

HIV enfeksiyonlu olgularda CMV

Bahadır Ceylan
Medipol Üniversitesi
Tıp Fakültesi

İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji

HIV pozitif hastalarda CMV

- Retinit
- Gastrointestinal tutulum
- Pulmoner tutulum
- MSS infeksiyonu

CMV retinitis

-ART öncesi dönem
-CD4<50



CMV retinitisi %21-44

ART



CMV retinitisi %80 azaldı

-CD4 sayısı düşer
-CD4 fonksiyonu azalır

-HLA B44
-HLADR7

CD4 bağımlı CMV spesifik
sitotoksik T lenfosit yanıtı azalır

CMV' ye daha az yanıt

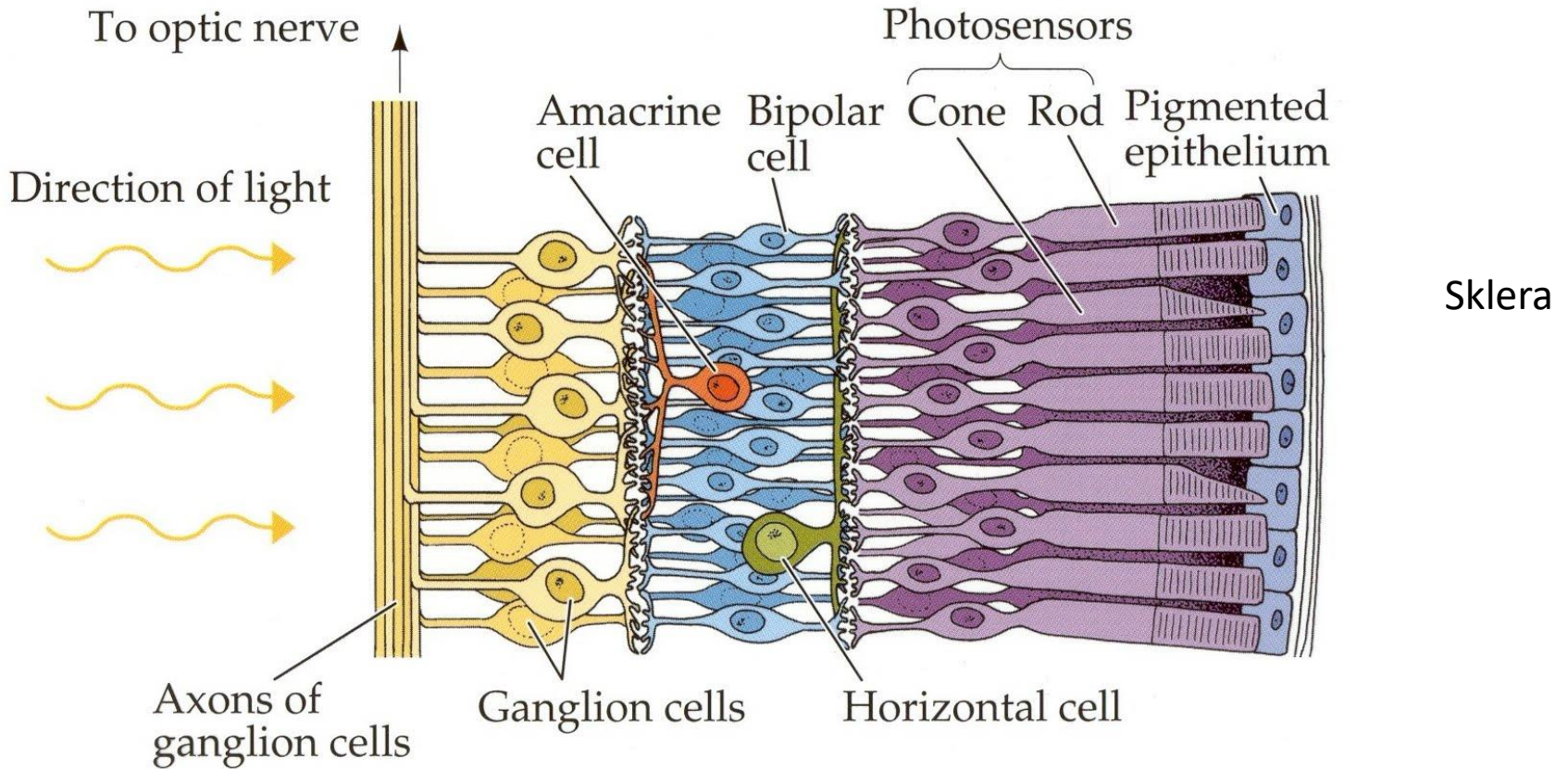
CMV aktivasyonu

Viremi

Retinit

CMV genomunda
IL-10 benzeri yapı içerir

Normal retina



CMV retiniti patolojisi



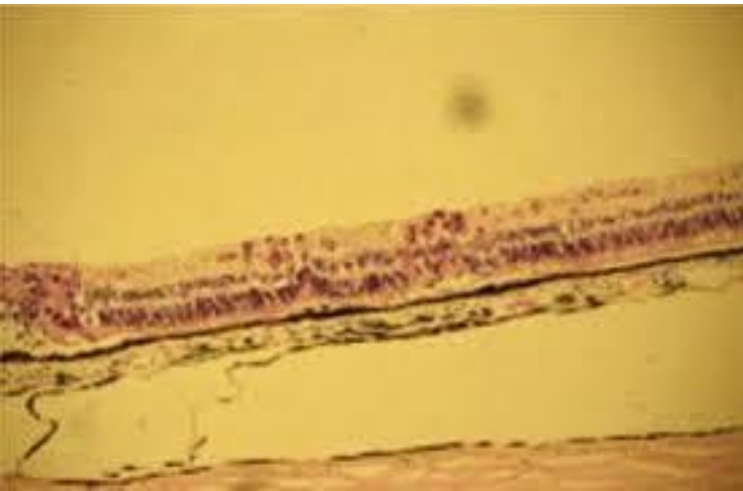
-Tam kat nekroz
-Ödem



Skar

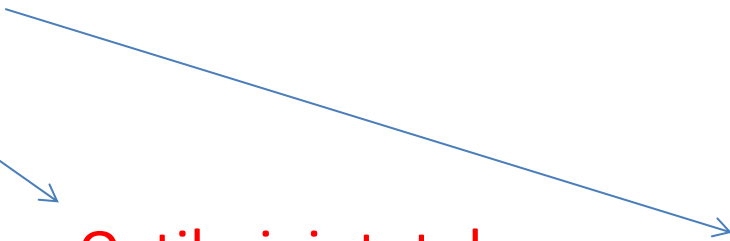
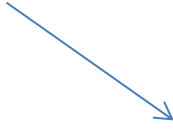


Retinal yırtılma



Retinal immunhistokimya

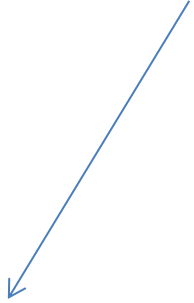
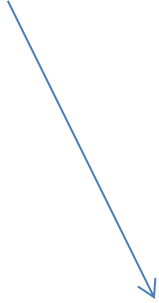
CMV retinitisi



Makuler tutulum

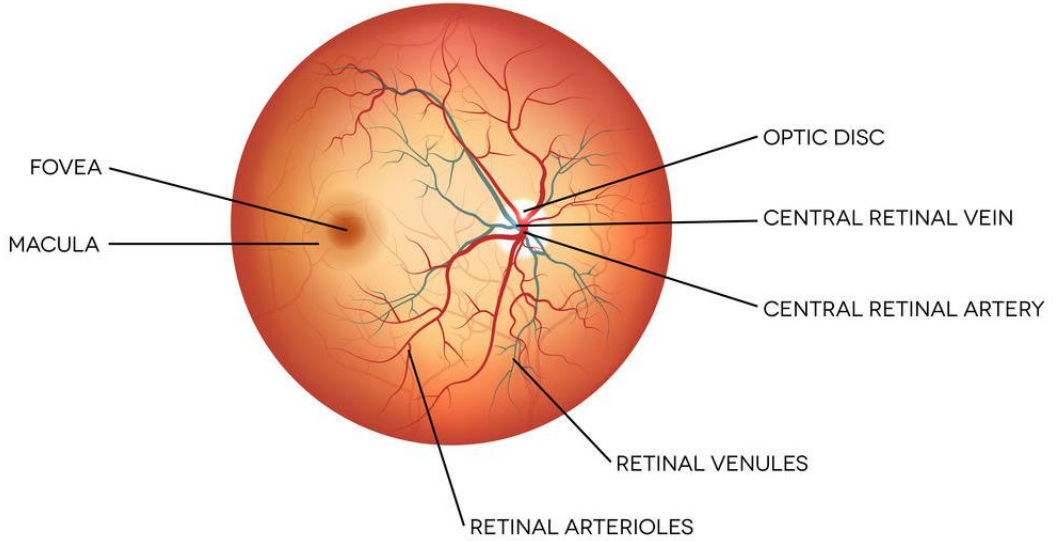
Optik sinir tutulumu

ART

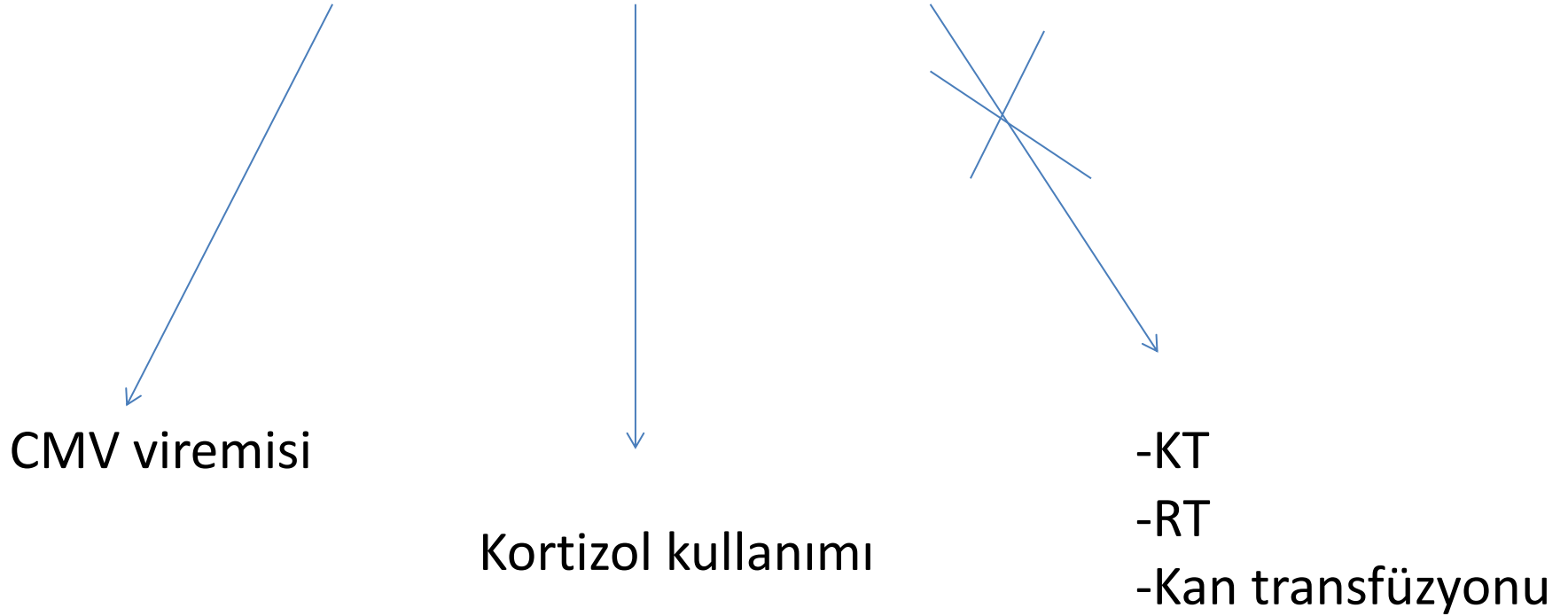


Görme bozukluğu

IRU (Immune recovery uveitis)

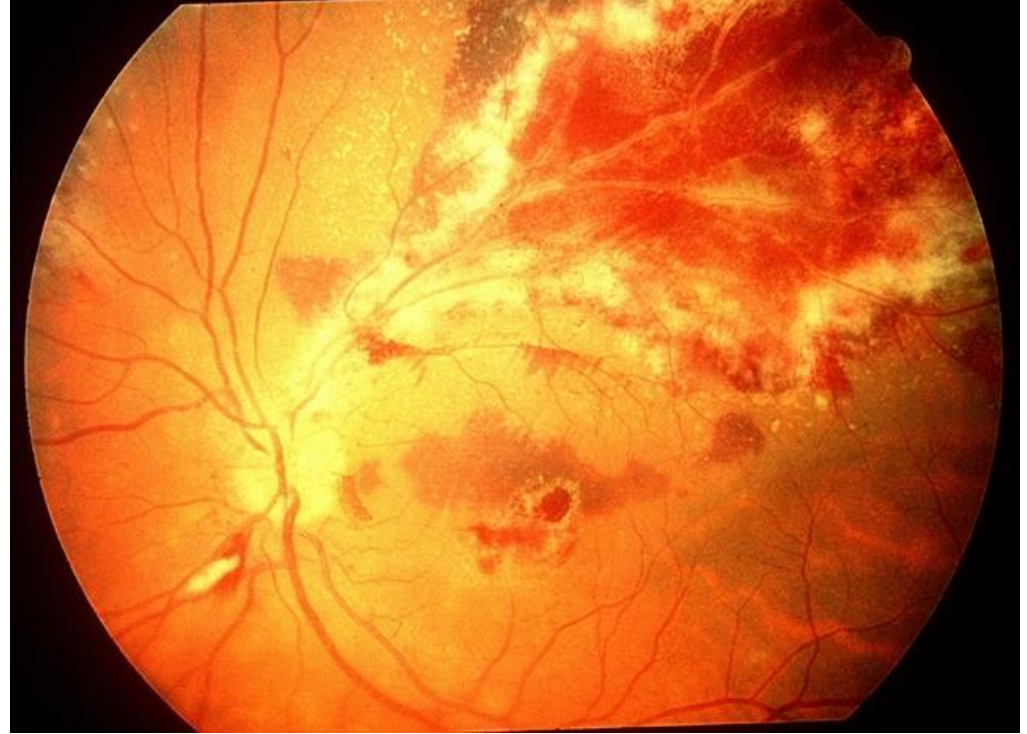


CMV retiniti risk faktörleri



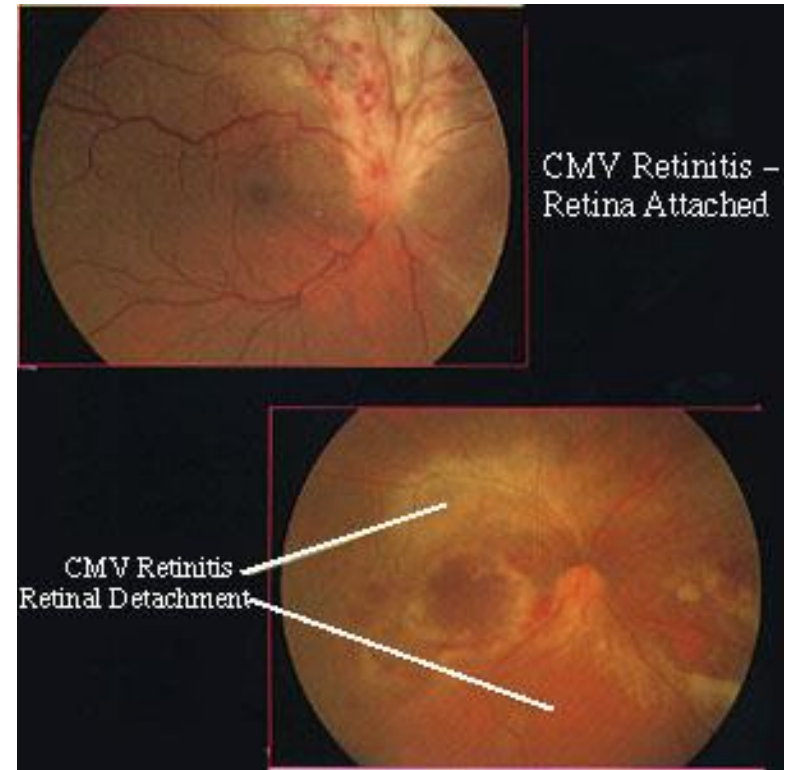
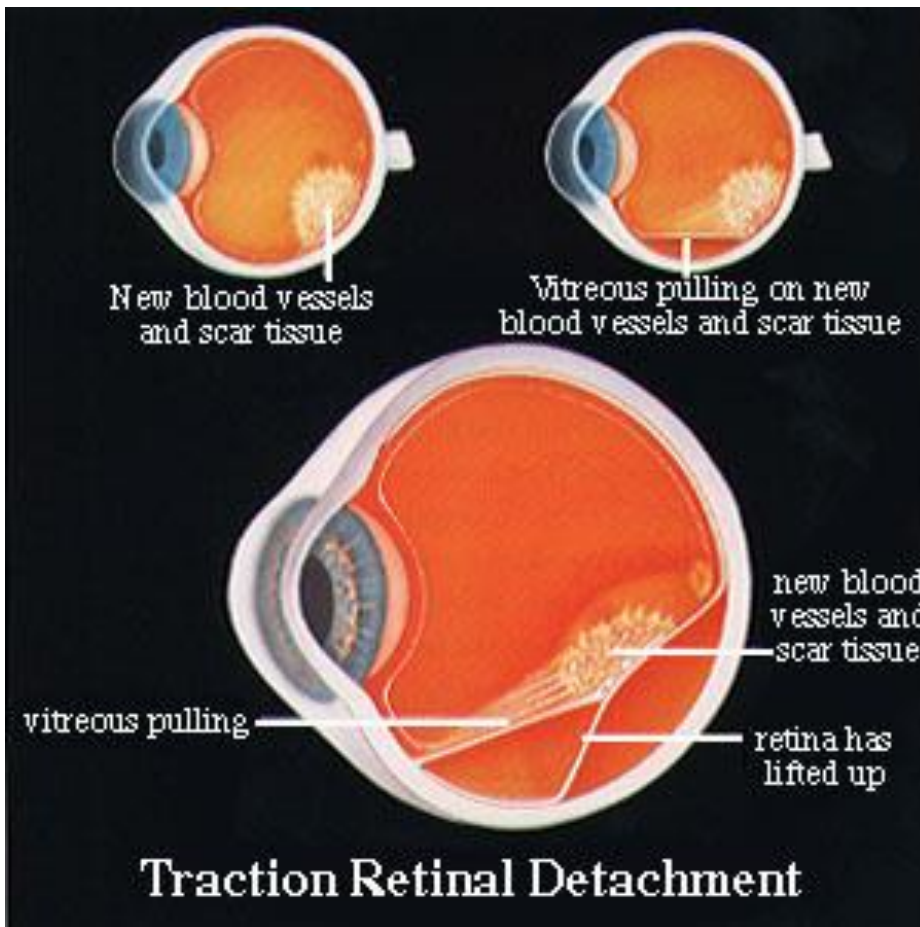
CMV retinitisi kliniđi

- En önemli semptomlar
 - Yüzen cisimler
 - Işık çakmaları
- Santral görme kaybı
- Skotom

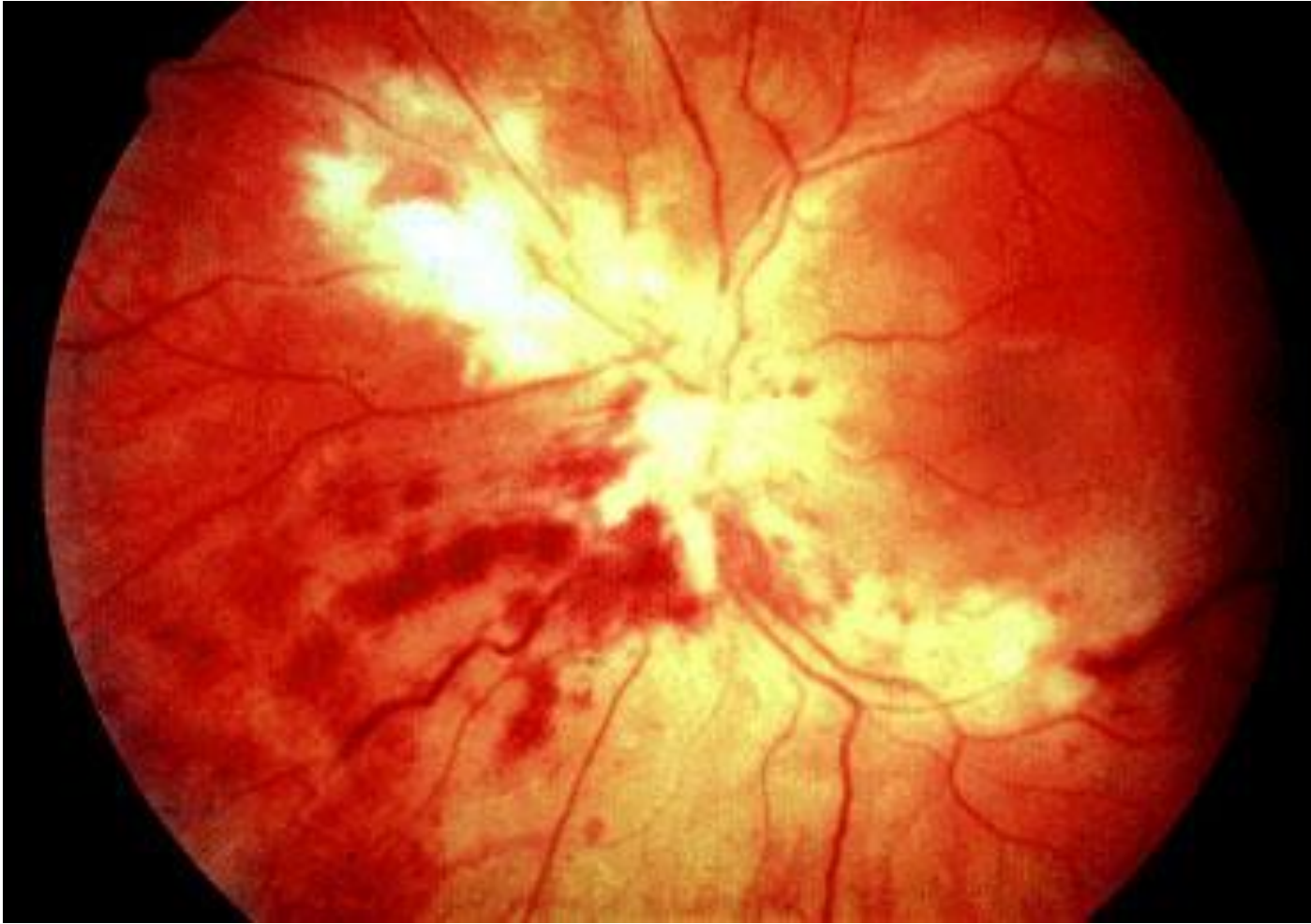


Damarlara yakın beyaz sarı granuler
Hemorajik retinit-makula veya optik
Sinire yakınsa görme kusuru olur

Önce 1 göz tutulumu → Tedavi yok → İkinci göze yayılım



Periferik retinitlerde daha sık



CMV-retiniti



%50 kanda CMV DNA pozitif

AIDS-CMV viremisi



1 yıl takip



% 50 organ hastalığı

CMV IgG negatifse CMV retiniti olasılığı çok az

Latent intraokuler CMV antijen

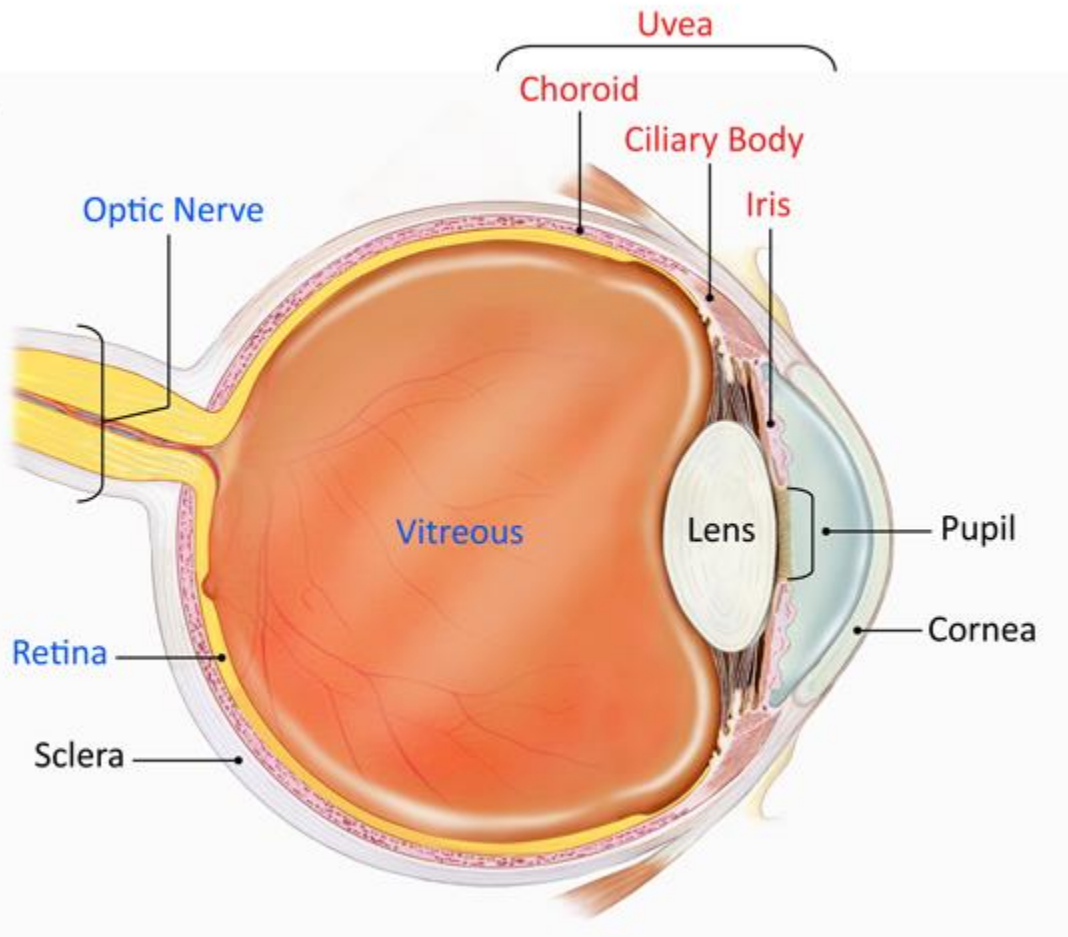
ART

T-hücre immun reconstitution

20 (2-84) hafta

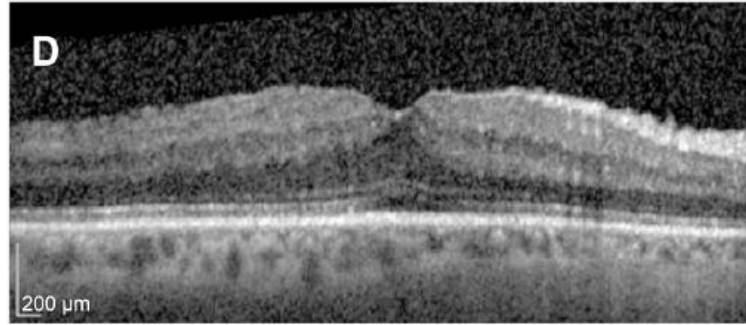
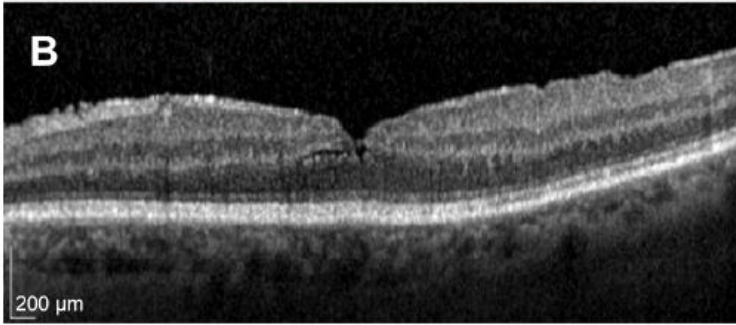
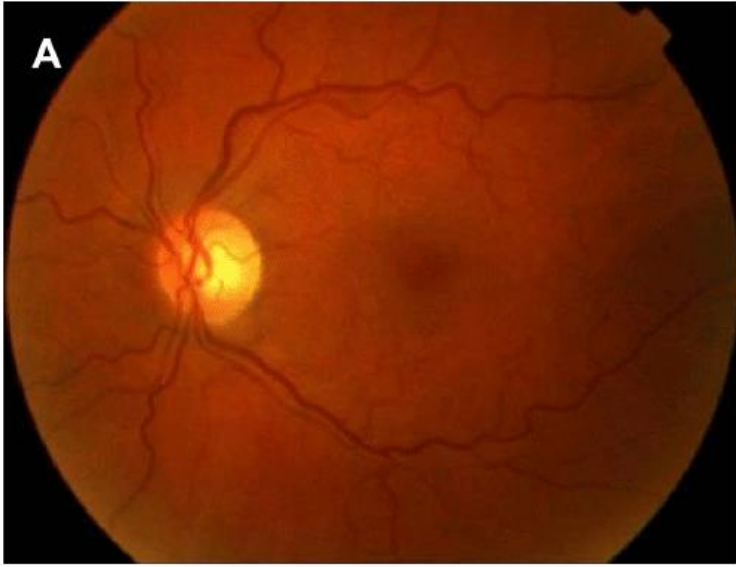
IRU (immune recovery uveitis)

Görme kaybının %50 sebebi

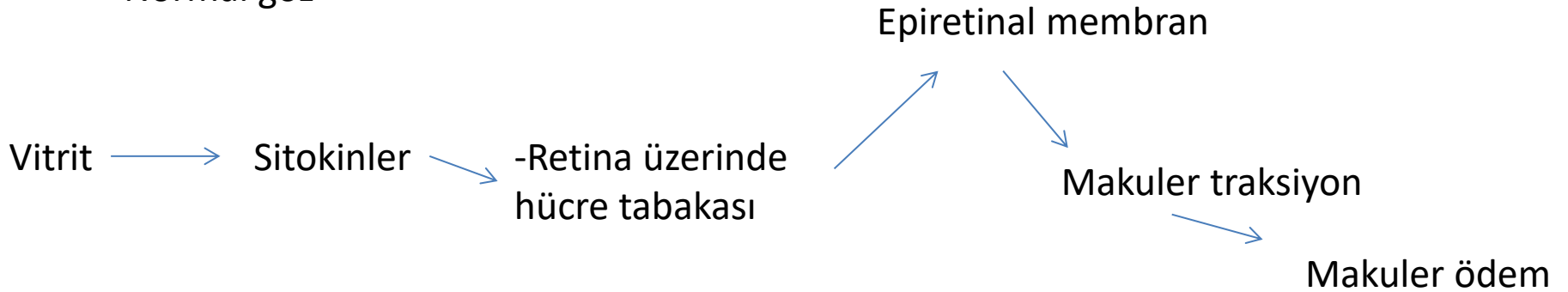


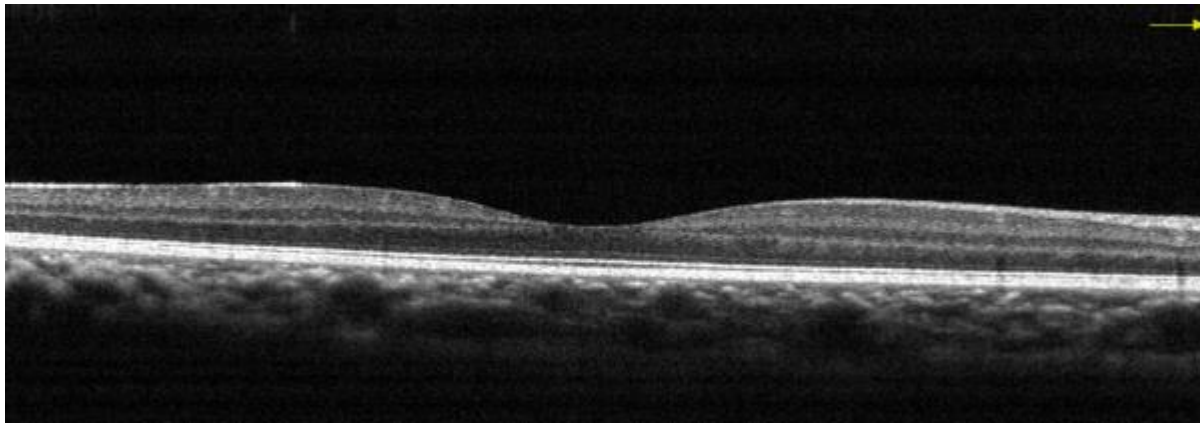
Vitritis



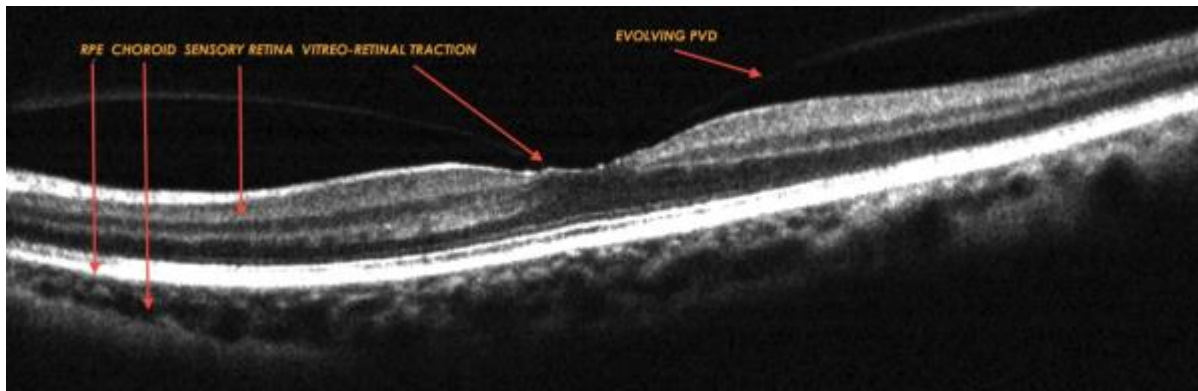


Normal göz

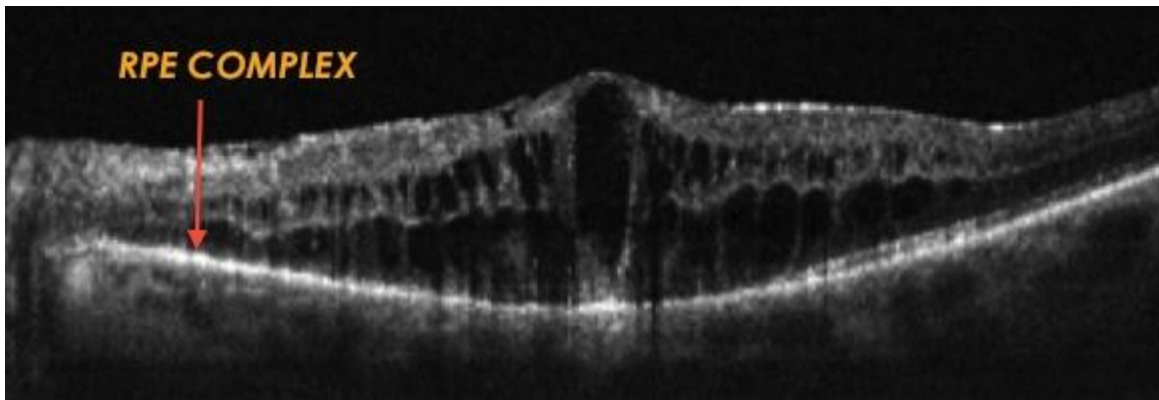




Normal makula



Makular kistoid ödem



Makular kistoid ödem

CMV retinitisi

Optik sinir veya makulaya uzaklık

<1500micron

>1500micron

Intravitreal gansiklovir veya foskarnet
+
Oral valgansiklovir

Oral valgansiklovir

Intravitreal tek doz sistemik tedavi için zaman kazandırır

Valgansiklovir

İV gansiklovir



Etki aynı



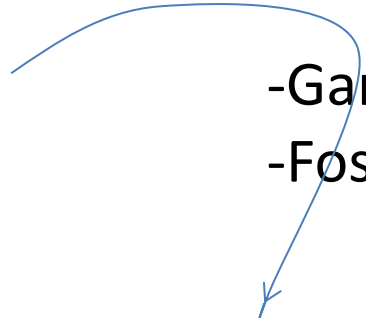
İV Gansiklovir



İV foskarnet

Cidofovir

-Gansiklovir
-Foskarnet



İn-vitro aktivite 10-100kat fazla

İndüksiyon tedavisi (2 hafta sonra ART başla)

2-3 hafta

İdame tedavisi

- En az 3 ay
- HIV RNA negatif
- CD4 > 100 (3 ay)

İdameyi kes

CMV retinitisi relapsı

Kandan ve vitreal sıvıdan CMV direnci

Valgansiklovir
+
İV foskarnet

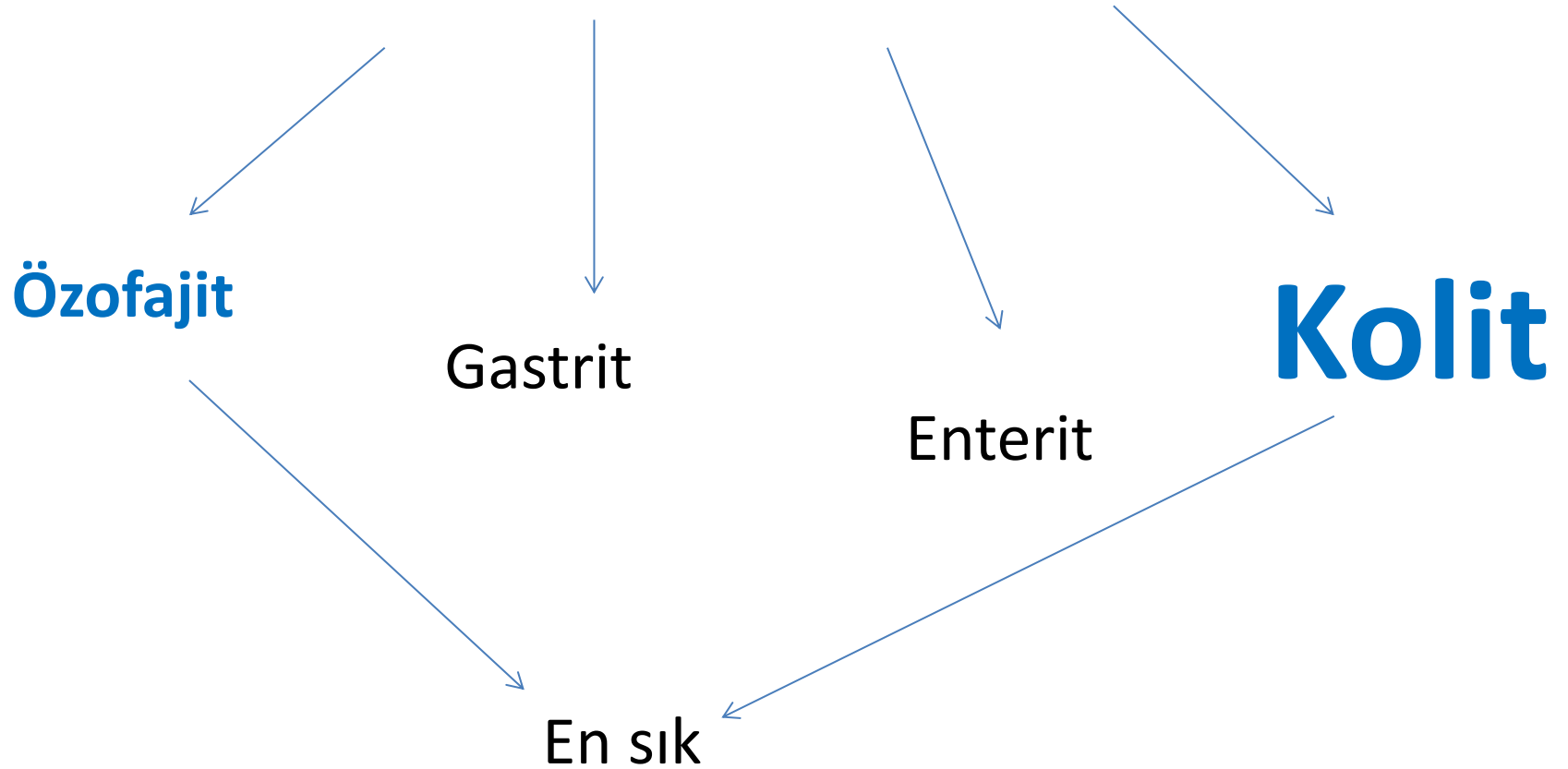
ART almayan hasta gansiklovire rağmen
muhakkak nükseder

Tolere edemezse
-Farklı ilaçla monoterapi

IRU tedavisi (görme bozulursa)

- Topikal steroid
- Göz içine kortikosteroid injeksiyonu

CMV-Gastrointestinal tutulum



Özofajit



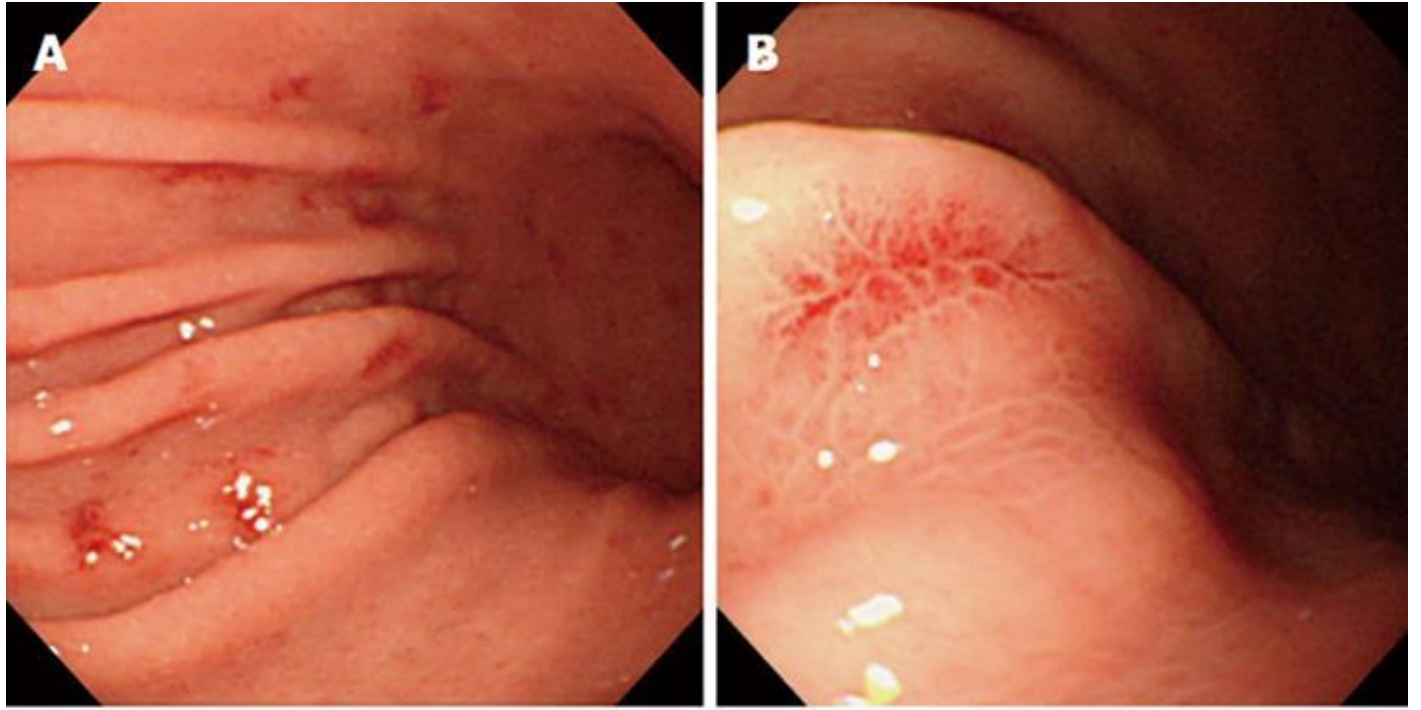
Alt özofagus sfinkterinde
çok sayıda ülser



- Odinofaji
- Substernal ağrı

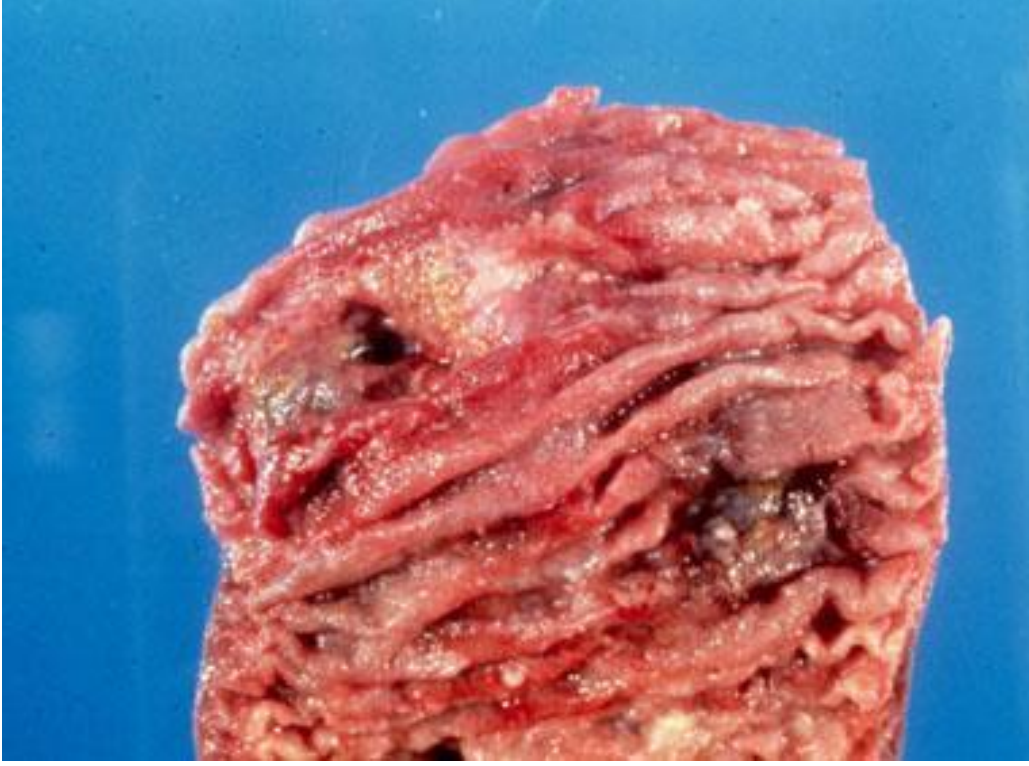


Geniş sığ ülser



CMV gastriti-eritematöz alanlar
-Epigastrik ağrı, bulantı

Geniş sığ ülser



- Ateş, bol sulu ishal
- Distal kolon tutulusa
 - tenezm, sık ve az dışkılama
- Kanama
- Perforasyon

CMV koliti



Erozyon



Derin ülser



Nekrotizan kolit

Semptom

+

Endoskopi bulgusu

+

Patolojik bulgu



CMV tedavisi

Klinik

+

Endoskopik bulgu

+

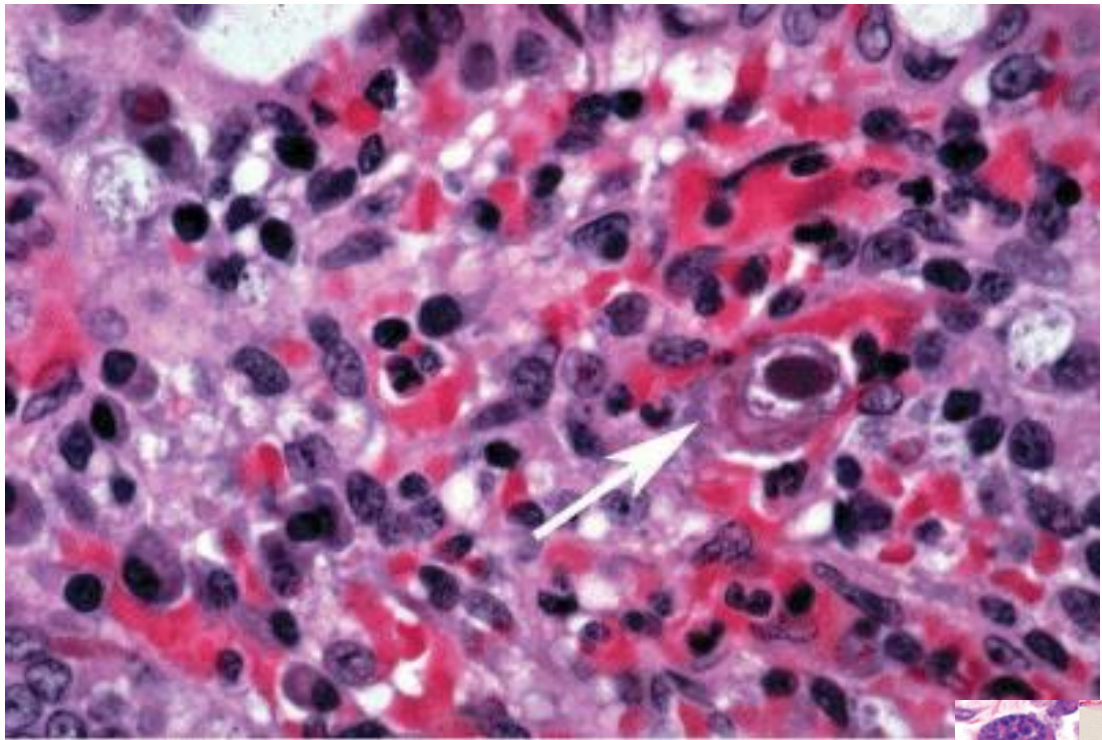
CD4<50



CMV empirik tedavisi

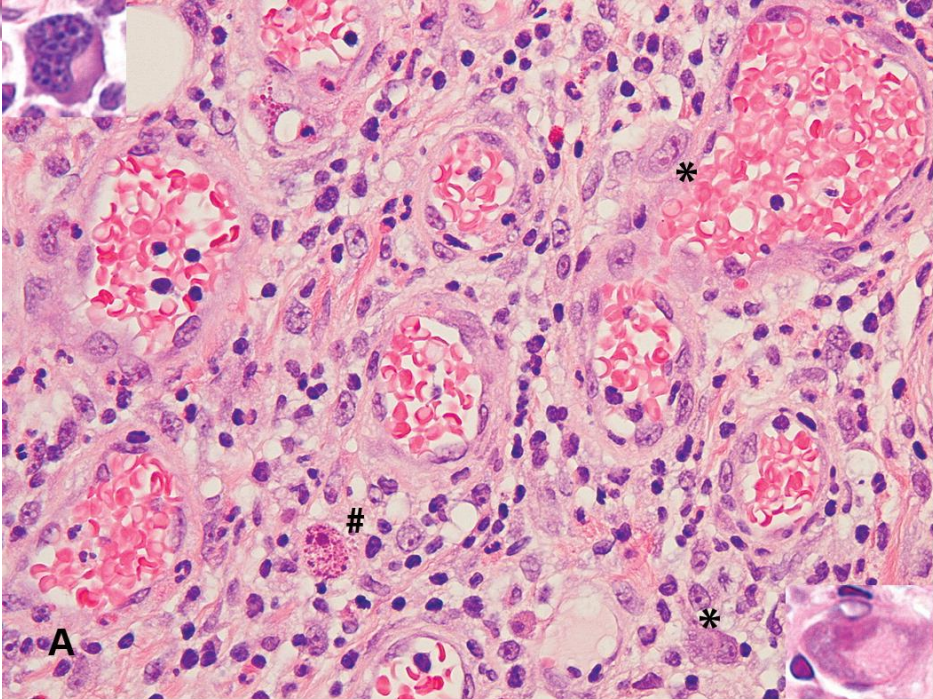
+

ART

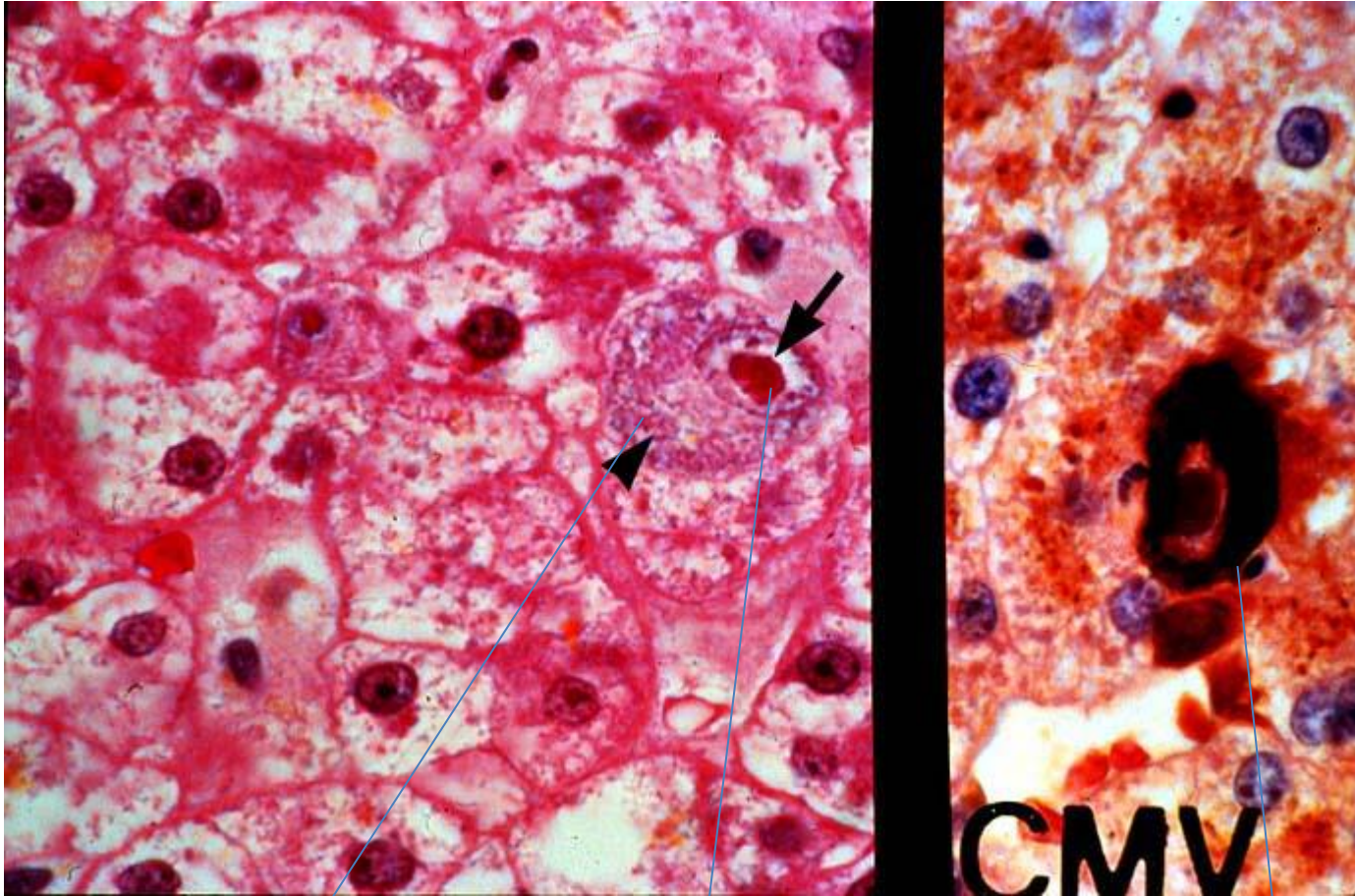


Eosinofilik intranükleer

Bazofilik sitoplazmik



HİSTOPATOLOJİ



Bazofilik, sitoplazmik, granüler

Eozinofilik, intranükleer

İmmünohistokimya

Daha duyarlı

- CMV DNA ÖLÇÜMÜ?

GIS CMV tutulumu



Göz muayenesi



Normalse



CD4 >50 olana kadar 6 ayda bir kontrol

CMV gastrointestinal tutulumu

İV gansiklovir

Kontrendikeyse foskarnet

Semptomlar azalınca ve
Absorbsiyon sorunu yoksa
oral gansiklovire geç

3-6 hafta **indüksiyon**

-Direnç?
-Başka etyoloji?

Düzelme yok

İdame

CD4>100 OLUNCAYA KADAR

CMV gastrointestinal tutulum



Valgansiklovir idame



- İlacın düzensiz kullanımı
- GIS absorpsiyonunda bozukluk
- Eskiden valgansiklovir alan

ilaç direnci



Relaps



CMV direnç testi gönder

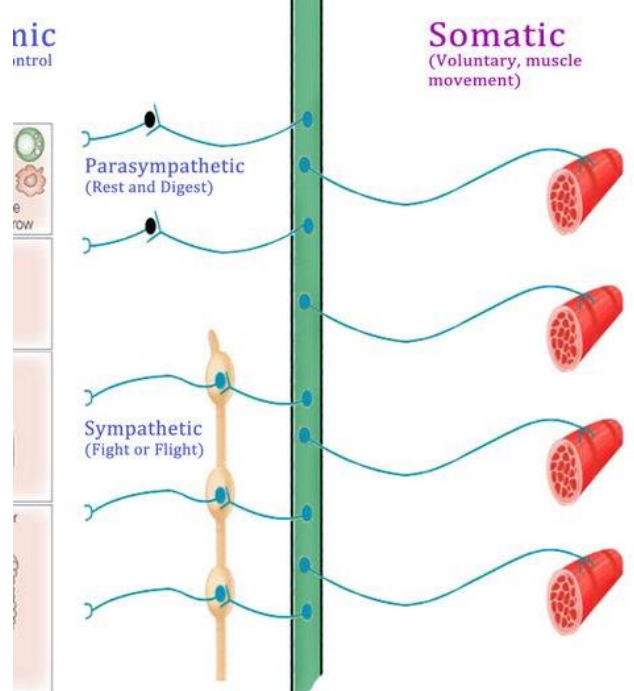
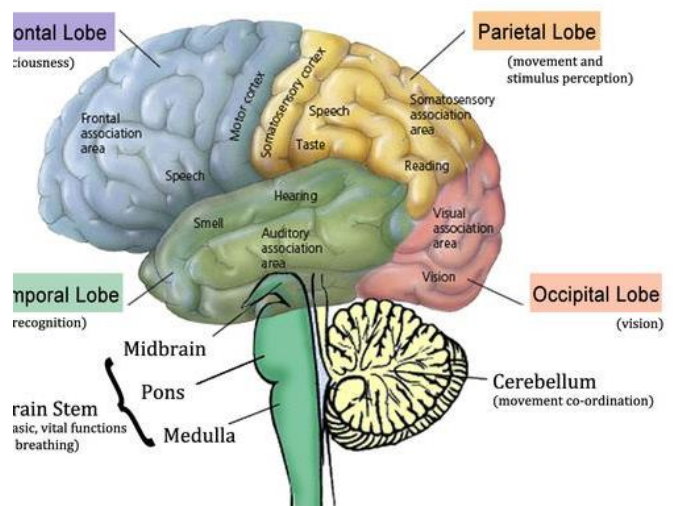
6 hafta



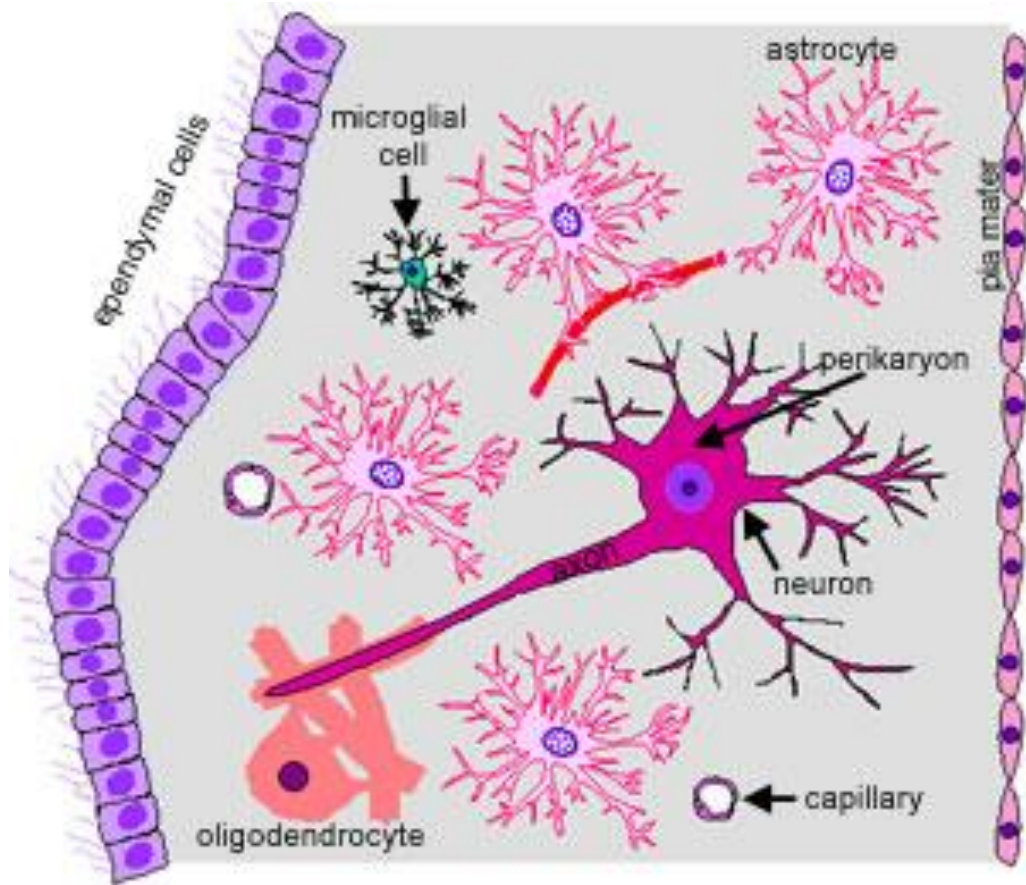
Gansiklovir
+
Foskarnet



CMV-Nörolojik hastalık



- Beyin
- Medulla spinalis
- Sinir kökleri
- Periferik sinirler

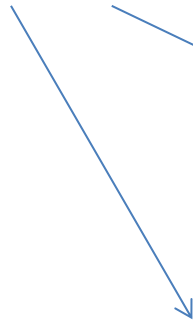


- Astrosit
- Oligodendrosit
- Ependimal hücre
- Nöron
- Kapiller hücre

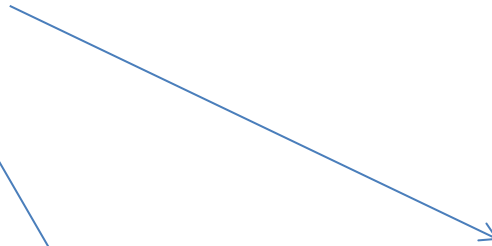
CMV ensefaliti



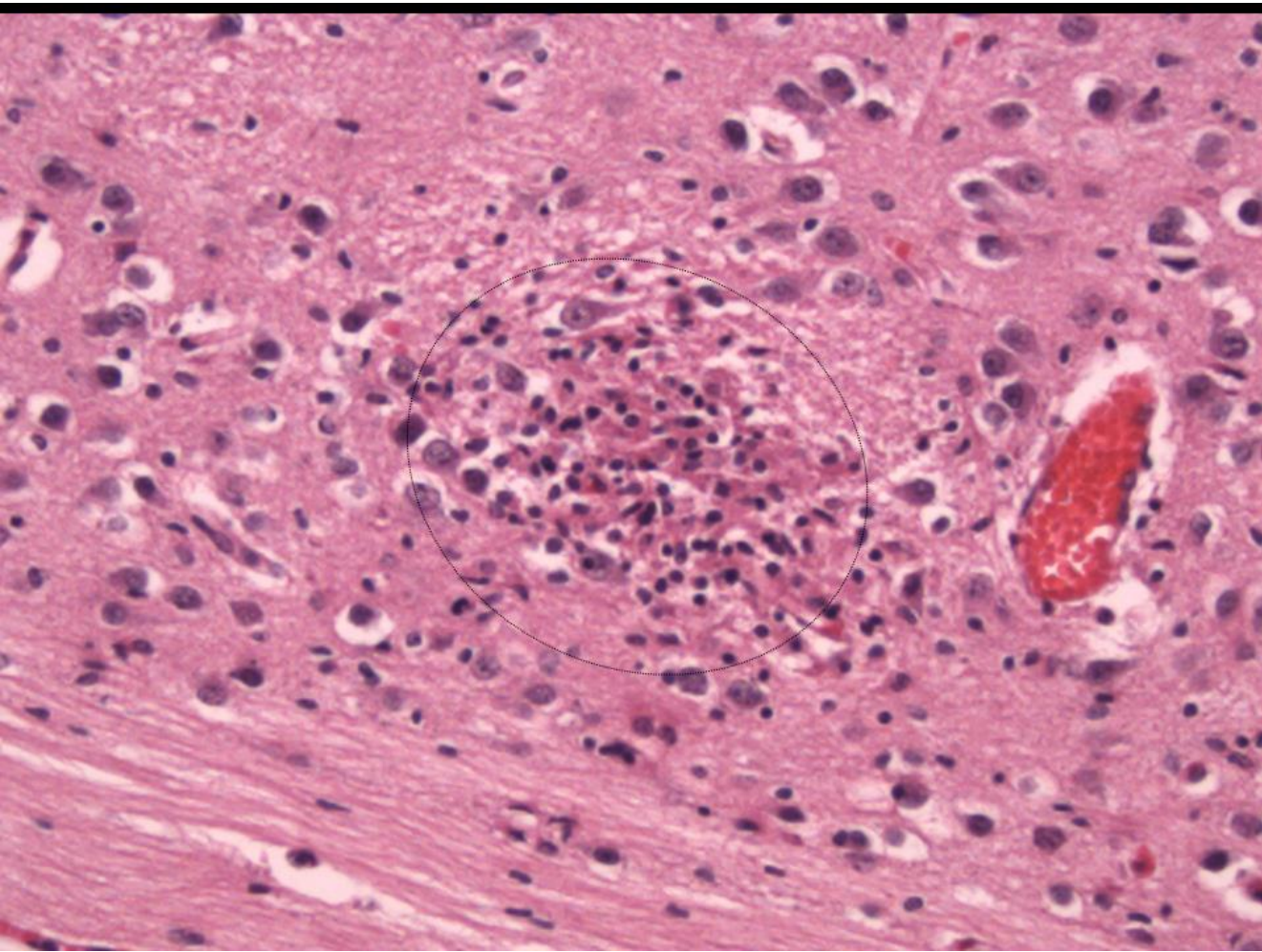
Mikroglial nodül



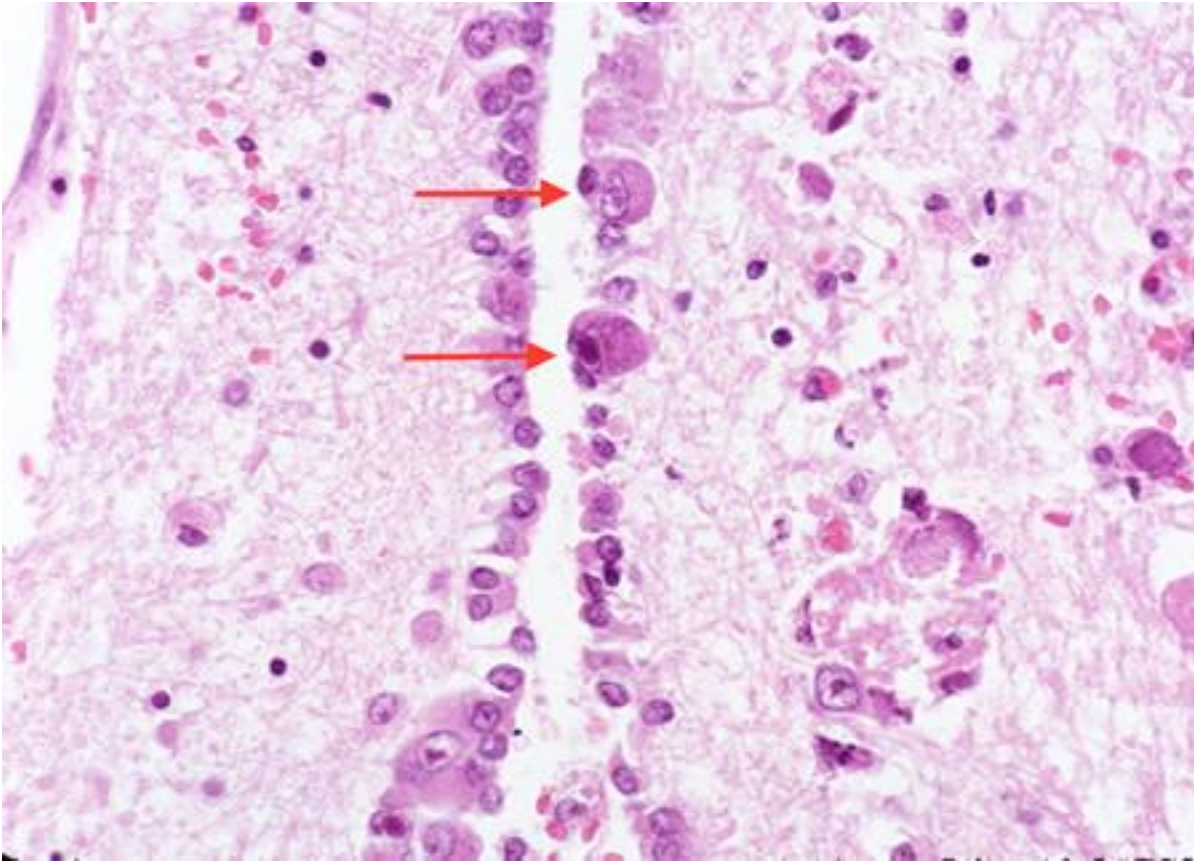
Ventriküloensefalit



Fokal parenkimal nekroz

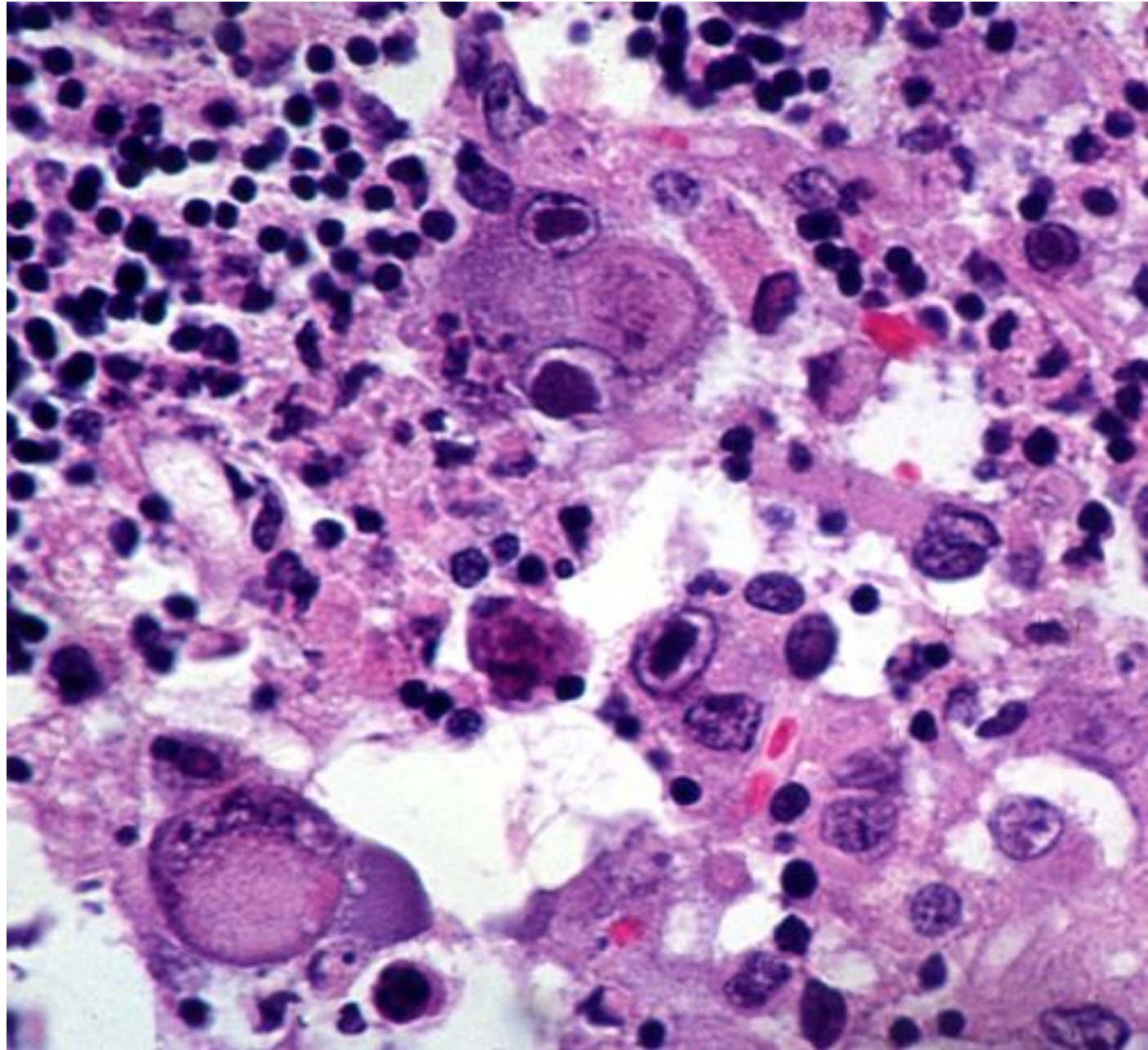


Mikroglial nodül. Lenfosit ve mikroglial aktivasyon



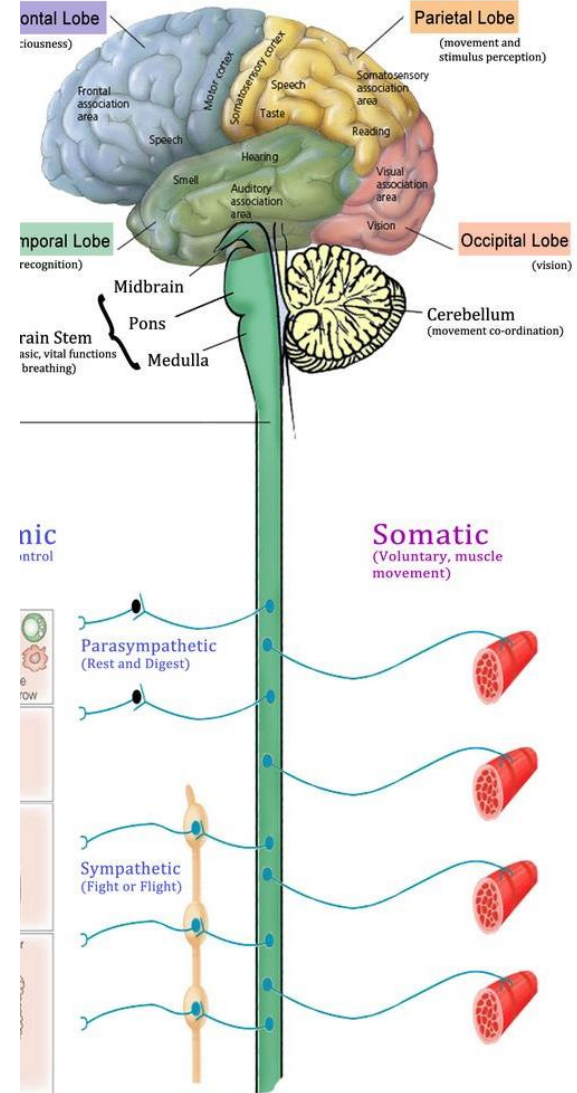
Ventriküloensefalit. Ependimal hücrelerde ve periventriküler dokuda fokal veya diffüz hasar

Intranükleer inklüzyonlar



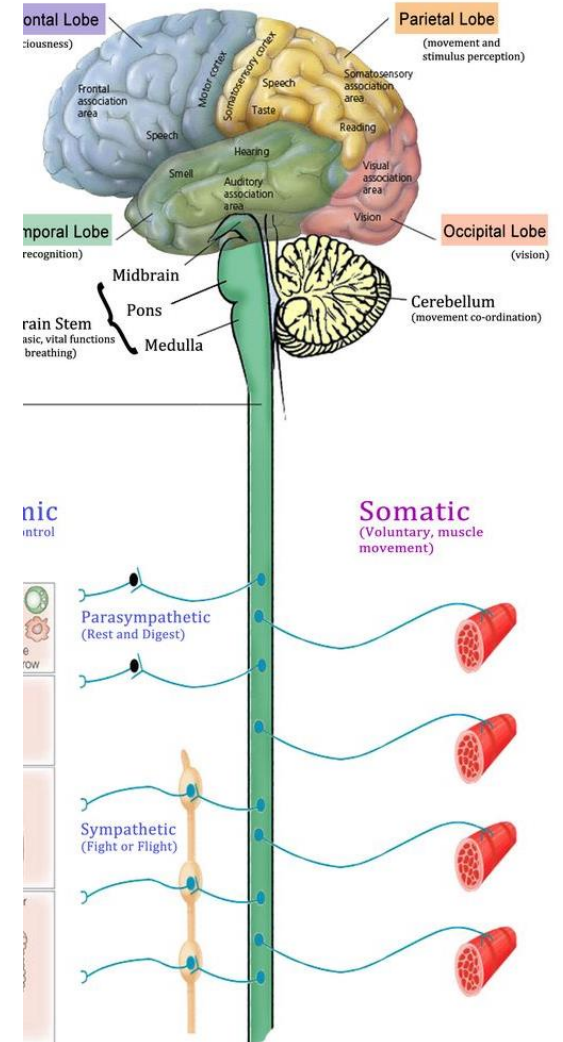
CMV ensefaliti

- Demans gibi
- Konfüzyon
- Konvülziyon
- Fokal nörolojik bulgu



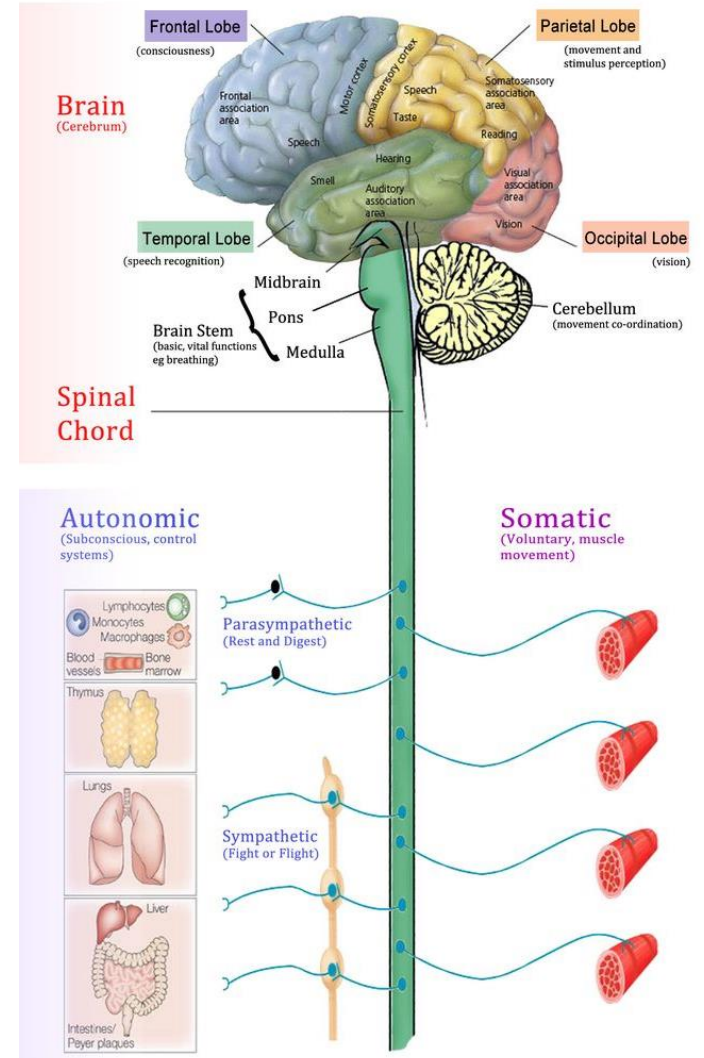
CMV miyeliti

- Alt ekstremitelerde güçsüzlük
- Tendon reflekslerinde artma



CMV Poliradikulopati

- Alt ekstremitede güçsüzlük
- Tendon reflekslerinde azalma
- Üriner retansiyon



CMV-periferik nöropati

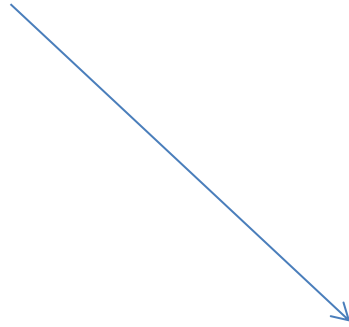
- **Mononöritis multipleks**

- Kranial sinirlerde asimetric multifokal sensoriyal ve motor kayıp

- Periferik sinirlerde asimetric multifokal sensoriyal ve motor kayıp

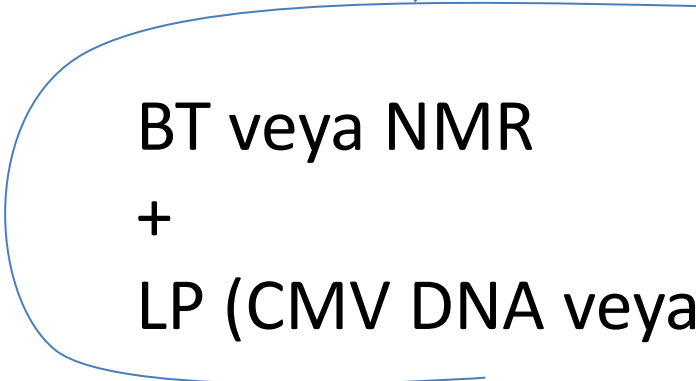
CD4 <50

Nörolojik semptom



CMV?

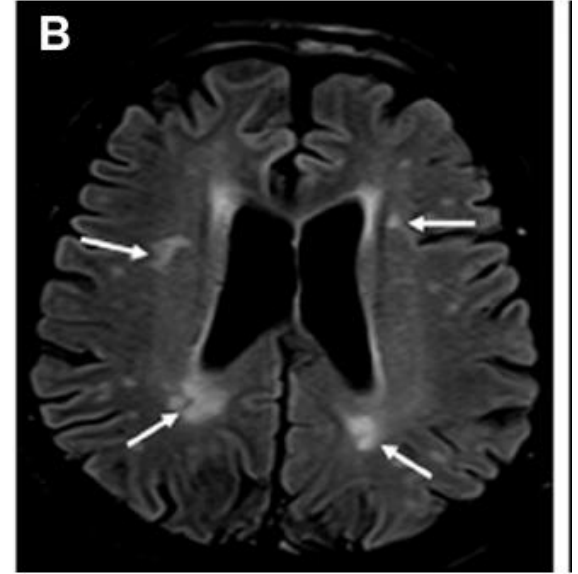
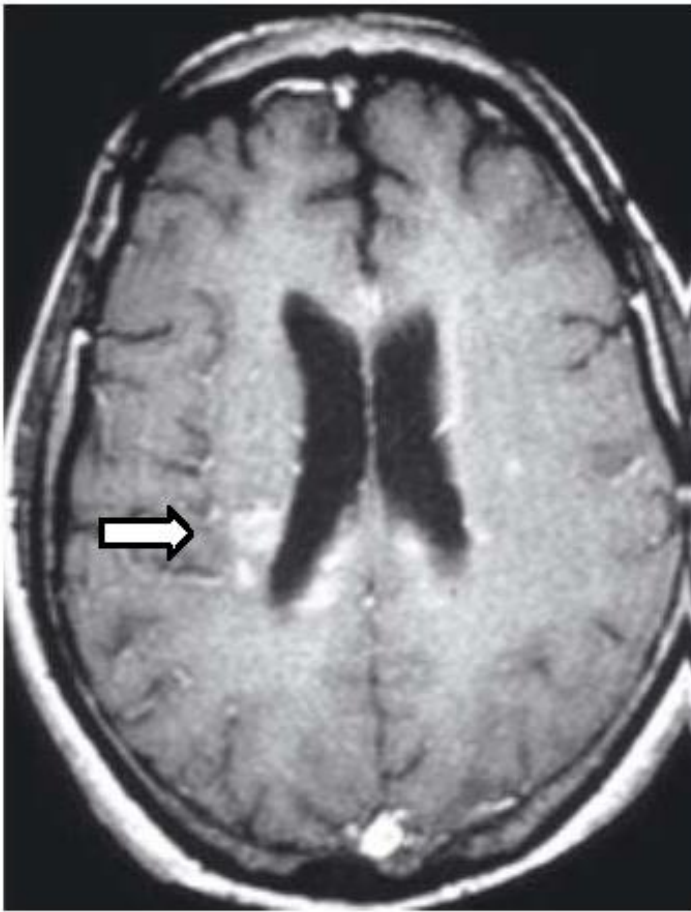
Kanda CMV DNA
ÖZGÜLLÜK?
DUYARLILIK?



BT veya NMR

+

LP (CMV DNA veya CMV anitijeni)



CMV-periventriküler ensefalit

Dışlanması gereken hastalıklar

- Tokso plazma
- PMLE
- Lenfoma

NMR



**Periventriküler ve
meningeal tutulum**



CMV?

-Duyarlılık?

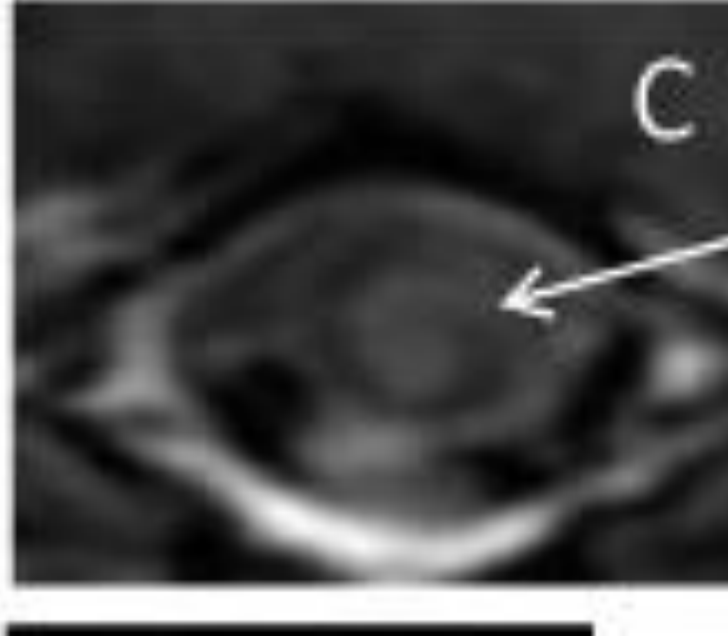
BOS CMV PCR



%100 duyarlı



NMR' da hiperintens görünüm
Kitlenin ekarte edilmesi



BOS' ta CMV DNA veya antijen pozitif

CMV radikülo Miyelopati

- NMR' DA sinir köklerinde kalınlaşma ve kitlenin ekarte edilmesi
- BOS' ta PNL, CMV DNA veya CMV antijeni

CMV periferik nöropati

- Sinir biyopsisi
- BOS CMV DNA pozitifliği

CMV MSS tutulumu

Şuur bozukluğu

-Mononöritis multiplex
-Poliradikulopati

İV gansiklovir

+

İV foskarnet

? (retinit)

Oral valgansiklovir

İdame (oral?-retinit)

ART' yi 2 hafta sonra başla

6 ay CD4>100 ise kes

Cidofovir alternatif

CMV-Pulmoner hastalık

75 HIV pozitif hasta-otopsi (38' i ARDS)



44(%59) CMV histolojisi pozitif



%50' sinde akciğer normal



21' inde akciğer patolojisi var

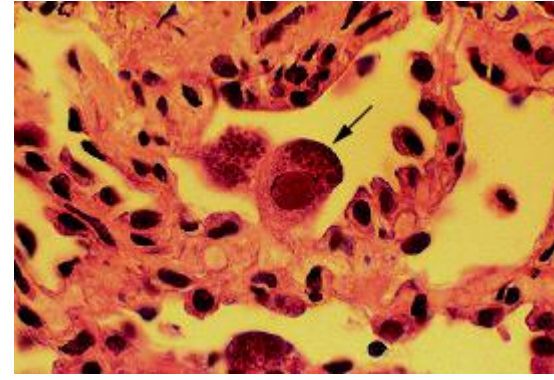


6' sında CMV tek başına



15' inde copatojen va

İnfekte pnömosit



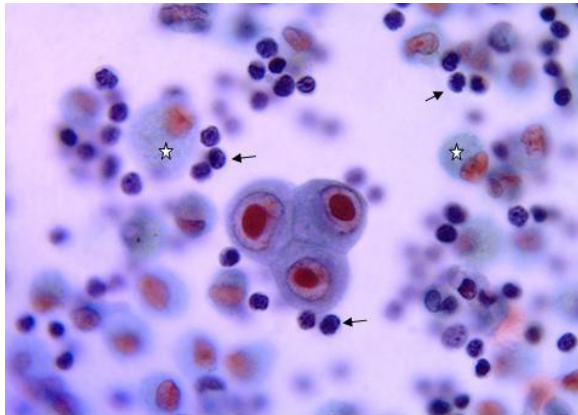
Pnömonili hasta, CD4<50

BAL CMV kültürü veya
CMV PCR

BAL immunhistokimya veya
Sitopatik etki

Akciğer biyopsisinde
İmmunhistokimya ve
Sitopatik etki

HIV pozitiflerin %50' sinde pozitif
Duyarlılık %50



Daha özgül

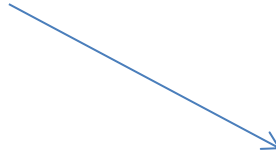
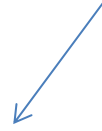
Duyarlılık az
(yamalı tutulum)

98 HIV pozitif hasta-PCP pozitif



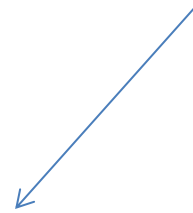
26' sında CMV pozitif

PCP ve CMV birlikteyse
GKK mortaliteyi artırır



13' üne CMV tedavisi + PCP tedavisi

13 hasta sadece PCP tedavisi



Mortalite aynı

