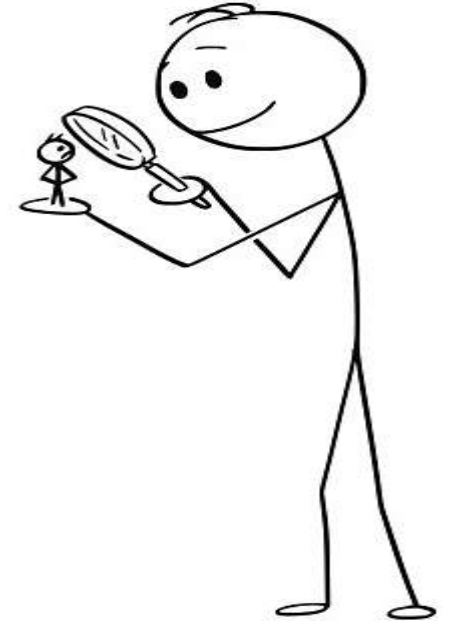
• **Conclusion:** In this study, 85% of undiagnosed cases of chronic meningitis were benign. No clinical or laboratory findings predicted those patients who had a fatal outcome. In our study population, the most useful empiric therapy was corticosteroids rather than antituberculous medications.

(*Mayo Clin Proc* 1994; 69:548-556)

CSF = cerebrospinal fluid; CT = computed tomography; ESR = erythrocyte sedimentation rate; HIV = human immunodeficiency virus; MRI = magnetic resonance imaging

SONUÇ

- Kronik merkezi sinir sistemi infeksiyonlarında süreç oldukça zor
- Titiz ve ısrarlı takip gerekir
- Tanı testleri akıllıca kullanılmalı
- Ülkemizde ilk planda tüberküloz akla gelmeli
- İnfeksiyon dışı nedenler unutulmamalı





İlginiz için teşekkürler