Diffüz Alveoler Hemoraji

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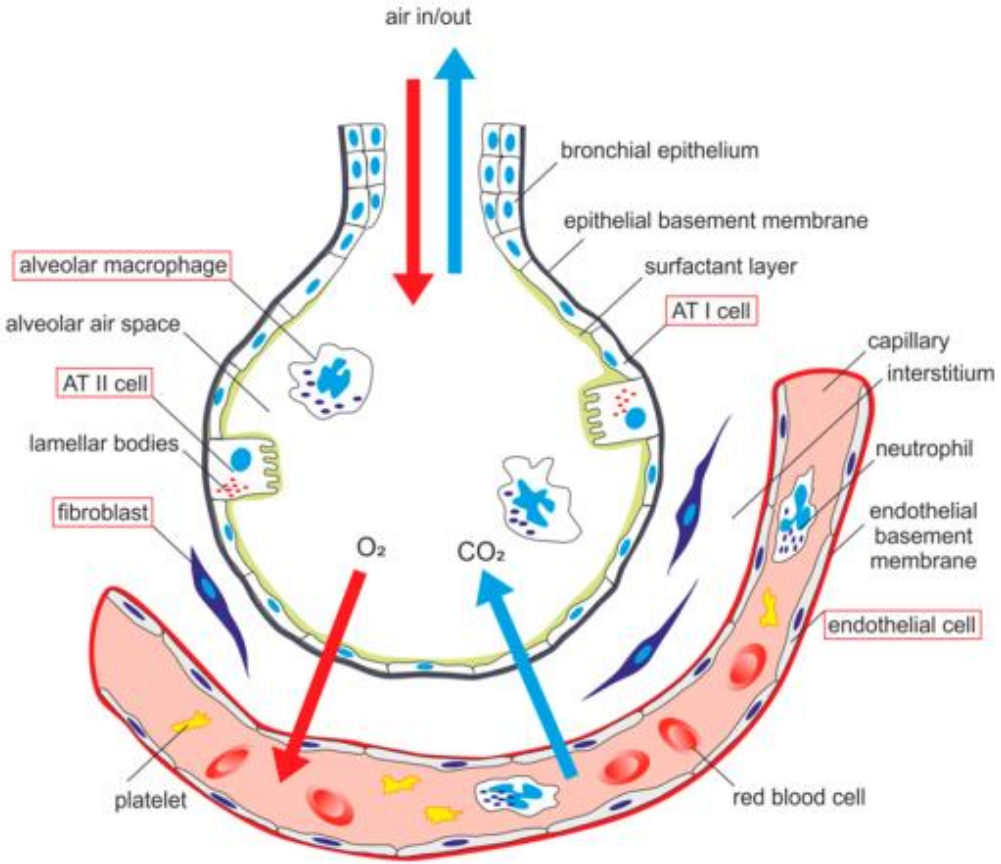
Ege ÜTF Göğüs Hast AD

Sunum Planı

- Diffüz alveoler hemoraji (DAH)
  - Tanım
  - Etiyoloji
  - Klinik
  - Tanı
  - Tedavi, prognoz
- İmmun DAH
- Non-immun DAH

Tanım

- Pulmoner mikrosirkülasyondan kaynaklanan, sıklıkla sistemik bir vakülitin neden olduğu, alveol içine eritrosit birikmesidir.



Tanım

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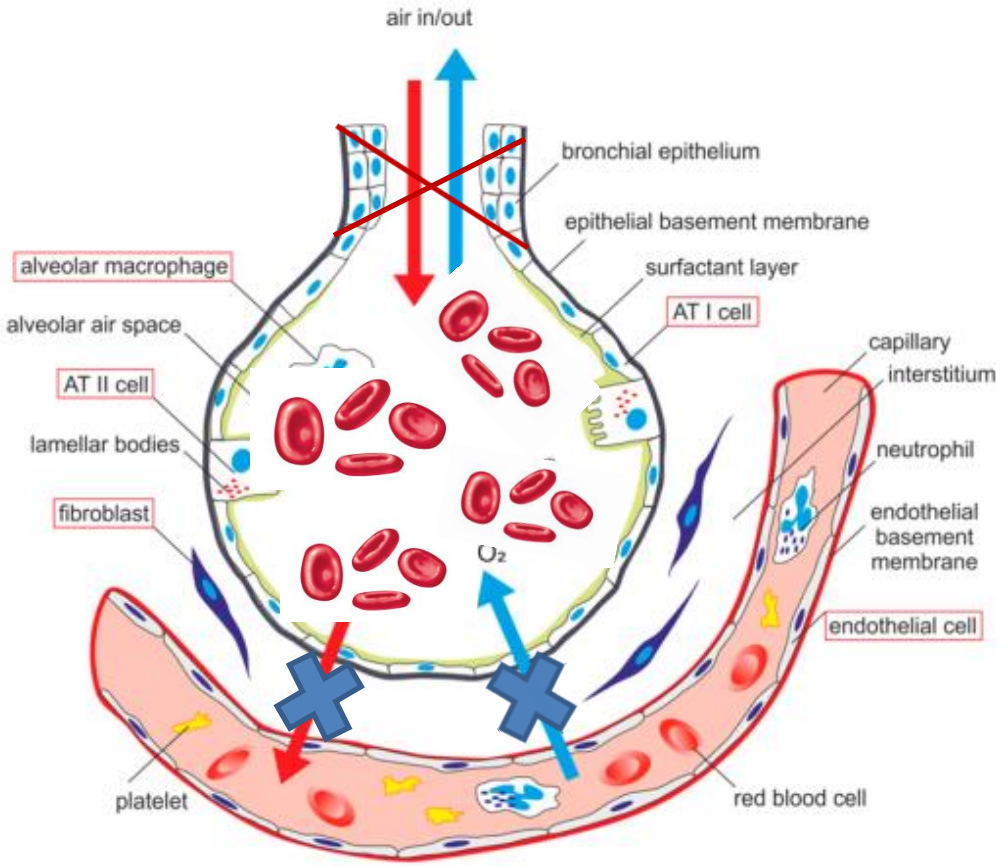
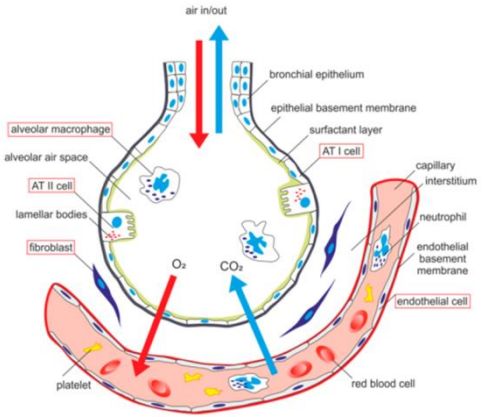


Etiyoloji

Table 1
Differential diagnosis of diffuse alveolar hemorrhage

Immune Mediated	Non–Immune Mediated
ANCA-Associated Vasculitis	Cardiac disease
Granulomatosis with polyangiitis (GPA)	Left ventricular dysfunction
Microscopic polyangiitis (MPA)	Valvular disease
Eosinophilic granulomatosis with polyangiitis (EGPA)	Infection
Isolated pulmonary capillaritis	Medications
Anti–glomerular basement membrane antibody syndrome	Acute respiratory distress syndrome
Connective tissue disease	Idiopathic pulmonary hemosiderosis
Systemic lupus erythematosus	Coagulopathy
Rheumatoid arthritis	Radiation exposure
Inflammatory myopathies	Occupational exposure
Antiphospholipid antibody syndrome	Crack cocaine inhalation
Henoch-Schönlein purpura/IgA vasculitis	Bone marrow transplant[a]
Cryoglobulinemic vasculitis	
Behçet disease	
Lung transplant rejection	
Hypocomplementemic urticarial vasculitis (anti-C1q vasculitis)	
Drug-induced vasculitis	
Bone marrow transplant[a]	



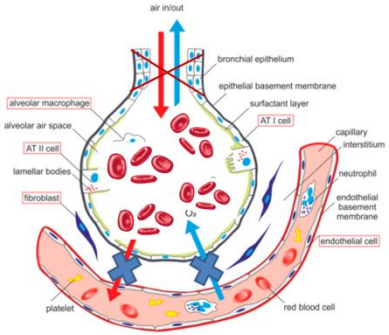
Etiyoloji

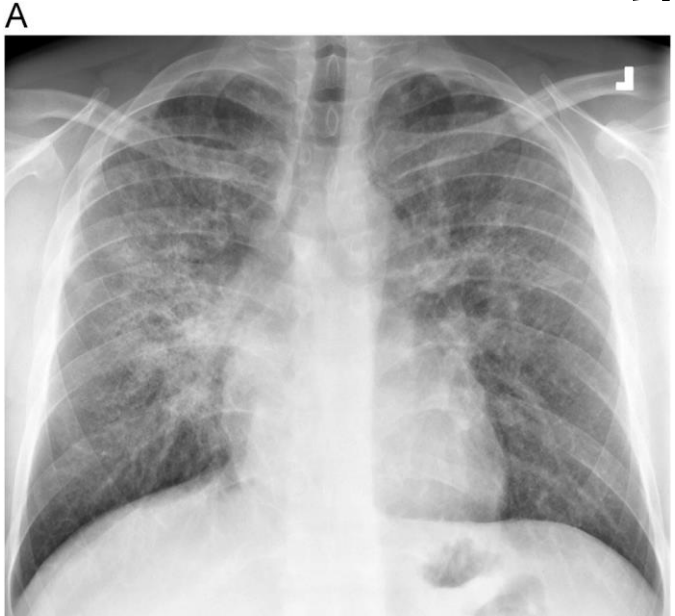
- 1998 - 2007
- DAHS 24 olgu (12'si E, yaş: 57.1 ± 18.9)
- DAHS'ye bağlı ARDS (%62.5)
- 9 olguda (%37.5) immun etiyoloji
- 16 olguda (%62.5) non-immun etiyoloji
  - Kanama diyatezi
  - Pnömoni
- 10 olguda (%41.7) hemoptizi
- 13 olguya (%54.2) anemi nedeniyele kan transfüzyonu

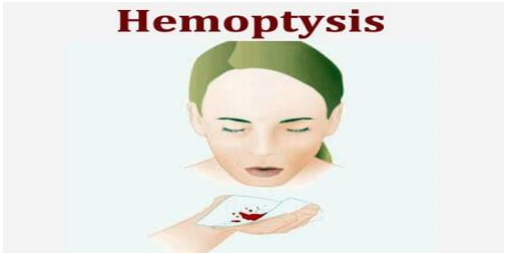
Türkiye Klinikleri Arch Lung 2009; 10(2): 39-44

Klinik

- Hemoptizi
- Anemi
- Nefes darlığı
- Diffüz radyolojik pulmoner infiltrasyon
- Hipoksemik solunum etmezliği



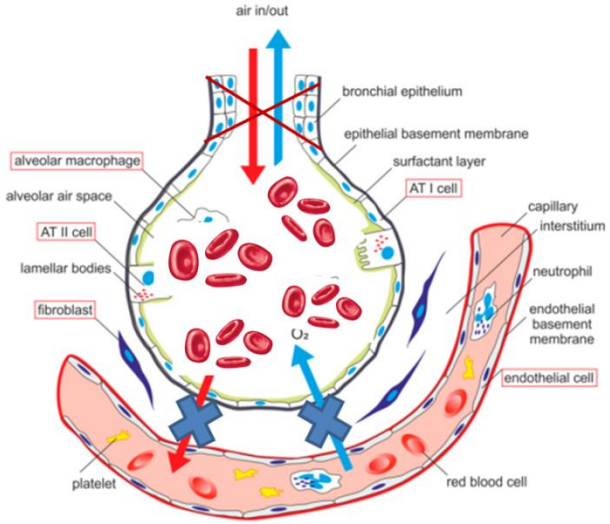




Tanı-Laboratuvar

- Tam kan sayımı
- Koagülasyon testleri
- Böbrek fonksiyon testleri
- c-ANCA, PR3-ANCA ve MPO-ANCA
- Anti-GBM Ab
- Antinuclear antibodies (ANA)
- Anticyclic citrullinated peptide antibodies (anti-CCP)
- Romatoid faktör (RF)
- Antifosfolipid antikoru
- Kreatinin kinaz
- İdrar sedimenti

Tanı- Radyoloji



Ground Glass Opacity

- Edema
- Infection such as pneumonia
- Neoplasm such as adenocarcinoma

DPH

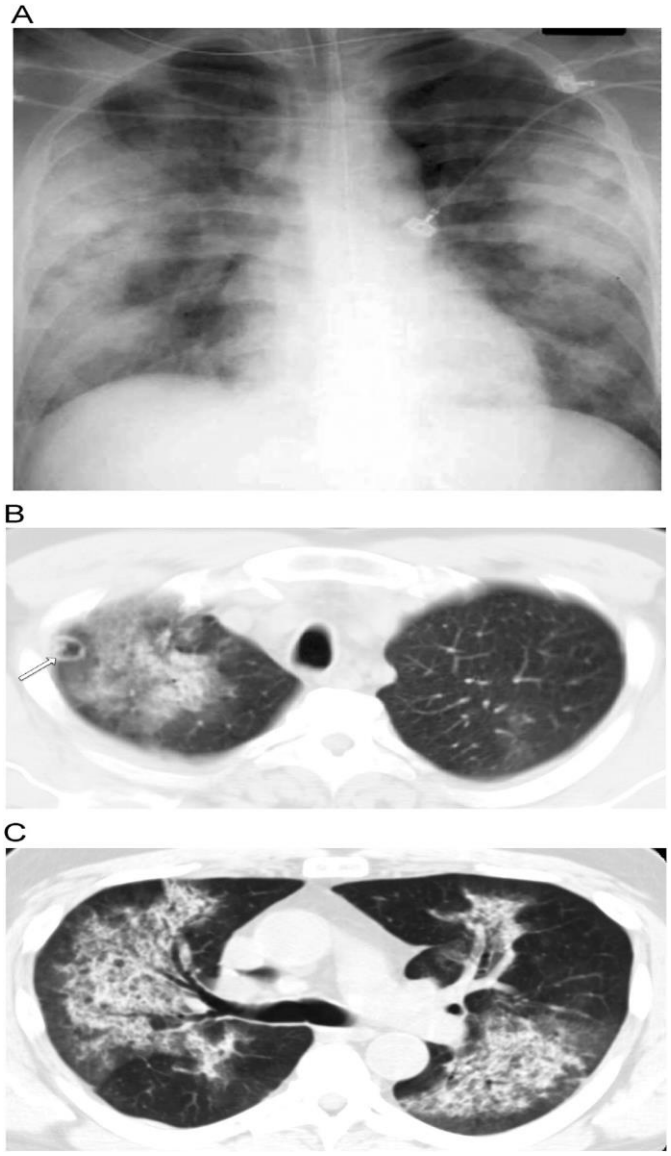
Centrilobular Nodules

- Endobronchial spread of infection such as tuberculosis
- Endobronchial spread of tumor
- Edema
- Hypersensitivity pneumonitis
- Organizing pneumonia

Septal Thickening

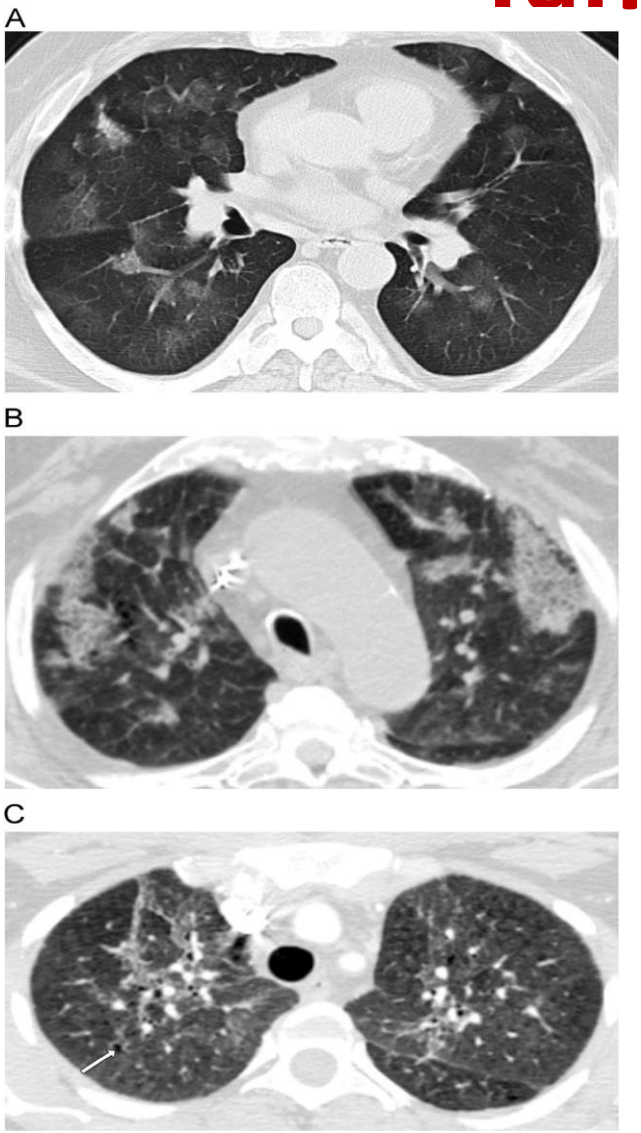
- Edema
- Lymphangitic carcinomatosis
- Interstitial pneumonia

Tanı- Radyoloji



- Nefes darlığı
- Kaviter nodül
- Buzlu cam
- Wegener granulomatosisi

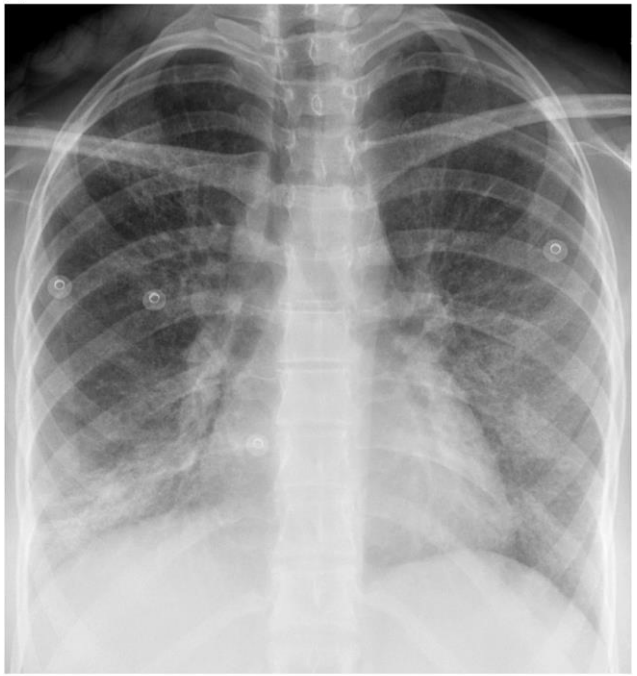
Tanı- Radyoloji



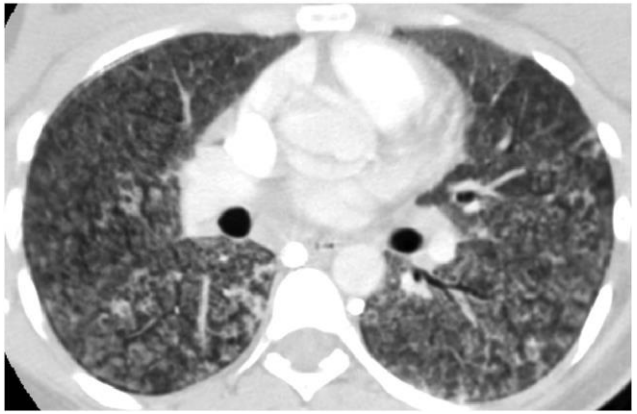
- Hemoptizi
- Good- pasture sendromu

Tanı- Radyoloji

A

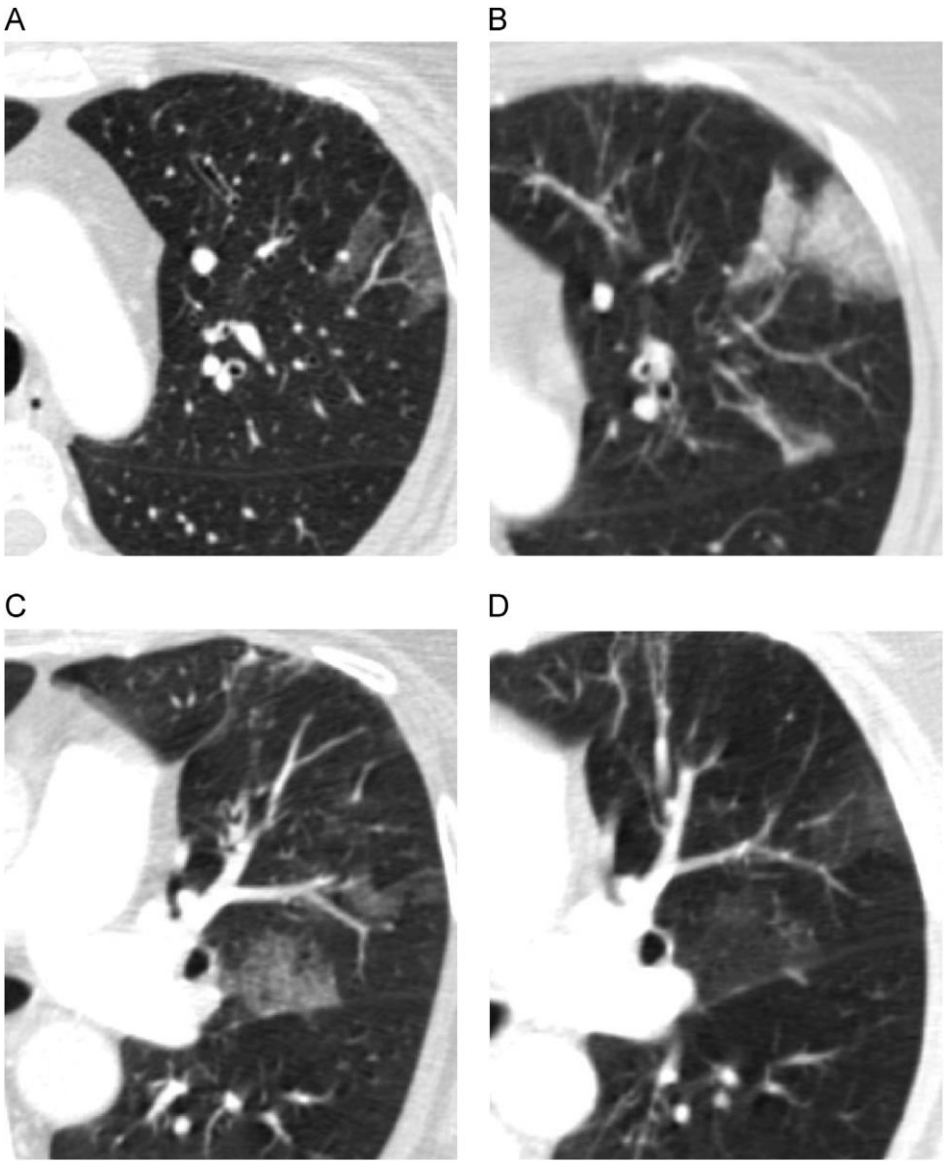


B



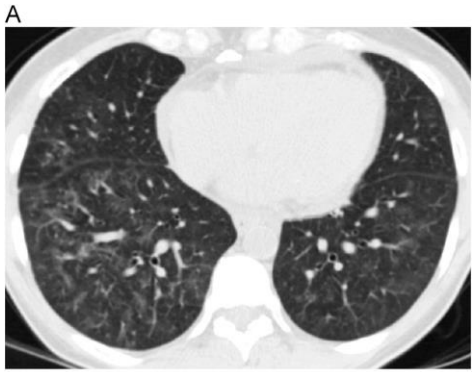
- Nefes darlığı
- Nonkardiyak akciğer ödemine benzer
- BT: Sentirlobüler opasite ve buzlu cam
- Bronkoskopi: Alveolar hemoraji
- Goodpasture syndrome

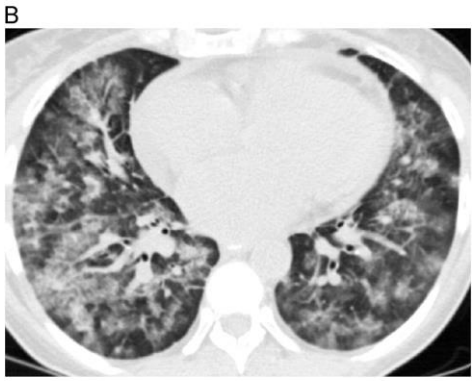
Tanı- Radyoloji

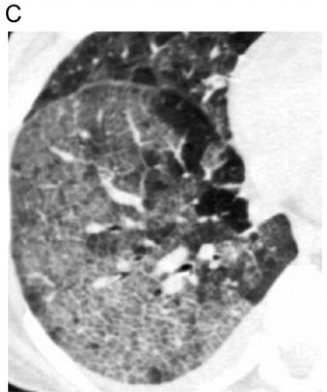


- Hemoptizi
- Nefes darlığı
- Periferik buzlu cam
- Churg-Strauss sendromu

Tanı- Radyoloji



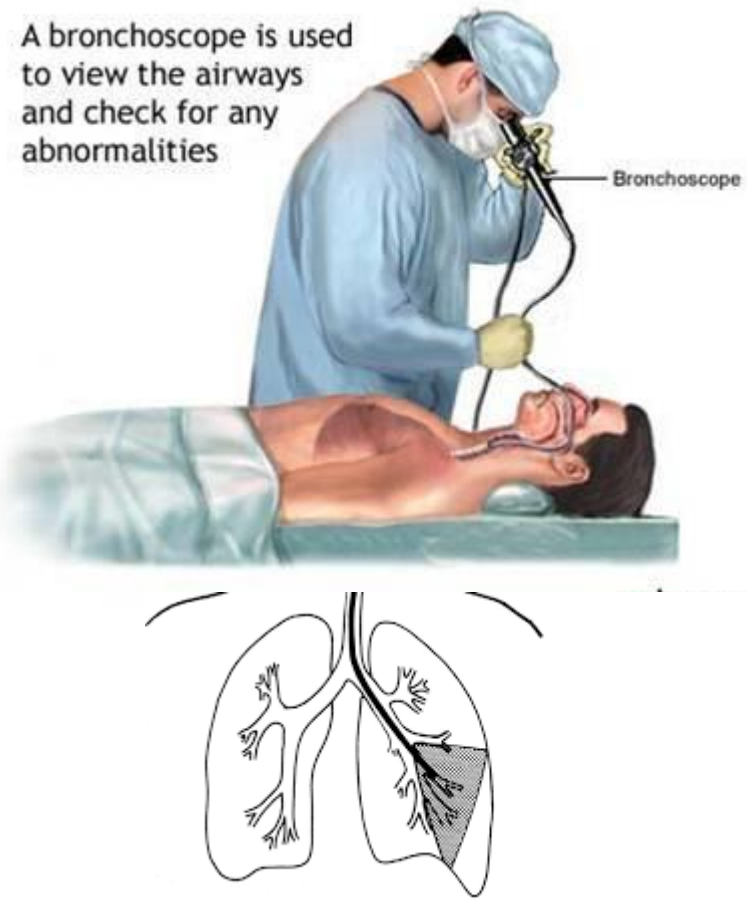


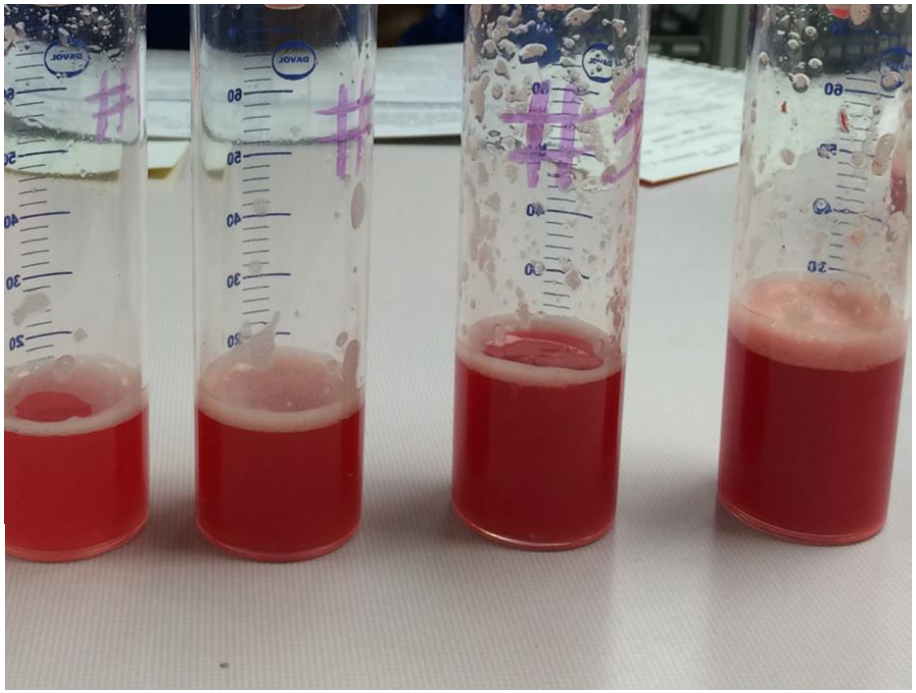


- SLE
- 1 ay ara ile BT
- Hemoptizi
- Bronkoskopi. Alveolar hemoraji

Tanı- Bronkoskopi

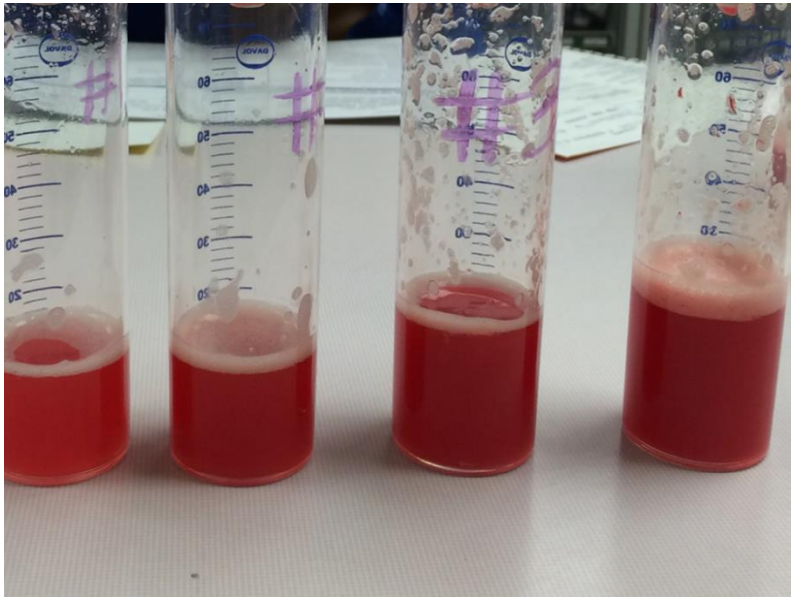
- Bronkoalveoler lavaj (BAL)

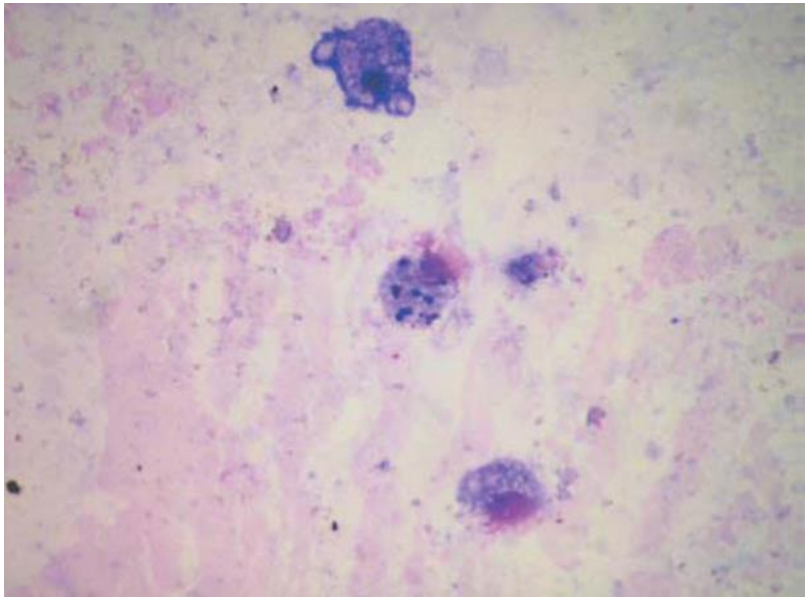




Tanı- Bronkoskopi

- Bronkoalveoler lavaj (BAL)

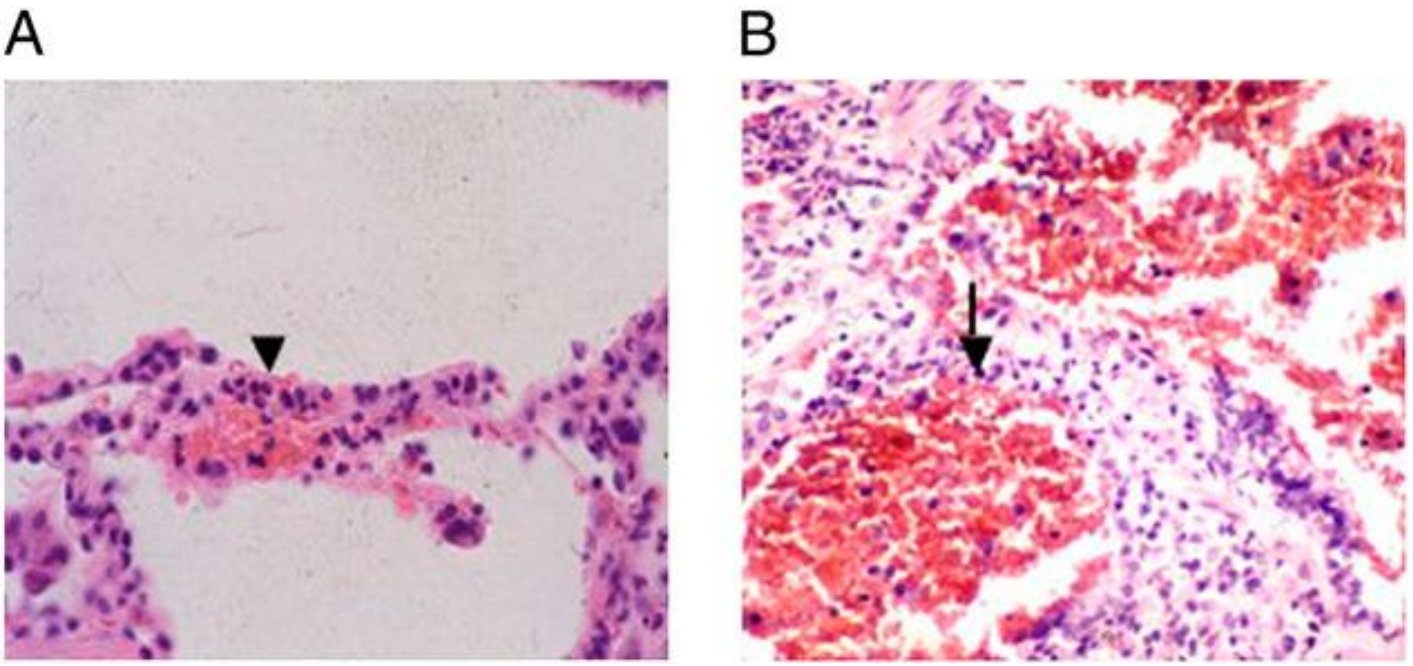




24-48 saat sonra
Makrofajların >5'inden fazlasında hemosiderin

Tanı-Bronkoskopi

- Biyopsi



Tedavi ve Prognoz

- **Tedavi**
  - Alta yatan nedene yönelik tedavi
  - İmmunsupressif tedavi

- **Prognoz**
- Altta yatan nedene bağlı (%20-50)
- 13/24 olguda (%54.2) mortalite
  - Başlangıç hemoglobin düzeyi 10 gr/dl ve altında
  - CRP düzeyi daha yüksek
  - Akut başlangıçlı olanlarda

Türkiye Klinikleri Arch Lung 2009; 10(2): 39-44

İmmun DAH

1. ANCA ilişkili vaskülitler
2. Sistemik lupus eritamatozis
3. Antifosfolipid sendromu

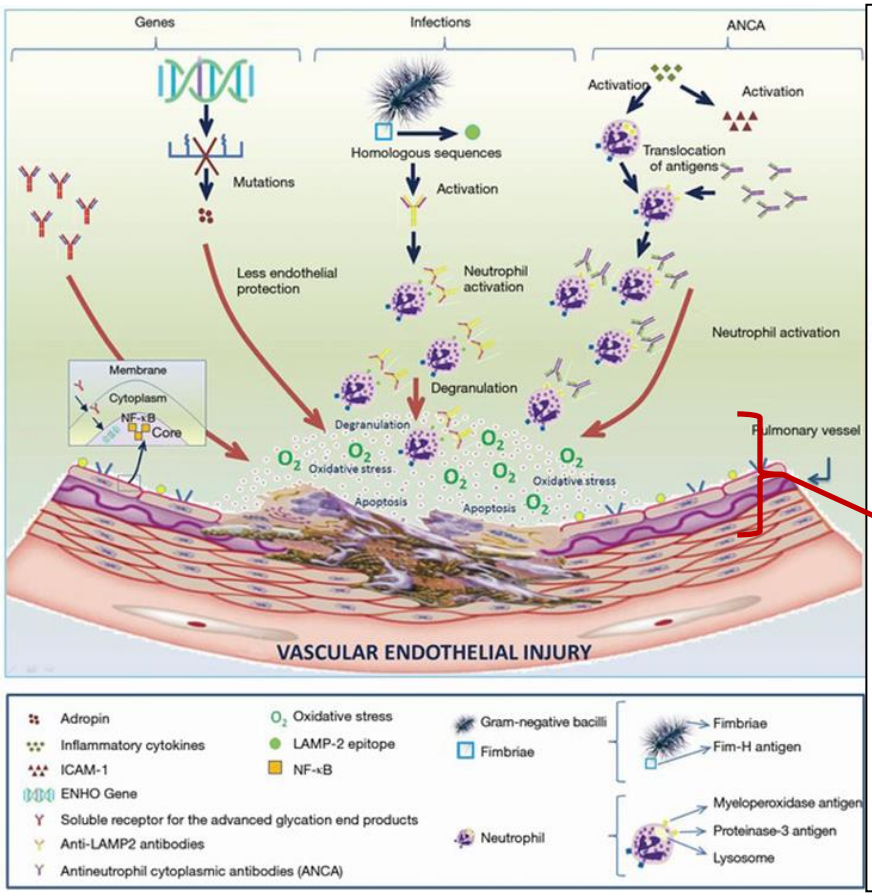
İmmun DAH

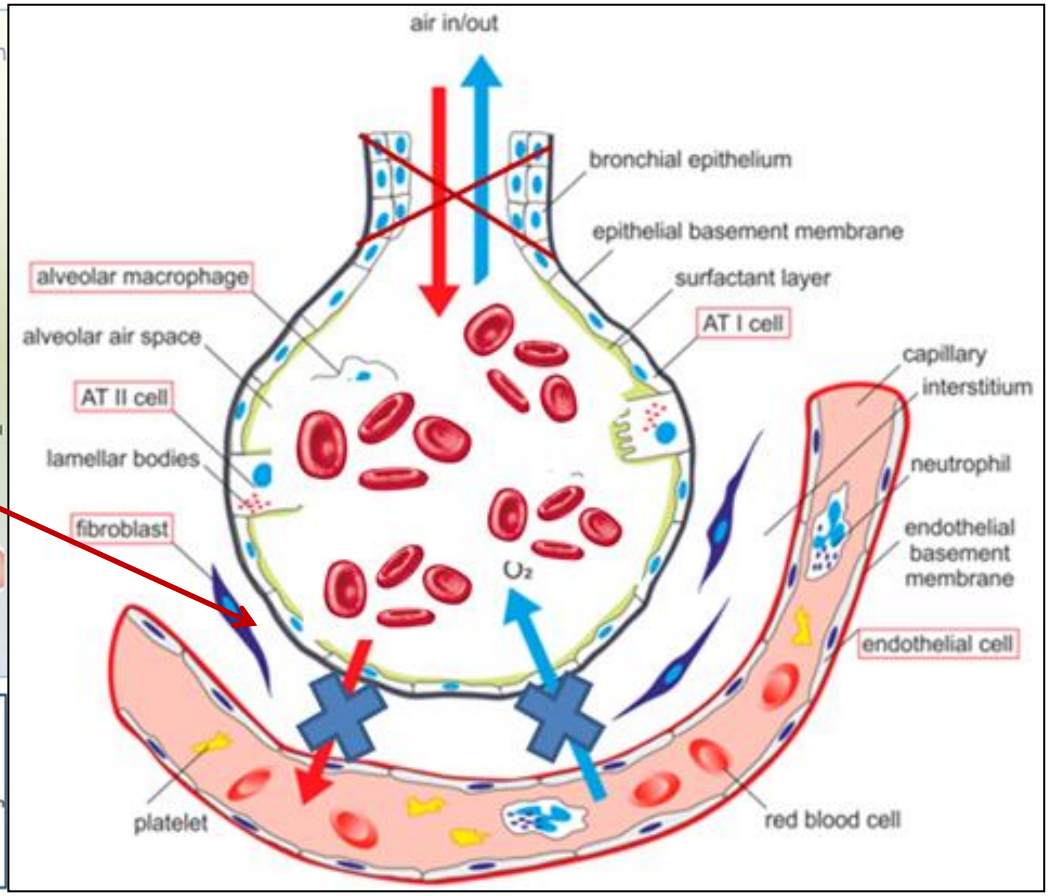
- 2010-2015,
- İmmunolojik orjinli 39 DAH
- Ortalama yaş: 44.8
- Etiyoloji
  - ANCA ilişkili vaskülit (n=29)
    - Granülamatöz polianjitis (n =14)
    - Mikroskopik polianjitis (n = 13)
  - SLE (n=10)

- Hemoptizi %76.9
- Radyolojide alveoler dolum defekti % 59
- 1-3 gr Hb düşüşü %100
- BAL'da makroskopik hemoraji % 43.6
- BAL'da hosiderin yüklü makrofaj %100

Respiratory Medicine (2017), doi: 10.1016/j.rmed.2017.06.003

ANCA ilişkili vaskülitler ve DAH





ANCA ilişkili vaskülitler ve DAH

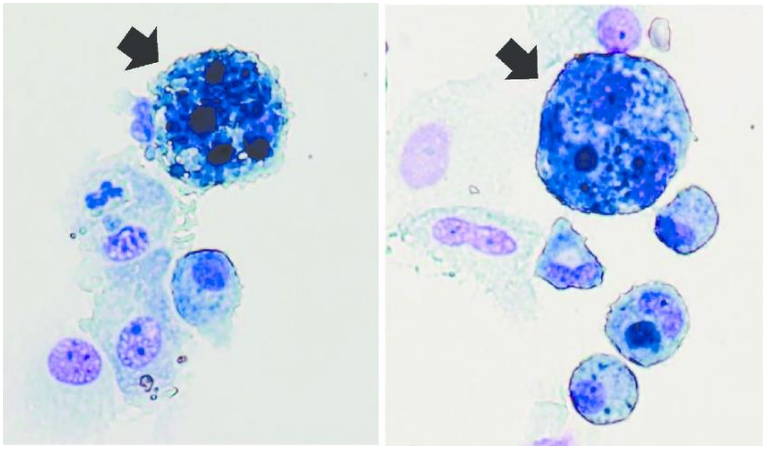
- Tüm DAH'nin %89'i
- En sık;
  - Polianjitisle ile birlikte olan granülomatoz
  - Mikroskopik polianjitis
  - Polianjitsi ile birlikte olan eozinofilik granülomatoz

ANCA ilişkili vaskülitler ve DAH

- **Klinik;**
  - Hemoptizi
  - Nefes darlığı
  - Hemoglobin düşüşü
- **Radyoloji;**
  - Normal
  - Buzlu cam
  - Konsolisasyon
  - Mozaik perfüzyon defekti (arterioler vaskülit)

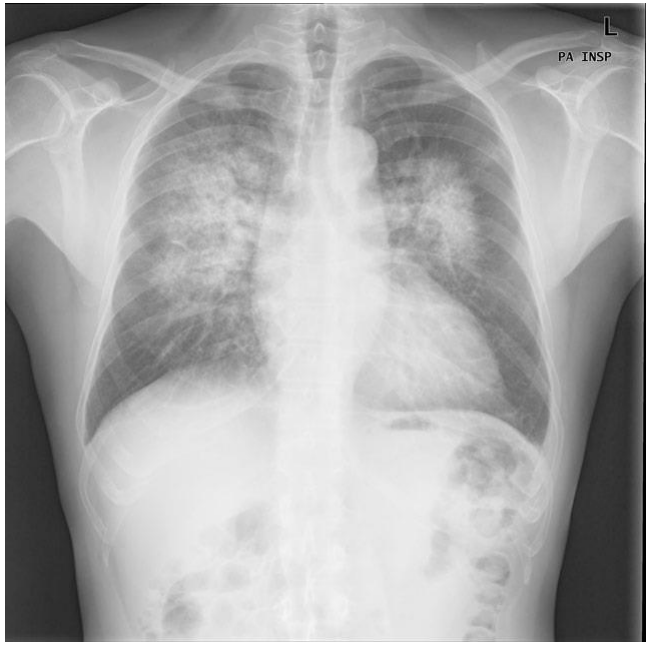
ANCA ilişkili vaskülitler ve DAH

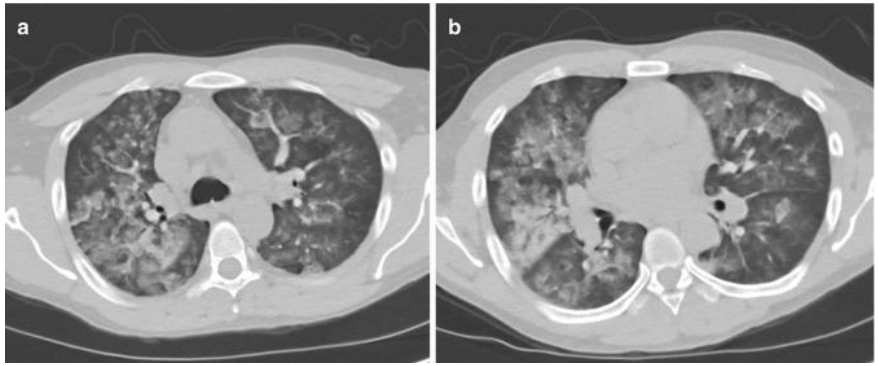
- **Tanı**
  - Bronkoskopi (BAL)
  - Makroskopi
  - Hemosiderin yüklü makrofaj



ANCA ilişkili vaskülitler ve DAH

- **Tanı**





ANCA ilişkili vaskülitler ve DAH

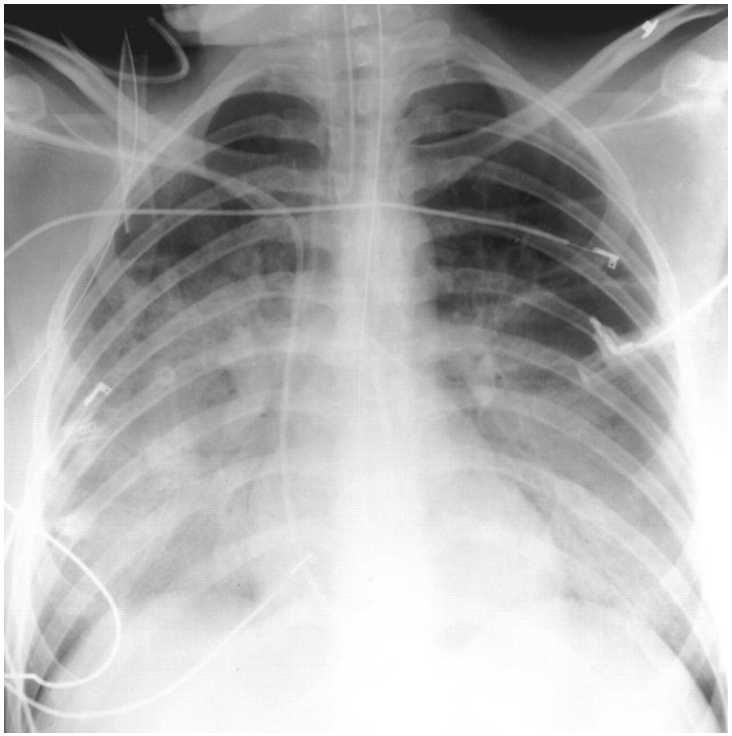
- **İndüksiyon tedavisi**
  - Pulse steroid (1 gr/gün 2-3 gün)
  - Siklofosfamid (15 mg/kg 3 haftada bir)

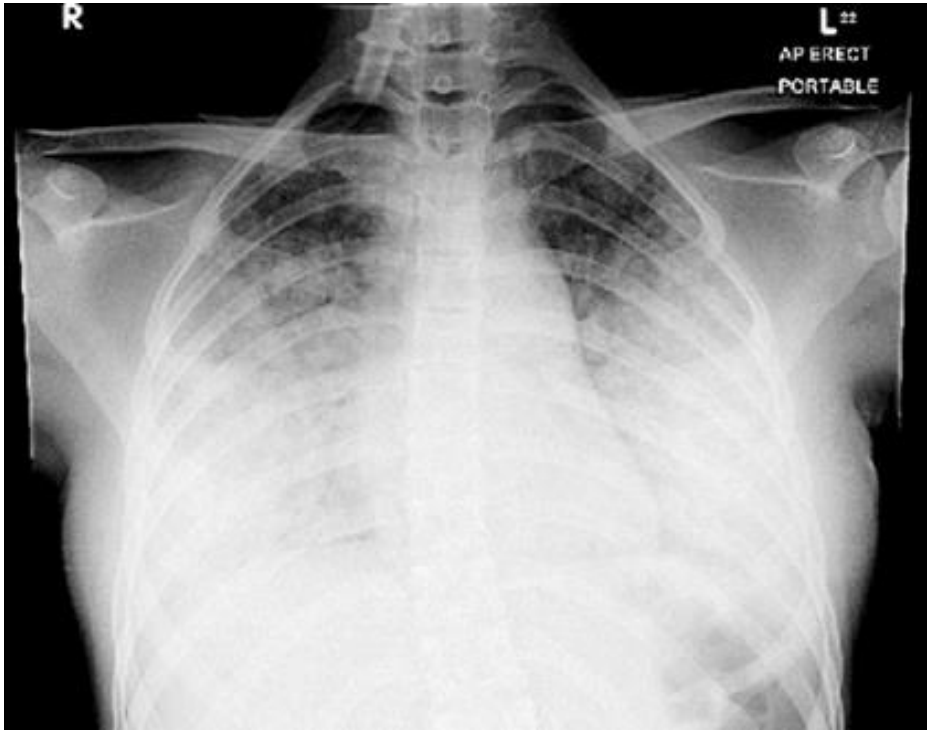
    ya da
  - Plazmaferez

    ya da
  - Rituksimab

Sistemik lupus eritematozis ve DAH

- %0.6-5.4
- Yüksek mortalite





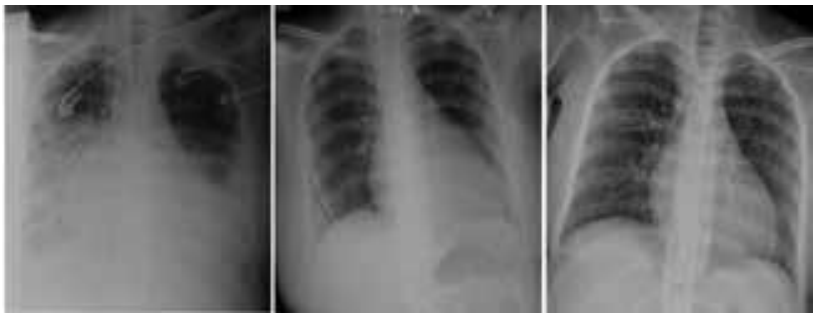
Sistemik lupus eritematozis ve DAH

Table 1 Signs, symptoms, and imaging signs in patients with DAH and SLE

Criteria	Frequency
Dyspnea	4+/4+
Radiograph or CT chest infiltrates	4+/4+
Hemoglobin drop ≥2 g/dl	4+/4+
Hemoptysis	2+/4+
Hemorrhagic BAL or presence	3+/4+
Increased DLCO	3+/4+

Sistemik lupus eritematozis ve DAH

- **Tedavi**
  - Pulse steroid (4-6 gr)
  - Siklofosfamid
  - Plazmaferez
  - Azotiopürin
  - IVIG
  - Antibiyotik (enf-DAH,SLE)



Sistemik lupus eritematozis ve DAH

140 hasta DAH ve SLE

TABLE 2. Therapeutic Agents Utilized to Treat DAH

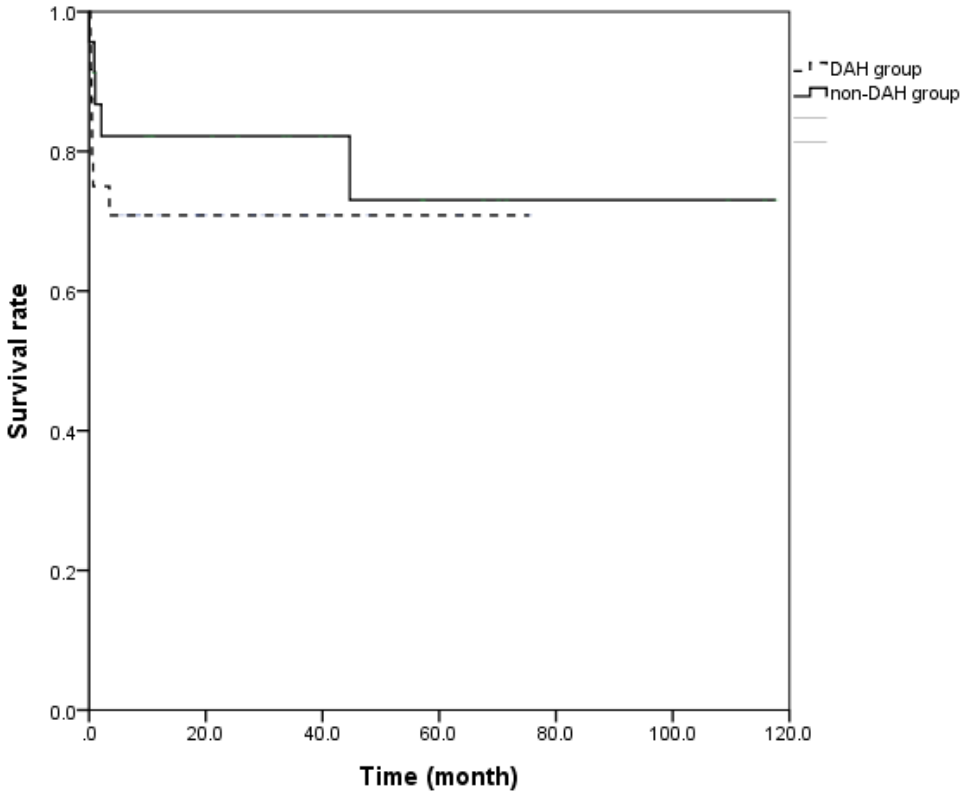
Corticosteroids	98%
Cyclophosphamide	54%
Plasmapheresis	31%
Azathioprine	7%
Intravenous immunoglobulin	5%
Mycophenolate	3%
Rituximab	6%
Stem cell transplantation	2%

J Clin Rheumatol 2015;21: 305–310

Sistemik lupus eritematozis ve DAH-Mortalite

1980'ler %75

2015 % 33



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J Clin Rheumatol 2015;21: 305–310

Sistemik lupus eritematozis ve DAH-Mortalite

- İMV gerekliliği
- Yüksek APACHE II skoru
- Yüksek kreatinin
- Enfeksiyon varlığı
- Trombositopeni varlığı
- SLEDAI>10

Antifosfolipid Sendromu ve DAH

- Primer APS ve SLE ile birlikte APS
- SLE'de %20-40 AP antikoru pozitif
- APS'da %2
- Klinik tablo SLE'ye benzer

Antifosfolipid Sendromu ve DAH

- **Klinik ve Tanı**
  - Nefes darlığı (%76)
  - Hemoptizi (%76)
  - Hipoksemi (%41)
  - İMV gerekliliği (%41)
  - BAL'da makroskopik hemoraji ve hemosiderin yüklü makrofaj
  - HRCT'de buzlu cam

Antifosfolipid Sendromu ve DAH

- **Tedavi**
  - Yüksek doz steroiv ve siklofosfamid
  - Mikofenolate mofetil
  - Metotreksat
  - Azothiyopürin
  - Rituksimab
  - IVIG

Hangi hastada immun DAH?

Clinical Investigations

Respiration

Respiration 2010;80:313–320
DOI: 10.1159/000315144

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Published online: May 22, 2010

Alveolar Haemorrhage in the Immunocompetent Host: A Scale for Early Diagnosis of an Immune Cause

Clément Picard[a, d] Jacques Cadranel[a] Raphaël Porcher[c] Hélène Prigent[a]
Pierre Levy[b] Muriel Fartoukh[a] Charles Mayaud[a] Antoine Parrot[a]

Hangi hastada immun DAH?

Table 2. Statistically different features between group 1 (DAH of immune cause) and group 2 (DAH of non-immune cause) in univariate analysis

	Group 1 (n = 32)	Group 2 (n = 44)	p value
Time since the first respiratory symptoms ≥11 days	26/32	16/44	10^{-4}
Systolic blood pressure >160 mm Hg (n = 64)[a]	11/26	6/38	0.018
Fatigue and/or weight loss[b]	16/32	6/44	10^{-3}
Arthralgia and/or arthritis	14/32	1/44	3.10^{-5}
Myalgias	9/32	1/44	3.10^{-3}
Ear-nose-throat symptoms	15/32	11/44	0.047
Cutaneous lesions	17/32	8/44	10^{-3}
Haematuria ≥10^4 cells/ml (n = 61)[a]	26/31	6/30	2.10^{-6}
Proteinuria ≥1 g/l (n = 67)[a]	19/30	5/37	7.10^{-5}
Glomerular filtration rate <80 ml/min (Cockroft formula; n = 65)[a]	23/27	17/38	2.10^{-3}
Haemoglobinemia <10 g/dl	22/32	12/44	3.10^{-4}
γ-globulin levels ≥9 g/l (n = 50)[a]	14/22	9/28	0.026

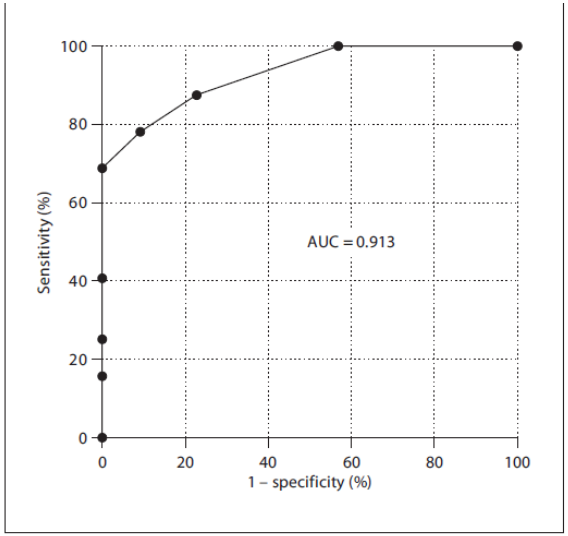
Respiration 2010;80:313–320

Hangi hastada immun DAH

Table 4. The scale defined using β-coefficients of the multivariate analysis

Variable	Points
Time since the first respiratory symptoms ≥11 days	+2
Fatigue and/or weight loss[a]	+2
Arthralgia/arthritis	+3
Proteinuria ≥1 g/l	+3

≥4



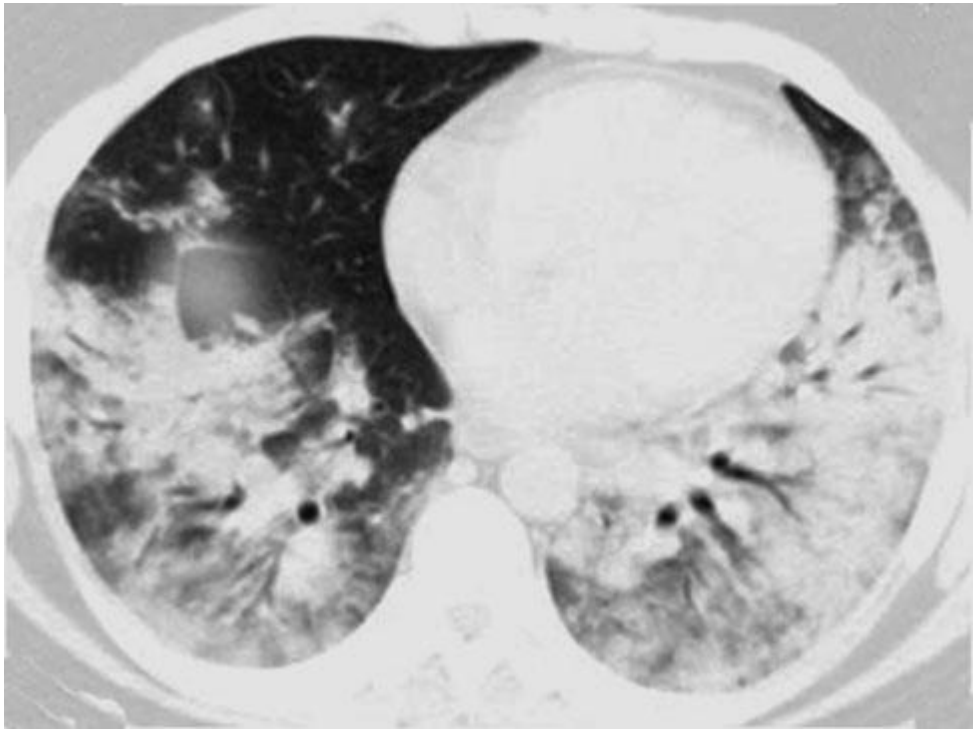
Respiration 2010;80:313–320

Non-immun DAH

- Enfeksiyonlar
- Koagülopati
- Kİ nakli
- Kalp ve kapak hastalıkları
- İlaçlar
- Radyasyon hasarı

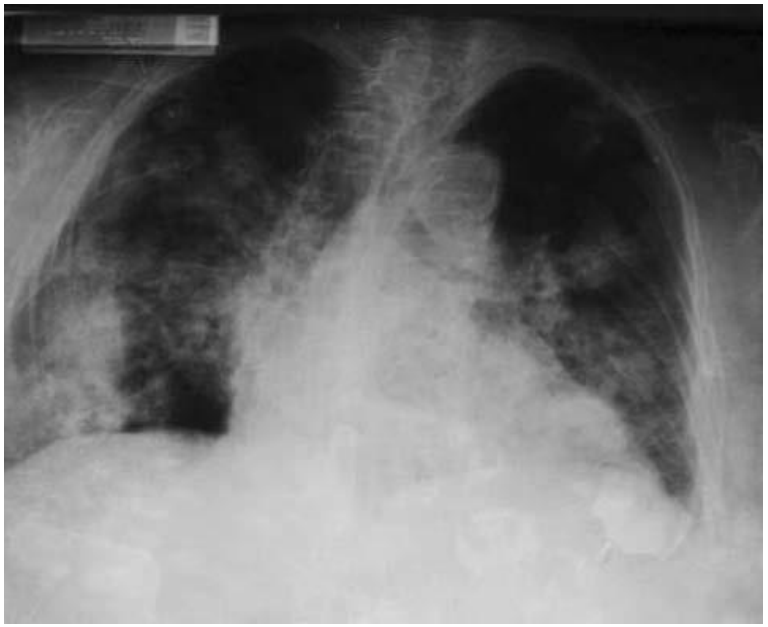
Non-immun DAH

- 28 Y, K
- Ateş
- Nefes darlığı
- Hemoptizi
- Anemi
- İnfluenza A (H1N1) pnömonisi



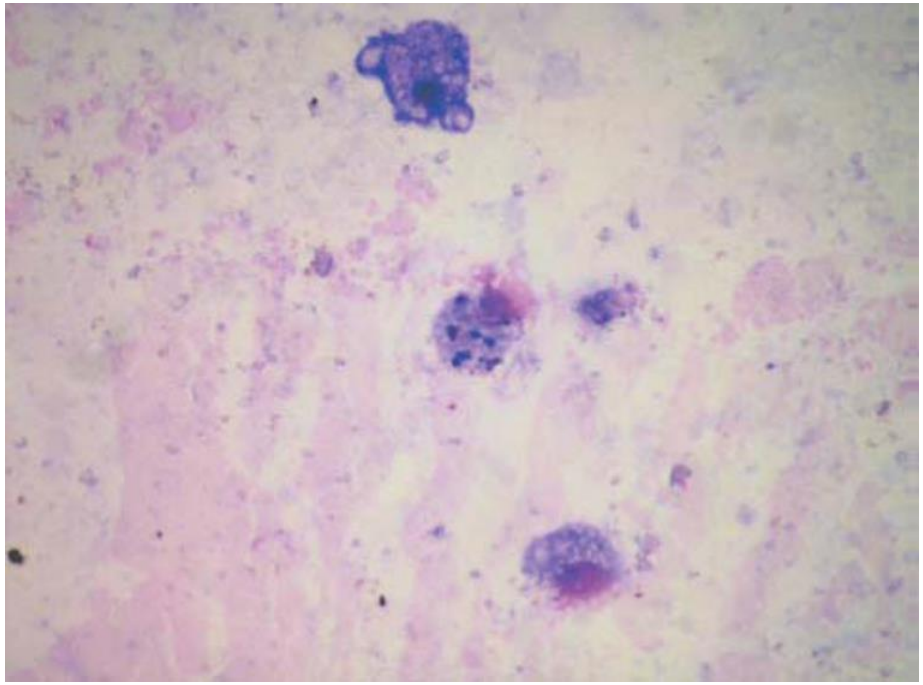
Non-immun DAH

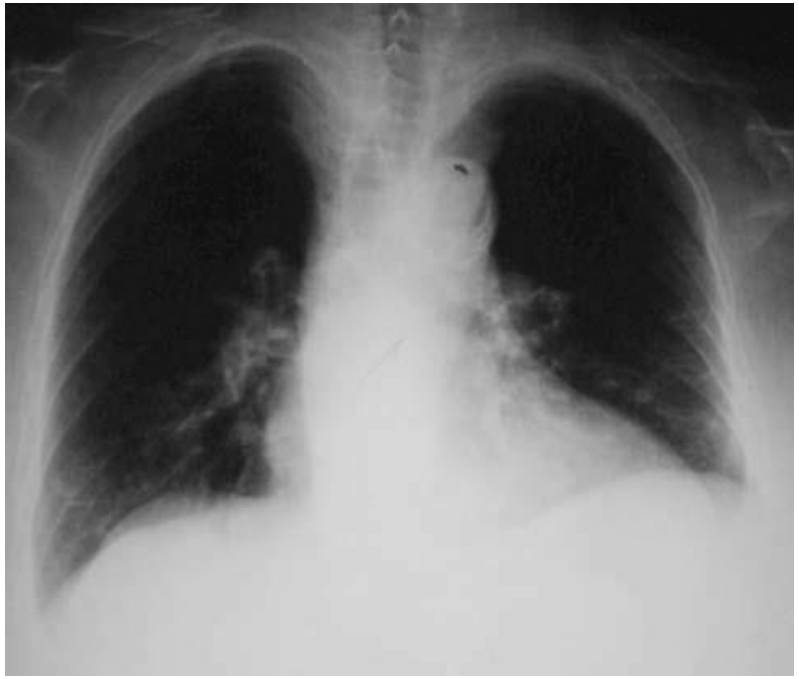
- 80 yaşında K
- Hemoptizi
- Solunum sıkıntısı
- Warfarin ve amiodoron
- PZ süresiz



Yoğun Bakım Dergisi 2010; 9(1): 57-63

Non-immun DAH





Yoğun Bakım Dergisi 2010; 9(1): 57-63

Non-immun DAH

- 34 Y, E
- Kİ nakli sonrası dispne, hemoptizi

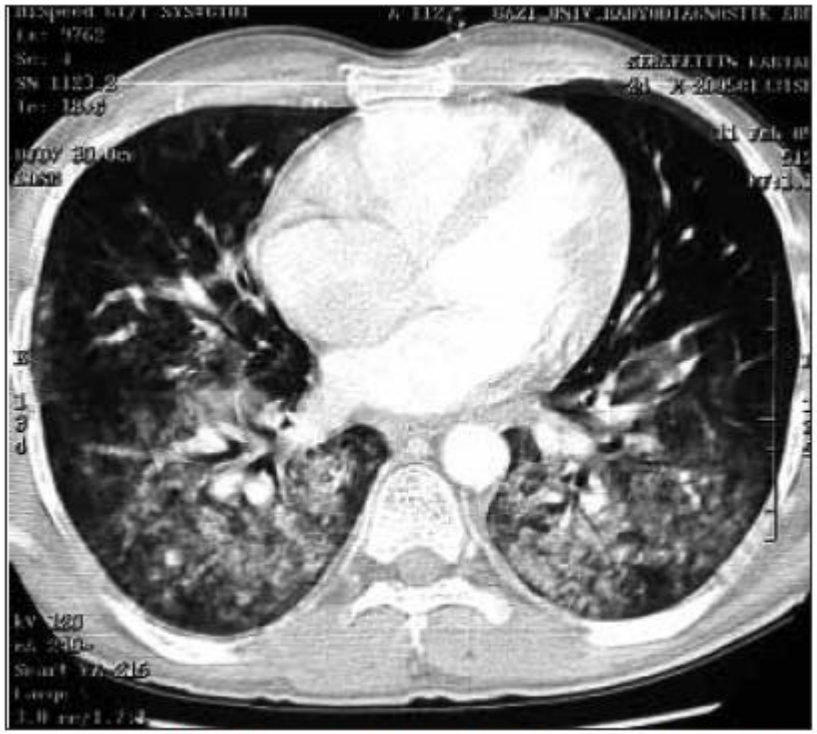


Figure 1. HRCT demonstrates bilateral alveolar infiltrates, predominantly in the lower zones

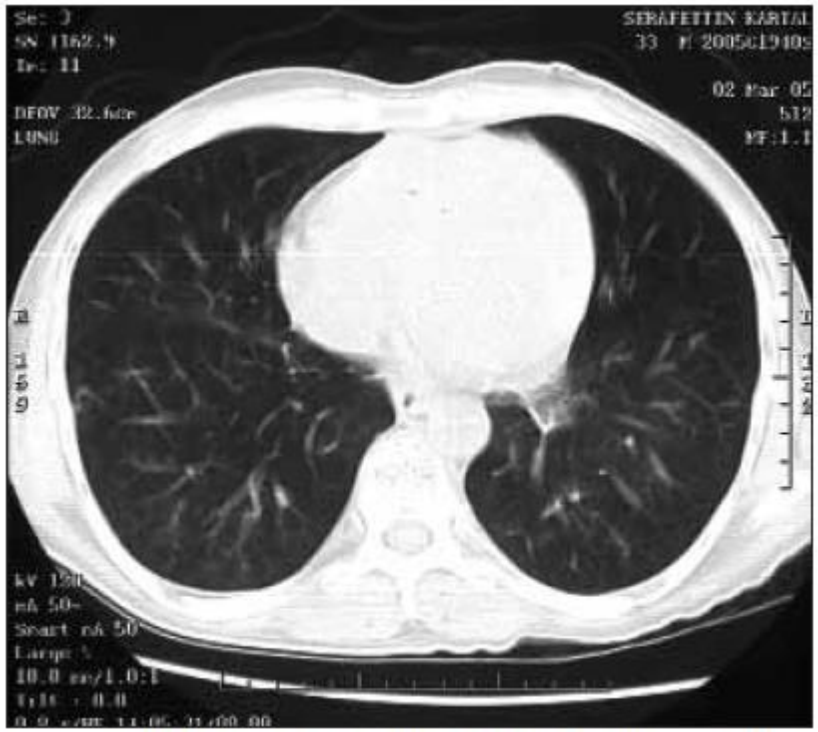
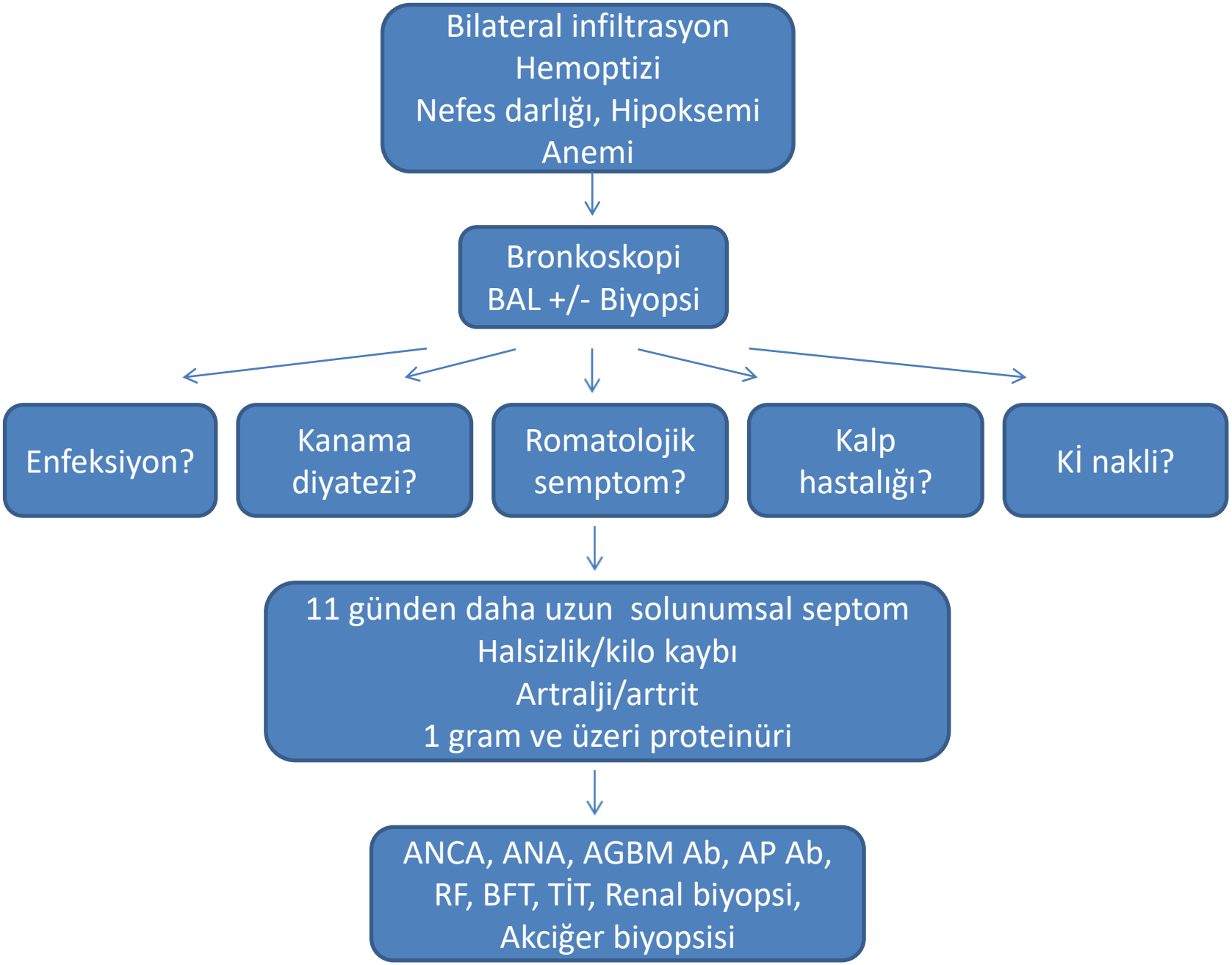


Figure 2. Control HRCT (2 weeks after steroid therapy) reveals complete disappearance of pulmonary infiltrates


Bilateral infiltrasyon
Hemoptizi
Nefes darlığı, Hipoksemi
Anemi
Bronkoskopi
BAL +/- Biyopsi
Enfeksiyon?
Kanama diyatezi?
Romatolojik semptom?
Kalp hastalığı?
Kİ nakli?
11 günden daha uzun solunumsal septom
Halsizlik/kilo kaybı
Artralji/artrit
1 gram ve üzeri proteinüri
ANCA, ANA, AGBM Ab, AP Ab,
RF, BFT, TİT, Renal biyopsi,
Akciğer biyopsisi

TEŞEKKÜRLER…