İSTANBUL
MEDENİYET ÜNİVERSİTESİ

TÜRKİYE EKMUD 2006

MUKORMİKOZİS YÖNETİMİ

Doç. Dr. Yasemin Çağ

İstanbul Medeniyet Üniversitesi

Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji AD

03.04.2019

- Mukormikoz tüm dünyada kandidiyazis ve aspergillozis'den sonra en sık üçüncü invaziv fungal enfeksiyon
- İnvaziv küf enfeksiyonlarında en yaygın ikinci etken
- İnsidansı giderek artmakta!
  - 1.2 (1988-2006) -3.3 (2007-2015) /100.000 hastane başvurusu
- Yüksek mortalite !
  - Mortalite altta yatan hastalık, tutulum yeri ve tedaviye bağlı değişmekte (20% - 80%)

- Bitar D *et al*. *Emerg Infect Dis* 2009
- Rees JR et al. *Clin Infect Dis* 1998
- Guinea J. et al. PLoS One 2017

- Mukormikoz ve zigomikoz terimleri sıklıkla birbirinin yerine kullanılmakta iken taksonomi yakın zamanda moleküler filogenetik analizlerden sonra değişmiştir
- Günümüzde, mukormikoz Mucorales takımından mantarların neden olduğu enfeksiyonları tanımlamaktadır
- **Mucorales Takımı**
  - *Rhizopus spp.* (En yaygın)
    - *Rhizopus oryzae*
  - *Mucor spp.*
  - *Lichtheimia spp.* (*Absidia*)
  - *Cunninghamella spp.*(Yüksek mortalite, virulans)
  - *Rhizomucor spp.*, *Apophysomyces spp.*, *Saksenaea spp.*

Epidemiyoloji ve Patogenez

- Çürümüş organik materyal ve toprak
- Konidiaların solunması, hasarlı deri veya mukozadan direk inokülasyon, gastrointestinal sistem
- Damar invazyonu, trombüs, nekroz, infarkt
- Komşuluk ve sinirler yoluyla yayılım

Risk Faktörleri

- Hematolojik malignite (AML) / HSCT
- Uzamış/ciddi nötropeni
- Kontrolsüz diabet
  - Ketoasidoz
- Solid organ malignitesi/transplatasyon
- Aşırı demir yüklenmesi, deferoxamin tedavisi
- Kemoterapi
- Biyolojik ajan kullanımı

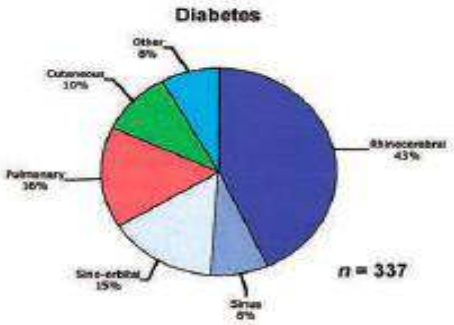
- Major travma
  - Yanık, penetran travma, cerrahi yara
- Uzamış kortikosteroid kullanımı
- Hemodiyaliz
- İV ilaç alışkanlığı
- Malnutrisyon
- Prematurite

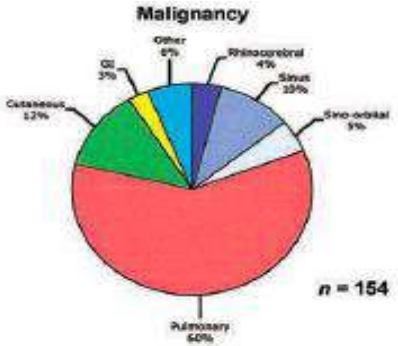
- Jeong, W., et al. *CMI* 2019
- Petrikkos et al. CID 2012

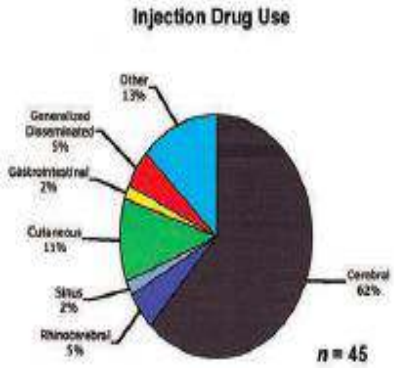
Klinik Formlar

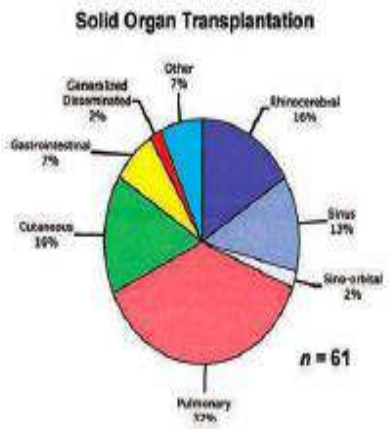
- Rino/orbito/serebral (en sık)
  - lokalize sinüs
  - lokalize orbital
  - lokalize sereral
  - sino-orbital
  - sino-serebral
  - rino-orbito-serebral
- Pulmoner
- Kutanöz
- Dissemine
- Diğer (Gastrointestinal, renal, hepatik, endokardit, peritonit)

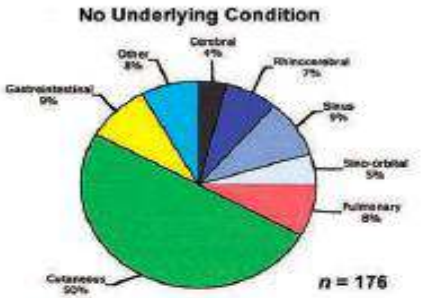
Hasta Populasyonu - Hastalık Formu İlişkisi

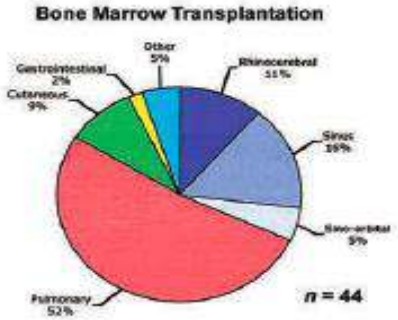


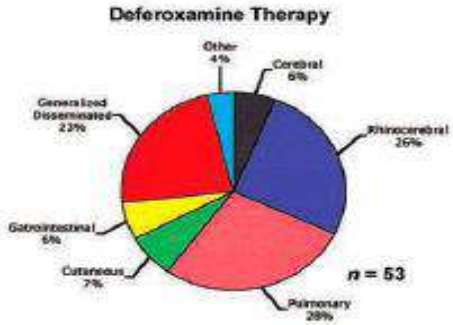












- Rino-orbito-serebral- En sık DM
- Pulmoner-En sık hematolojik malignite
- Kutanöz- En sık travma veya cerrahi

Roden, Maureen M., et al. Clinical Infectious Diseases 41.5 (2005): 634-653.

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Systematic review

The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports

W. Jeong [1], C. Keighley [2, 3], R. Wolfe [4], W.L. Lee [1], M.A. Slavin [5, 6], D.C.M. Kong [1, 7, 8], S.C.-A. Chen [2, 3, *]

Available online 21 July 2008

Disease manifestations[a] for 851 cases of mucormycosis

Disease manifestations	No of patients *n* (%)	No of proven cases *n* (%)	Overall mortality *n* (%)
Rhino-orbito-cerebral mucormycosis	288 (34%)	254 (88%)	120 (42%)
Localized sinus	158 (55%)	136 (86%)	53 (34%)
Localized orbital	6 (2%)	6 (100%)	2 (33%)
Localized cerebral	16 (6%)	16 (100%)	11 (69%)
Sino-orbital	82 (28%)	75 (91%)	35 (43%)
Sino-cerebral	20 (7%)	16 (80%)	15 (75%)
Generalized rhino-orbital-cerebral	6 (2%)	5 (83%)	4 (67%)
Pulmonary mucormycosis	172 (20%)	132 (77%)	87 (51%)
Localized	168 (98%)	128 (76%)	84 (50%)
Deep extension	4 (2%)	4 (100%)	3 (75%)
Cutaneous mucormycosis	187 (22%)	172 (92%)	58 (31%)
Localized	150 (80%)	137 (91%)	46 (31%)
Deep extension	37 (20%)	35 (95%)	12 (32%)
Disseminated mucormycosis	110 (13%)	101 (92%)	75 (68%)
Gastrointestinal mucormycosis	72 (8%)	71 (99%)	39 (54%)
Others[b]	22 (3%)	20 (91%)	10 (46%)

Tanı

- Risk faktörleri + klinik veya radyolojik şüphe
- Mukormikoz enfeksiyonu genellikle hızla ilerleyen ve yıkıcı bir enfeksiyon olduğundan hastalıktan şüphe durumunda acil müdahale gerektirir.
- Kesin tanı için klinik örnek gerekli (Biyopsi, BAL, balgam, BOS)
  - Direk mikroskopi
  - Kültür
  - Histopatoloji

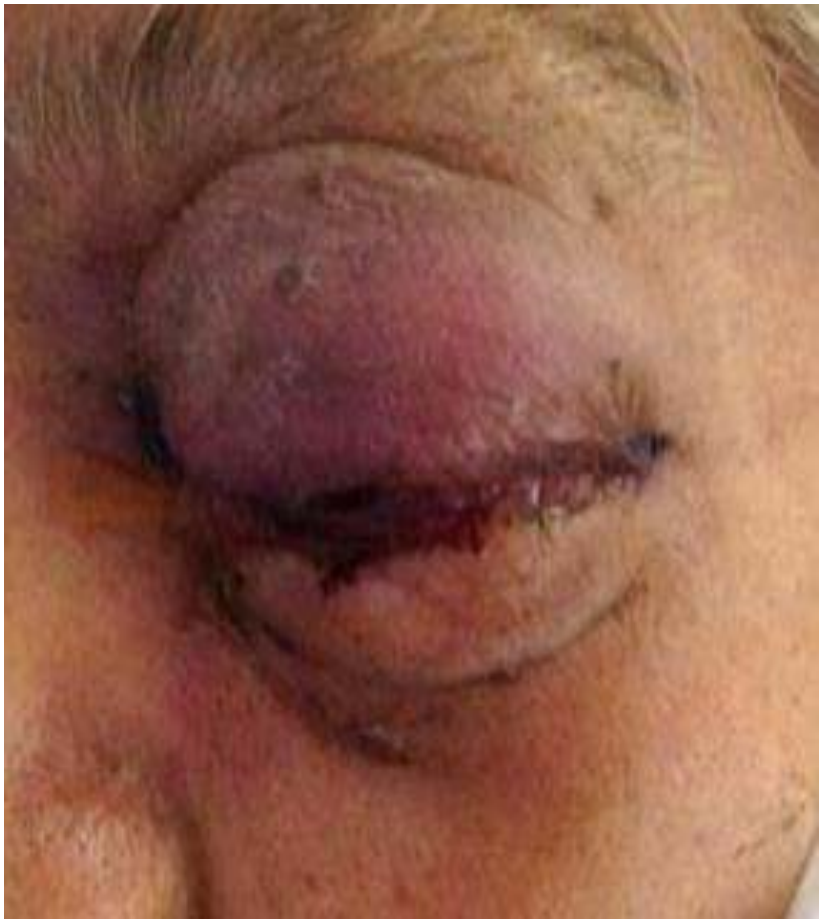
Klinik Şüphe !!!

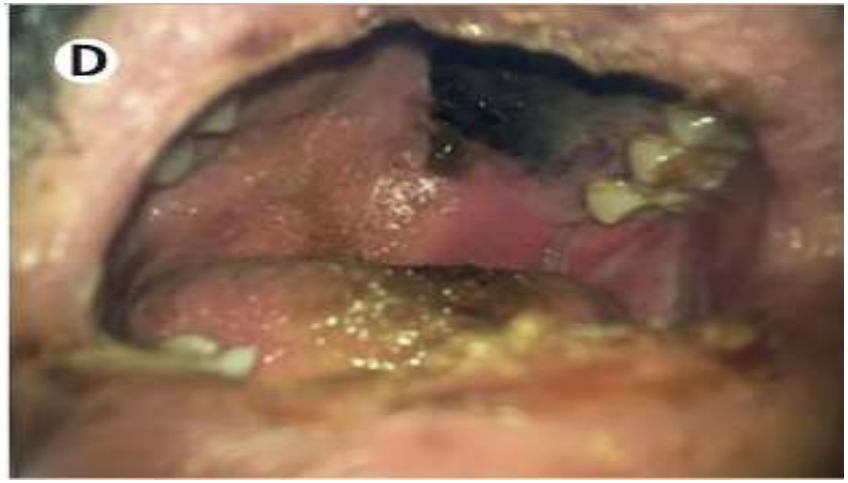
Risk faktörleri olan hastada

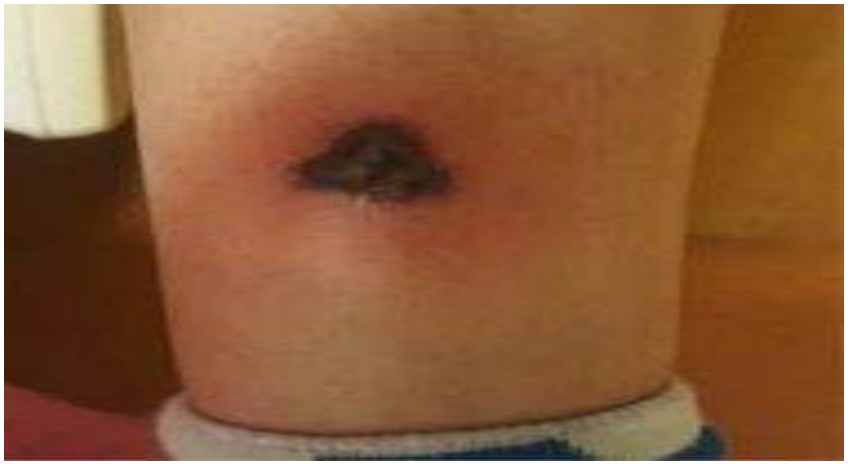
- İmmun supresif ve kontrolsuz diyabet

- Yüzde veya sino-orbital bölgede hızlı ilerleyen enfeksiyon
- Yüzde tek taraflı ağrı
- Eşlik eden ani gelişen diplopi
- Nekrotik siyah renkli skar (geç dönem bulgusu)

Rino-orbito-serebral tutulum düşünülmeli







Cornely, Oliver A., et al. "*The Lancet infectious diseases* 2019

Görüntüleme

- Tanı ve takipte yol gösterici
  - CT (sinüs, AC)
  - MRI (orbita, beyin, batın)

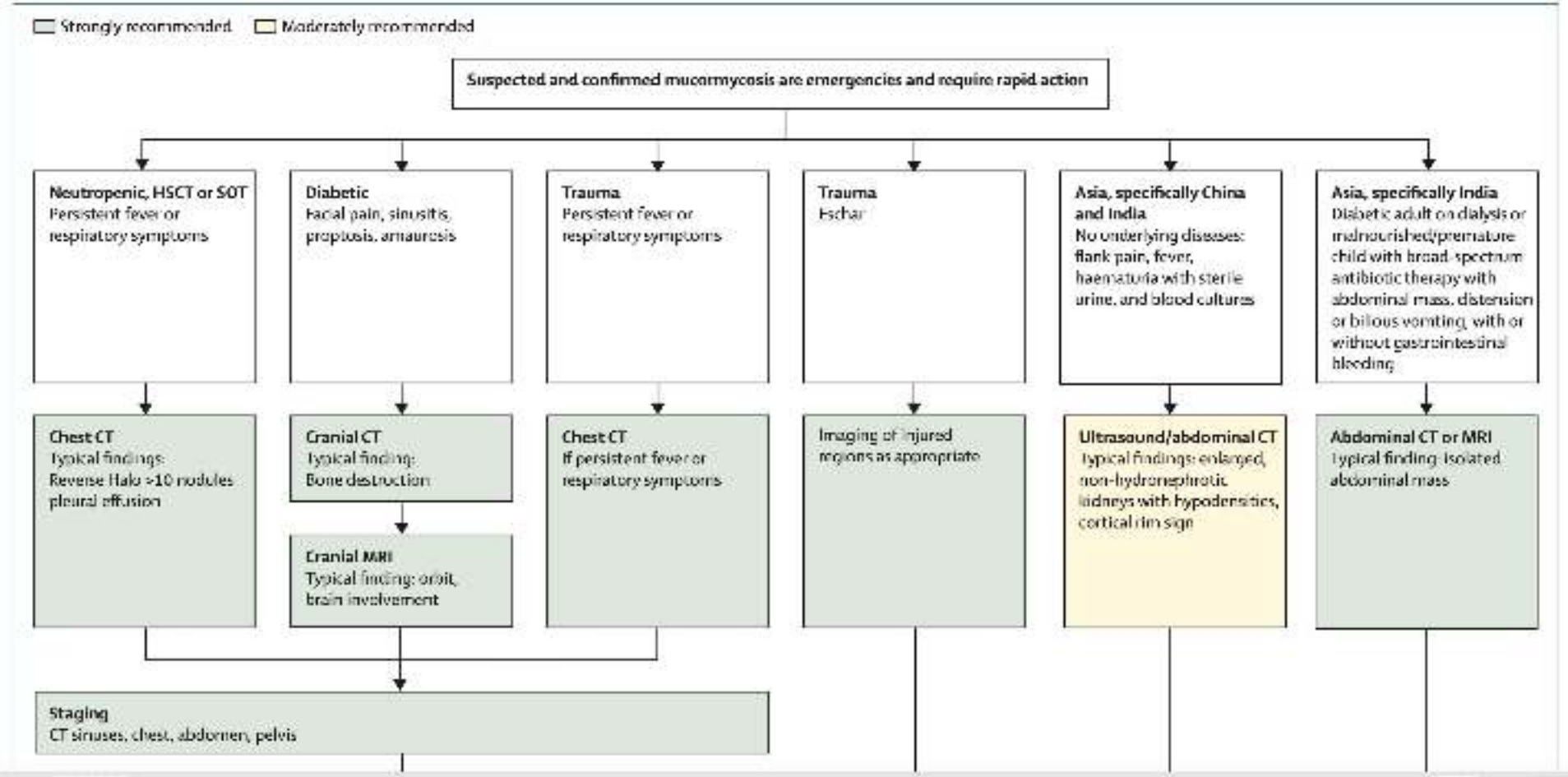
Görüntüleme

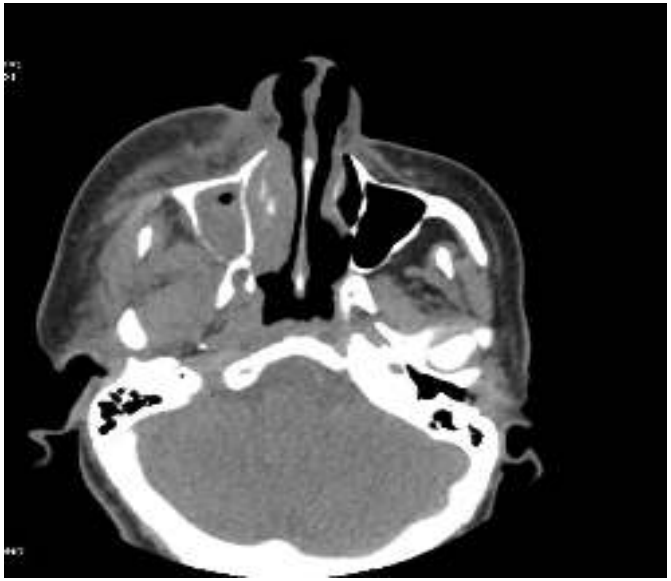
- Akciğer: Hematolojik maligniteli hastalarda mucor'un en sık tutulduğu alan (Aspergillus akciğerin en sık İFİ)
  - Ters halo (%10) (tuberküloz, Aspergillus …..)
  - >10 nodüler infiltrat
  - >3 cm nodül
  - Plevral efüzyon
  - Halo (Aspergillus, tuberküloz, CMV, Nocardia……)
- Rhino-orbita-cerebral : Hematolojik maligniteli hastada çoğunlukla etken mucor (Aspergillus….)
  - Kemik yıkımı
  - Mukozal kalınlaşma
  - İntrakranial yayılım

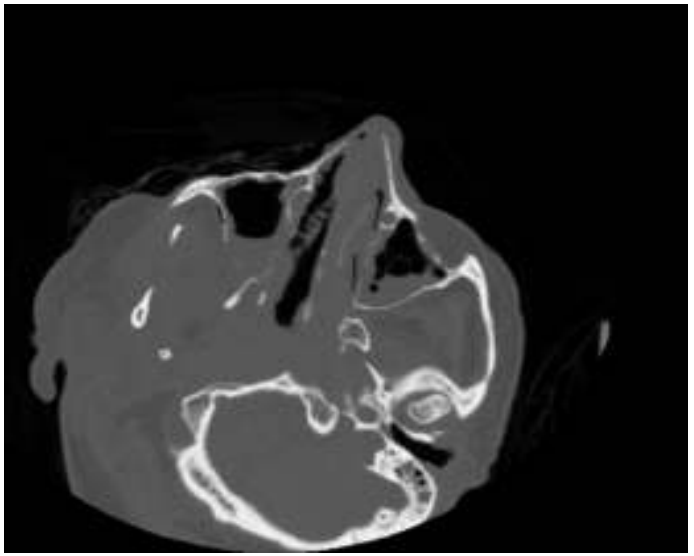
Bu bulgular mukormikozu destekleyen bulgular ancak spesifik bulgular değil

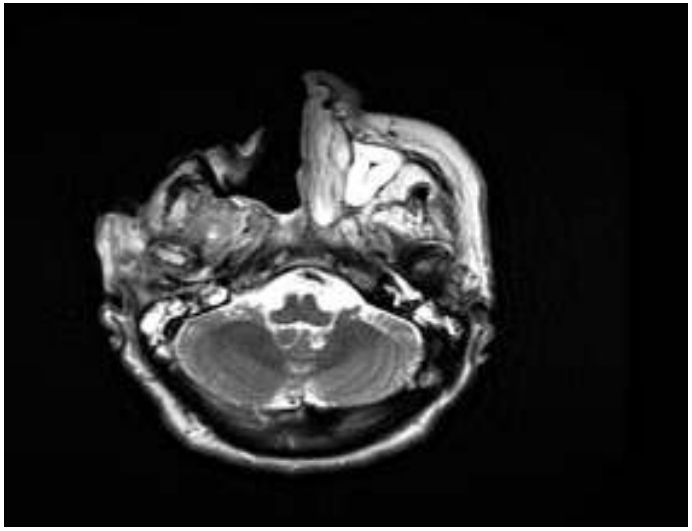
Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium

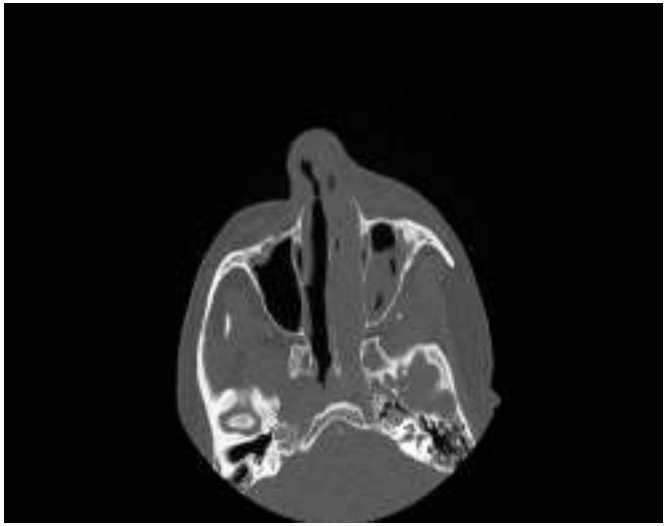
Oliver A Cornely, Ana Alastruey-Izquierdo, Dorothee Arenz, Sharon C A Chen, Eric Dannaoui, Bruno Hochhegger, Martin Hoenigl, Henrik E Jensen, Katrien Lagrou, Russell E Lewis, Sibylle C Mellinghoff, Mervyn Mer, Zoi D Pana, Danila Seidel, Donald C Sheppard, Roger Wahba, Murat Akova, Alexandre Alanio, Abdullah M S Al-Hatmi, Sevtap Arikan-Akdagli, Hamid Badali, Ronen Ben-Ami, Alexandro Bonifaz, Stéphane Bretagne, Elio

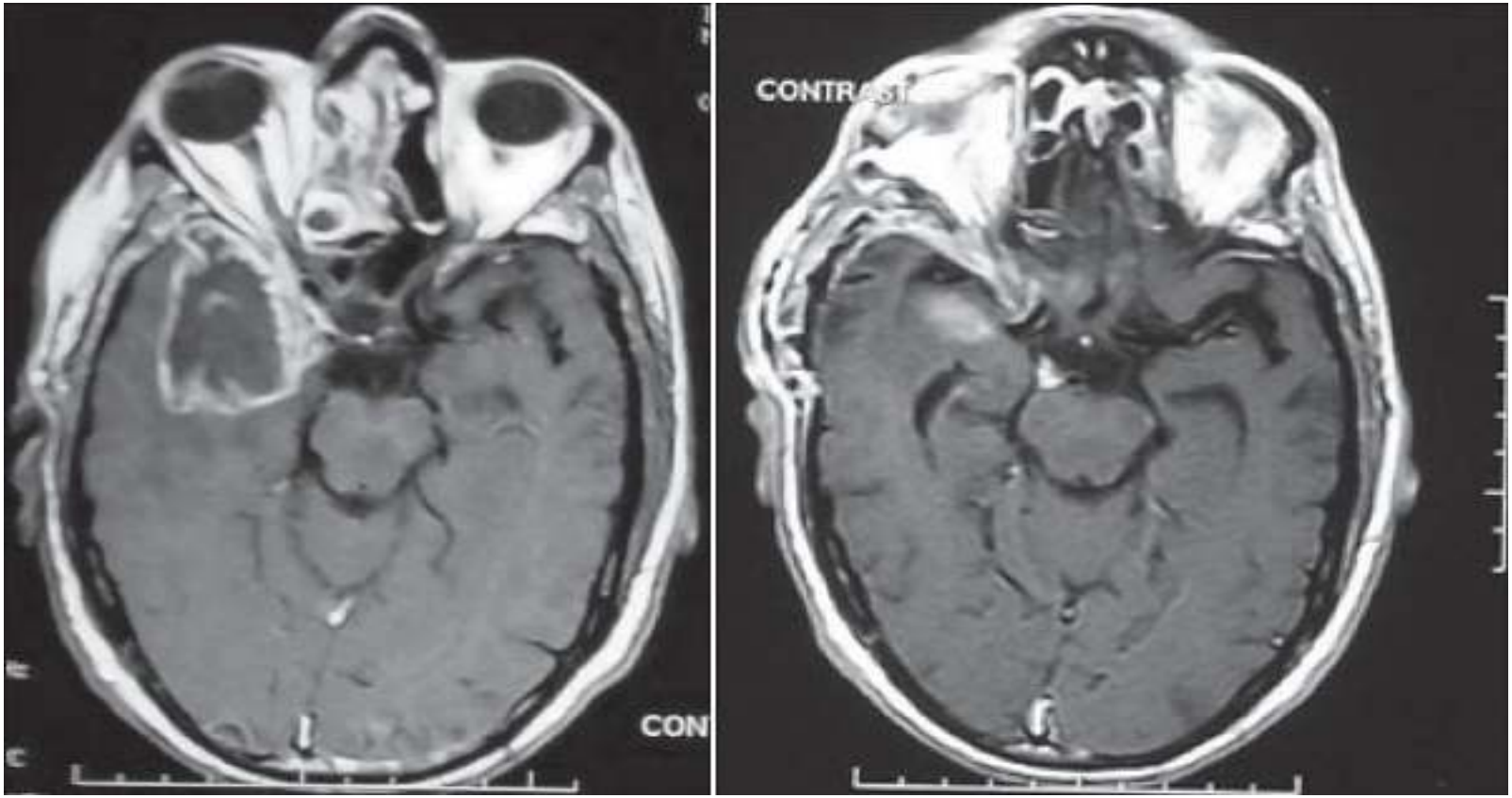


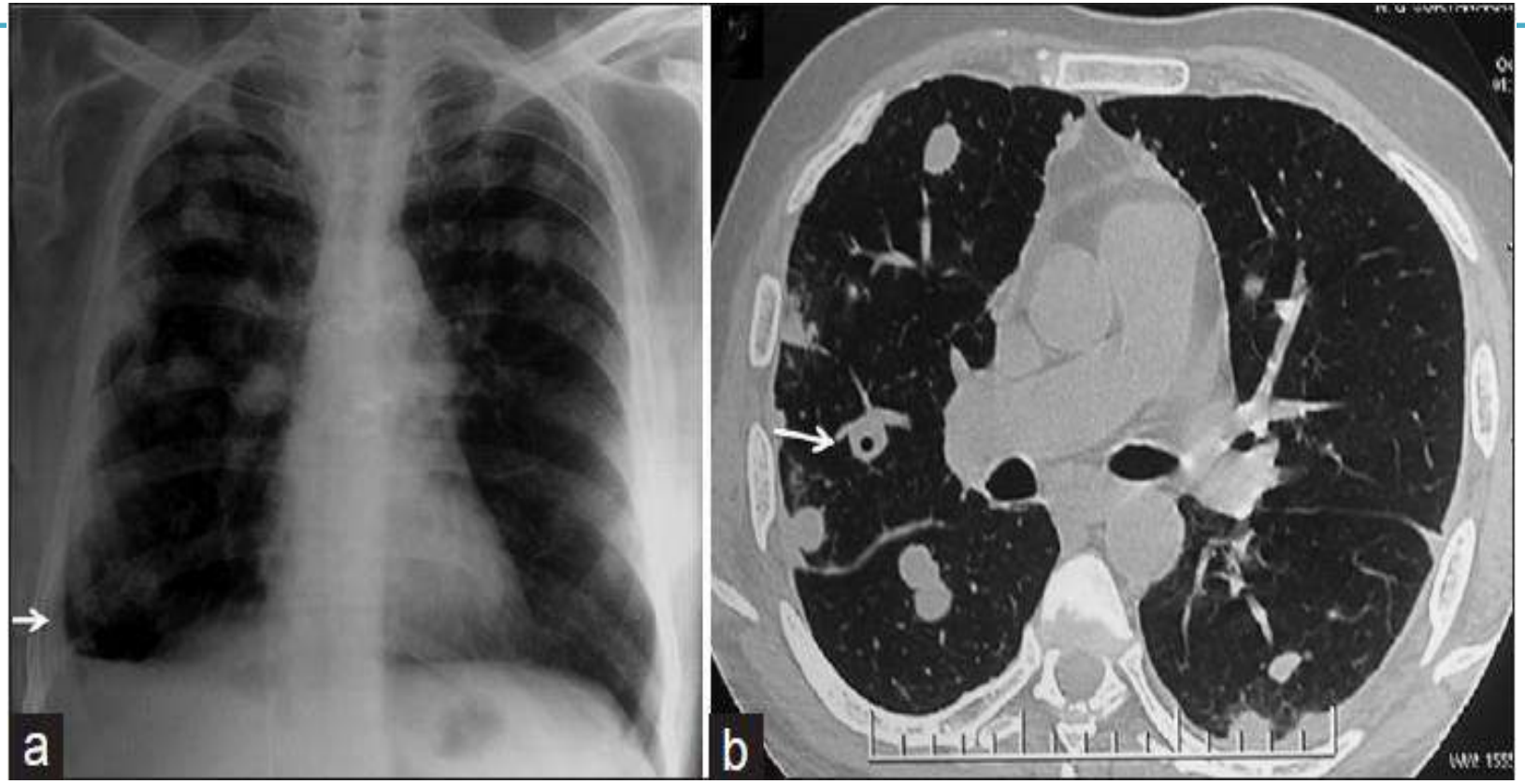


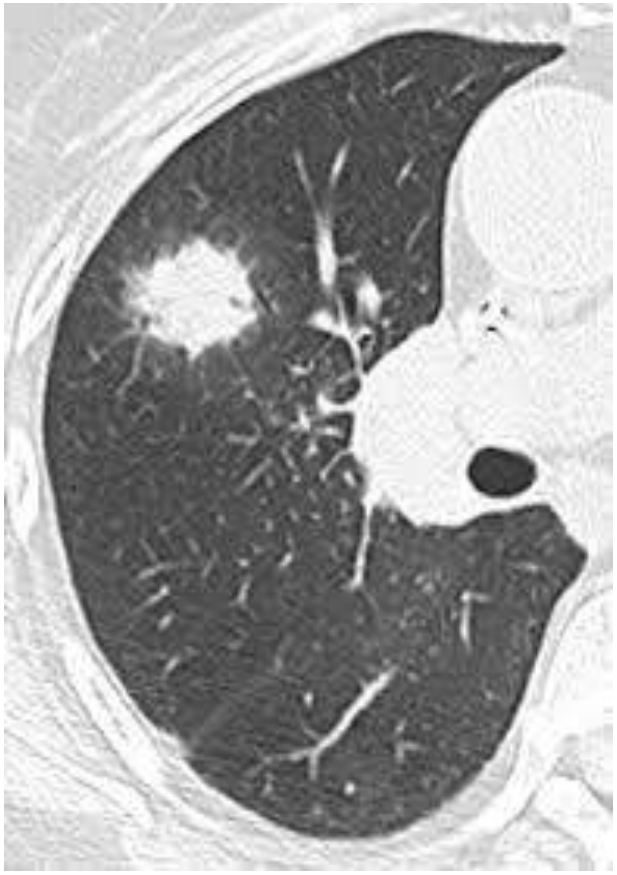


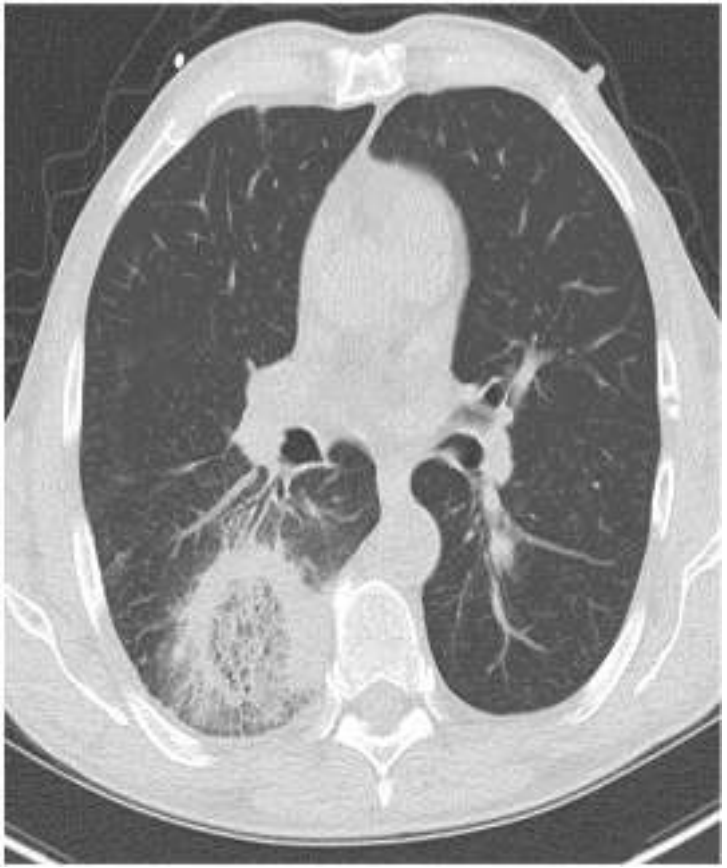





CON
CONTRAST

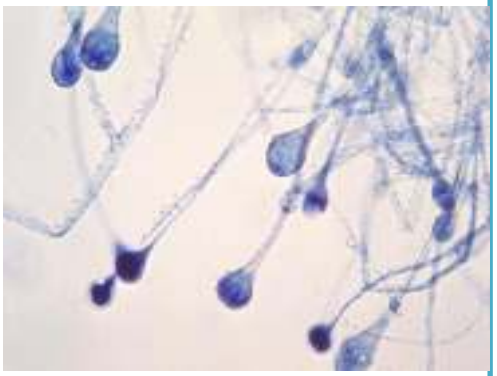

a
b





Mikrobiyolojik İnceleme

- Direk mikroskopi: Hızlı, yol gösterici, kültürle doğrulanmalı
- KOH ile muamele, kalkoflor beyazı veya Gomori methamine- silver ile boyama
  - Hiyalen
  - Septasız, veya seyrek septalı
  - Serit benzeri dik açı ile dallanan
  - Geniş (6-16 µm) çaplı
  - Düzensiz, hifler



Kültür

- 30-37C^0 de, genellikle 24-48 saatte ürer
- Petri kutusunu dolduran yünümsü örgüde koloni (3-5 gün)
- Biyopsi materyali ezilmemeli
- Kan kültüründe üremez (Kontaminasyon??)
- BOS nadiren üreme
- **Cins ve tür düzeyinde tanımlama imkanı**

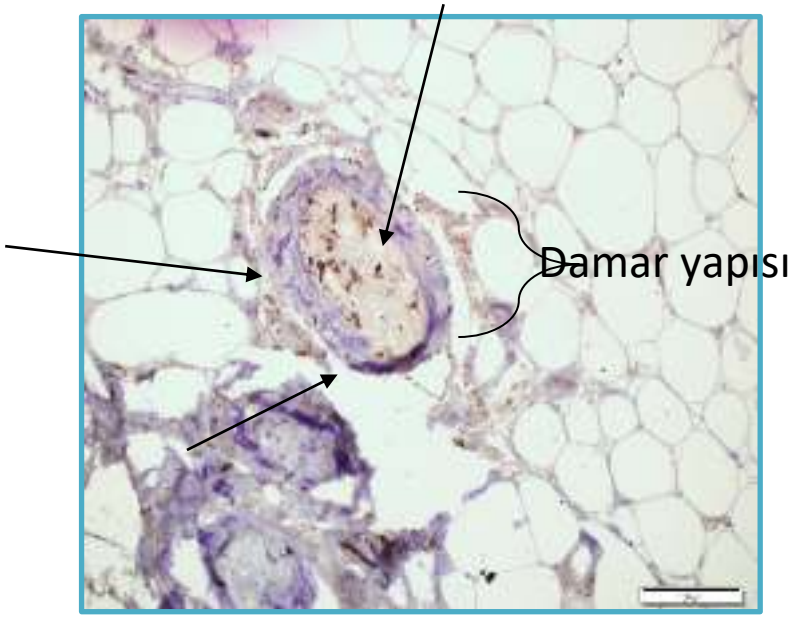
- Etkenin cins ve tür düzeyinde tamınlanmasının antifungal tedaviyi yönlendirecek etkisi gösterilememiş
- Tür düzeyinde tanımlama epidemiyolojik veriler ve salgın araştırmalarında önemli

Salas V et al. AAC 2012

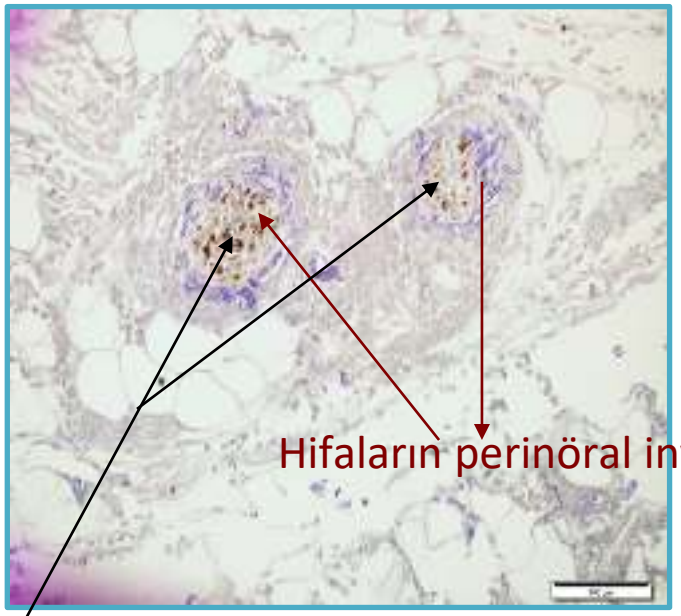
Rammaert B, et al. *CID* 2012

Histopatoloji

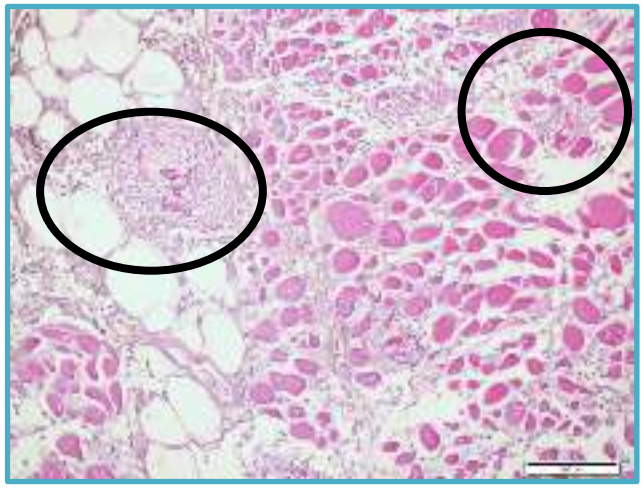
- **Nekrotik doku içinde Mucorales takımına ait fungal hifler**
- **Perinöral invazyon**
- İnfarkt (Hemorajik)
- Damar invazyonu
- Nötrofilik infiltratlar
- Granülom
- **Tür ve cins ayırımı yapılamaz**



Damar duvarlarında mantar hifaları



Sinir dokusu (s100 boyama)



Kas dokusu içerisinde geniş, ince duvarlı, irreguler non-paralel konturlu tipik mucor hifaları

Serolojik Testler

- Galaktomannan: Negatif
- 1,3 Beta-D Glukan: Negatif

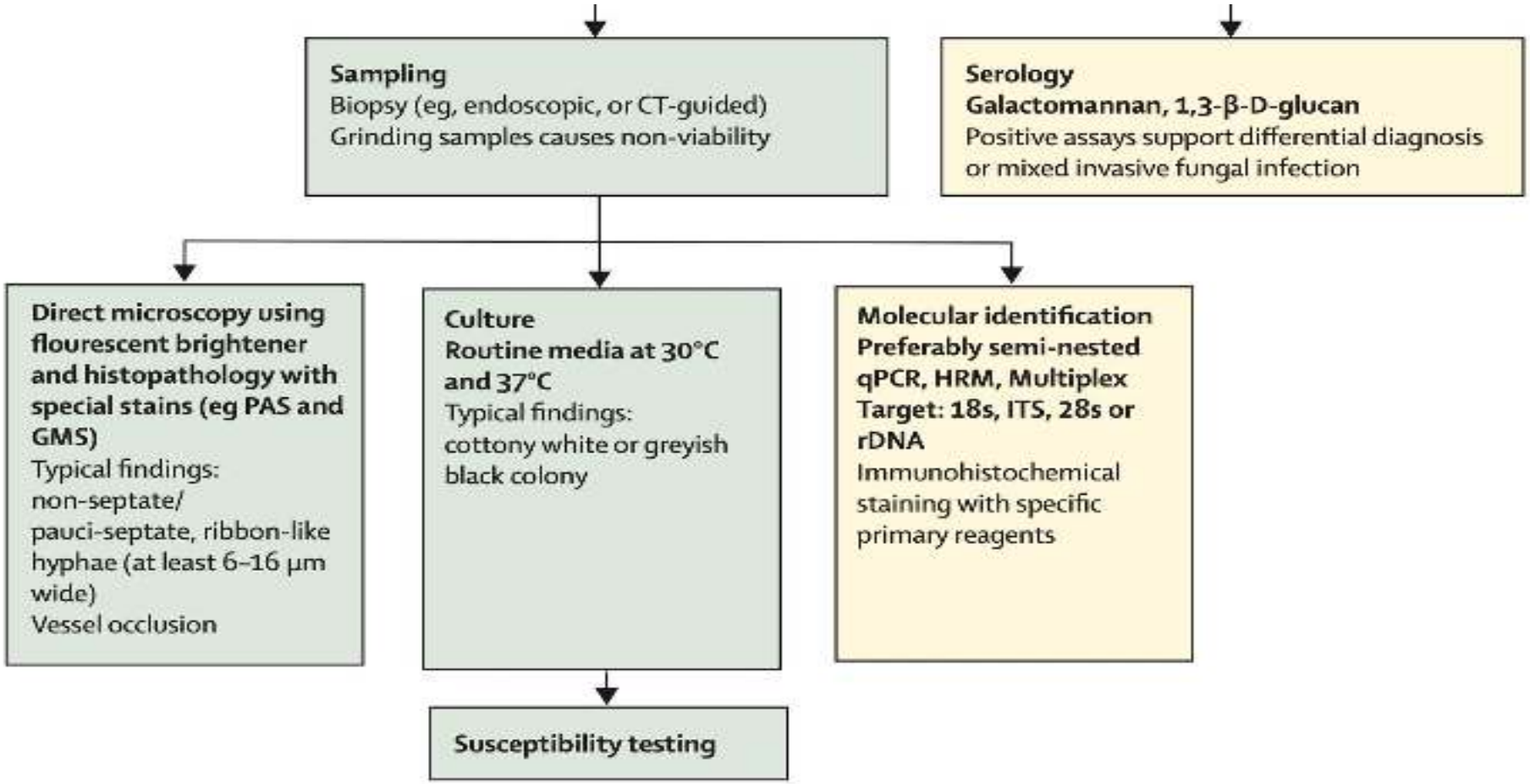
Yeni Tanısal Yaklaşımlar

- ELISPOT (Mucorales-specific T cells saptanması)
- Moleculer testler (PCR)
  - Taze klinik materyal
  - Parafinli örnek
  - Serum
  - Kültür
- MALDI-TOF

Henüz standardize edilememiştir

Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium

Oliver A Cornely, Ana Alastruey-Izquierdo, Dorothee Arenz, Sharon C A Chen, Eric Dannaoui, Bruno Hochhegger, Martin Hoenigl, Henrik E Jensen, Katrien Lagrou, Russell E Lewis, Sibylle C Mellinghoff, Mervyn Mer, Zoi D Pana, Danila Seidel, Donald C Sheppard, Roger Wahba, Murat Akova, Alexandre Alanio, Abdullah M S Al-Hatmi, Sevtap Arikan-Akdagli, Hamid Badali, Ronen Ben-Ami, Alexandro Bonifaz, Stéphane Bretagne, Elio



Tedavi

- Antifungal tedavi
- Uygun ve erken cerrahi debritman
- Altta yatan koşulların kontrolü/tedavisi

Spellberg B. Clin Microbiol Rev 2005

- Empiric (ateşe dayalı) tedavi önerilmez
- Preemptive (tanısal testlere dayalı) tedavi:
  - Hasta immunsupresif
  - Mukormikoz şüpheli tedavi hemen başlanmalıdır
- Hedefe yönelik tedavi: Tedavi hemen başlanmalıdır

Clin Infect Dis. 2008 Aug 15;47(4):503-9. doi: 10.1086/590004.

Delaying amphotericin B-based frontline therapy significantly increases mortality among patients with hematologic malignancy who have zygomycosis.

Chamilos G[1], Lewis RE, Kontoyiannis DP.

Author information

Abstract

BACKGROUND: Zygomycosis is an emerging opportunistic mycosis among immunocompromised patients with a particularly poor prognosis.

METHODS: We analyzed the impact of delaying effective amphotericin B-based therapy on outcome among 70 consecutive patients with hematologic malignancy who had zygomycosis in our institution during the period 1989-2006. We used classification and regression tree analysis to identify the mortality breakpoint between early and delayed treatment.

RESULTS: Delayed amphotericin B-based therapy (i.e., initiating treatment >/=6 days after diagnosis) resulted in a 2-fold increase in mortality rate at 12 weeks after diagnosis, compared with early treatment (82.9% vs. 48.6%); this remained constant across the years of the study and was an independent predictor of poor outcome (odds ratio, 8.1; 95% confidence interval, 1.7-38.2; P = .008) in multivariate analysis. Active malignancy (P = .003) and monocytopenia (P = .01) at the time of diagnosis of infection were also independently associated with a poor

Tedaviye erken başlanması mortaliteyi 2 kat azaltmış

hematological malignancy who are at an increased risk for zygomycosis.

PMID: 18611163 DOI: 10.1086/590004

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, May 2002, p. 1581–1582 Vol. 46, No. 5
0066-4804/02/$04.00+0 DOI: 10.1128/AAC.46.5.1581–1582.2002

In Vitro Activities of Posaconazole, Itraconazole, Voriconazole, Amphotericin B, and Fluconazole against 37 Clinical Isolates of Zygomycetes

Qiu N. Sun,[1,2] Annette W. Fothergill,[3]* Dora I. McCarthy,[3] Michael G. Rinaldi,[3,4] and John R. Graybill[1,4]

Int J Antimicrob Agents. 2019 Jan 9. pii: S0924-8579(19)30002-0. doi: 10.1016/j.ijantimicag.2019.01.002. [Epub ahead of print]

The contemporary management and clinical outcomes of mucormycosis: a systematic review and meta-analysis of case reports.

Jeong W[1], Keighley C[2], Wolfe R[3], Lee WL[1], Slavin MA[4], Chen SC[2], Kong DCM[5].

- İnvitro çalışmalarda amfoterisin B ve posakonazol mucorales takımına en etkili ajanlar

- İsavukonazol mukorales takımına etkili (*M. circinelloides* hariç), ancak MİK değerleri posakonazolden 2-3 adım daha yüksek

Isavuconazole treatment for mucormycosis: a single-arm open-label trial and case-control analysis

*Francisco M Marty, Luis Ostrosky-Zeichner, Oliver A Cornely, Kathleen M Mullane, John R Perfect, George R Thompson III, George J Alangaden, Janice M Brown, David N Fredricks, Werner J Heinz, Raoul Herbrecht, Nikolai Klimko, Galina Klyasova, Johan A Maertens, Sameer R Melinkeri, Ilana Oren, Peter G Pappas, Zdeněk Ráčil, Galia Rahav, Rodrigo Santos, Stefan Schwartz, J Janne Vehreschild, Jo-Anne H Young, Ploenchan Chetchotisakd, Sutep Jaruratanasirikul, Souha S Kanj, Marc Engelhardt, Achim Kaufhold, Masanori Ito, Misun Lee, Carolyn Sasse, Rochelle M Maher, Bernhardt Zeiher, Maria J G T Vehreschild, for the VITAL and FungiScope Mucormycosis Investigators**

Summary

Background Mucormycosis is an uncommon invasive fungal disease with high mortality and few treatment options. Isavuconazole is a triazole active in vitro and in animal models against moulds of the order Mucorales. We assessed the efficacy and safety of isavuconazole for treatment of mucormycosis and compared its efficacy with amphotericin B in a matched case-control analysis.

Methods In a single-arm open-label trial (VITAL study), adult patients (≥18 years) with invasive fungal disease caused by rare fungi, including mucormycosis, were recruited from 34 centres worldwide. Patients were given isavuconazole

Lancet Infect Dis 2016

Published Online
March 8, 2016
http://dx.doi.org/10.1016/S1473-3099(16)00071-2

See Online/Comment
http://dx.doi.org/10.1016/S1473-3099(16)00127-4

Isavukonazol

- İkinci kuşak triazol
- Oral ve IV formları mevcut
- Mart 2015 mukormikoz için FDA onayı

Isavuconazole treatment for mucormycosis: a single-arm open-label trial and case-control analysis

Francisco M Marty, Luis Ostrosky-Zeichner, Oliver A Cornely, Kathleen M Mullane, John R Perfect, George R Thompson III, George J Alangaden, Janice M Brown, David N Fredricks, Werner J Heinz, Raoul Herbrecht, Nikolai Klimko, Galina Klyasova, Johan A Maertens, Sameer R Melinkeri,

	Isavuconazole	Amphotericin B	p value
Crude all-cause mortality, n/N (%; 95% CI)*	7/21 (33%; 14·6–57·0)	13/33 (39%; 22·9–57·9)	p=0·775†
Weighted all-cause mortality (%;‡ 95% CI)*	33%; 13·2–53·5	41%; 20·2–62·3	p=0·595§
Crude mortality by matching covariates, n/N (%)			
Haematological malignancy	5/11 (45%)	7/18 (39%)	NA
Severe disease¶	6/12 (50%)	8/13 (62%)	NA
Surgical treatment‖	4/9 (44%)	3/13 (23%)	NA

Primary treatment with isavuconazole-treated cases (VITAL) versus amphotericin B-treated controls (FungiScope). *95% CI are based on an exact binomial distribution (crude) or normal approximation (weighted). †Calculated from Fisher's exact test. ‡Weights were applied according to the ratio of the number of controls matched to each case. §Calculated from a χ^2 test. ¶CNS involvement or disseminated disease (defined as disease involving >1 non-contiguous organ). ‖Resection or debridement at the site of infection at treatment start (SD 7 days).

Table 5: **All-cause mortality through day 42 for a matched case-control analysis of patients with mucormycosis**

İsavukonazol ve AmB etkinlik açısından benzer bulunmuş

L-AmB ve Posakonazol Kombinasyon Tedavisi

Combined antifungal approach for the treatment of invasive mucormycosis in patients with hematologic diseases: a report from the SEIFEM and FUNGISCOPE registries

Table 1. Clinical characteristics and risk factors of 32 patients who developed invasive mucormycosis.

	N	%
Gender		
M	18	56
F	14	44

- 32 vaka (SEİFEM ve FUNGİSOPE)
- 27 (posakonazol + L-AmB)
- 5 (posakonazol + ABLC)
- **Posakonazol çoğunlukla kurtarma tedavisi olarak kullanılmış**
- Tedavi yanıtı= %56

Pagano L, Cornely O. Haematologica 2013

Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium

Oliver A Cornely, Ana Alastruey-Izquierdo, Dorothee Arenz, Sharon C A Chen, Eric Dannaoui, Bruno Hochhegger, Martin Hoenigl, Henrik C Jensen, Kristina Lagrou, Russell E Lewis, Sibylle C Mellinghoff, Melvyn Mer, Priti D Perti, Dimitri Seidel, Donald C Sheppard, Roger Wahlin, Murat Akova, Alexandre Alanio, Abdullah M S Al-Hatmi, Sevtap Arikan-Akdagli, Hamid Badali, Ronen Ben-Ami, Alexandro Bonifaz, Stéphane Bretagne, Elio

Strongly recommended | Moderately recommended | Marginally recommended | Recommended against

A

Suspected and confirmed mucormycosis are emergencies and require rapid action

Surgical debridement with clean margins
for 3 purposes: (1) disease control, (2) histopathology, (3) microbiological diagnostics
Plus
Immediate treatment initiation

Avoid slow escalation of doses	If brain involvement	If SOT	If preexisting renal compromise	Isavuconazoayle IV 3×200 mg day 1–2 1×200 mg per day from day 3 Posaconazole IV 2×300 mg day 1 1×300 mg per day from day 2	Posaconazole oral suspension 4×200 mg per day	Liposomal amphotericin B <5 mg/kg per day	Avoid amphotericin B deoxycholate Any dose
Liposomal amphotericin B 5–10 mg/kg per day from day 1	Avoid slow escalation of doses **Liposomal amphotericin B** 10 mg/kg per day from day 1	Avoid slow escalation of doses **Liposomal amphotericin B or amphotericin B lipid complex** 10 mg/kg per day from day 1	**Isavuconazoayle IV** 3×200 mg day 1–2 1×200 mg per day from day 3 **Posaconazole IV** 2×300 mg day 1 1×300 mg per day from day 2				

Response assesment
(eg weekly imaging)

Stable disease or partial response	Progressive disease		Toxicity	
Continuation of 1st line treatment or change to oral treatment **Isavuconazoayle PO** 3×200 mg day 1–2 1×200 mg per day from day 3 or **Posaconazole DR tablets** 2×300 mg day 1 1×300 mg per day from day 2	**Isavuconazoayle IV** 3×200 mg day 1–2 1×200 mg/day 2 from day 3 or **Posaconazole IV or DR tablets** 2×300 mg day 1 1×300 mg per day from day 2 **Posaconazole oral suspension** 4×200 mg per day	**Liposomal amphotericin B** 10 mg /kg per day from day 1 **Amphotericin B lipid complex** or **Liposomal amphotericin B** 5 mg /kg per day from day 1 **Combination with pozaconazole**	**Isavuconazoayle IV** 3×200 mg day 1–2 1×200 mg/day 2 from day 3 or **Posaconazole IV or DR tablets** 2×300 mg day 1 1×300 mg per day from day 2 **Posaconazole oral suspension** 4×200 mg per day	**amphotericin B lipid complex or liposomal amphotericin B** 5 mg /kg per day from day 1

Altta Yatan Koşulların Kontrolü

- Diyabetin kontrolü
- Hasta nötropenikse hemopoietik growth faktör verilmesi
- Steroidin kesilmesi veya azaltılması
- Deferoxamin tedavisinin kesilmesi
- İmmun supresyonun azaltılması

Spellberg B. Clin Microbiol Rev 2005

Hiperbarik Oksijen

- Mukorales takımının üremesini inhibe eder (in vitro)
- Doku hipoksisi ve asidozu azaltır
- Polienlerin oksidatif öldürme etkisini arttırır
- Anjiogenezi artırır ve iyileşmeyi hızlandırır

Tragiannidis A. Clin Microbiol İnfect 2009

- Diyabetik hastalarda daha yararlı

Tedavi Süresi

- Hasta bazında değerlendirilmeli
- Klinik ve radyolojik tam iyileşme
- Altta yatan risk faktörleri düzelene kadar

Tedaviye devam edilmeli

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Contemporary management and clinical outcomes of mucormycosis: A systematic review and meta-analysis of case reports ☆

Wirawan Jeong [a], Caitlin Keighley [b,c], Rory Wolfe [d], Wee Leng Lee [a], Monica A. Slavin [e,f],

Accepted 6 January 2019

ABSTRACT

With the advent of newer antifungals, optimum treatment of mucormycosis remains to be fully elucidated. This study systematically evaluated the contemporary management and outcomes of mucormycosis. Mucormycosis cases in patients aged ≥18 years published between January 2000 and January 2017 were identified through Ovid MEDLINE and Embase. Of the 3619 articles identified, 600 (851 individual patient cases) were included in the review. Of the 851 patient cases, antifungal treatment details were available for 785. Intravenous (i.v.) amphotericin B formulations remained the most commonly prescribed first-line antifungals (760/785; 96.8%); 88.2% (670/760) were initiated as monotherapy and 11.8% (90/760) as combination antifungal therapy. Posaconazole oral suspension monotherapy was prescribed as an initial antifungal in 11 cases. It was also administered as maintenance or salvage therapy in 39 and 25 cases, respectively. Itraconazole capsule monotherapy ($n = 10$) was prescribed primarily for cutaneous disease in patients not receiving any immunosuppressive therapy. All-cause 90-day mortality was 41.0% (349/851). Initial treatment with combination antifungals did not reduce 90-day mortality compared with i.v. conventional amphotericin B or i.v. liposomal amphotericin B monotherapy [35/90 (38.9%) vs. 146/369 (39.6%) vs. 91/258 (35.3%), respectively; $P = 0.541$]. Concomitant surgical and antifungal therapy was associated with significantly lower 90-day mortality compared with treatment with antifungals alone (OR = 0.23, 95% CI 0.13–0.41; $P < 0.001$). The findings suggest that first-line antifungals with good efficacy remain an urgent unmet need. Whilst surgery is fundamental to improving survival, the clinical utility of combination antifungal therapy or posaconazole monotherapy requires further investigation.

Treatment modality	Compared with antifungal alone	<0.001		<0.001
Surgery	0.88 (0.24–3.28)	0.851	0.47 (0.09–2.44)	0.372
Antifungal and surgery	0.28 (0.17–0.43)	<0.001	0.23 (0.13–0.41)	<0.001
Antifungal and adjunctive therapy	0.44 (0.09–2.05)	0.297	0.38 (0.06–2.31)	0.293
Antifungal and surgery and adjunctive therapy	0.11 (0.04–0.28)	<0.001	0.07 (0.02–0.20)	<0.001

OR, odds ratio; CI, confidence interval.

[a] Complete details of demographic data and underlying conditions are presented in [17].

Mycopathologia
https://doi.org/10.1007/s11046-021-00528-2

CASE REPORT

Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM): Case Report and Systematic Review of Literature

Deepak Garg · Valliappan Muthu · Inderpaul Singh Sehgal · Raja Ramachandran ·

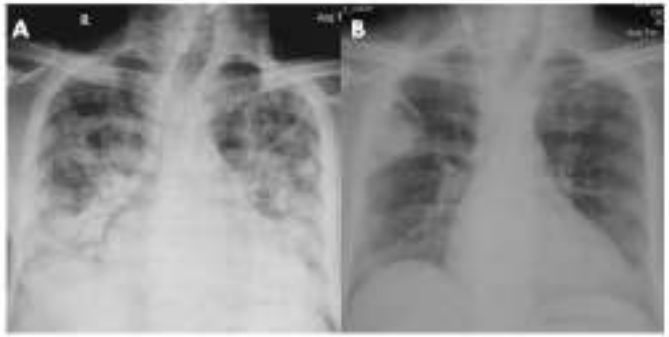


Fig. 1 Chest radiograph at admission a showing bilateral diffuse infiltrates and cardiomegaly. In the third week of hospitalization, a cavity with intracavitary content b can be seen in the right upper zone

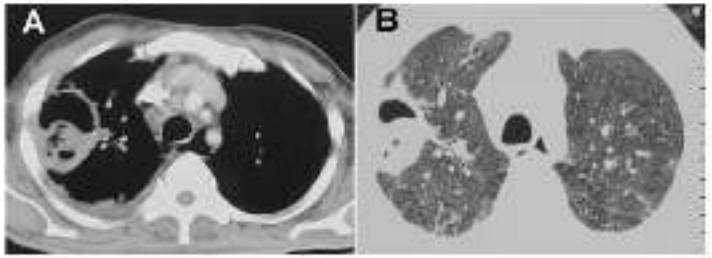


Fig. 2 Computed tomography showing thick-walled cavity in the right upper lobe in the corresponding mediastinal A and lung window B sections

Sonuç

Sağ kalım oranlarını arttırabilmek;

- Tıbbi, cerrahi, radyolojik ve laboratuar temelli multidisipliner bir yaklaşım ve
- Hızlı teşhis ve
- Hızlı tedavi ile mümkündür