OLGU SUNUMU

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Antalya Eğitim ve Araştırma Hastanesi

Olgu

- AG G, 32 Yaş, Kadın
- Antalya'da yaşıyor
- Seks işcisi
- Heterosexüel multiple partner
- <u>Özgeçmiş:</u>
  - DM (10 yıldır düzensiz OD kullanımı)
  - Psöriasis vulgaris* (20 yıldır steroid krem kull.)

*HIV ile birliktelik sık!!

11 Kasım 2016
Nöroloji Kliniği

- Psöriasis vulgaris'te son 2 yılda şiddetlenme
- Halsizlik, yorgunluk, kilo kaybı (1 yılda 40 kg)
- Bacaklarda yavaş ilerleyen güçsüzlük
- EMG: yaygın sensörimotor periferik nöropati

- Guillain-Barre Sendromu ön tanısıyla Nöroloji kliniğine yatırılıyor
  - 5 gün 0.4 mg/kg IVIG veriliyor

Nöroloji Kliniği

- **Anti HIV: Reaktif**

- **Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji konsültasyonu isteniyor**

- **HIV RNA, $CD4^+$ sayısı, PA Akciğer grafisi, Batın USG isteniyor**

  (WB gönderilmiş)

Enfeksiyon Hastalıkları ve KM Kliniği

- Nöropati ve parezi edinsel immun yetmezlik sendromuna bağlı olarak yorumlanıyor

- Tüberküloz açısından göğüs hastalıkları görüşü isteniyor

- Hasta AIDS ± tüberküloz ? ön tanısıyla 22.11.2016'da kliniğimize devir alınıyor

CMV Nörolojik Tutulum

- Demans
- Ensefalit
- Poliradikülomyelopatiler

(Gullian Barre-benzeri sendroma neden olabilir!)

Fizik Muayene

- Ateş yok, vital bulguları stabil
- Kaşektik görünümde, saçlı deri dahil tüm vücutta hiperkeratoz (+)
- Bilinç açık, oryante-koopere, ense sertliği yok
- Denge bozukluğu ve her iki alt ekstremitede hareket kısıtlılığı (+)
- Dinlemekle bilateral akciğer sesleri azalmış
- Batın rahat, hepatomegali yok, traube kapalı
- Periferik LAP yok, tinea pedis ve onikomikoz (+)

Laboratuvar Bulguları

- Hgb:9.1g/dL WBC:7600/mm^3 (lenfosit:500) PLT: 120.000/mm^3
- $CD4^+$: %1 (5)
- HIV RNA: 1.757.446 kopya/ml
- Glukoz:185 mg/dl AST:147 u/L ALT:36 u/L
  GGT:825 u/L ALP:395 u/L LDH:345
  total /direkt bilirubin: 2.1 /0.94 mg/dl
  Hba1c: 9.3 Kr: 0.62 mg/dl
- Trigliserid: 373 diğer lipid profili normal
- CRP:59mg/L Sedimentasyon:58mm/saat
- TFT ve TİT normal, kan ve idrar kültürü steril

Laboratuvar

- HBs Ag(-) anti HBs(-)
- anti HCV(-)
- anti HAV IgM (-) IgG (+)
- VDRL(-) TPHA(-)
- Toxo IgG(-) Toxo IgM(-)
- CMV IgG(+) IgM(-)
- VZV IgG(+) IgM(-)
- HSV 1 ve 2 IgG(+) IgM(-)
- HIV direnç testi gönderildi (direnç yok)

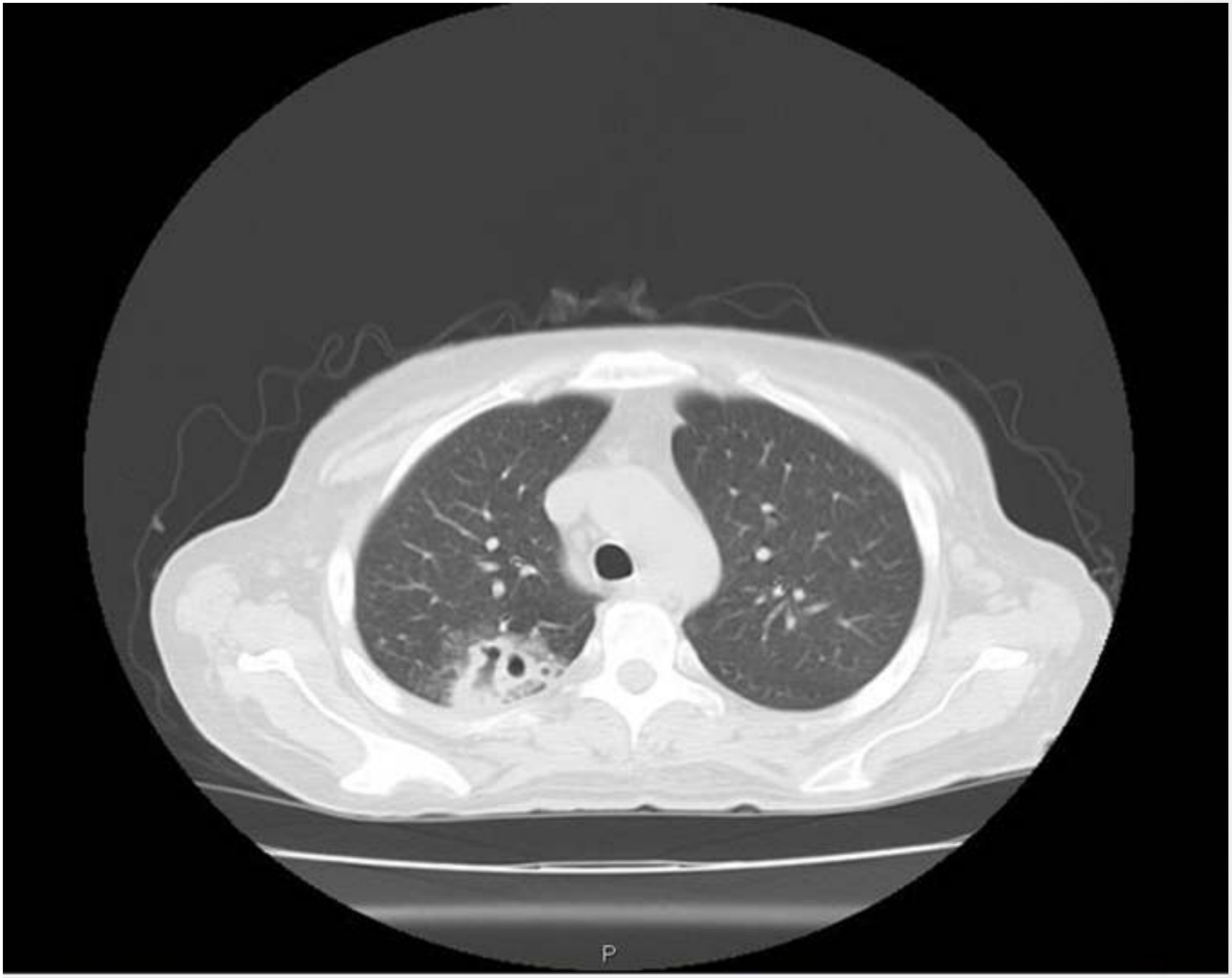
Laboratuvar

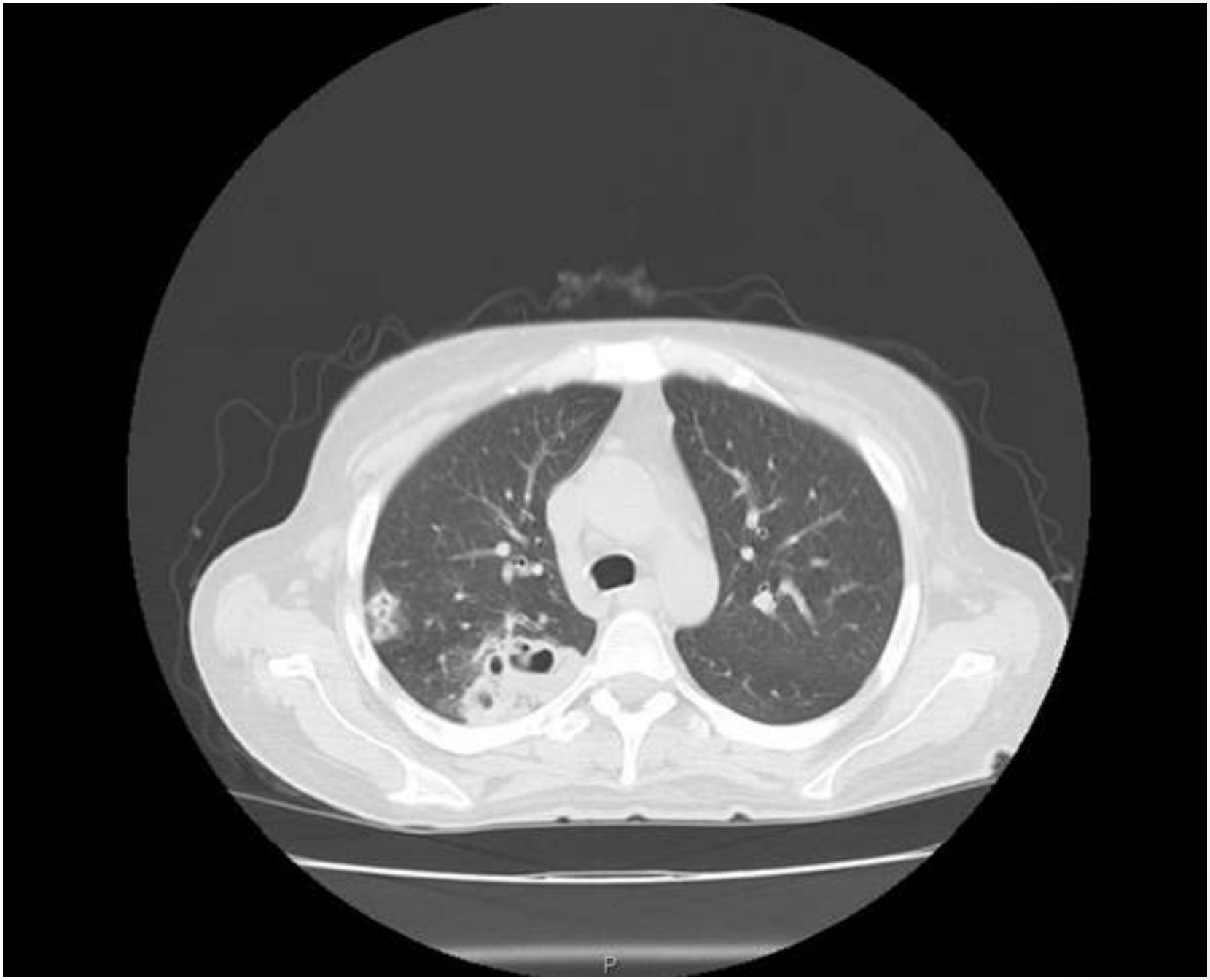
- **PA AC Grafisi:** Sağ üst lobda dansite artışı!

- **Batın USG:** Dalak 150 mm KC 175 mm
  (grade 3 hepatosteatoz)

- **Toraks BT:** Sağ üst lob posteriorda kalın cidarlı, kaviteleşme gösteren konsolidasyon alanı, aynı lokalizasyonda 1-2 adet kaviter lezyon ve komşuluğunda buzlu cam dansiteleri , sol akciğer alt lobda asinenodüler infiltrasyon
- Yorum Tbc'ye benzemiyor!

- **PPD:** 0 mm **IGRA:** independent


P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24 Kasım 2016 Tedavi?

- Tüberküloz?
- CMV?
- PCP?
- Septik emboli?
- Kaviter pnömoni?
- Pulmoner vaskülitler?
- Acil ART başlanmalı mı?

AIDS Patient Care STDS. 2001 Jul;15(7):353-61.

Cavitary lung disease in AIDS: etiologies and correlation with immune status.

Aviram G[1], Fishman JE, Sagar M.

Author information

1 Department of Radiology, Jackson Memorial Hospital, University of Miami School of Medicine, Miami, Florida.

Abstract

To investigate the etiology and differential features of cavitary lung disease in patients with acquired immune deficiency syndrome (AIDS), chest computed tomography (CT) records from a 2-year period were reviewed to identify all human immunodeficiency virus (HIV)-positive patients with cavitary lung disease. Medical records were reviewed for the documentation of specific causes of lung cavitation and the CD4 count at the time of imaging. Of 25 HIV-positive patients with cavitary lung disease, 20 had specific diagnoses. Infection was the etiology in all the cases. Polymicrobial infection was found in 17 patients (85%) and unimicrobial in 3 (15%). Seventeen patients (85%) had bacterial organisms, 10 of whom had other pathogens as well. Mycobacteria were isolated in 8 patients (40%), fungi in 3 (15%), cytomegalovirus (CMV) in 3 (15%), and Pneumocystis carinii pneumonia (PCP) in 1 (5%). Mediastinal or hilar lymphadenopathy and additional noncavitary ill-defined nodular opacities were found more frequently in patients with mycobacterial pathogens. Mean CD4 count in patients with cavitary disease because of bacterial pathogens alone was significantly higher than in patients with nonbacterial pathogens (alone or combined with bacterial pathogens) (203 vs. 42, $p < 0.05$). Four patients expired during the diagnostic hospital admission; 2 of them had pulmonary cavitary disease associated with Nocardia asteroides. Cavitary lung disease in patients with AIDS undergoing chest CT should be assumed infectious and is generally polymicrobial.

Rev Chilena Infectol. 2011 Aug;28(4):343-8. doi: /S0716-10182011000500007.

[Etiology of pneumonia in chilean HIV-infected adult patients].

[Article in Spanish]

Pérez C[1], García P, Calvo M, Labarca J, Bustos M, Beroíza T, Gaete P, Moreno R, Acuña G, Vial P.

Author information

Abstract

OBJECTIVES: To establish the etiology of pneumonia and to compare the yield of diagnostic techniques for diagnosis of Pneumocystis jiroveci and Mycobacterium tuberculosis infections in HIV-1-infected patients.

PATIENTS AND METHODS: Subjects underwent sputum induction and bronchoalveolar lavage (BAL). Gram, Ziehl-Neelsen, silver stain (SS) and immunofluorescense staining (IF) for P. jiroveci, fluorescent stain for mycobacteria, PCR for P. jiroveci and M. tuberculosis, aerobic, fungal and mycobacterial cultures, respiratory viruses and CMV cultures were performed on the sputum and BAL. IgM for Mycoplasma pneumoniae and Chlamydophyla pneumoniae, and Legionella pneumophila urinary antigen were also obtained.

RESULTS: Sixty patients were included. An etiologic diagnosis was made in 97%. Pneumocystis jiroveci was the most frequent etiology (58%) followed by Streptococcus pneumoniae (12%), and Mycobacterium avium complex (12%). Mycobacterium tuberculosis was found in 5%.

CONCLUSIONS: The comparison of diagnostic methods for P. jiroveci showed a higher sensitivity of IF and SS in BAL than in sputum, however PCR was equally sensitive in both samples. With this approach a precise etiologic diagnosis was reached in the great majority of patients. The most common etiology was P. jiroveci. IF in BAL remains the gold standard for diagnosis of P. jiroveci pneumonia.

PMID: 22052399 DOI: /S0716-10182011000500007

REHBER NE DİYOR?

Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

CMV ?

End-organ disease caused by CMV occurs in patients with advanced immunosuppression, typically those with CD4 T lymphocyte cell (CD4) counts <50 cells/mm^3, who are either not receiving or have failed to respond to antiretroviral therapy (ART).[1-3] Other risk factors include previous opportunistic infections (OIs), a high level of CMV viremia (most often measured by polymerase chain reaction [PCR]), and high plasma HIV RNA levels (>100,000 copies/mL).

PCP?

Hypoxemia, the most characteristic laboratory abnormality, can range from mild (room air arterial oxygen [pO_2] ≥70 mm Hg or alveolar-arterial O_2 difference, [A-a] DO_2 <35 mm Hg) to moderate ([A-a] DO_2 ≥35 and <45 mm Hg) to severe ([A-a] DO_2 ≥45 mm Hg). Oxygen desaturation with exercise is often abnormal but is non-specific.[21] Elevation of lactate dehydrogenase levels to >500 mg/dL is common but non-specific.[22] Chest radiograph typically demonstrates diffuse, bilateral, symmetrical interstitial infiltrates emanating from the hila in a butterfly pattern;[19] however, a chest radiograph may be normal in patients with early disease.[23] Atypical radiographic presentations also occur, such as nodules, blebs and cysts, asymmetric disease, upper lobe localization, and pneumothorax. Spontaneous pneumothorax in a patient with HIV infection should raise the suspicion of PCP.[24,25] Cavitation, intrathoracic adenopathy, and pleural effusion are uncommon in the absence of other pulmonary pathogens or malignancy, and their presence may indicate an alternative diagnosis. Approximately 13% to 18% of patients with documented PCP have another concurrent cause of pulmonary dysfunction, such as tuberculosis (TB), Kaposi sarcoma (KS), or bacterial pneumonia.[26,27]

Toxoplazmoz?

Clinical Manifestations

Among patients with AIDS, the most common clinical presentation of *T. gondii* infection is focal encephalitis with headache, confusion, or motor weakness and fever.[1,3,9] Patients may also present with non-focal manifestations, including only non-specific headache and psychiatric symptoms. Focal neurological abnormalities may be present on physical examination, and in the absence of treatment, disease progression results in seizures, stupor, and coma. Retinochoroiditis, pneumonia, and evidence of other multifocal organ system involvement are rare in patients with AIDS. Computed tomography (CT) scan or magnetic resonance imaging (MRI) of the brain will typically show multiple contrast-enhancing lesions in the grey matter of the cortex or basal ganglia, often with associated edema.[1,9,12-14] Toxoplasmosis also can manifest as a single brain lesion or diffuse encephalitis without evidence of focal brain lesions on imaging studies.[15] This latter presentation tends to be rapidly progressive and fatal.

Biz Ne Yaptık?

- PCP ve Toxoplazma profilaksisi için TMP/SXT ve
- MAC profilaksisi için klaritromisin ve
- TKP için SAM 4x2 gr İV başlandı

- İndüksiyonla balgam alınamadı, mide açlık suyunda Tbc PCR ve ARB: negatif
- Cilt lezyonları için dermatoloji görüşü alındı
  - Psöriaisle uyumlu bulundu
  - Lokal tedavi önerildi

25-26 Kasım 2016

- Kan kültüründe MSSA üredi
- Endokardit?
- EKO: patoloji yok
  - WBC:4000; Hgb:7.9; PLT:133.000
  - Sedim: 59
  - CRP: 35
- Parezisi olan hastada santral tutulum açısından kraniyal MR çekildi ve LP yapıldı

BOS İncelemesi

- Hücre sayımı: 10/mm^3 lökosit, 70/mm^3 eritrosit
- Glukoz: 75 (KŞ: 120)
- Protein: 77 mg/dl
- Tbc PCR-ARB: negatif
- VDRL: negatif
- Kriptokok Ag: negatif
- Toxo PCR: negatif
- Brucella aggl: negatif
- CMV DNA: negatif
- HIV RNA: 100.248 kopya/ml

28.11.2016'da BAL yapıldı

- **BAL Tbc PCR ve ARB: negatif**
- **BAL kültür: *P. aeruginosa ve Klebsiella spp. ve Candida albicans (kolonizasyon)***
- **BAL mikroskobik inceleme: Bol PNL, ara ara mononükleer hücreler, gram pozitif koklar ve gram negatif basiller**
- **BAL CMV DNA: 10.000.000 kopya/ml !!**

CMV Infection Presenting as a Cavitary Lung Lesion in a Patient with Systemic Lupus Erythematosus Receiving Immunosuppressive Therapy

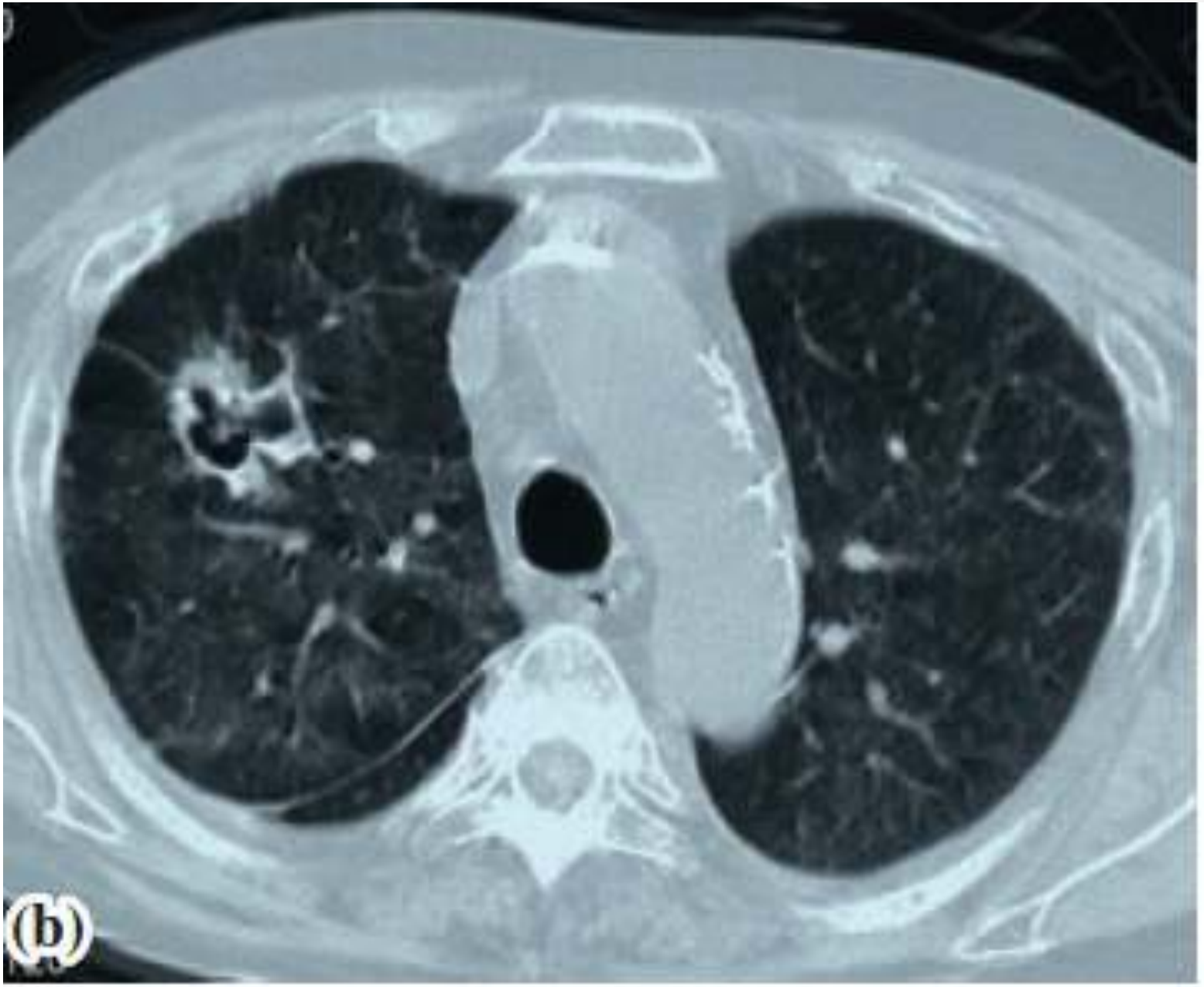
Naoto Azuma[1], Naoaki Hashimoto[1], Akihiro Yasumitsu[2], Kazuya Fukuoka[2], Kazunori Yokoyama[1], Hisashi Sawada[1], Aki Nishioka[1], Masahiro Sekiguchi[1], Masayasu Kitano[1], Takanori Kuroiwa[1,3], Kiyoshi Matsui[1] and Hajime Sano[1]

Abstract

We report a case of cytomegalovirus (CMV) pneumonitis that presented as a cavitary lung lesion in a patient with systemic lupus erythematosus receiving immunosuppressive treatment. The lesion was confirmed by positive polymerase chain reaction (PCR) for CMV in bronchoalveolar lavage fluid (BALF) and CMV antigenemia. PCR for CMV in BALF was demonstrated to be useful for the diagnosis of CMV pneumonitis on the basis of high sensitivity and specificity. After initiating ganciclovir, the lesion gradually regressed. A cavitary lung lesion associated with CMV is extremely rare. This presentation suggests that the differential diagnosis of cavitary lung lesion in immunocompromised individuals should include CMV.

Key words: cavitary lung lesion, cytomegalovirus, immunosuppressant, opportunistic infection, systemic lupus erythematosus

(Inter Med 48: 2145-2149, 2009)


(b)

CMV Pneumonia in HIV-Infected Ventilated Infants

P. Goussard,[1]* S. Kling,[1] R.P. Gie,[1] E.D. Nel,[1] L. Heyns,[1]
G.J. Rossouw,[2] and J.T. Janson[2]

Summary. Background: The contributing role of cytomegalovirus (CMV) in infants treated for *Pneumocystis jiroveci* pneumonia (PJP) is unknown. High dose steroids used in the treatment of PJP may further immunocompromise these infants contributing to the development of CMV pneumonia. Aim: The aim of this study was to determine the role of CMV pneumonia in infants being ventilated for suspected PJP. Methods: In this prospective study HIV infected infants being treated with trimethoprim–sulfamethoxazole (TMP/SMX) and ventilated for suspected PJP were included if they had not responded to treatment. Open lung biopsy was performed if there was no improvement in ventilatory requirements. Results: Twenty-five HIV positive infants with a mean age of 3.3 months were included. Lung biopsy was performed in 17 (68%) and post-mortem lung tissue was obtained in 8 (32%). After evaluation of the histology, immunohistochemistry, and viral cultures from lung tissue, the most likely causes of pneumonia were: CMV and PJP dual infection 36% (n = 9), CMV pneumonia 36% (n = 9), and PJP 24% (n = 6). The pp65 test for CMV antigen was falsely negative in 24%. The mean blood CD4 count was 287/μl. There was an association between the CD4 lymphocyte status and the final diagnosis, with the CMV and PJP group (CD4 110/μl) having the lowest CD4 status ($P = 0.0128$). Pediatric Intensive Care Unit (PICU) mortality was 72% (n = 18) and in hospital mortality 88%. Conclusion: Of the ventilated infants failing to respond to treatment, 72% had histologically confirmed CMV pneumonia, probably accounting for the high mortality in this cohort. The incidence of CMV disease in HIV infected infants being ventilated for severe pneumonia warrants that ganciclovir is used empirically until CMV disease is excluded. The role of lung biopsy in these circumstances needs to be researched. **Pediatr Pulmonol. 2010; 45:650–655.**

Key words: CMV pneumonia; HIV-infected; ventilation; PJP; pp65; HIV related lung disease; Ventilation index; Lung biopsy.

Prevalence and Outcome of Cytomegalovirus-associated Pneumonia in Relation to Human Immunodeficiency Virus Infection

Marco Zampoli, MB BCh, FCPaeds, Cert Paed Pulm, Brenda Morrow, PhD,†*
Nei-Yaun Hsiao, MB BCh, MMed,‡ Andrew Whitelaw, MB BCh, MSc, FCPath,§ and Heather J. Zar, PhD§

Aim: To investigate the antemortem prevalence and outcome of cytomegalovirus (CMV)-associated pneumonia in African children.
Methods: A total of 202 children (median age, 3.2 months; 124 human immunodeficiency virus [HIV]-infected, 62%; 87 severely malnourished, 43%) sequentially hospitalized for severe pneumonia were prospectively investigated. In addition to routine microbiologic investigations, respiratory tract secretions and blood were submitted for CMV culture and qualitative and quantitative CMV polymerase chain reaction.
Results: CMV-associated pneumonia was common (28%, 47/169) and more prevalent in HIV-infected than uninfected children (36% vs. 15%; odds ratio [OR], 3.0; 95% confidence interval, 1.3–7.4). CMV-associated pneumonia was more common than *Pneumocystis* pneumonia (27%) and other viral-associated pneumonia (19%) in HIV-infected children. In-hospital mortality was 25% (51/202) with increased mortality in HIV-infected compared with uninfected children (43/124 [35%] vs. 8/76 [11%]; OR, 4.5; 1.9–11.8). Increased mortality occurred in HIV-infected children with CMV-associated pneumonia (OR, 2.5; 1.04–6.5) but this association was not evident after adjusting for CD4 <15% (adjusted OR, 1.78; 0.6–4.6).
Conclusions: CMV-associated pneumonia is common and associated with a poor outcome in children with advanced HIV disease. Improved diagnostic testing and increased access to antiviral therapy might improve the outcome of HIV-infected children with CMV-associated pneumonia.

Key Words: cytomegalovirus, pneumonia, HIV, children

(*Pediatr Infect Dis J* 2011;30: 413–417)

CMV mi?

- **Kan CMV DNA: 232.974 kopya/ml**

- **CMV Retinit ?**
  - **Bilateral optik disk etrafında cotten-wool spot ile uyumlu değişiklikler (+)**
  - **HIV retinopatisi ?**

CMV Klinik Tutulumları

- Göz tutulumu
  - Retinit (en sık!)
- Gastrointestinal tutulum
  - Kolit
  - Özofajit
  - Hepatit
- Solunum sistemi tutulumu
  - Pnömoni
- Nörolojik tutulum

CMV Tanı

- Kan, BOS, BAL, vitreus sıvısı veya humor aköz de CMV DNA PCR (+) olması anlamlı
- Retinada tipik lezyonun görülmesi
- Kolit veya özofajitte biyopside intranükleer ve intrasitoplazmik inklüzyon cisimciği görülmesi
- Pnömonide tanı klinik bulgular (ateş ve öksürük veya dispne) ile birlikte radyolojik olarak diffüz pulmoner infiltrasyonların görülmesi ile konur
- Nörolojik tutulumda klinik ile birlikte BOS veya beyin dokusunda PCR pozitifliği

Olgumuzda

- CMV viremisi (+)
- CMV pnömonisi (+)
- CMV retiniti, koliti yoktu

- CMV özofajiti (-)
- CMV poliradikülomyelopatisi ?
- CMV hepatiti ?

TEDAVİ ??

- Tüberküloz düşündürecek bulgu ve laboratuvar sonuçlarının olmaması
- CMV pnömonisi ve CMV hepatit? tablosu olan hasta için
- CMV tedavisi ve ART başlanmasının öncelikli olmasına karar verildi

1 Aralık 2016

- Solunum sıkıntısı gelişti- YBÜ'ye alındı
- SAM kesildi ve piperasilin –tazobactam 3x4.5 gr iv başlandı
- TMP/SXT PCP tedavi dozuna geçildi (iv)
- O_2 saturasyonu %70 altına düşmedi, entübe edilmedi bu nedenle steroid başlanmadı

1 Aralık 2016
Tedavinin 1. Günü

- WBC:7400/mm^3
- Sedimentasyon:120mm/saat
- CRP:100 g/dl
- KCFT/ AST:87 ALT:66 GGT:1008 ALP:442
- Böbrek FT:normal

Managing Well-Documented CMV Pneumonitis:

- Doses are the same as for CMV retinitis.
- Treatment experience for CMV pneumonitis in HIV patients is limited. Use of IV ganciclovir or IV foscarnet is reasonable **(CIII)**.
- The role of oral valganciclovir has not been established.
- The optimal duration of therapy has not been established.

Managing CMV Neurological Disease

- Doses are the same as for CMV retinitis.
- **Treatment should be initiated promptly**.
- Combination of ganciclovir IV plus foscarnet IV to stabilize disease and maximize response **(CIII)**.
- Optimal duration of therapy has not been established.
- The role of oral valganciclovir has not been established.
- Optimize ART to achieve viral suppression and immune reconstitution **(BIII)**.

Preferred Therapy:

- Intravitreal injections of ganciclovir (2 mg/injection) or foscarnet (2.4 mg/injection) for 1–4 doses over a period of 7–10 days to provide higher intraocular levels of drug and faster control of the infection until steady state intraocular ganciclovir concentrations are achieved **(AIII)**; *plus*
- Valganciclovir 900 mg PO BID for 14–21 days, then 900 mg once daily **(AI)**

Alternative Therapy

- Intravitreal injections as listed above **(AIII)**; *plus* one of the following systemic therapy:
  - Ganciclovir 5 mg/kg IV q12h for 14–21 days, then 5 mg/kg IV daily **(AI)**, *or*
  - Ganciclovir 5 mg/kg IV q12h for 14–21 days, then valganciclovir 900 mg PO daily **(AI)**, *or*
  - Foscarnet 60 mg/kg IV q8h or 90 mg/kg IV q12h for 14–21 days, then 90–120 mg/kg IV q24h **(AI)**, *or*
  - Cidofovir 5 mg/kg/week IV for 2 weeks, then 5 mg/kg every other week with saline hydration before and after therapy and probenecid 2 g PO 3 hours before the dose followed by 1 g PO 2 hours after the dose, and 1 g PO 8 hours after the dose (total of 4 g) **(BI)**.

  Note: This regimen should be avoided in patients with sulfa allergy because of cross hypersensitivity with probenecid

1 Aralık 2016
ART ve CMV Tedavisi

- Tenofovir disproksil fumarat (TDF) ve Emtristabin 1x1 po (Hivent)
- Dolutegravir 1x1 po (Tivicay)
- Gansiklovir 2x5 mg/kg (50 kg)-

  2x250 mg yükleme
- Flukonazol 1x800 mg/1x400 mg İV

(oral kandidiyazis var kandida özofajiti ?)

5 Aralık 2016 YBÜ'den çıkarıldı

- GD orta ateş yüksekliği yok
- Bilinç açık, kooperasyon/oryantasyon tam değil, O_2 ihtiyacı yok
- Sakral ve sol gluteal dekübit yarası (+)
  - Plastik cerrahi: Günlük pansuman sonrasında rekonstrüksiyon önerdi
- WBC:4200
- Sedim:120
- CRP:37

7 Aralık 2016

- Hastanın genel durumu iyi
- Solunum sıkıntısı geriledi

- Kan CMV DNA: 81.603 kopya/ml
  (232.974 kopya/ml idi)

- Karaciğer biyopsisi yapıldı
  - Kronik hepatit bulguları var
  - CMV boyası negatif

Karaciğer ve Özefagus CMV Tutulumu ?? 8 Aralık 2016

- USG'de portal venöz çap artışı (+)
- Üst GİS Endoskopi: Özofagogastrik bileşkede yüzeyel ülserasyon- displazi yok, özofagus doğal (kandida özofajiti yok)
- Patoloji: Ülser gelişimine reaktif atipi
  - CMV boyası yapılmamış

9 Aralık 2016
Gansiklovir Bitti!!

- **Gansiklovir hastane eczanesi tarafından temin edilemediğinden ☹**

- **Valgansiklovir 1x900 po başlandı**

15 Aralık 2016
Gansiklovir Temin Edildi ☺

- GD iyi ateşi yok
- WBC:4400 mm^3, Hgb: 10.7 g/dl
- Sedim:79 mm/saat
- CRP:37 mg/dl

19 Aralık 2016

- ART 20. gün
- CMV Ted. 20. gün
- TMP/SXT 27. gün (20 gündür PCP tedavisi)
- Klaritromisin 27. gün

- WBC: 2500/mm^3, $CD4^+$ %8, CRP: 50, Sedim:70
- GD orta, ateş: 38.7 ^oC
- AC oskültasyon: kaba ral ve ronküs(+)
- PA AC: Sağ bazalde yeni infiltratif alan (+)

AIDS. 2012 Mar 27;26(6):721-30. doi: 10.1097/QAD.0b013e3283511e91.

Immune reconstitution inflammatory syndrome: incidence and implications for mortality.

Novak RM[1], Richardson JT, Buchacz K, Chmiel JS, Durham MD, Palella FJ, Wendrow A, Wood K, Young B, Brooks JT; HIV Outpatient Study (HOPS) Investigators.

Collaborators (33)

Author information

Abstract

OBJECTIVE: To describe incidence of immune reconstitution inflammatory syndrome (IRIS) and its association with mortality in a large multisite US HIV-infected cohort applying an objective, comprehensive definition.

DESIGN: We studied 2,610 patients seen during 1996-2007 who initiated or resumed highly active combination antiretroviral therapy (cART) and, during the next 6 months, demonstrated a decline in plasma HIV-RNA viral load of at least 0.5 log(10) copies/ml or an increase of at least 50% in CD4 cell count per microliter. We defined IRIS as the diagnosis of a type B or C condition [as per the Centers for Disease Control and Prevention (CDC) 1993 AIDS case definition] or any new mucocutaneous disorder during this same 6-month period.

METHODS: We assessed the incidence of IRIS and evaluated risk factors for IRIS using conditional logistic regression and for all-cause mortality using proportional hazards models.

RESULTS: We identified 370 cases of IRIS (in 276 patients). Median and nadir CD4 cell counts at cART initiation were 90 and 43 cells/μl, respectively; median viral load was 2.7 log(10) copies/ml. The most common IRIS-defining diagnoses were candidiasis (all forms), cytomegalovirus infection, disseminated Mycobacterium avium intracellulare, Pneumocystis pneumonia, varicella zoster, Kaposi's sarcoma and non-Hodgkin lymphoma. Only one case of Mycobacterium tuberculosis was observed. IRIS was independently associated with CD4 cell count less than 50 cells/μl vs. at least 200 cells/μl [odds ratio (OR) 5.0] and a viral load of at least 5.0 log(10) copies vs. less than 4.0 log(10) copies (OR 2.3). IRIS with a type B-defining or type C-defining diagnosis approximately doubled the risk for all-cause mortality.

CONCLUSION: In this large US-based HIV-infected cohort, IRIS occurred in 10.6% of patients who responded to effective ART and contributed to increased mortality.

Immune reconstitution inflammatory syndrome associated with pulmonary pathogens

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ABSTRACT Immune reconstitution inflammatory syndrome (IRIS) is an exaggerated immune response to a variety of pathogens in response to antiretroviral therapy-mediated recovery of the immune system in HIV-infected patients. Although IRIS can occur in many organs, pulmonary IRIS, associated with opportunistic infections such as *Mycobacterium tuberculosis* and *Pneumocystis jirovecii*, is particularly associated with high morbidity and mortality. The pathology of IRIS is associated with a variety of innate and adaptive immune factors, including $CD4^+$ T-cells, $CD8^+$ T-cells, γδ T-cells, natural killer cells, macrophages, the complement system and surfactant proteins, Toll-like receptors and pro-inflammatory cytokines and chemokines. Although there are numerous reports about the immune factors involved in IRIS, the mechanisms involved in the development of pulmonary IRIS are poorly understood. Here, we propose that studies using gene-deficient murine and nonhuman primate models will help to identify the specific molecular targets associated with the development of IRIS. An improved understanding of the mechanisms involved in the pathology of pulmonary IRIS will help to identify potential biomarkers and therapeutic targets in this syndrome.

Immune Reconstitution Inflammatory Syndrome: Opening Pandora's Box

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One of the purposes of antiretroviral therapy (ART) is to restore the immune system. However, it can sometimes lead to an aberrant inflammatory response and paradoxical clinical worsening known as the immune reconstitution inflammatory syndrome (IRIS). We describe a 23-year-old male, HIV1 infected with a rapid progression phenotype, who started ART with TCD4+ of 53 cells/mm^3 (3,3%) and HIV RNA = 890000 copies/mL (6 log). Four weeks later he was admitted to the intensive care unit with severe sepsis. The diagnostic pathway identified progressive multifocal leukoencephalopathy, digestive Kaposi sarcoma, and *P. aeruginosa* bacteraemia. Five weeks after starting ART, TCD4+ cell count was 259 cells/mm^3 (15%) and HIV RNA = 3500 copies/mL (4 log). He developed respiratory failure and progressed to septic shock and death. Those complications might justify the outcome but its autopsy opened *Pandora*'s box: cerebral and cardiac toxoplasmosis was identified, as well as hemophagocytic syndrome, systemic candidiasis, and *Mycobacterium avium complex* infection. IRIS remains a concern and eventually a barrier to ART. Male gender, young age, low TCD4 cell count, and high viral load are risk factors. The high prevalence of subclinical opportunistic diseases highlights the need for new strategies to reduce IRIS incidence.

CMV- IRIS

- CMV retiniti olan olgularda IRIS'in oküler formu ART başlangıcından sonra CD4'ün hızla yükseldiği ilk 4-12 haftada ortaya çıkar.
- Ancak başarılı CMV tedavisinden aylar veya yıllar sonra da ortaya çıkabilir!
- Sıklığı 0.02/kişi-yıl
- Makular ödem ve görme kaybına yol açabilir
- Tedavide steroid (anti-CMV tedavi +steroid)

IRIS

- Prednol 2x40 mg ve Pip/Tazo 3x4.5 gr başlandı
  - Steroid tedavinin 2. gününde
  - GD orta, ateş yok, takipne yok
  - AC oskültasyon: ral ve ronküs yok

23 Aralık 2016

- GD iyi, ateş yüksekliği yok
- Dilde kandida plakları (+)
- WBC 1700, CRP:24, Sed: 24
- Mukostatin ve Flukonazol başlandı
- Lökopeni nedeniyle gansiklovir kesildi
- Valgansiklovir 1x900 mg başlandı
- Prednol azaltılmaya başlandı (2x20 mg)
- Pip tazo kesildi (4.gün)
- TMP/SXT profilaksi dozuna indirildi

9 Ocak 2017

- GD iyi
- CD4+: %12
- CMV DNA: 555 kopya/ml
- HIV RNA: Negatif
- ART, Bactrim, Gansiklovir tedavilerinin 40. gününde taburcu edildi
- Hastanın CD4 sayısı 200'ün üzerinde 6 ay seyredene kadar Bactrim forte tb 1x1 ve azitromisin 1x1200 mg tb kullanması planlandı

CMV Tedavi

- CMV tedavisi ART ile $CD4^+$ sayısı >100/mm^3 olana ve bu düzey 3-6 ay devam edecek kadar verilmelidir
- Akut CMV tedavisi sonrasında CMV retiniti veya relaps yok ise
- CMV gastrointestinal tutulum, pnömoni ve SSS tutulumunda tedavinin devamı önerilmemektedir!

CMV Tedavi

- Relaps oranı %3
- CMV tedavisi kesilmesi için tam güvenli bir $CD4^+$ düzeyi yok
- Relaps olan bir olguda CD4 sayısı 1250 hücre/mm^3
- Anti CMV tedavisi bitirildikten sonra retinit açısından en az 3 ay arayla periyodik kontroller yapılması önerilir
- CMV viral yük takibi önerilmez

Poliklinik Kontrolleri

- Hasta taburculuk sonrası kontrole gelmedi
- Telefonla hasta yakını (!) arandı
- Ulaşılamadı

Hazin Son??

- 29 Ocak 2017 ‘de evden atıldığı için hastanemiz acil servisine başvuruyor
  - WBC:3500, Lenfosit 400
  - Hgb:12.2, PLT:78.000 CRP: 11 g/dl
  - AST:292 ALT: 24 GGT:163 LDH:379
  - GD iyi, yatış önerilmiyor
  - Poliklinik takibine çağırılıyor
- 2 gün sonra evde ölü bulunuyor
- Yüksek doz uyuşturucu ?