

İMMÜNSUPRESİF HASTADA PNÖMONİ



Prof Dr Zekaver Odabaşı, Marmara Üniversitesi

İmmünsupresif hastaya yaklaşırken

- İmmünsupresif durumun **sebebi** nedir
- Etkilenen **immünolojik yanıt** nedir
- **Hangi enfeksiyon etkenleri** ile risk altındadır
- **Anti-enfektif profilaktif** ajan kullanılmaktadır
- Yeni tedavi ajanları (kanser, otoimmün hastalık)
 - ▣ **Monoklonal antikolar**
 - ▣ **Tirozin kinaz enzim inhibitörleri**
 - ▣ **İmmünoterapi ajanları**

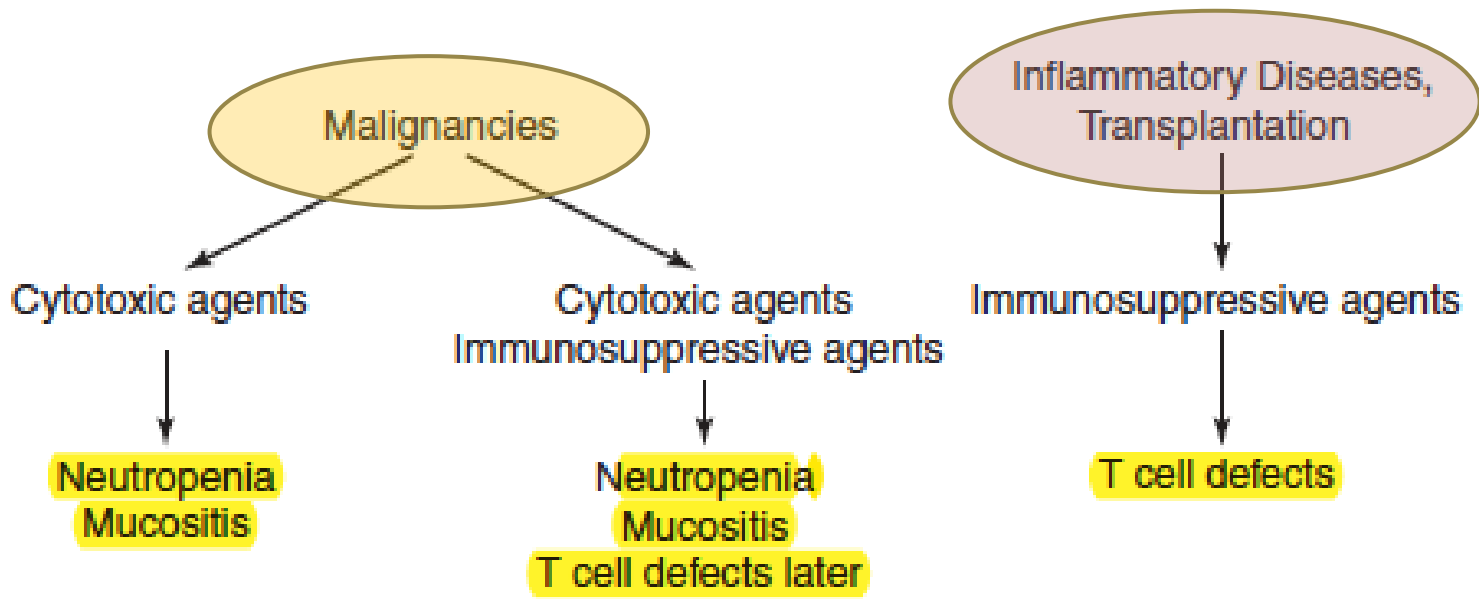
İmmünsupresyon

- **Primer (konjenital)**
- **Sekonder (edinilmiş)**
 - Kanser kemoterapisi
 - Nötropeni
 - Ajana özgün immünsupresyon
 - Solid organ nakli
 - Kök hücre nakli ve GVHH
 - Kortikosteroid kullanımı
 - AIDS
 - Splenektomi
 - Diğer: otoimmün hastalıklar, travma, siroz, KBY, yanık

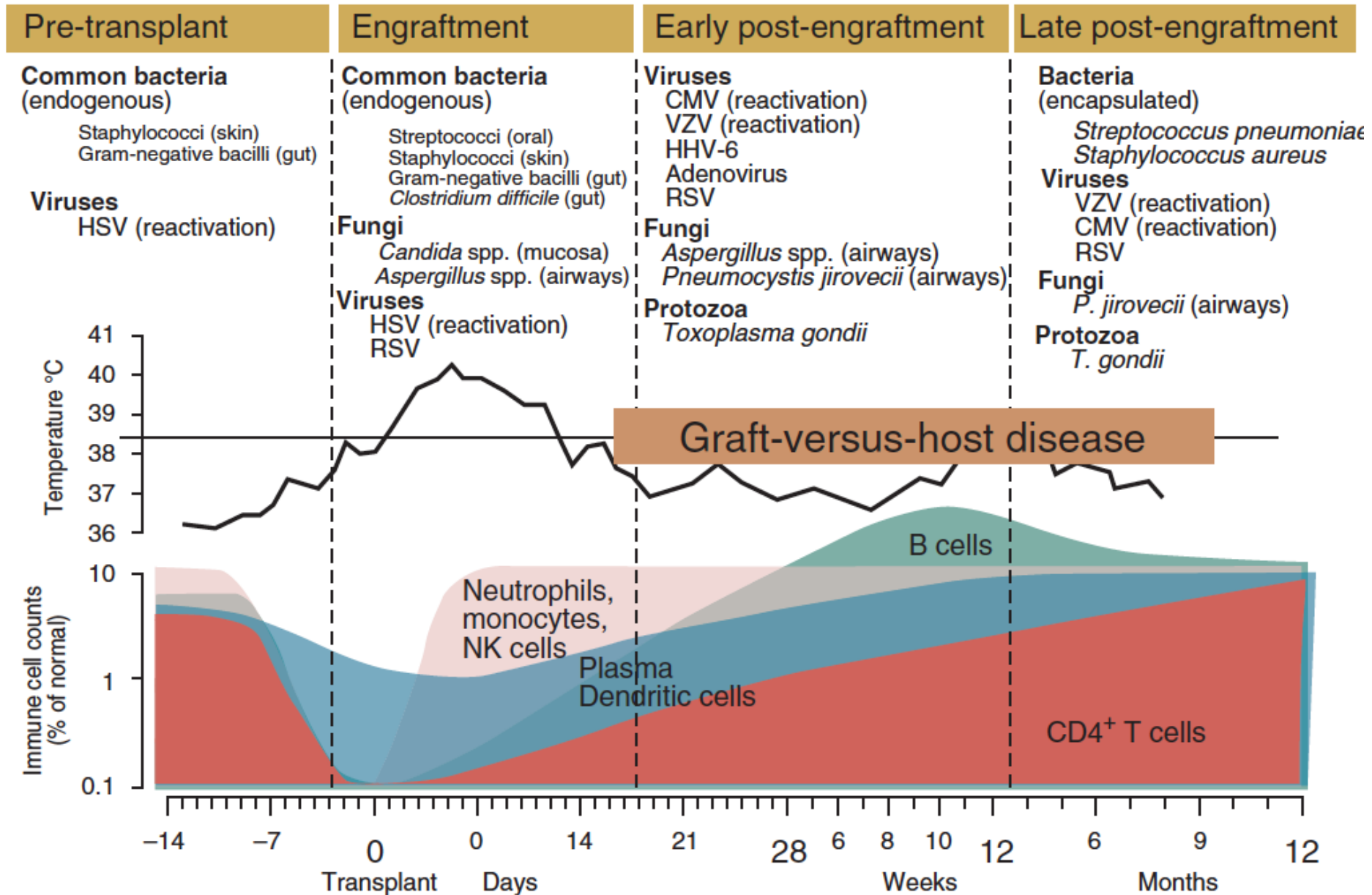
Beş Majör İmmün Defekt ve Pnömoni Etiyolojisi

Table 1. Types of immunological defects, predisposing factors, and common pathogens which cause pulmonary infections

Defects	Bacteria	Fungi	Viruses	Parasites
Phagocytes nötropeni	<i>Staphylococcus aureus</i> <i>Pseudomonas aeruginosa</i> <i>Klebsiella pneumoniae</i> <i>Escherichia coli</i>	<i>Aspergillus</i> spp. <i>Candida</i> spp.		
B-cell	<i>Streptococcus pneumoniae</i> <i>S. aureus</i> <i>Haemophilus influenzae</i> <i>P. aeruginosa</i>			
T-cell	<i>Legionella</i> spp. <i>Nocardia</i> spp. <i>Mycobacteria</i> spp.	<i>Pneumocystis jirovecii</i> <i>Cryptococcus neoformans</i> <i>Histoplasma capsulatum</i> <i>Coccidioides immitis</i> <i>Candida</i> spp.	Cytomegalovirus Varicella-zoster virus Herpes simplex virus	<i>Toxoplasma gondii</i> <i>Strongyloides stercoralis</i>
Splenectomy	<i>S. pneumoniae</i> <i>S. aureus</i> <i>H. influenzae</i>			
Steroid therapy	<i>S. aureus</i> <i>Legionella</i> spp. <i>Nocardia</i> spp. <i>Mycobacteria</i> spp. <i>P. aeruginosa</i> Other gram-negative bacteria	<i>Aspergillus</i> spp. <i>Candida</i> spp. <i>C. neoformans</i> <i>H. capsulatum</i> <i>C. immitis</i>	Cytomegalovirus Varicella-zoster virus Herpes simplex virus	<i>T. gondii</i> <i>S. stercoralis</i>



Kök Hücre nakli hastaları



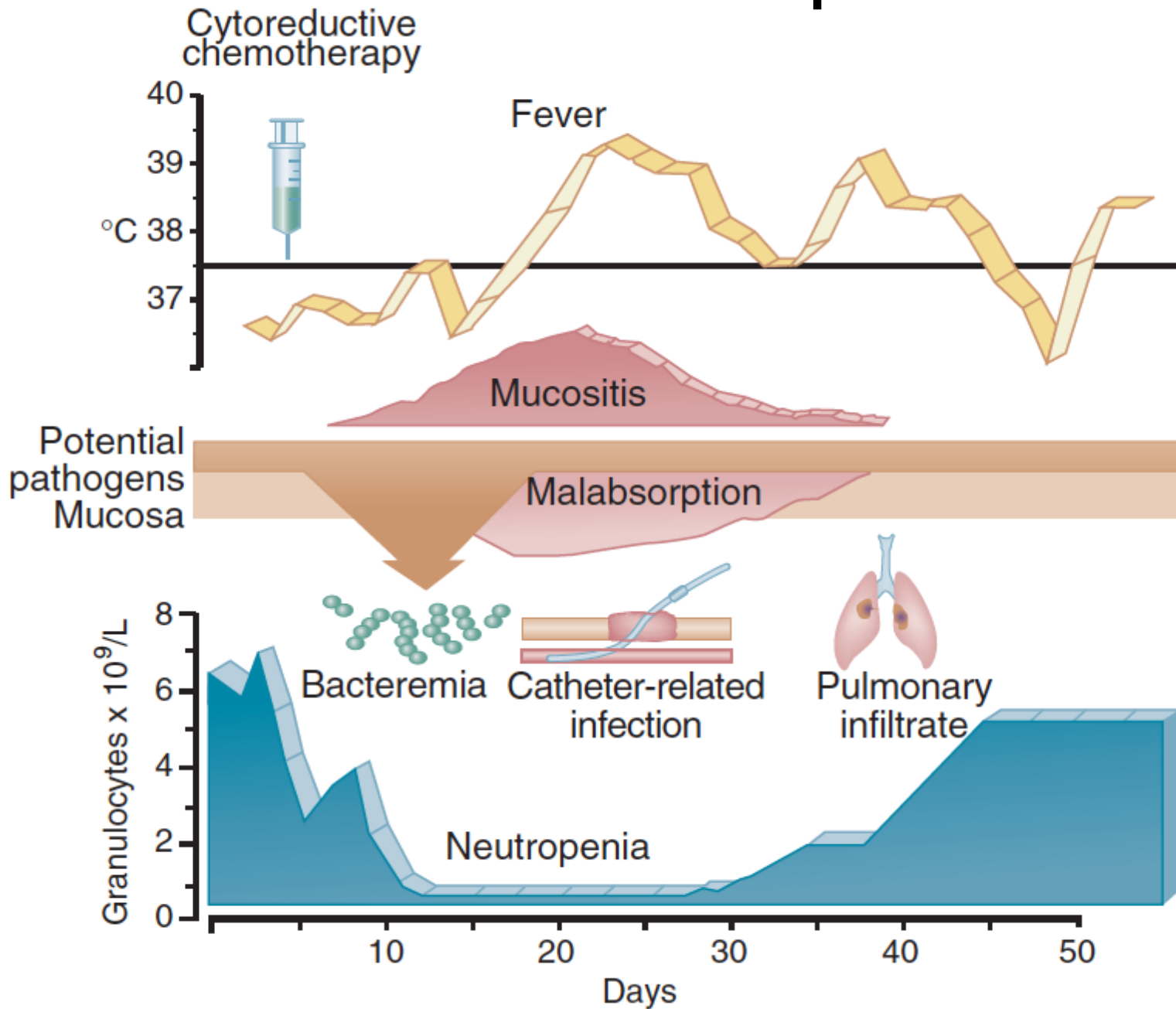
Kök Hücre nakli hastaları – Pnömoni etkenleri

Table 2. Pulmonary infection after hematopoietic stem cell transplantation

Pre-engraftment (day 0–30)	Post-engraftment (day 31–100)	Late engraftment (day >100)
Neutropenia	Defect in CMI & humoral immunity	Community-acquired infection
Aspiration	CMV	<i>Streptococcus</i>
G (-) bacilli	<i>Pneumocystis jirovecii</i>	<i>Staphylococcus</i>
<i>Aspergillus</i>	Idiopathic pneumonitis	Varicella
	GVHD	GVHD
		Bronchiolitis obliterans
		BOOP

CMI, cell-mediated immunity; CMV, cytomegalovirus; GVHD, graft-versus-host disease; BOOP, bronchiolitis obliterans organizing pneumonia.

Kemoterapi - Febril nötropeni



Febril nötropeni - muhtemel Enfeksiyon Etkenleri

- **Gram Pozitif Bakteriler**
 - Stafilokoklar (S. aureus ve koagülaz negatifler)
 - Viridans streptokoklar
 - Enterokoklar
- **Gram Negatif Bakteriler**
 - E. coli
 - Klebsiella pneumoniae
 - Pseudomonas aeruginosa
- **Viral:** HSV, VZV
- **Fungal:** Candida, Aspergillus

Fonksiyonel Hiposplenizm

TABLE 316-1 Medical Conditions Associated with Functional Hyposplenism

MEDICAL CONDITION	PREVALENCE OF HYOSPLENISM	DEGREE OF HYOSPLENISM	STRENGTH OF EVIDENCE FOR RISK OF SEPSIS
Sickle cell anemia	100%	Severe	+++
Graft-versus-host disease	15%-40%	Moderate to severe	+++
Celiac disease	33%-76%	Moderate to severe	+++
Human immunodeficiency virus–acquired immunodeficiency syndrome	36%	Moderate to severe	+++
Alcoholic liver disease	37%-100%	Moderate to severe	+++
Inflammatory bowel disease			++
Ulcerative colitis	35%-45%	Moderate	
Crohn's disease	9%-37%	Mild	
Primary amyloidosis	28%	Moderate	++
Systemic lupus erythematosus	5%-7%	Mild to moderate	++

++, moderate evidence; +++, strong evidence.

Modified from Di Sabatino A, Carsetti R, Corazza GR. Post-splenectomy and hyposplenic states. *Lancet*. 2011;378:86-97.

Solid organ nakli

TABLE 313-3 Frequency, Types of Infections, and Sources of Infections Occurring in the First Year after Transplantation

TYPE OF TRANSPLANT	INFECTION EPISODES PER PATIENT	BACTEREMIA (%)	CMV DISEASE* (%)	FUNGAL INFECTIONS (%)	MOST COMMON SOURCE
Kidney	0.98	5-10	8	0.7	Urinary tract
Heart	1.36	8-11	25	8	Lung
Heart-lung	3.19	8-25	39	23	Lung
Liver	1.86	10-23	29	16	Abdomen and biliary tract

*Numbers reflect CMV disease rates in the absence of routine antiviral prophylaxis.

- ❑ Özellikle **T hücre fonksiyonları** baskılanır
 - ❑ mTor inhibitörleri: **evrolimus, sirolimus**
 - ❑ Kalsinörin inhibitörleri: **siklosporin, takrolimus**
 - ❑ **Viral**: toplum kökenli viruslar ve CMV, HSV, VZV
 - ❑ **Fungal**: P jirovecii, Aspergillus sp, Kriptokokal enf.
 - ❑ **Paraziter**: Toxoplasma

TABLE 313-4 Microbial Causes of Pneumonia in Transplant Recipients

Early Pneumonia (≤ 30 Days)

Common Causes

Gram-negative bacilli

Staphylococcus aureus

Aspiration

Less Common Causes

Aspergillus

Herpes simplex virus

Legionella

Toxoplasma gondii

Late Pneumonia (>30 Days)

Common Causes

Pneumococcus

Haemophilus influenzae

Influenza

No cause identified

Less Common Causes

Pneumocystis

Nocardia

Legionella

Aspergillus

Gram-negative bacilli

Staphylococcus aureus

Aspiration

Cytomegalovirus

Varicella-zoster virus

Paramyxoviruses

Tuberculosis

Coccidioidomycosis

Histoplasmosis

Cryptococcus

Respiratory viruses*

*These include parainfluenza, respiratory syncytial virus, metapneumovirus, coronavirus, rhinovirus, and adenovirus.

TABLE 313-5 Etiology of Pulmonary Nodules in Organ Transplant Recipients

Infectious

Bacterial

Nocardia

Mycobacteria

Legionella

Staphylococcus aureus (septic emboli)

Fungal

Aspergillus

Cryptococcus

Mucormycosis

Endemic fungi (histoplasmosis and coccidioidomycosis)

Other non-*Aspergillus* molds

Viral

Cytomegalovirus

Noninfectious

Malignancies

Post-transplantation lymphoproliferative disorder and other lymphomas

Carcinomas (typically lung neoplasms and hepatocellular carcinoma)

Nonmalignant Lesions

Rounded atelectasis

Data from Copp DH, Godwin JD, Kirby KA, et al. Clinical and radiologic factors associated with pulmonary nodule etiology in organ transplant recipients. *Am J Transplant*. 2006;6:2759-2764; and Paterson DL, Singh N, Gayowski T, et al. Pulmonary nodules in liver transplant recipients. *Medicine*. 1998;77:50-58.

Glukokortikoidler

- Ana etki **hücresel immünite** üzerine
 - **T – B hücre cevabını baskılar**
- **Alveoler makrofajların fagositik etkinliği azalır**
- Monosit, lenfosit ve eozinofiller baskılanır
- **Bakteriyel, viral, fungal enfeksiyon riski artar**
- Uzun süreli kullanımında
 - ***P. jirovecii* profilaksisi**
 - **Latent tüberküloz tedavisi**

RESEARCH ARTICLE

Common Infections in Patients Prescribed Systemic Glucocorticoids in Primary Care: A Population-Based Cohort Study

Laurence Fardet^{1,2,3*}, Irene Petersen¹, Irwin Nazareth¹

1 Department of Primary Care and Population Health, University College London, London, United Kingdom, 2 Department of Dermatology, Henri Mondor Hospital, Paris, France, 3 EA 7379 Epidémiologie en Dermatologie et Evaluation des Thérapeutiques, Université Paris–Est Créteil, UPEC Paris 12, Créteil, France

* laurence.fardet@aphp.fr



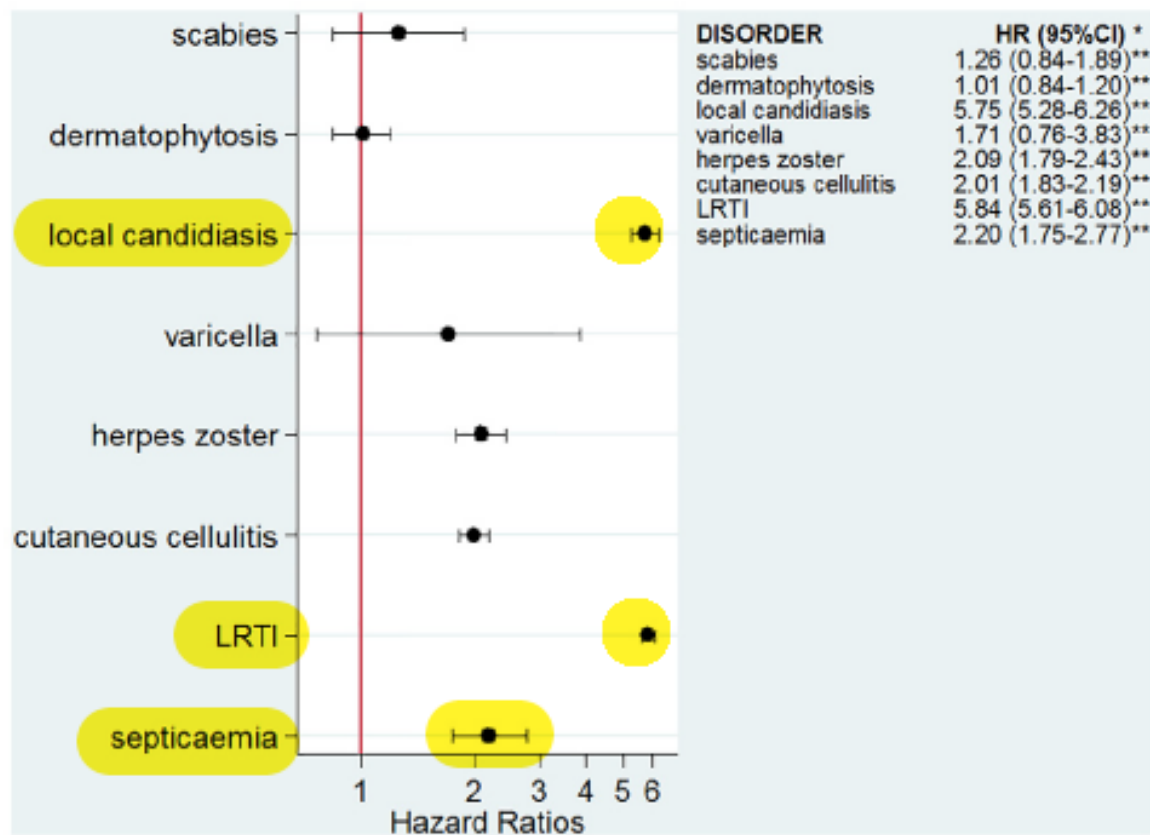


Fig 3. Risk of infection in glucocorticoid-exposed patients with one of the seven diseases of interest compared to those with the same underlying diseases but unexposed to glucocorticoids. *Models adjusted for sex, age, diabetes, use of other immunosuppressants, and the underlying disease. ** p -Value < 0.001 for all infections except for scabies, $p = 0.25$; varicella, $p = 0.20$; and dermatophytosis, $p = 0.97$.

Steroid dozu ve enfeksiyon riski

Format: Abstract

Send to

Rev Infect Dis. 1989 Nov-Dec;11(6):954-63.

Risk of infectious complications in patients taking glucocorticosteroids.

Stuck AE¹, Minder CE, Frey FJ.

Author information

Abstract

The association between corticosteroid therapy and subsequent infections was calculated by pooling data from 71 controlled clinical trials. The overall rate of infectious complications was 12.7% in the 2,111 patients randomly allocated to systemic corticosteroids and 8.0% in the 2,087 controls (relative risk [RR], 1.6; 95% confidence interval [CI], 1.3-1.9; P less than .001). The risk of infection was particularly high in patients with neurologic diseases (RR, 2.8; 95% CI, 1.9-4.3; P less than .001) and less pronounced in patients with intestinal (RR, 1.4; 95% CI, 1.1-1.7; P = .02), hepatic (RR, 1.4; 95% CI, 0.9-2.3; P = .25), and renal (RR greater than 1; P = .03) diseases. The rate was not increased in patients given a daily dose of less than 10 mg or a cumulative dose of less than 700 mg of prednisone. With increasing doses the rate of occurrence of infectious complications increased in patients given corticosteroids as well as in patients given placebo, a finding suggesting that not only the corticosteroid but also the underlying disease state account for the steroid-associated infectious complications observed in clinical practice.

PMID: 2690289

[Indexed for MEDLINE]



Prednizon günlük dozu 10 mg veya kümülatif dozu 700 mg 'ın altında ise risk artmıyor

HIV

CD 4 Sayısı*	Enfeksiyöz komplikasyonlar	Non-enfeksiyöz komplikasyonlar
>500 /mm ³	<ul style="list-style-type: none">➤ Akut retroviral sendrom➤ Kandida vajiniti	<ul style="list-style-type: none">➤ Persistan generalize lenfadenopati➤ Guillain Barre➤ Aseptik menenjit
200-500 /mm ³	<ul style="list-style-type: none">➤ Pnömonokokal pnömoni➤ Pulmoner tüberküloz➤ Zona➤ Orofarengeal kandidiyaz➤ Kaposi sarkomu➤ Oral lökoplaki	<ul style="list-style-type: none">➤ Servikal kanser➤ B hücreli lenfoma➤ İTP➤ Mononöritis multipleks➤ Anemi➤ Hodgkin lenfoma
<200 /mm ³	<ul style="list-style-type: none">➤ P jirovecii pnömonisi➤ Milier tüberküloz➤ PML (lökoensefalopati)	<ul style="list-style-type: none">➤ HIV erimesi➤ Non-hodgkin lenfoma➤ HIV demansı
<100 /mm ³	<ul style="list-style-type: none">➤ Disemine herpes➤ Toksoplazmoz, kriptokokkoz➤ Kriptosporidiyoz, mikrosporodiyoz➤ Kandida özefajiti	
<50 /mm ³	<ul style="list-style-type: none">➤ CMV➤ Mikobakterium avium kompleks	<ul style="list-style-type: none">➤ SSS lenfoması

* Belirtilen komplikasyonlar sıklıkla bu CD4 düzeylerinde gerçekleşse de, farklı CD4 düzeylerinde de görülebilirler.

Table 3. Pulmonary infection in AIDS

CD4 >200 cells/ μ L	CD4 between 50 and 200 cells/ μ L	CD4 <50 cells/ μ L
Bacterial pneumonia	Bacterial pneumonia	Bacterial pneumonia
TB (reinfection)	Primary TB	Atypical appearances of TB
	<i>Pneumocystis jirovecii</i>	<i>P. jirovecii</i>
	Fungal infection	Fungal infection
		MAC
		CMV

AIDS, acquired immunodeficiency syndrome; CD4, cluster of differentiation 4; TB, tuberculosis; MAC, *Mycobacterium avium* complex; CMV, cytomegalovirus.

Pnömonisi olan immünsupresif hastada önemli bazı noktalar

- **Çoğul** (miks) **enfeksiyon** riski unutulmamalıdır
 - *P. jirovecii* ve CMV
 - Influenza virüs ve Aspergilloz
- **Erken görüntüleme (BT) ve özgün mikrobiyolojik değerlendirme** yapılmalıdır
 - Düz akciğer grafisi yerine mümkünse tomografi tercih edilir
 - Duyarlılık testleri, moleküler testler
- **İnvaziv işlem sıklıkla gerekir**: Bronkoskopi, biyopsi
- Önceki enfeksiyon ve tedavi öyküsü, duyarlılık testleri

Pnömonisi olan immünsupresif hastada önemli bazı noktalar

- **İmmün supresyonu mümkünse azaltmalıdır**
- **Antikor bazlı serolojik testler genelde kullanışsızdır**
 - Yeterince antikor cevabı gelişmemiş olabilir
- **Antijen tespiti ve/veya moleküler (PCR) bazlı mikrobiyolojik testler tercih edilmelidir**
- **Klinik olarak stabil olmayan**, akut ve hızlı progresyon gösteren vakalarda **ampirik tedavi** başlanabilir
 - Etiyolojiye göre tedavi daraltılmalıdır
- **Epidemiyolojik risk faktörlerine** dikkat edilmelidir (tbc vb)

TABLE 1. Etiology of Febrile Pneumonitis Syndrome in 100 Cancer Patients and 51 Renal Transplant Patients at Massachusetts General Hospital^a

Etiology (Percent)	Number of patients		
	Cancer	Renal transplant	Total
Infectious causes			
Conventional bacterial infection (23.8)	26	10	36
Viral infection (13.2)	11	9	20
Fungal infection (10.6)	10	6	16
<i>Nocardia asteroides</i> (8.6)	5	8	13
<i>Pneumocystis carinii</i> (5.3)	6	2	8
<i>Mycobacterium tuberculosis</i> (0.7)	1	0	1
Mixed infections (9.9)	14	1 ^b	15
Total (72.2)	73	36	109
Noninfectious causes			
Pulmonary emboli (7.9)	3	9	12
Recurrent tumor (5.3)	8	0	8
Radiation pneumonitis (4.6)	7	0	7
Pulmonary edema (4.6)	1	6	7
Drug-induced pneumonitis (3.3)	5	0	5
Leukoagglutinin reaction (1.3)	2	0	2
Pulmonary hemorrhage (0.7)	1	0	1
Total (27.8)	27	15	42

^aData taken and modified from Rubin³ and Ramsey *et al.*²

^bThis one case was that of an aspiration pneumonia from whom mixed oropharyngeal floras were grown from a transtracheal aspirate. In addition, 23 renal transplant patients with a primary pulmonary process developed superinfection.

Kanser hastalarında pulmoner enfeksiyon etiyolojisi

Bakteriyel – %37

Fungal – %14

Viral – %15

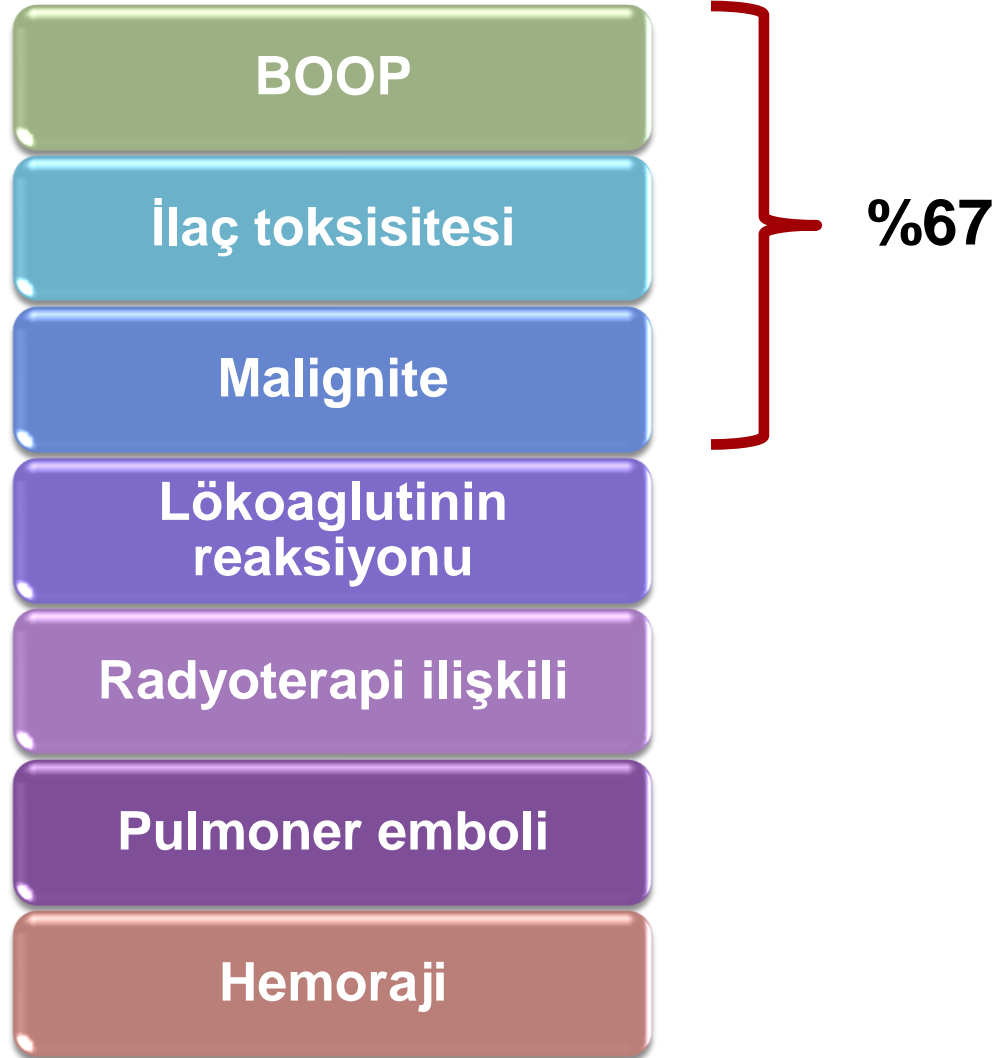
P. jirovecii – %8

Nocardia spp – %7

Mycobacterium tuberculosis – %1

Miks enfeksiyon – %20

Kanser hastalarında non - enfeksiyöz pulmoner infiltrat etiyolojisi



Tanısal Yaklaşım

- Vital bulgular ve **oksijen satürasyonu**
- Tam kan sayımı ve periferik yayma
- Elektrolitler, BUN ve kreatinin
- **Kan kültürü**
- İdrar sedim incelemesi ve kültürü
- **İdrarda pnömokok ve legionella antijenleri**
- **Solunum örneği incelemesi**
- **Radyolojik görüntüleme**
- Diğer sistem muayeneleri (disseminasyon)

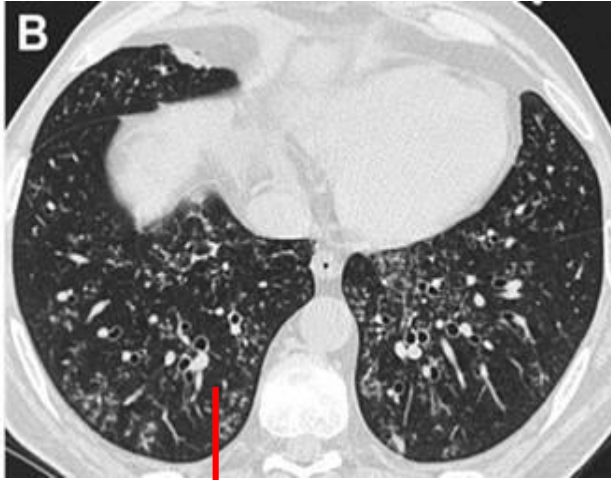
Radyolojik bulgular ve Etiyolojik Etken

- **Akut** gelişmiş fokal veya multifokal **konsolidasyonlar**
 - Genelde **bakteriyel pnömoni** lehinedir
- **Subakut** fokal veya multifokal **konsolidasyonlar**
 - **Nocardia spp, Actinomyces spp, Tüberküloz ve fungal enfeksiyonlar** lehine
- **Nodüler: Fungal enfeksiyon ya da Nocardia spp** lehine
- **Subakut diffüz peribronkovasküler** ya da miliyer
 - **Viral (CMV) , P jirovecii** ya da akciğer naklinde rejeksiyon
- **Kavite**
 - Anaeroblar, bazı gram negatifler (P aeruginosa, Klebsiella), Nocardia spp, Aspergilloz, Tüberküloz

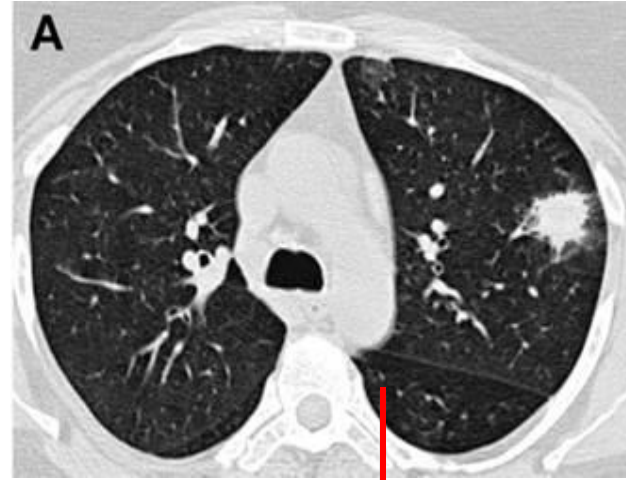
Chest radiograph or CT abnormality	Etiology by rate of disease progression	Etiology by rate of disease progression
	Acute <24 hours*	Chronic
Consolidation	Any organism (especially bacteria)	Fungi <i>Nocardia</i> spp, <i>Actinomyces</i> spp Mycobacteria Bronchoalveolar cancer Bronchiolitis obliterans organizing pneumonia
Diffuse interstitial infiltrate	<i>Pneumocystis jirovecii</i> Bacteria (especially <i>Haemophilus influenzae</i>) Virus (Influenza, CMV) Pulmonary edema Acute respiratory distress syndrome	Mycobacteria Drug toxicity Lymphocytic interstitial pneumonia Metastatic disease Pulmonary alveolar proteinosis
Nodular infiltrate	Bacteria	<i>Nocardia</i> spp, <i>Actinomyces</i> spp Fungi Kaposi's sarcoma Other tumors (especially lung cancer) Castleman's Disease
Adenopathy		Lymphoma Kaposi's sarcoma Castleman's Disease Lung cancer Tuberculosis
Pleural effusion	Bacteria (parapneumonic) Tuberculosis Empyema	Lymphoma (especially non-Hodgkin's lymphoma and primary effusion lymphoma) Kaposi's sarcoma
Pneumothorax	<i>P. jirovecii</i>	

Aspergillozun Farklı Hastalıklarda Prezantasyonu

Hava yolu invaziv



Anjiyo - invaziv

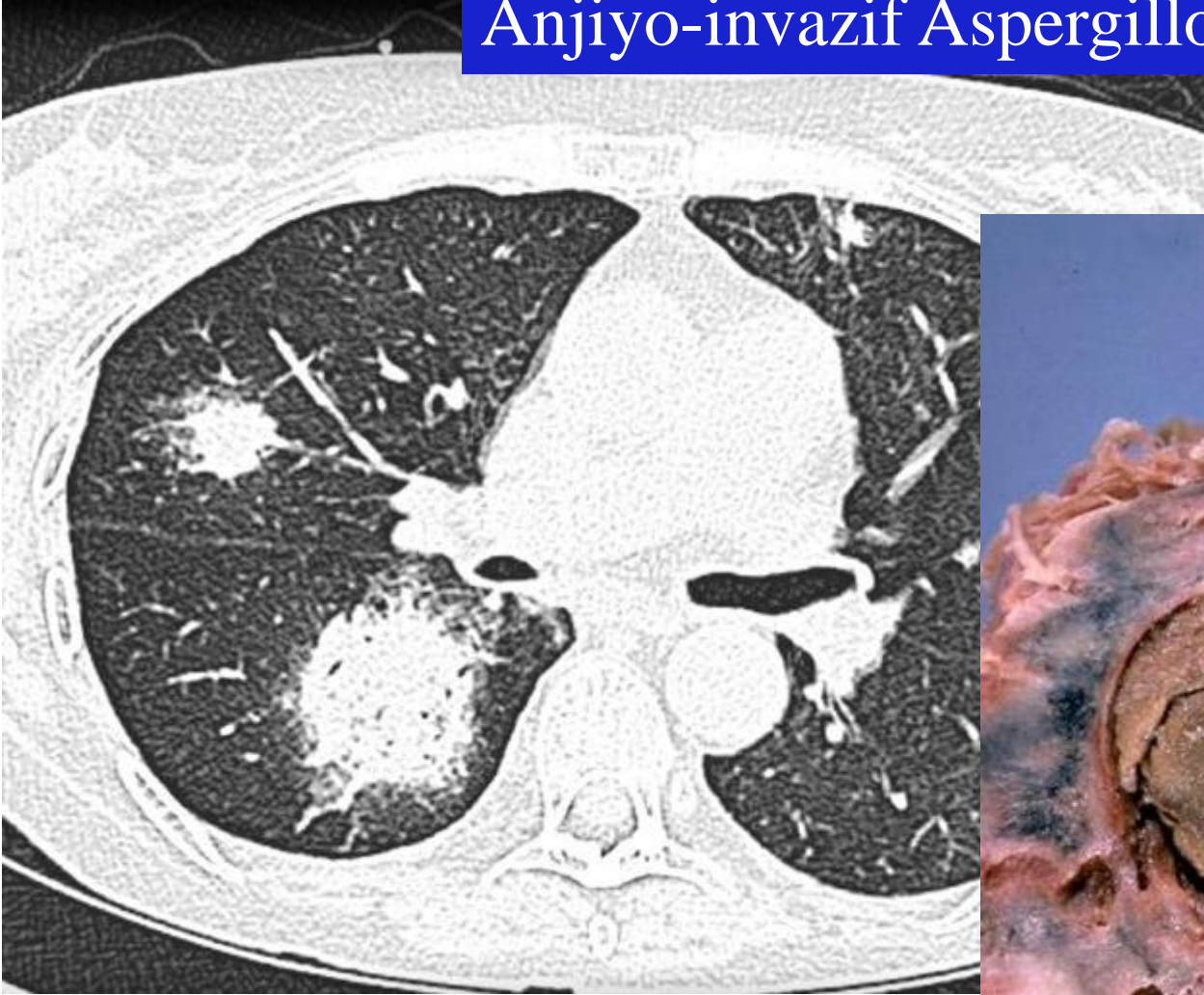


Bulgular	İlik Nakli (n=23)	Akut lösemi (n=22)	Diğer (n=10)
Anjiyoinvazif	3 (13%)	10 (45%)	1 (10%)
Hava yolu invazif*	10 (44%)	3 (14%)	2 (20%)
Her ikisi birden	3 (13%)	2 (9%)	2 (20%)
İkisi de olmadan	7 (30%)	7 (32%)	5 (50%)

* Sentrilobüler infiltrat, tree in bud

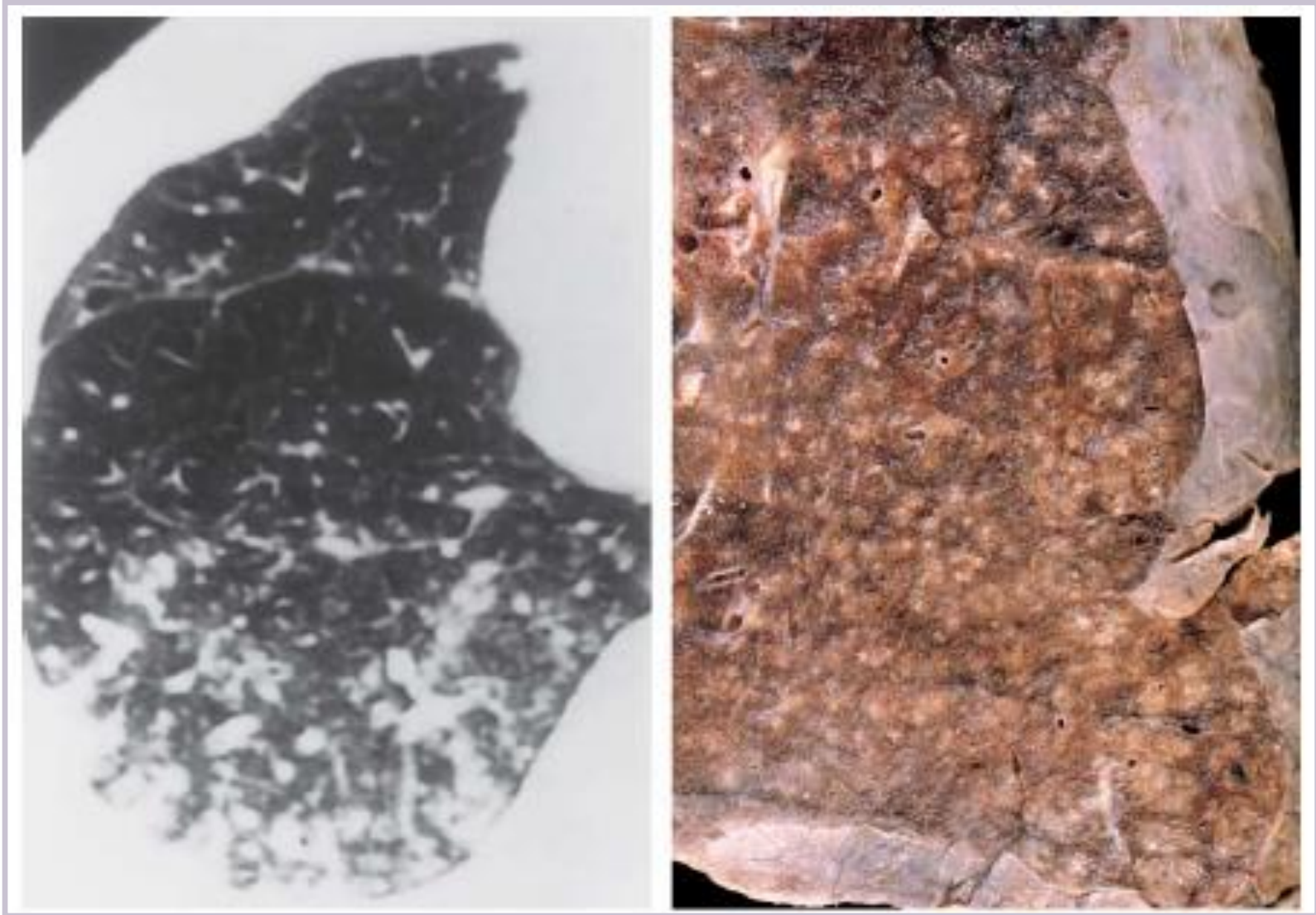
Bergeron A. Blood 2012;119(8):1831-7

Anjiyo-invazif Aspergilloz



Küçük – orta boy pulmoner arter dallarının infiltrasyonu ve kanama

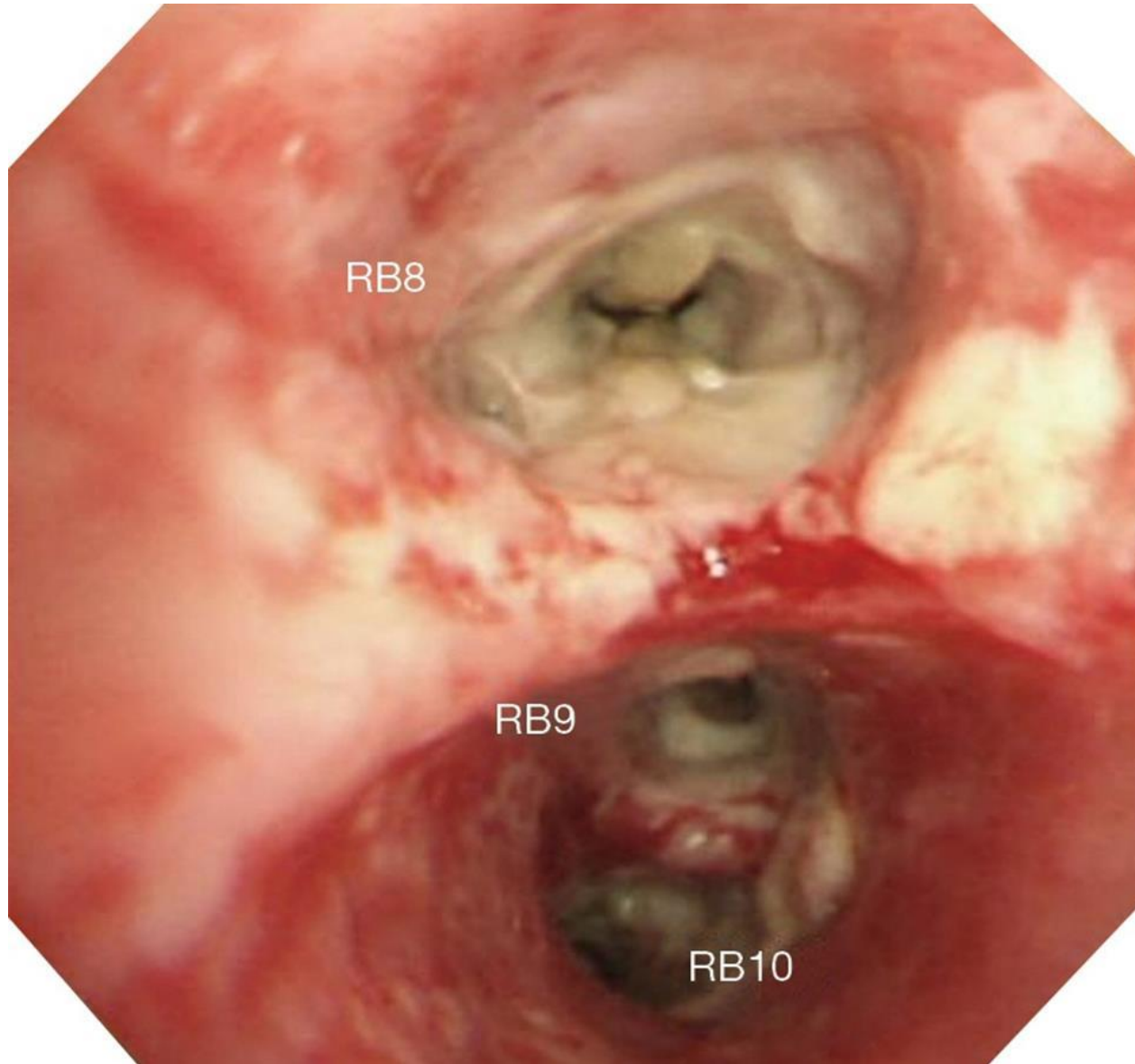
Havayolu invazif Aspergilloz



İnvazif bronşial aspergilloz

Franquet T, RadioGraphics 2001

Havayolu-invazif Aspergilloz



CT scan evolution during IPA

Peripheral halo

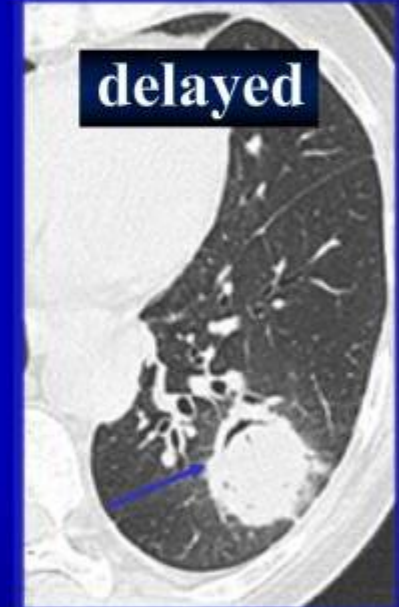
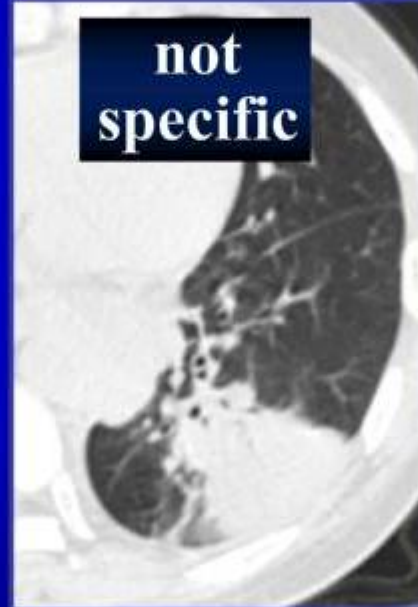
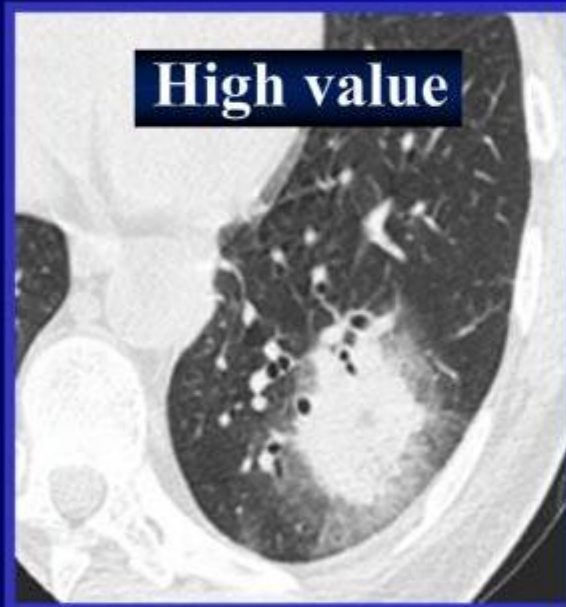
triangular shape

Air-crescent sign

d0 - d5

d5 - d10

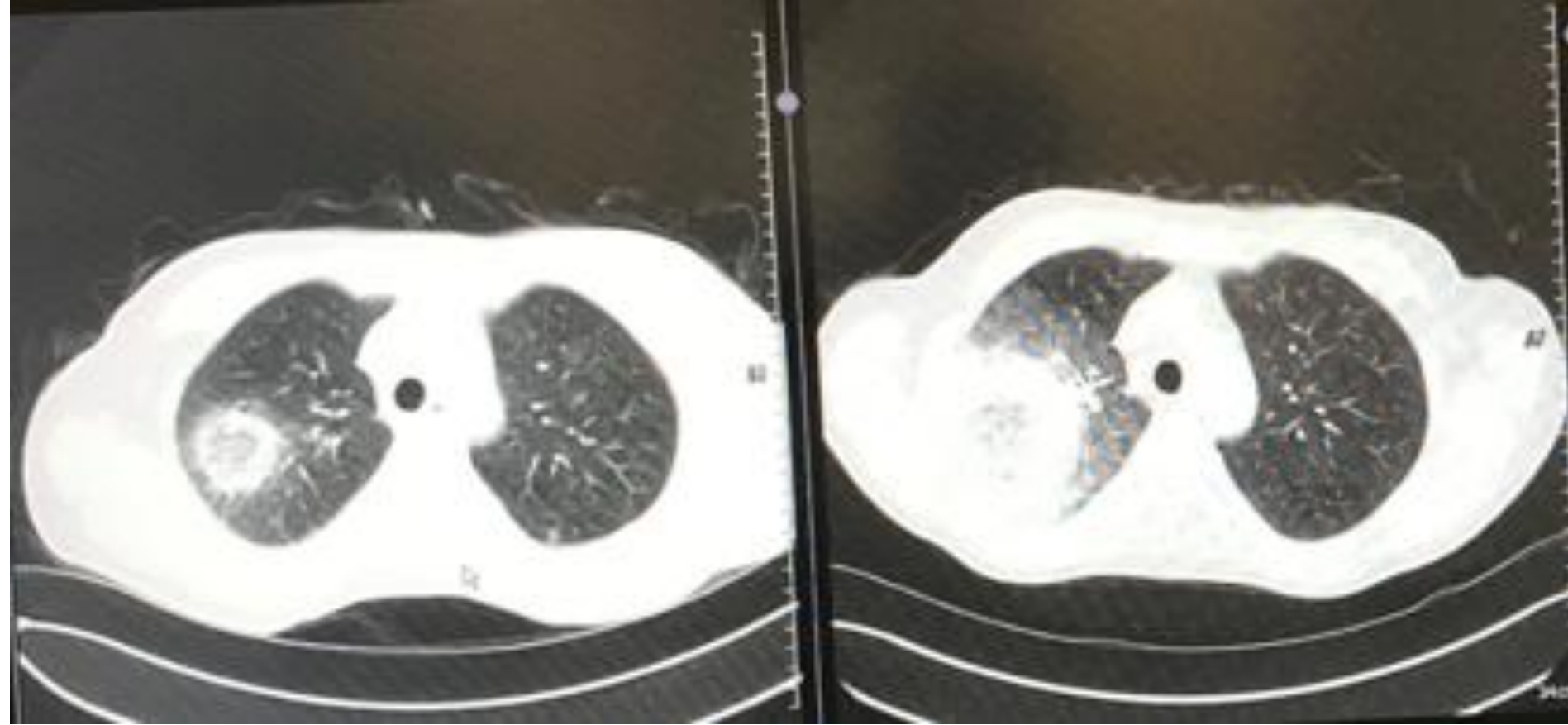
d10 - d20



Neutropenia

PMN >> 500

1 hafta ara ile çekilen iki tomografi, AML vakası



Ters halo: mukormikoz

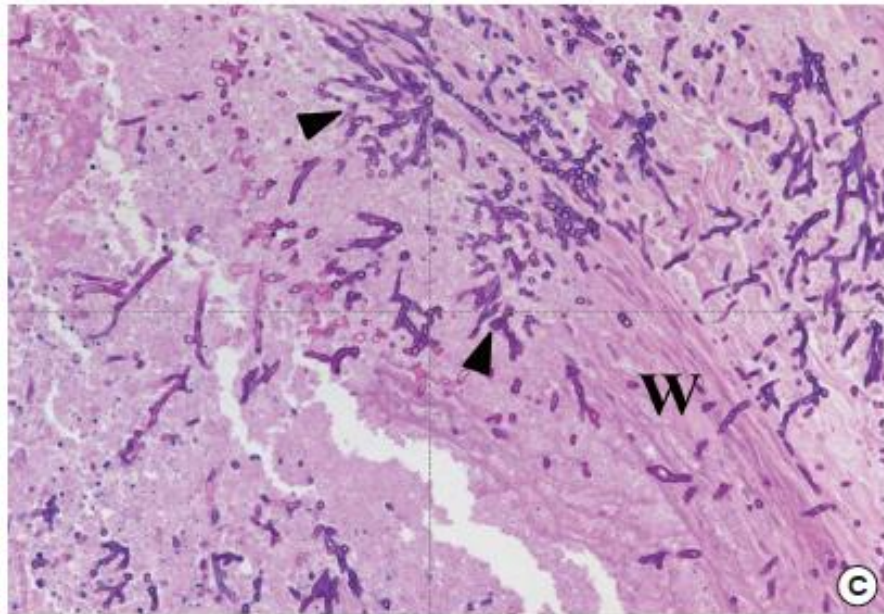


Fig. 1. Angioinvasive aspergillosis in a 63-year-old woman with acute lymphoblastic leukemia. (A) Lung window image of computed tomography (CT) scan (2.5-mm-section thickness) obtained at level of carina shows dense consolidation with internal air-density (arrowhead) showing so called “**reversed CT halo sign.**” (B) Follow-up CT image obtained 2 weeks later demonstrates a so-called lung ball with air-crescent sign (arrowhead). Soft tissue lesion (asterisk) within the cavity represents necrotic lung (sequestrum). (C) Photomicrograph (H&E stain, $\times 200$) shows infiltration of aspergillus colonies (arrowheads) into the wall of adjacent pulmonary artery (W).

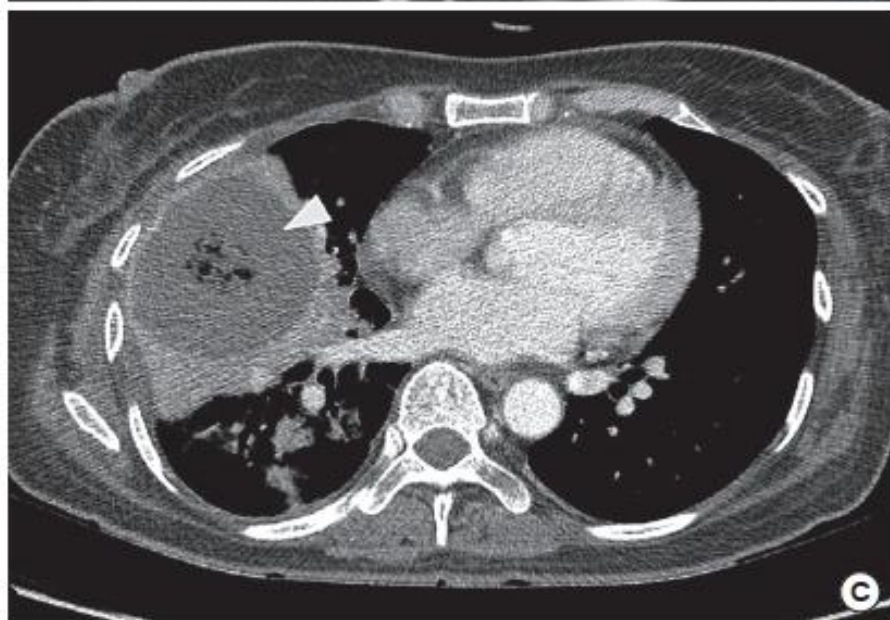
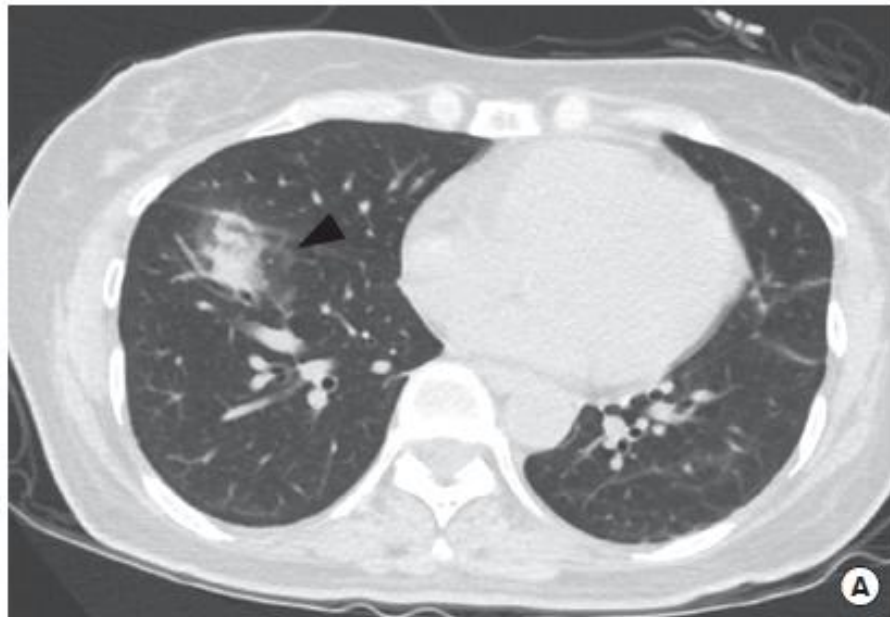


Fig. 6. Evolution of computed tomography (CT) findings in pulmonary mucormycosis in a 50-year-old woman with acute myelogenous leukemia. (A) Lung window image of CT scan (2.5-mm-section thickness) demonstrates ill-defined focal consolidation with ground-glass halo (arrowhead) in right lower lobe. (B) Lung window image of CT scan (2.5-mm-section thickness) obtained 3 weeks later shows progression of right lower lobe consolidation extending to right middle lobe. Note central low-attenuation area (arrowhead) within the dense consolidation representing ischemic change. (C) Mediastinal window image of CT scan (2.5-mm-section thickness) obtained 1 week after (B) shows large area of central necrotic area (arrowhead) within the dense consolidation.

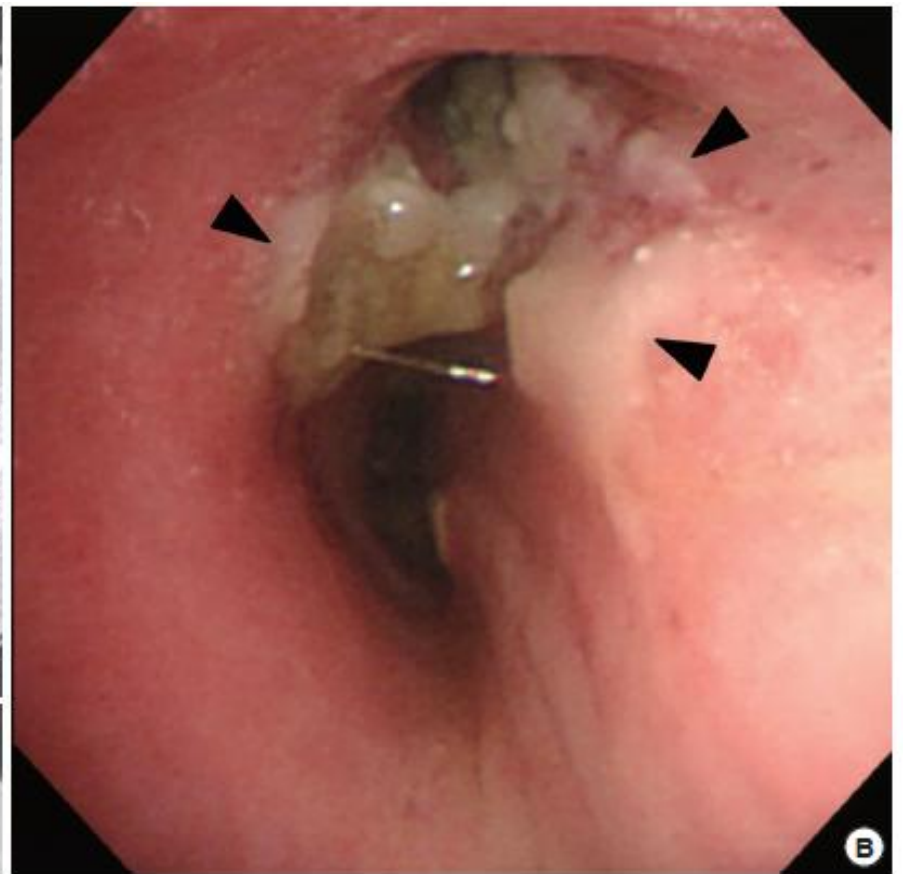
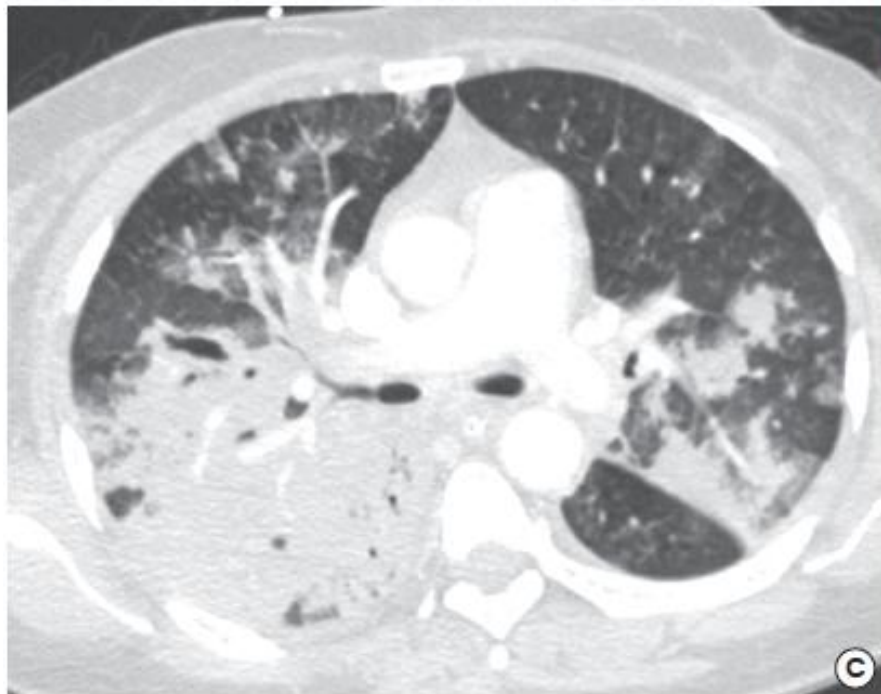
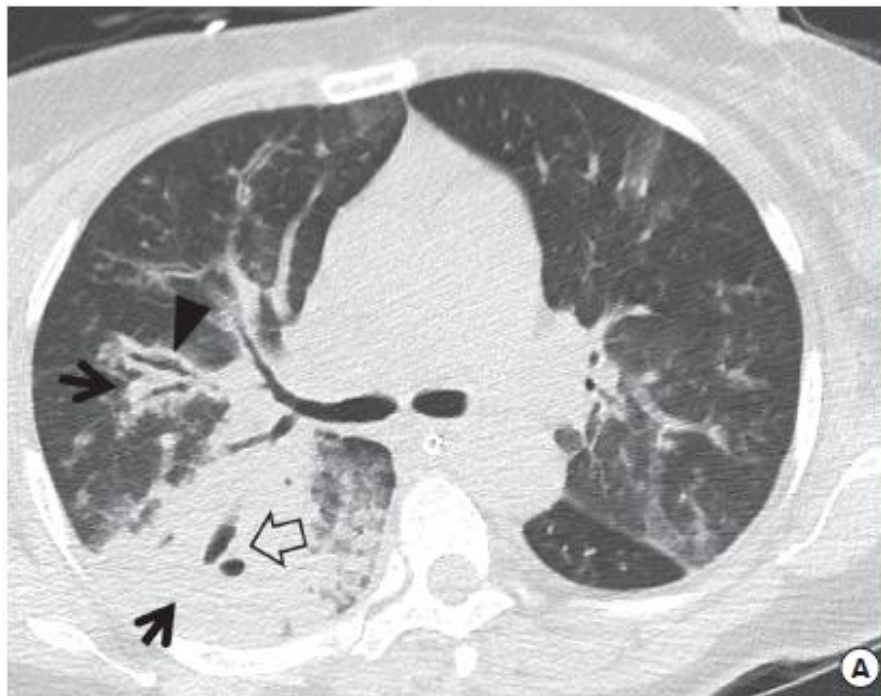


Fig. 2. Airway invasive aspergillosis in a 56-year-old woman with acute myelogenous leukemia. (A) Lung window image of computed tomography (CT) scans (2.5-mm-section thickness) obtained at level of main bronchi shows dense area of consolidation in a predominantly peribronchial distribution (arrows). Also note diffuse bronchial wall thickening (arrowhead) representing aspergillus tracheobronchitis. Cavity formation is seen within the consolidation (open arrow). (B) Bronchoscopy revealed multifocal mucosa hyperemia and pseudo-membrane formation (arrowheads) in the bronchial lumen. (C) Follow-up CT Image obtained 3 days later shows rapid progression of multifocal consolidation in both lungs. The patient expired despite the use of antifungal agents.

Aspergillus Türlerinde Büyüme Hızı

24 saatte 1-2 cm büyüme gösterir

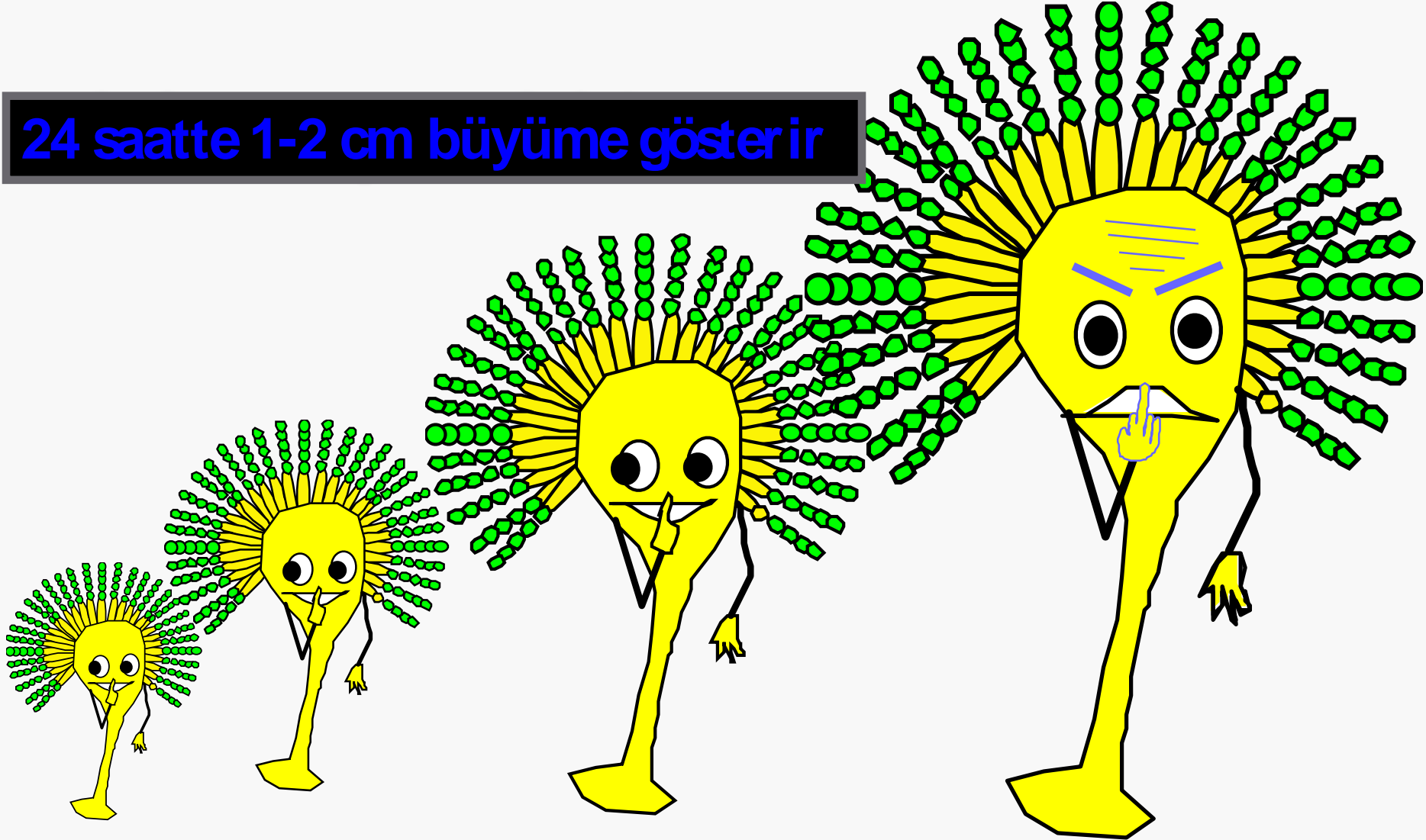




Fig. 8. Cryptococcosis in a 70-year-old woman with uncontrolled diabetes mellitus. Lung window images of computed tomography scans (2.5-mm-section thickness) obtained at level of right main bronchus depicts multifocal nodular consolidation with variable size (arrowheads) in both lungs.

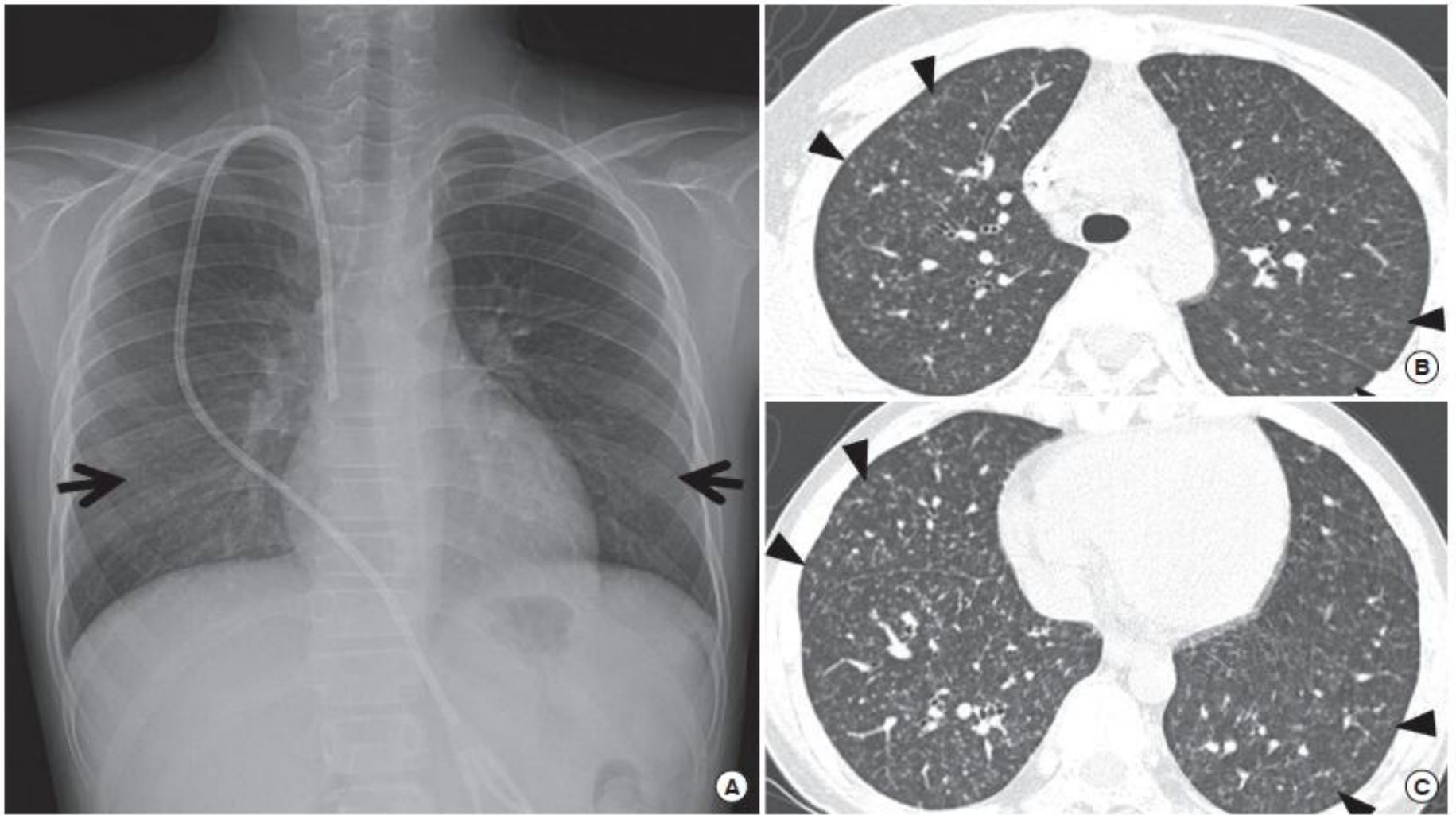
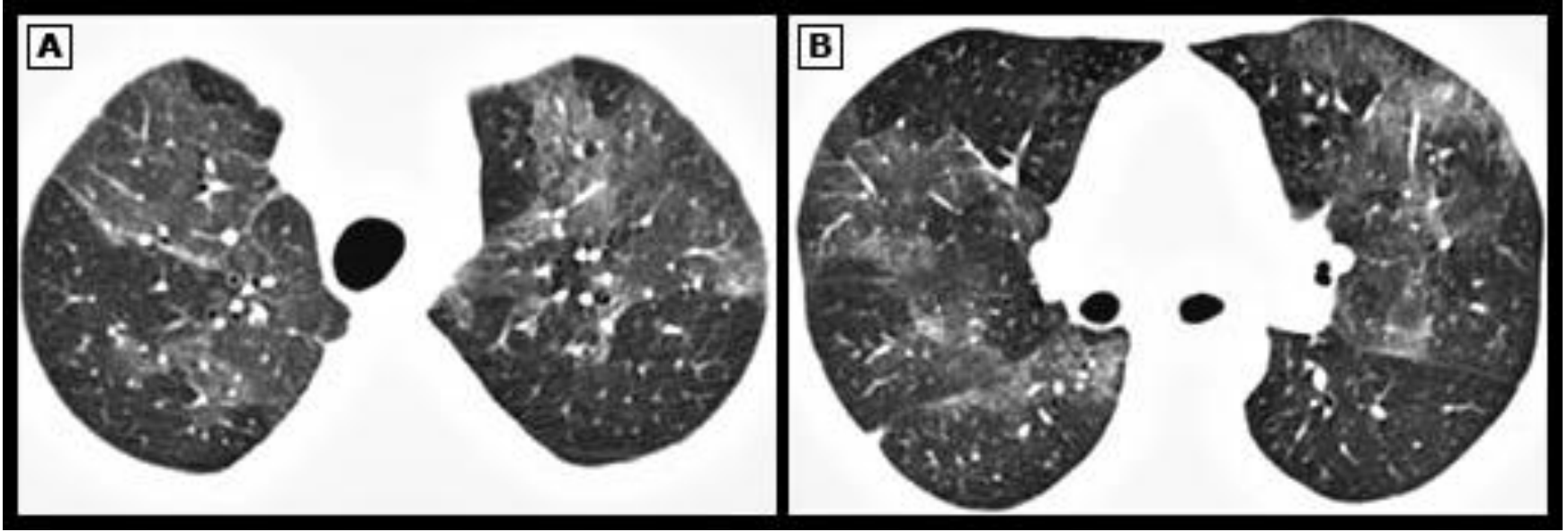
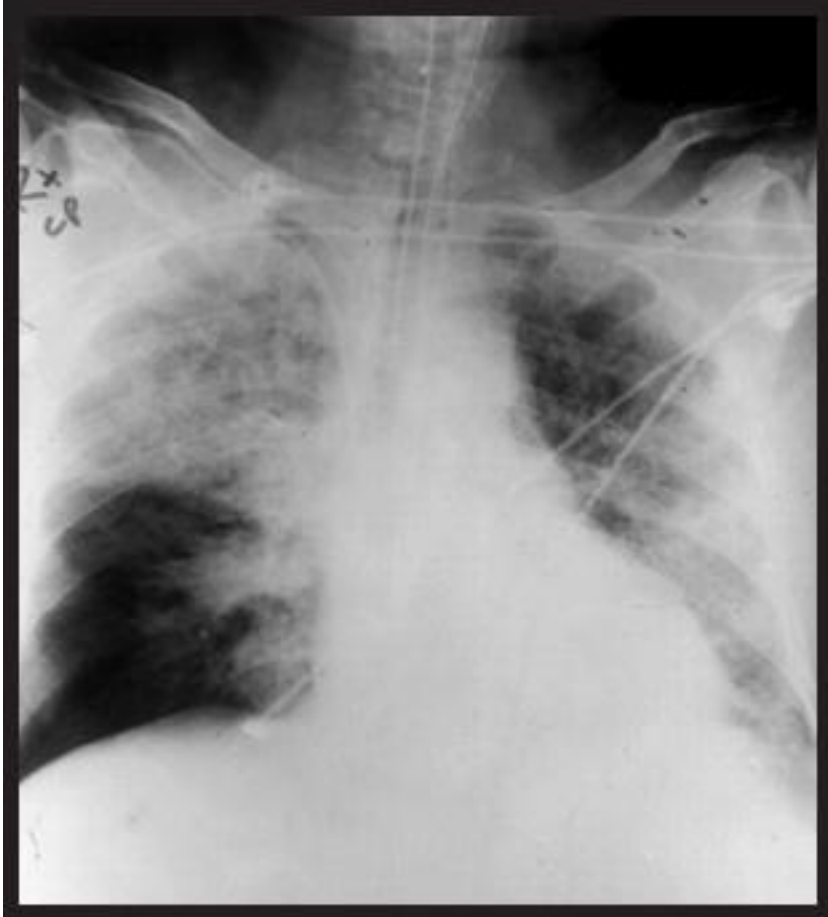


Fig. 3. Cytomegalovirus pneumonia In a 14-year-old male who underwent allogeneic hematopoietic stem cell transplantation 2 months ago. (A) Chest radiograph shows diffuse ill-defined ground-glass opacities in both lower lung zones (arrows). (B, C) Lung window images of computed tomography scans (2.5-mm-section thickness) obtained at levels of aortic arch (B) and left ventricle (C), respectively, depict diffuse and poorly-defined ground-glass opacity nodules (arrowheads) in both lungs.



Akut CMV pnömonisi

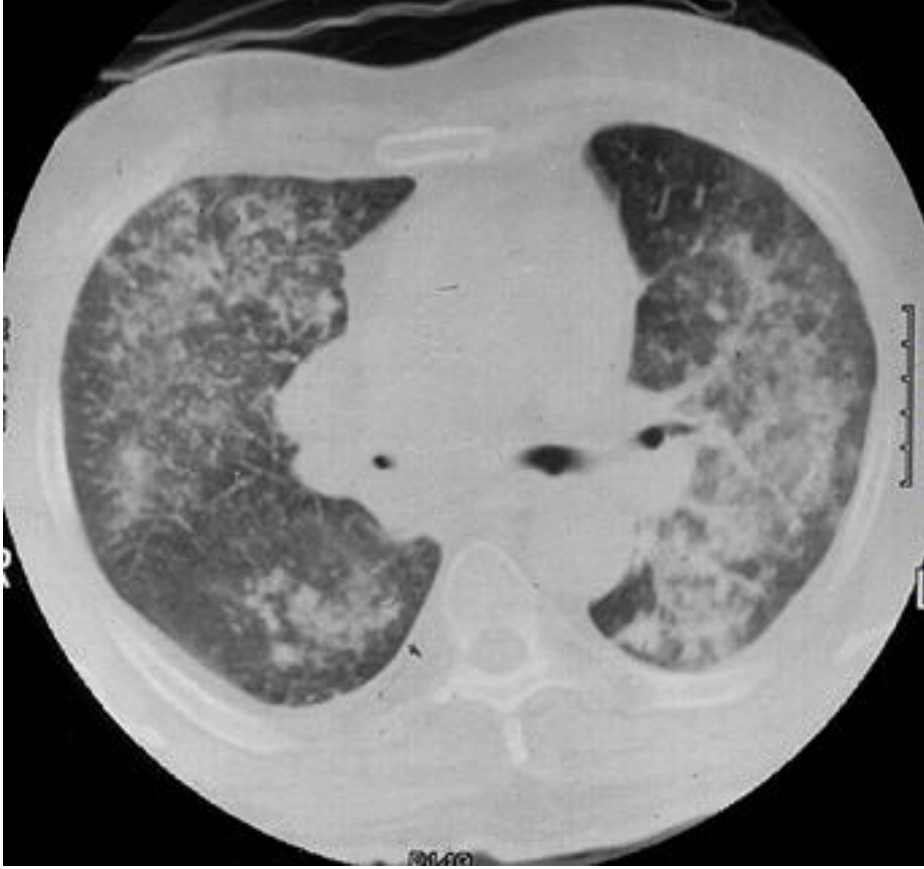
Bilateral buzlu cam manzarası



Wegener granülomatozu

Tanı

CMV + Legionella pnömonisi



İnterstisyel pnömoni

Karaciğer nakli vakası

Tanı: transbronşiyal biyopsi

CMV + Pneumocystis jirovecii

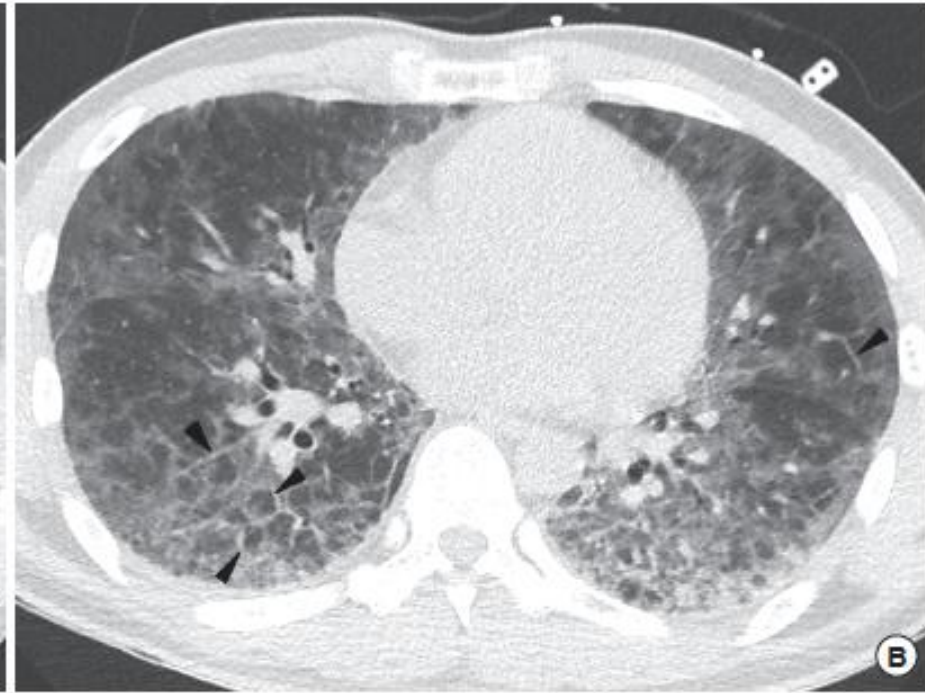
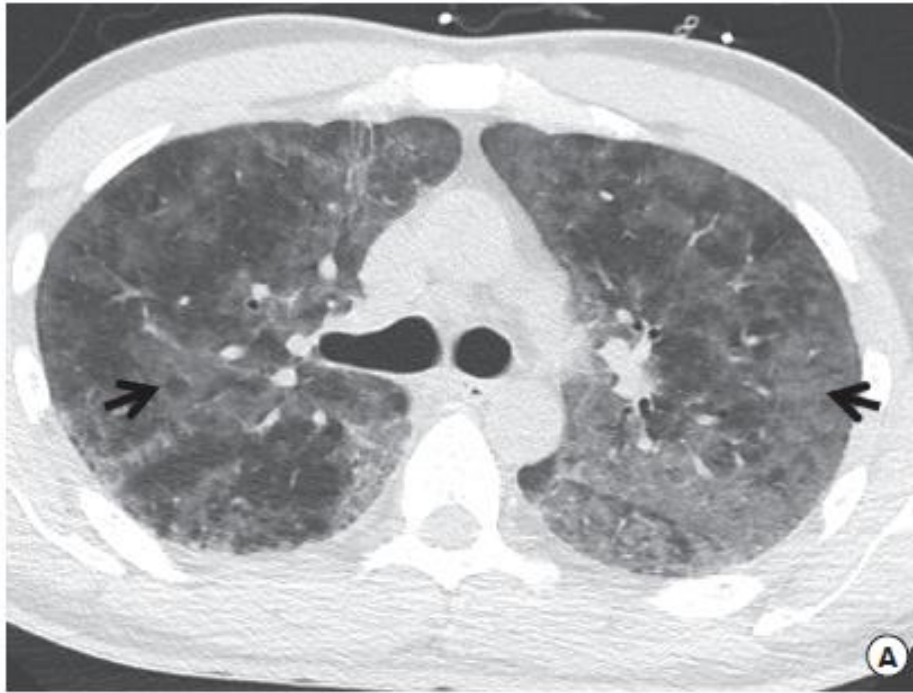
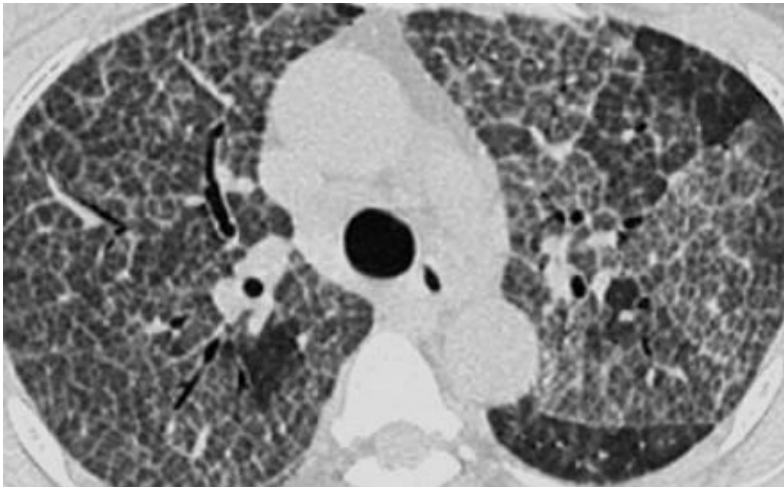


Fig. 4. Pneumocystis pneumonia in a 37-year-old man with acquired immunodeficiency syndrome (AIDS) (cluster of differentiation 4+ [CD4+] count, 75 cells/ μ L). (A, B) Lung window image of computed tomography scan (2.5-mm-section thickness) obtained at levels of carina and lung base, respectively, demonstrate **diffuse ground-glass opacity with geographic pattern** (arrows). Also note smooth interlobular septal thickening showing **crazy-paving** appearance (arrowheads).



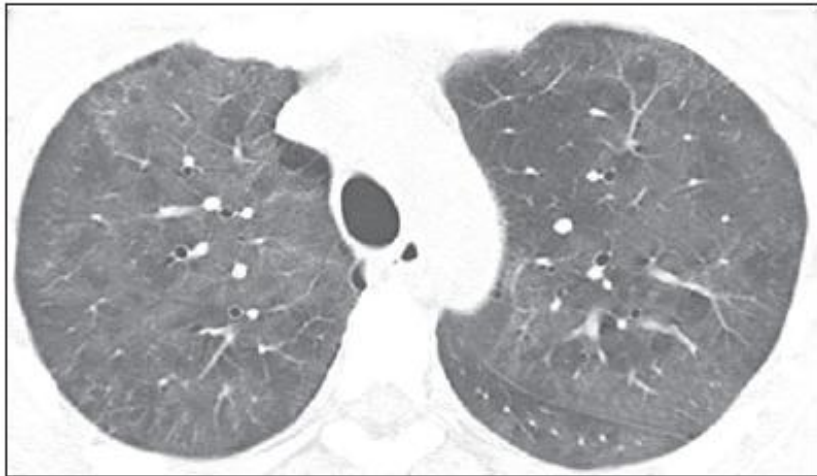
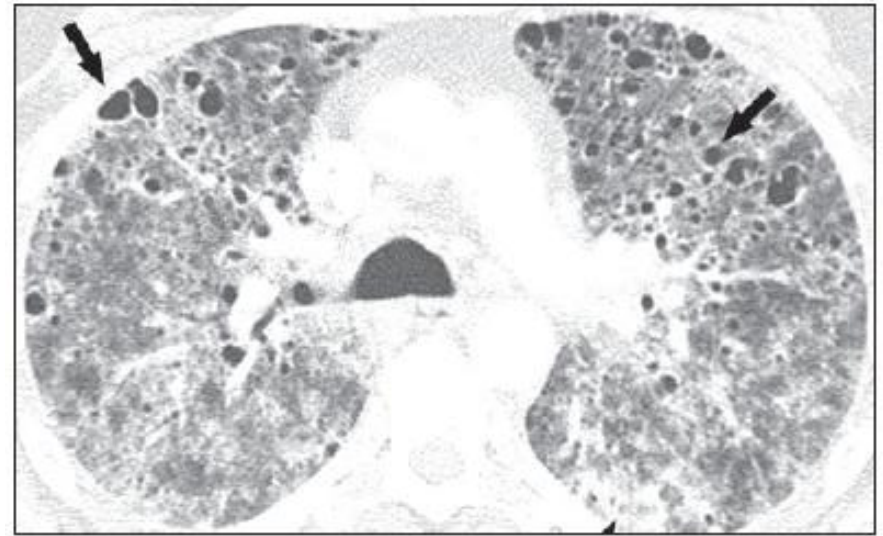
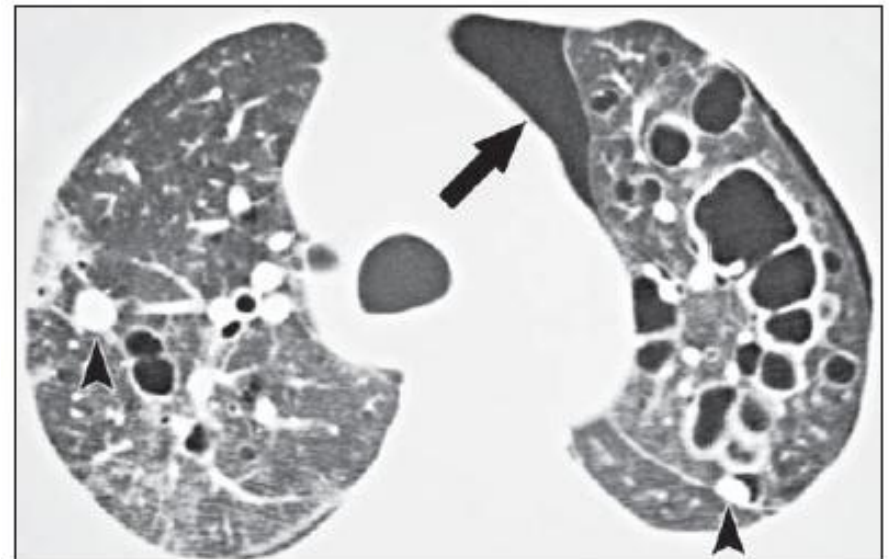


Fig. 10—37-year-old man with AIDS and *Pneumocystis jiroveci* pneumonia. High-resolution CT image shows numerous thin-walled cysts (arrows) on background of patchy ground-glass opacity. Mild focal consolidation (arrowhead) is present in left lower lobe. (Courtesy of Sirajuddin A, Northwestern Memorial Hospital, Chicago, IL)





Pulmoner Nokardiyoz

Çok farklı infiltrasyon patrni gösterebilir

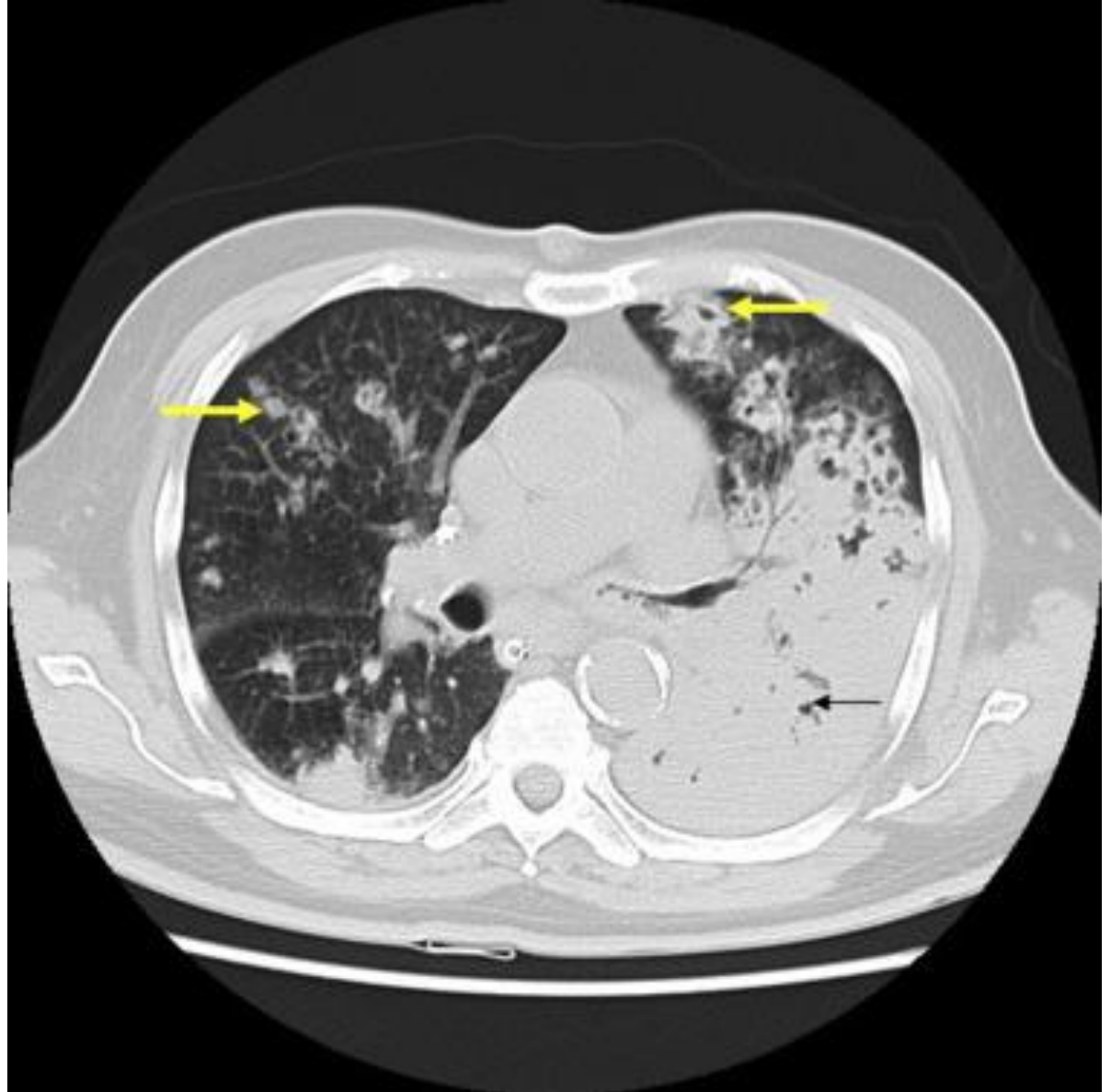
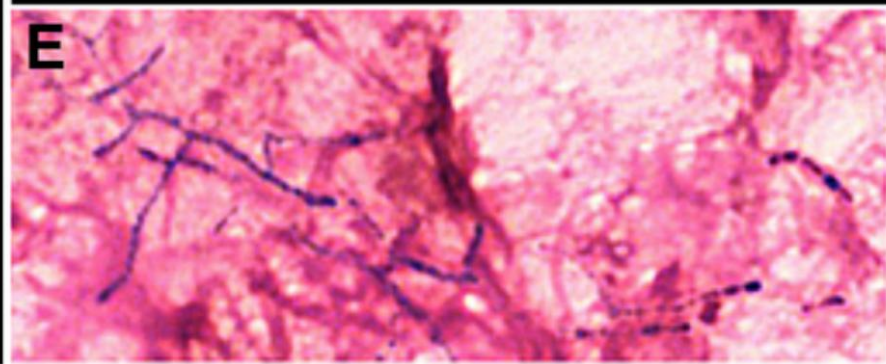
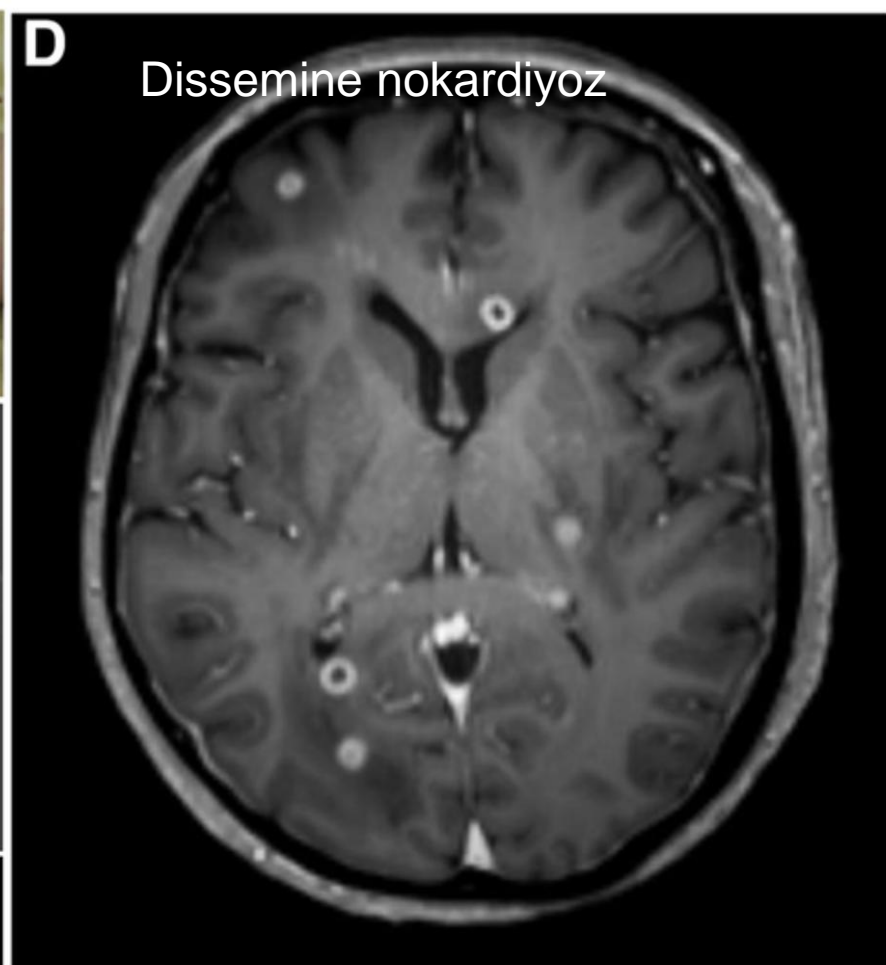
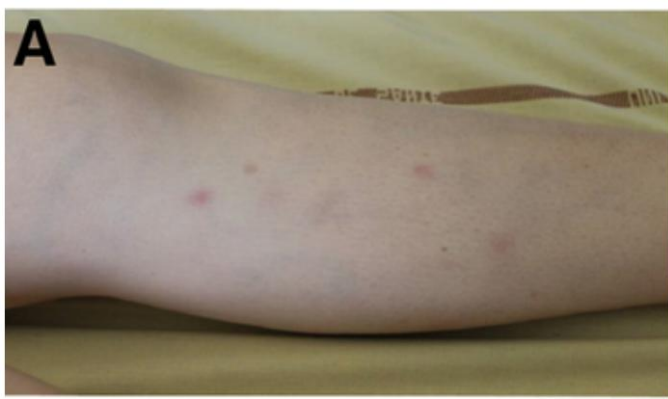


Table 5. Main radiological findings of our and other patients.

	Our patients (n=7)	Published reports (n=33)
Nodule (<3 cm)	5 (71.4%)	8 (24.2%)
Solitary	1	1
Multiple	4	7
Cavitation	1 (14.3%)	11 (33.3%)
Solitary	0	3
Multiple	1	8
Mass (≥3 cm)	0	5 (15.1%)
Solitary	0	4
Multiple	0	1
Consolidation	1 (14.3%)	8 (24.2%)
Empyema	0	1 (0.03%)



Disseminated nocardiosis. (A) Subcutaneous nodules of the lower extremities; (B) right hilar lymph node (indicated by asterisk); (C) retroperitoneal nodules (arrows); (D) multiple brain abscesses (MRI); (E) Gram stain

Solunum Yolu Örneklemesi

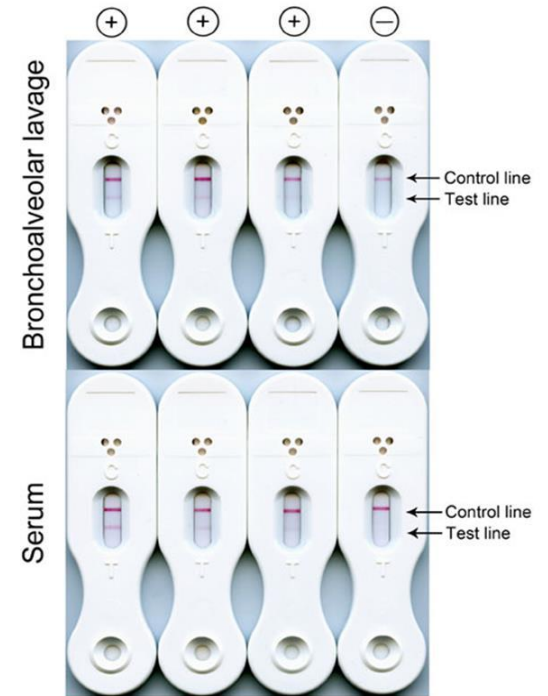
- Balgam
- Nazofarengeal örnekleme
- Bronkoskopi
- BAL
- Transbronşiyal biyopsi
- Trans – torasik BT eşliğinde biyopsi
- Video-assisted thorascopic biyopsi (VATS)
- Açık akciğer biyopsisi

Mikrobiyolojik inceleme

- **Balgam / BAL** : direk inceleme, rutin bakteriyel kültür
- **Aside dirençli ve modifiye aside dirençli boyama**
- **Tüberküloz ve fungal kültür**
- **Pneumocystis jirovecii için boya**
- **İnfluenza virüs için hızlı test, PCR**
- **Nazofarengeal sürüntü**: multiplex PCR (solunum paneli)
 - BAL sıvısında da yapılabilir
- **İdrarda pnömokok ve Legionella antijeni**
- **BAL tüberküloz PCR**

Mikrobiyolojik inceleme

- Serum / BAL **CMV** yük tayini
- Serum **kriptokok antijen testi**
- Serum / BAL **Galaktomannan antijen** testi
- Serum / BAL **Aspergillus lateral flow**



The FilmArray® Respiratory Panel 2 (RP2)

Sample type: Nasopharyngeal Swab

Viruses

Adenovirus
Coronavirus HKU1
Coronavirus NL63
Coronavirus 229E
Coronavirus OC43
Human Metapneumovirus
Human Rhinovirus/Enterovirus
Influenza A
Influenza A/H1
Influenza A/H1-2009
Influenza A/H3
Influenza B
Parainfluenza Virus 1
Parainfluenza Virus 2
Parainfluenza Virus 3
Parainfluenza Virus 4
Respiratory Syncytial Virus

Bacteria

Bordetella parapertussis
Bordetella pertussis
Chlamydia pneumoniae
Mycoplasma pneumoniae



21 | 1
Pathogens | Test

97.1%
Sensitivity*
99.3%
Specificity*

*Data on file.

Tedavi - genel

- **Akut başlangıçlı** pnömoni vakalarında ampirik antibakteriyel tedavi başlanır
 - Tipik – atipik bakteriler
- **Febril nütropenik hastada** anti – psödomonal beta laktam
- **Fırsatçı etiyolojik etken ihtimalini artıran durumlar**
 - >7 günü geçen semptom
 - Non – prodüktif öksürük
 - Diffüz ya da nodüler infiltrat varlığı

Nötropenik hastada risk durumu belirleme

Düşük riskli

Yüksek riskli

MASCC skoru ≥ 21

MASCC skoru < 21

Hastane dışında ateşin olması

Ateşin hastane kaynaklı

Nötropeni beklentisi < 7 gün

Beklenen nötropeni > 7 gün

Böbrek yetmezliği yok

Kreatinin klerensi < 30 ml/dk

Karaciğer yetmezliği yok

Transaminazlar ≥ 5 kat artmış

Hemodinamisi stabil

Hemodinamik instabilite

Performans skoru iyi

Kontrolsüz ilerleyici malignite

Enfeksiyon odağı yok

Eşlikenden pnömoni, ishal vb ciddi

Komorbid hastalık yok

enfeksiyon odağı var

Ateş $< 39^{\circ}\text{C}$

Allogeneik kök nakli

MASCC skorlaması

Kriter	Puan
Yaş < 60	→ 2
Hastanede yatmıyor olmak	→ 3
Başvuru anında klinik durumu	
• Hipotansiyon yok	→ 5
• Parenteral sıvı gerektiren dehidratasyon yok	→ 3
Febril nötropeniye bağlı semptomlar	
• Semptom yok veya hafif	→ 5
• Orta derecede semptom	→ 3
KOAH yok	→ 4
Hastanın altta yatan hastalığı	
• Solid tümör hastası olması	→ 4
• Hematolojik hastalığı olup öyküde invaziv pulmoner aspergilloz olmaması	→ 4

Nocardia pnömonisi

- Daha çok **immün düşkün kişilerde** enfeksiyon yapar
- Gram boyamada **Gr (+), dallanan filamentöz bakteri**
- **Pnömoni** en sık klinik enfeksiyon tablosudur,
- **%50 hematogen yayılır en sık beyin,**
- **Mutlaka kraniyal MR kontrolü yapılmalıdır**
 - Diğer: **cilt, böbrek, kemik, göz**
- Akciğer grafide tek veya multiple **nodül, kavite** görülür
- Tedavi
 - **Trimetoprim/sülfametoksazol + imipenem** 3-4 hafta
 - Sonra trim sülfam ile 3-6 ay devam edilir
 - Diğer: Amikasin, seftriakson, linezolid, amoks/klav, klaritromisin, moksifloksasin, minosiklin

Pneumocystis jirovecii

- Bağışıklığı baskılanmış kişilerde pnömoni yapan fırsatçı
 - ▣ Organ nakli
 - ▣ İlik nakli
 - ▣ ≥ 20 mg/gün steroid
 - ▣ CD4 düzeyi <200 hücre/ μ l (HIV)
- Akut veya subakut pnömoni yapar
 - ▣ HIV de klinik tablo genelde günler – haftalar içerisinde oturur
- Lab: **LDH yüksekliği** olabilir (%90)
- **Kültür edilemez, direnç bakılamaz**
- Düz grafi: **bilateral diffüz infiltrat, CT de buzlu cam**
 - ▣ Kistler ve pnömotoraks göreceğimiz diğer bulgular

Pneumocystis jirovecii

- Tanı: solunum örneklerinde **metanamin silver**, toluidin mavi, giemza veya immünfloresan boya ile **kistler gösterilir**
 - ▣ Beta glukan testi, PCR
- Aşağıdaki durumlarda profilaksi önerilir:
 - ▣ **CD4 sayısı < 200** olan HIV hastaları
 - ▣ Bir aydan uzun ≥ 20 mg/gün **steroid** kullanımı
 - ▣ **Fludarabin** (KLL tedavisi), Alemtuzumab, Temozolomid
 - ▣ **İlik ve organ nakli** hastaların immünsupresif dönemlerinde
 - ▣ **Steroid + siklofosfamid alacak Wegener granülomatozu**
- Tedavi: **Trimetoprim/sülfametoksazol**, 21 gün,
 - ▣ PaO₂ < 70 ise **steroid** eklenir

İnvazif Pulmoner Aspergilloz

- Özellikle immünsupresiflerde (**nötropeni, GVHH**) gelişir
 - ▣ Antibiyotiklere cevap vermeyen **nodül ve kavitasyon** olur
 - ▣ **Akciğer ve sinüslerde** enfeksiyon tablosu oluşturur
 - ▣ Akciğerlerde erken dönemde etrafında **halo olan nodül** yapar
 - ▣ İleri dönemde **hava hilal işareti** ile giden nekroz ve kavite olur
- Tanı: **tomoğrafi ve galaktomannan antijen testi**
 - ▣ Kesin tanı biyopsi kültürü veya patolojide dar açılı septalı hifler
- Tedavi
 - ▣ **Vorikonazol** (ilk tercih), izavukonazol eşit derecede etkili
 - ▣ **Amfoterisin B** (diğer alternatif), İtrakonazol, Kaspofungin
 - ▣ **Flukonazolün *Aspergillus türlerine* etkisi yoktur**

Joost Wauters
Ingrid Baar
Philippe Meersseman
Wouter Meersseman
Karolien Dams
Rudi De Paep
Katrien Lagrou
Alexander Wilmer
Philippe Jorens
Greet Hermans

Invasive pulmonary aspergillosis is a frequent complication of critically ill H1N1 patients: a retrospective study

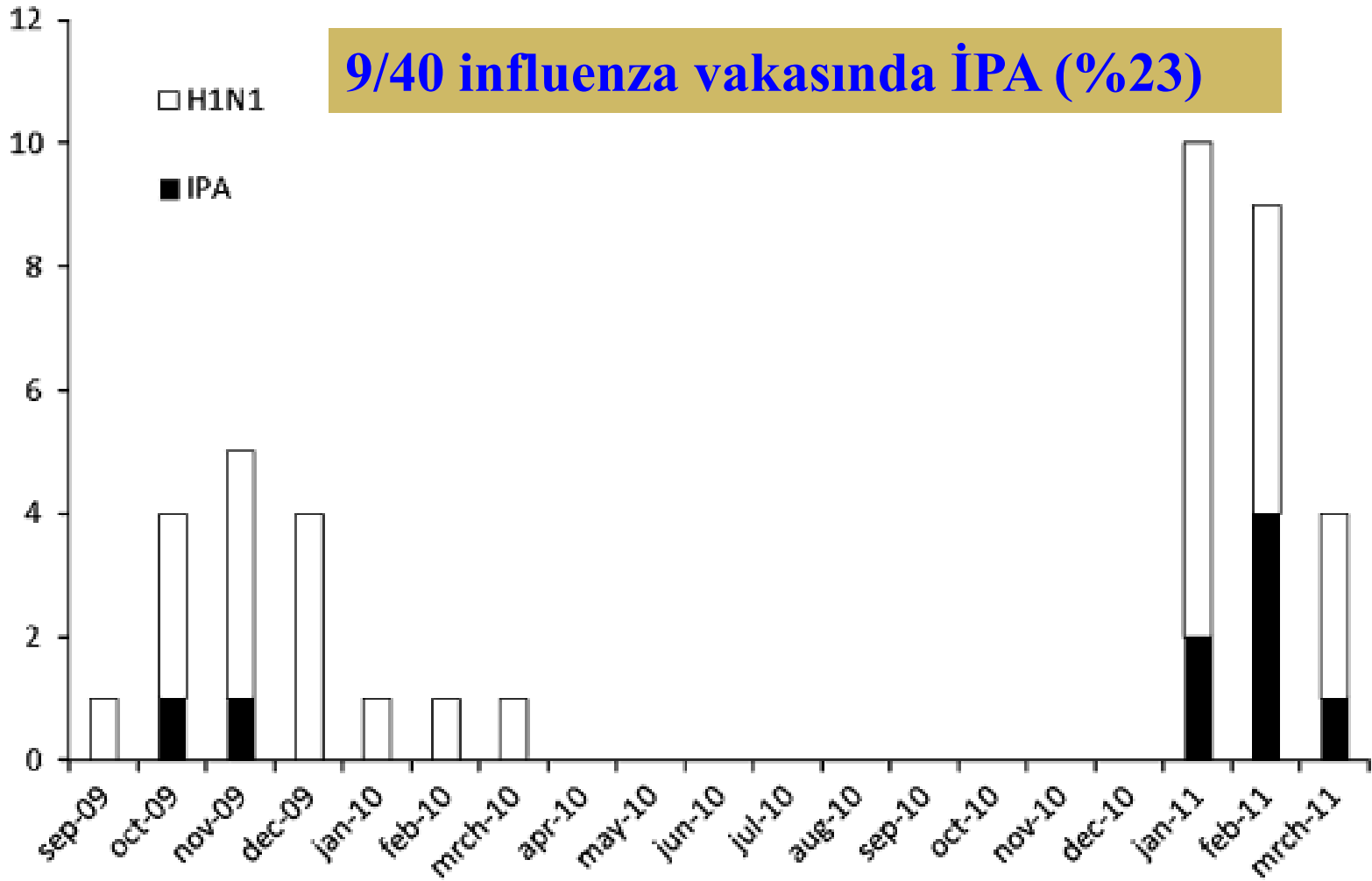
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doi :[10.1007/s00134-012-2677-y](https://doi.org/10.1007/s00134-012-2677-y).

Abstract *Purpose:* Despite their controversial role, corticosteroids (CS) are frequently administered to patients with H1N1 virus infection with severe respiratory failure secondary to viral pneumonia. We hypothesized that invasive pulmonary aspergillosis (IPA) is a frequent complication in critically ill patients

$p = 0.002$). IPA patients also received significantly higher doses of CS before ICU admission [hydrocortisone equivalent 800 (360–2,635) versus 0 (0–0) mg, $p = 0.005$]. On multivariate analysis, use of CS before ICU admission was independently associated with IPA [odds ratio (OR) 14.4 (2.0–101.6), $p = 0.007$].

9/40 influenza vakasında İPA (%23)



Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study

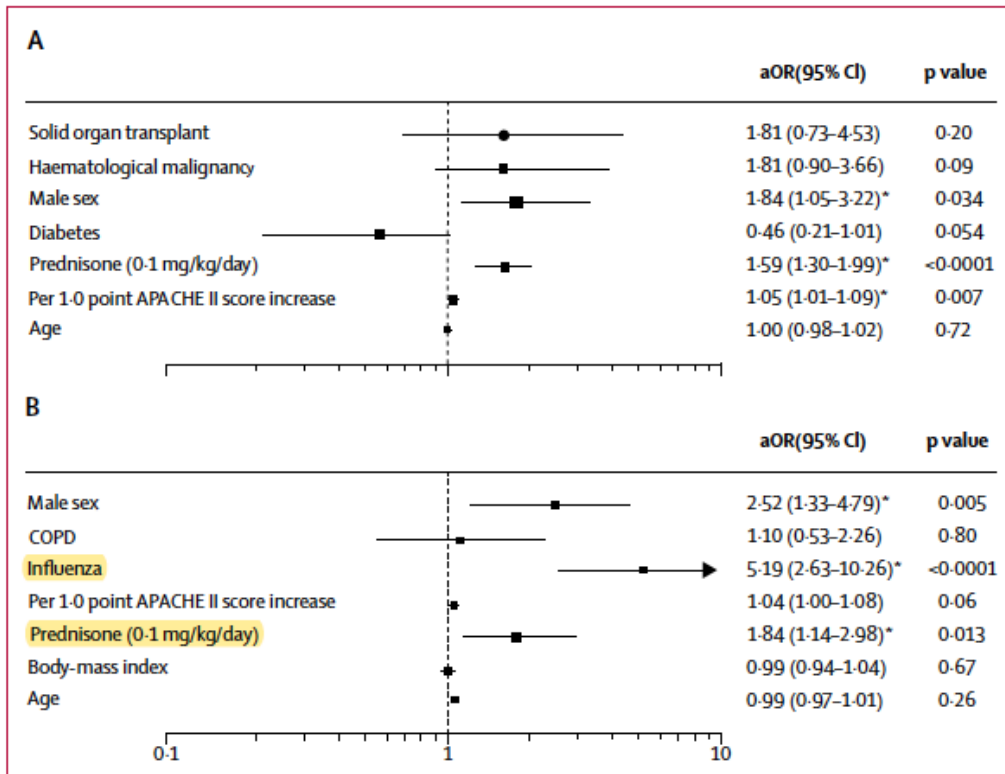


Figure 2: Forest plots of risk factors for the development of invasive pulmonary aspergillosis. These have been corrected for centre as well but this is not depicted here as no significant differences were found. (A) Analysis of risk factors for the influenza cohort to develop invasive pulmonary aspergillosis. (B) Overview of comparison between the influenza case group and the control group. aOR=adjusted odds ratio. APACHE=acute physiology and chronic evaluation score. COPD=chronic obstructive pulmonary disease. *Factors independently associated with the development of invasive pulmonary aspergillosis.

- 2009 – 2016 arası
- **83 / 432** influenza vakasında invazif aspergilloz (**%19**)
- **İmmün-supresif** influenza vakalarında **%34**
- **Non-immün-supresif** vakalarda **%14**
- **Mortalite – İA: %52**
- **Mortalite İA yok: %28**

Teşekkürler