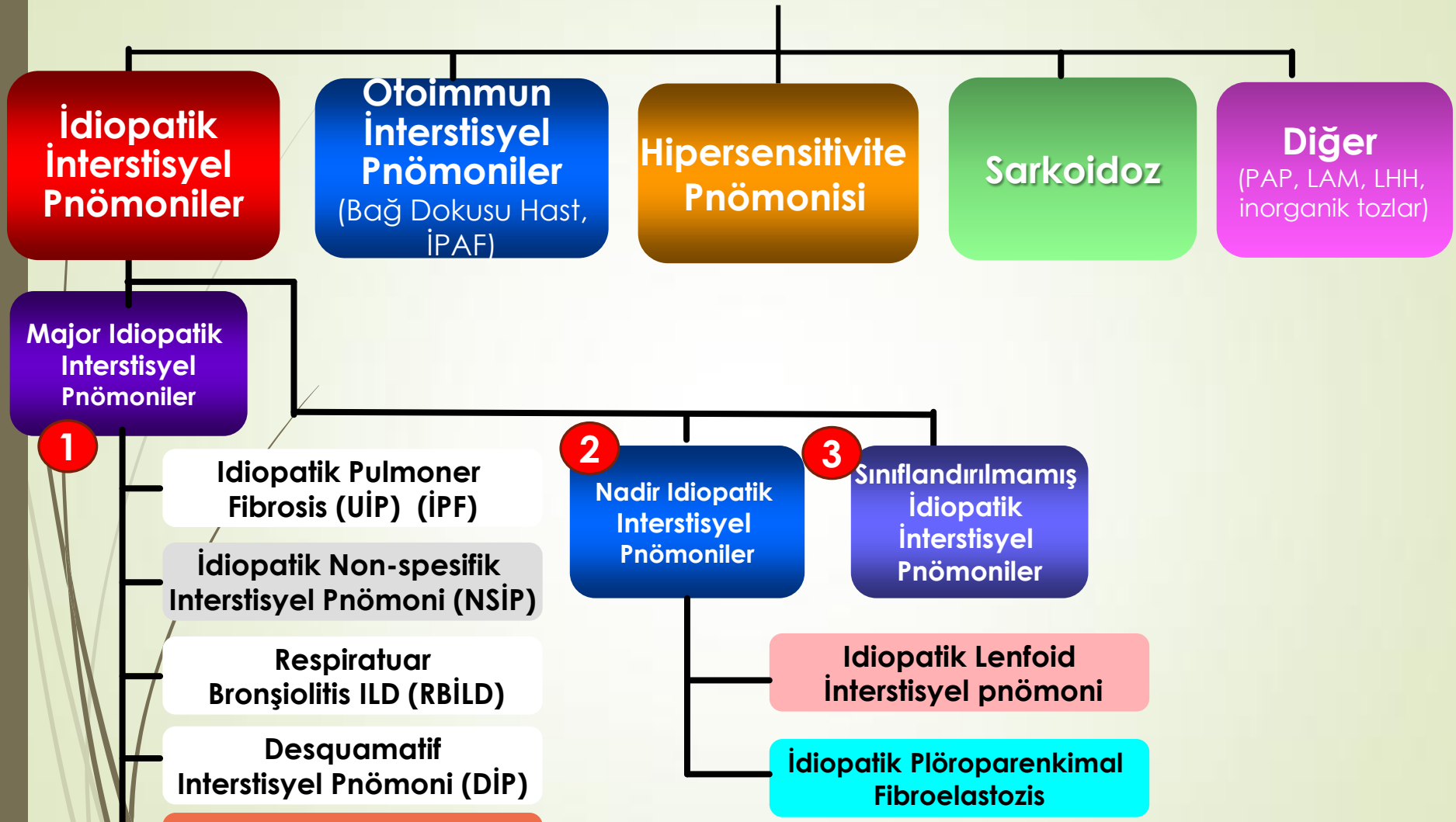
Kriptojenik Organize Pnömoni (KOP)

Songül Özyurt

İnterstisyel Akciğer Hastalıkları Sınıflaması



Am J Respir Crit Care Med **2013**; 188;733–748

- Organize pnömoni nadir görülen bir klinikopatolojidir
- Gerçek insidansı ve prevalansı bilinmemektedir ancak 100.000 de 1-3 civarında olduğu düşünülmektedir
- Her iki cinsiyette görülme oranı benzerdir
- Ortalama 50-60 yaşlarında sık rastlanılmaktadır
- Sigara?

Altta yatan hastalık ya da neden belli değilse kriptojenik organize pnömoni (KOP) olarak adlandırılır

Organize Pnömoni (OP)

- **Enfeksiyonlar:**

  Bakteriler: klamidya, legionella, mycoplasma, streptokoklar

  Virusler: HIV, CMV, Influenza, Herpes V

  Mantarlar: Cryptococ neoformans, P jirovei

- **İlaçlar:** ASA, Amiodaron, Bleomisin, Karbamazepin, Fenitoin, Metotreksat , biyolojik ajanlar……
- **Kollajen vaskuler hastalıklar:** RA, Sjögren S, MPA,SLE….
- **Akciğer nakli, kemik iliği nakli**
- **Diğer:** Toksik gaz, GÖR, radyoterapi

Baque-Juston M, Pellegrin A, Leroy S, Marquette CH, Padovani B. Organizing pneumonia: what is it? A conceptual approach and pictorial review. Diagn Interv Imaging. 2014 Sep;95(9):771-7. doi: 10.1016/j.diii.2014.01.004

Kriptojenik Organize Pnömoni

- 1980'lerin başında Davison ve Epler tarafından tanımlanmıştır
- Distal hava yollarında granulasyon dokusu ile karakterize hastalıktır
- Özellikle alveoller, alveoler kanallar ve kısmen bronşioler lümende myofibroblast, fibroblast ve özellikle de kollagen birikimini içeren organize pnömoni tablosu

Handra D, Hershberger DM. Pneumonia, Cryptogenic Organizing. 2018 Oct 27.StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-.Available from http://www.ncbi.nlm.nih.gov/books/NBK507874

- **KOP:** genellikle subakut seyirli, tanı öncesi ortalama semptom süresi 2-6 haftadır
- En yaygın semptomlar öksürük, nefes darlığı, ateş, balgam, iştahsızlık ve kilo kaybıdır
- Hemoptizi, bol balgam, göğüs ve eklem ağrısı, gece terlemesi daha seyrektir
- ESR, CRP yüksekliği ve lökositoz görülür

Drakopanagiotakis F, Paschalaki K,at all. Cryptogenic and secondary organizing pneumonia: clinical presentation, radiographic findings, treatment response, and prognosis. Chest. 2011 Apr;139(4):893-900. doi: 10.1378/chest.10-0883

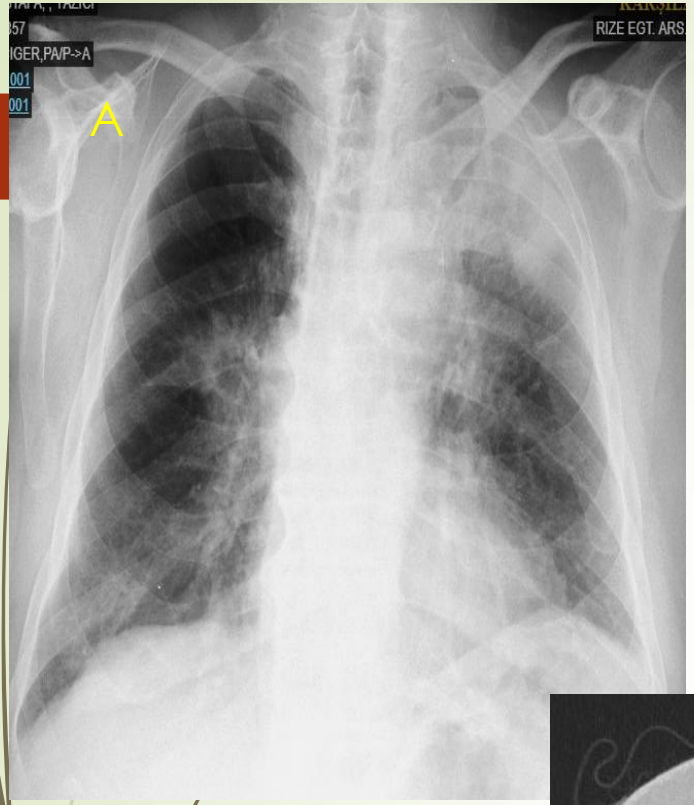
- Temel radyolojik görünüm genellikle periferik yerleşimli buzlu cam veya hava bronkogramı içeren konsolidasyonlar (%90)

- Daha seyrek olarak diffüz bilateral infiltrasyon, soliter fokal kitle ya da metastazı düşündüren yaygın nodüler lezyonlar da gözlenebilmektedir

- Drakopanagiotakis F, Paschalaki K,at all. Cryptogenic and secondary organizing pneumonia: clinical presentation, radiographic findings, treatment response, and prognosis. Chest. 2011 Apr;139(4):893-900. doi: 10.1378/chest.10-0883

- Nodüler lezyonlar oranı %10
- Nodüllerin boyutları ancak hastaların %15'inde 1 cm'den büyüktür
- HRCT: ters halo işareti olarak da bilinen atoll işareti (%20)

Typical pattern (most common)	Patchy alveolar opacities (typical COP)
Less common patterns	Solitary opacity (focal COP) Infiltrative opacities (infiltrative COP)
Rare patterns	Reversed halo sign or atoll sign Progressive fibrosis with reticulation and areas of consolidation Multiple nodules Multiple masses or nodules Bronchocentric consolidation Irregular lines or bands Perilobular opacities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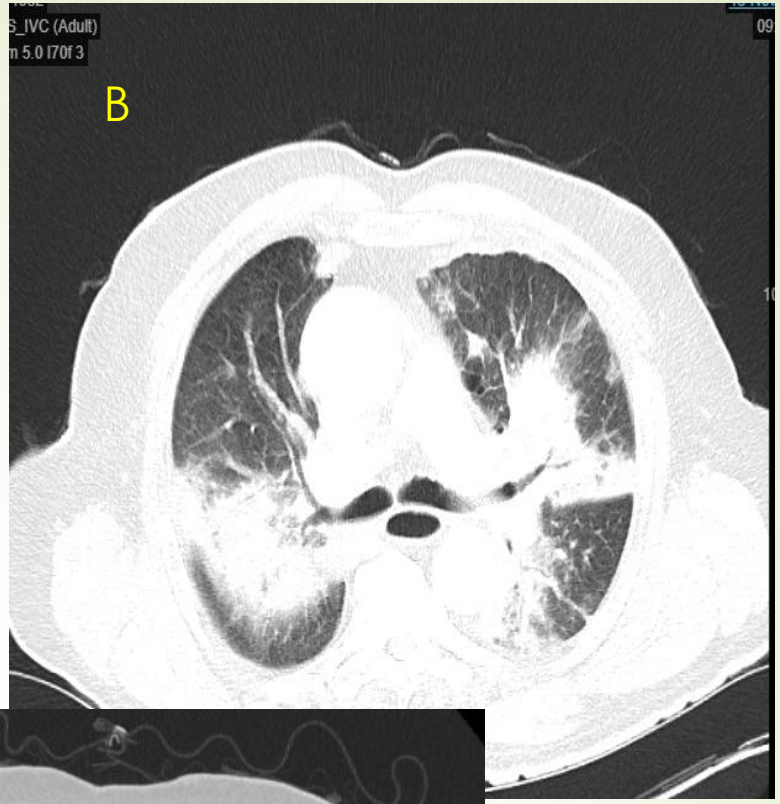
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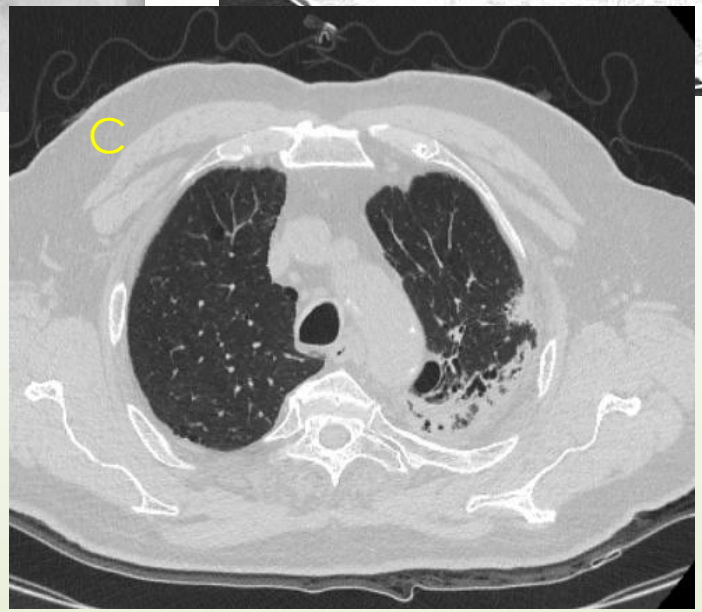
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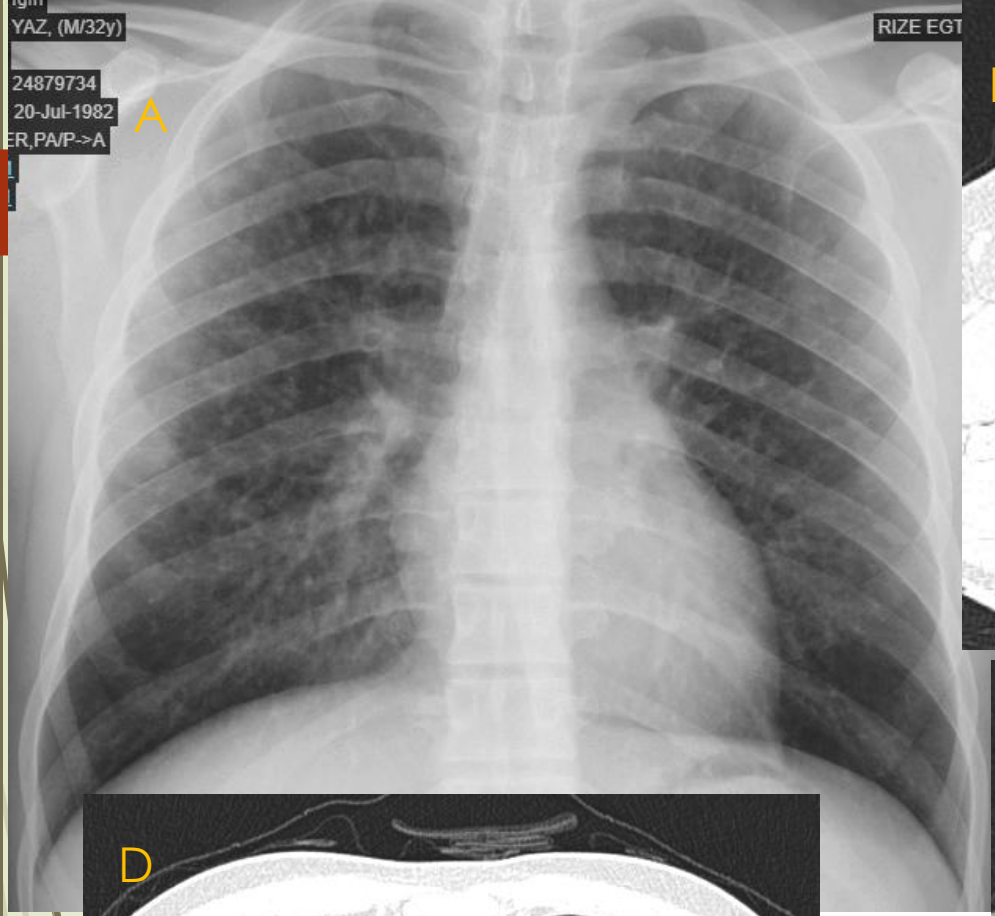
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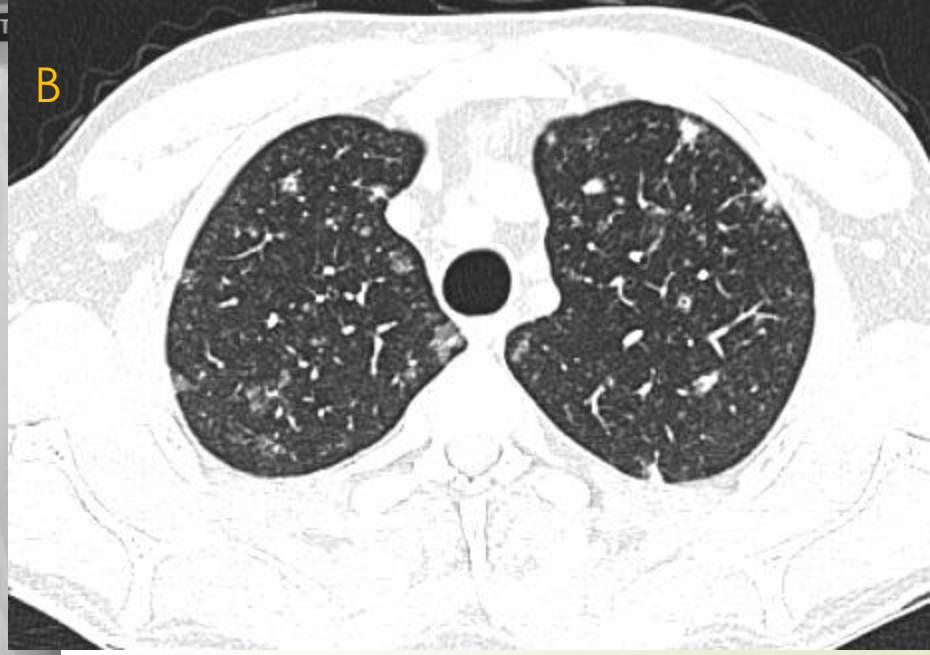
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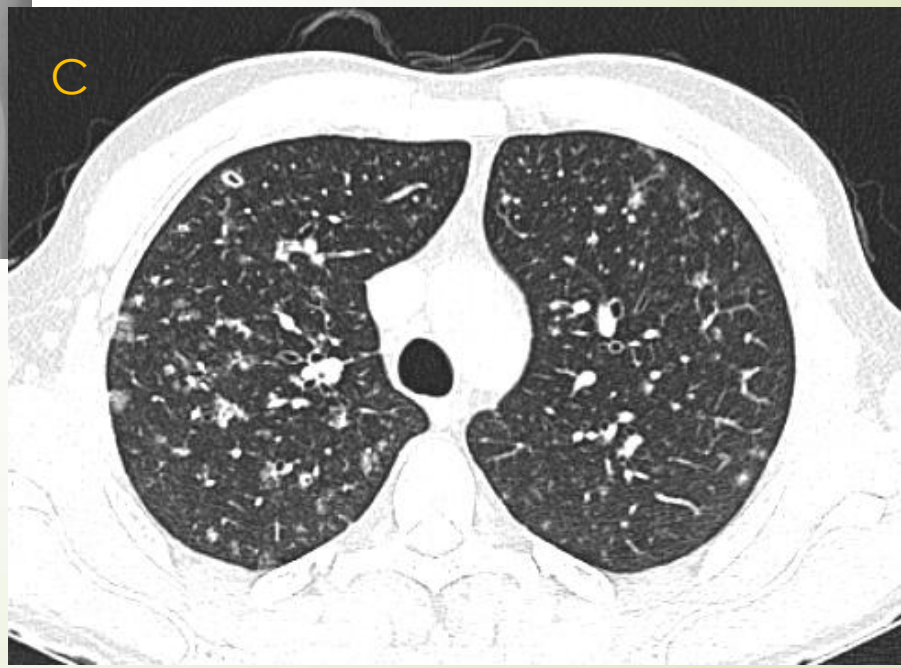
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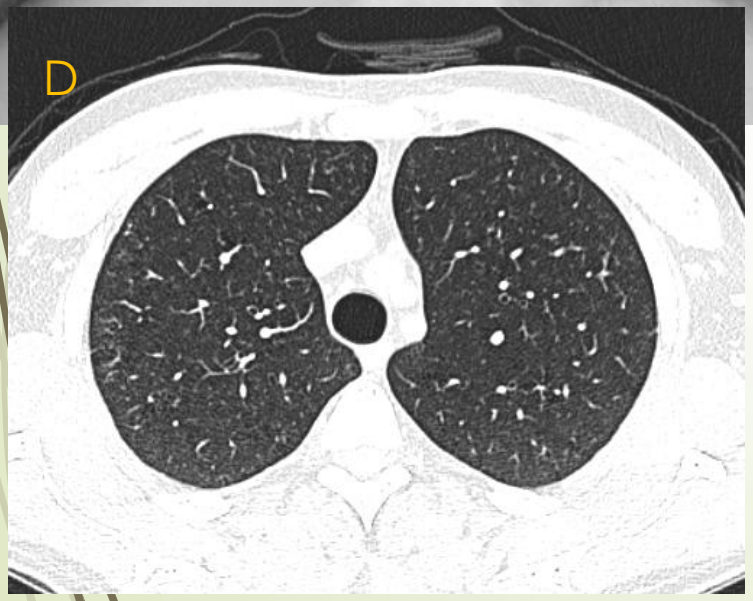
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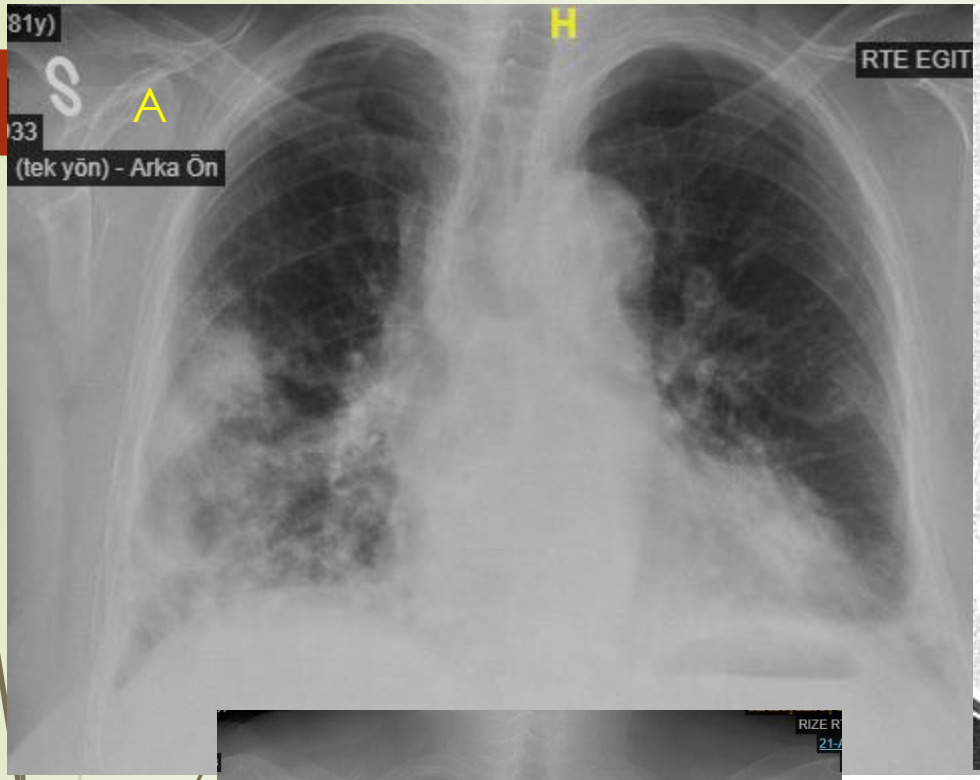
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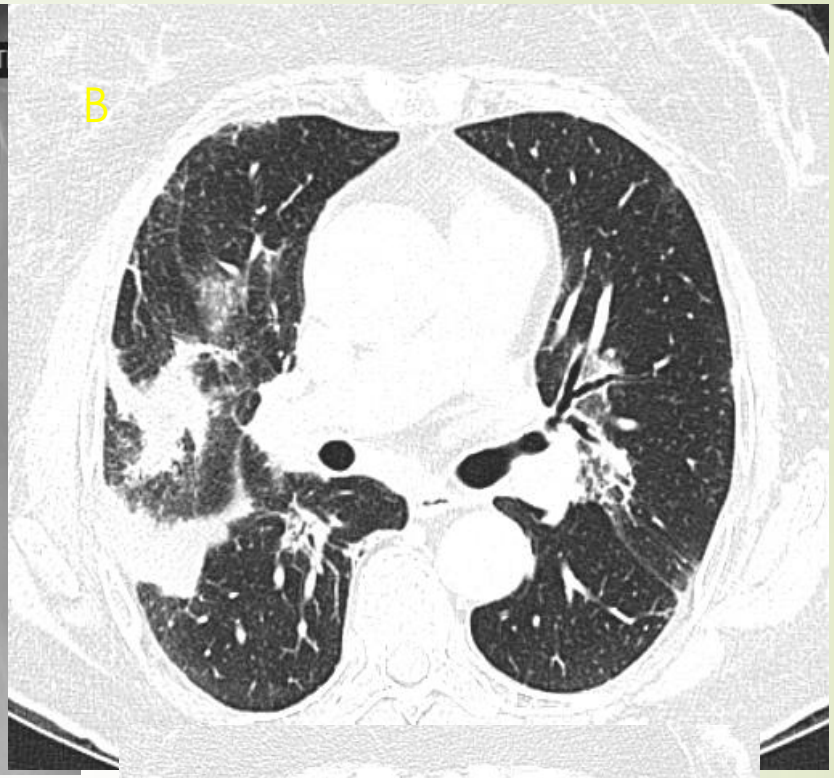
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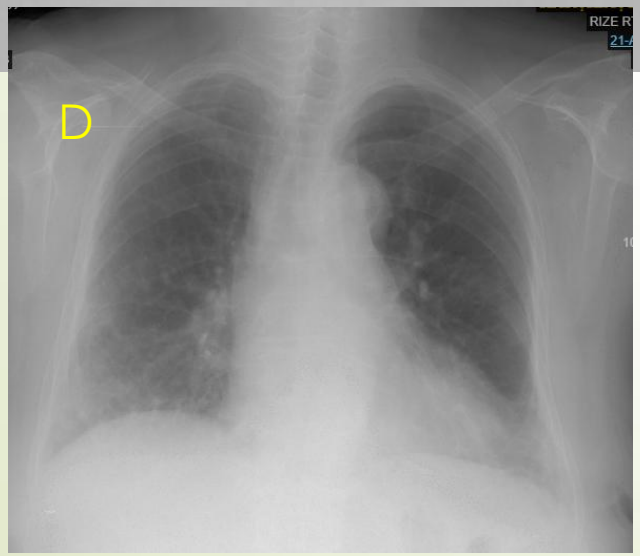
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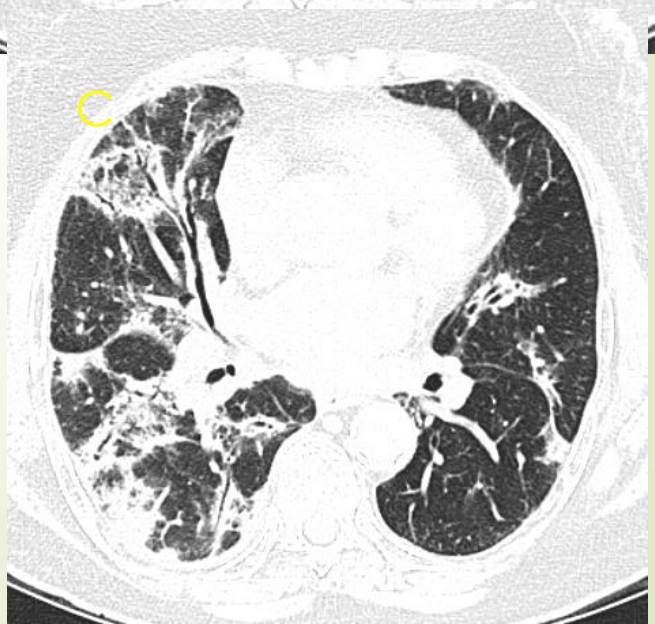
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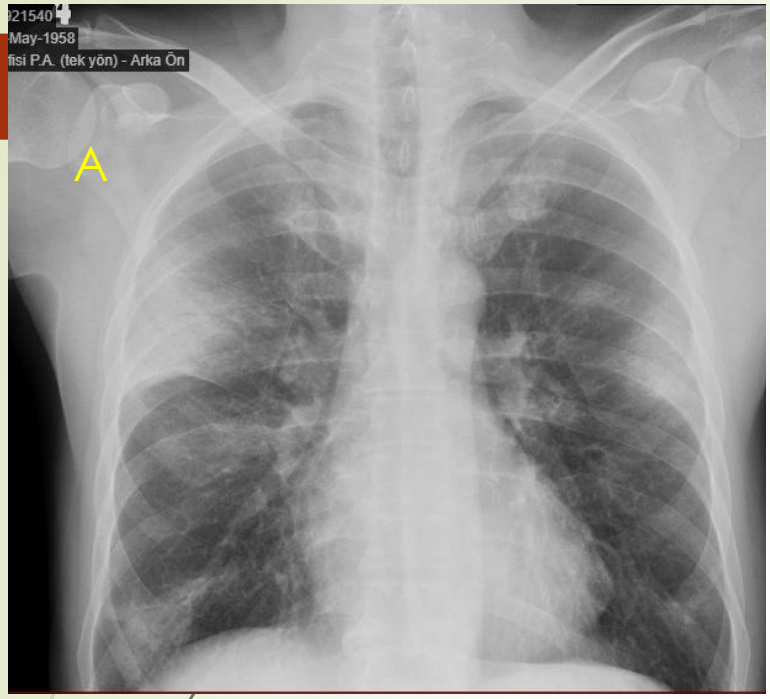
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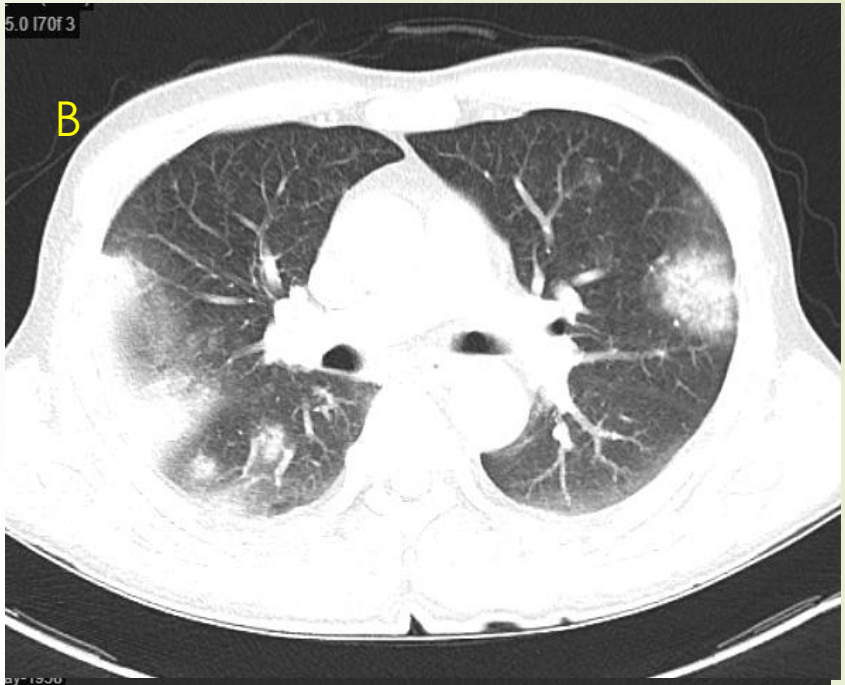
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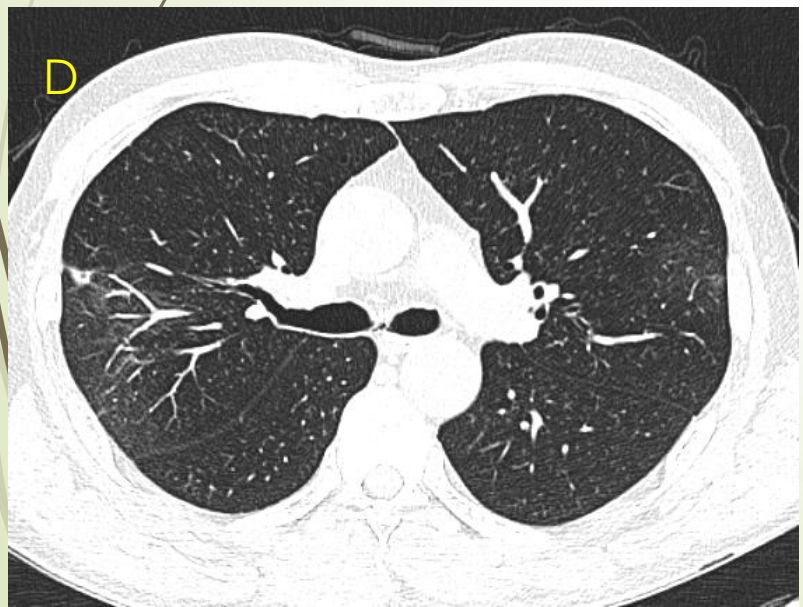
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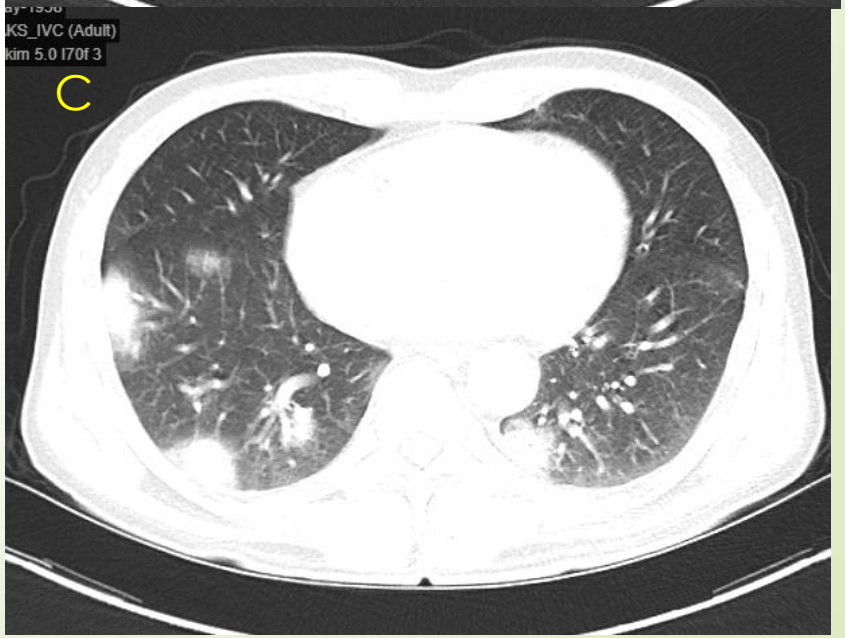
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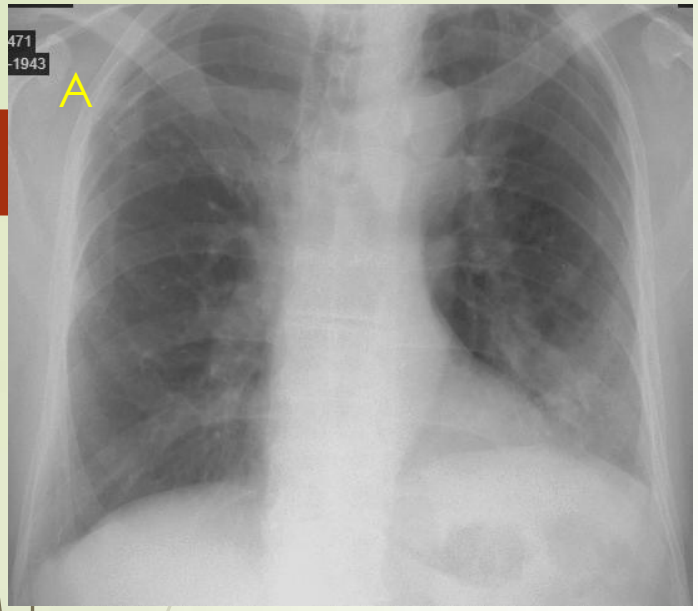
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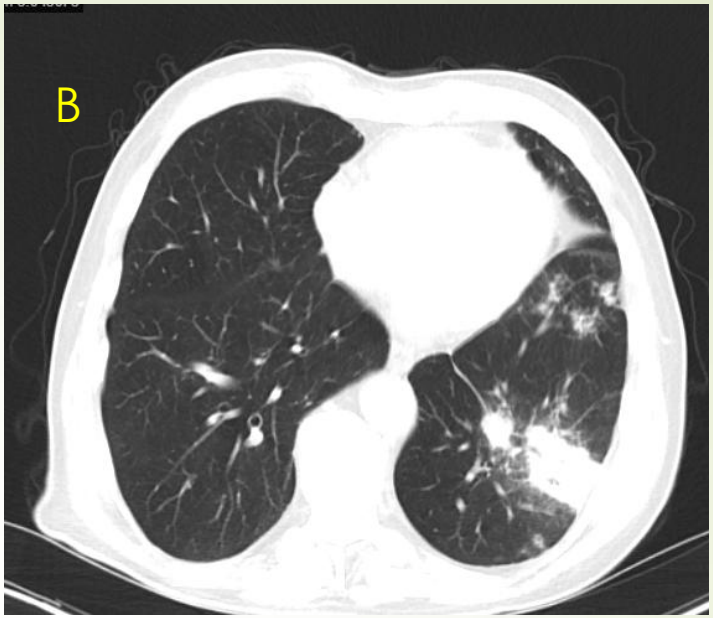
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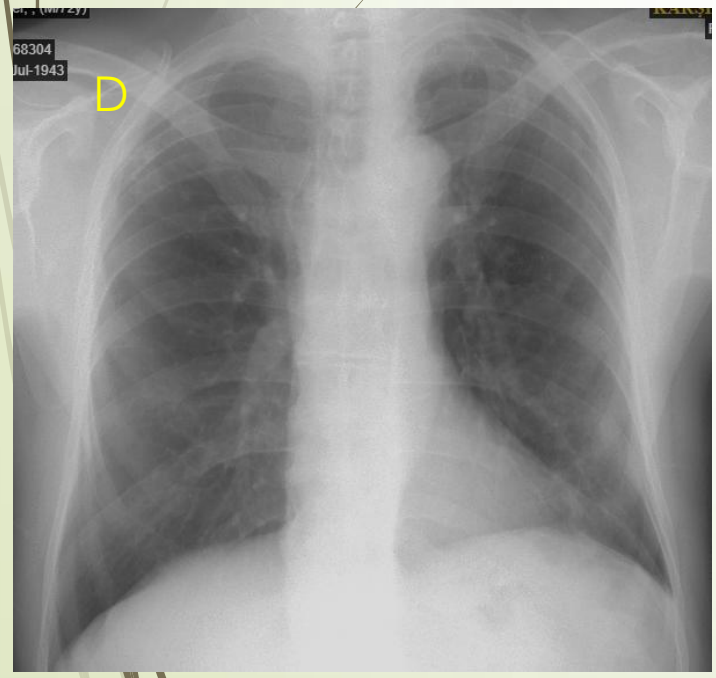
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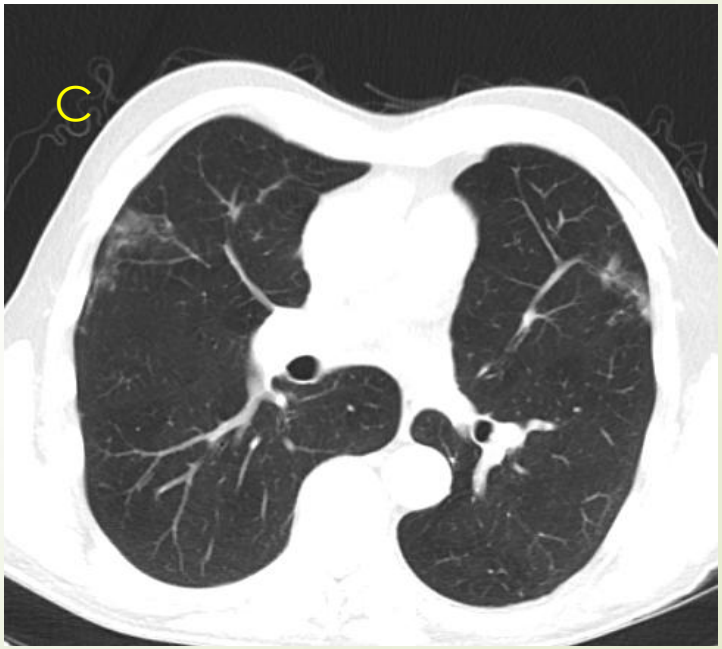
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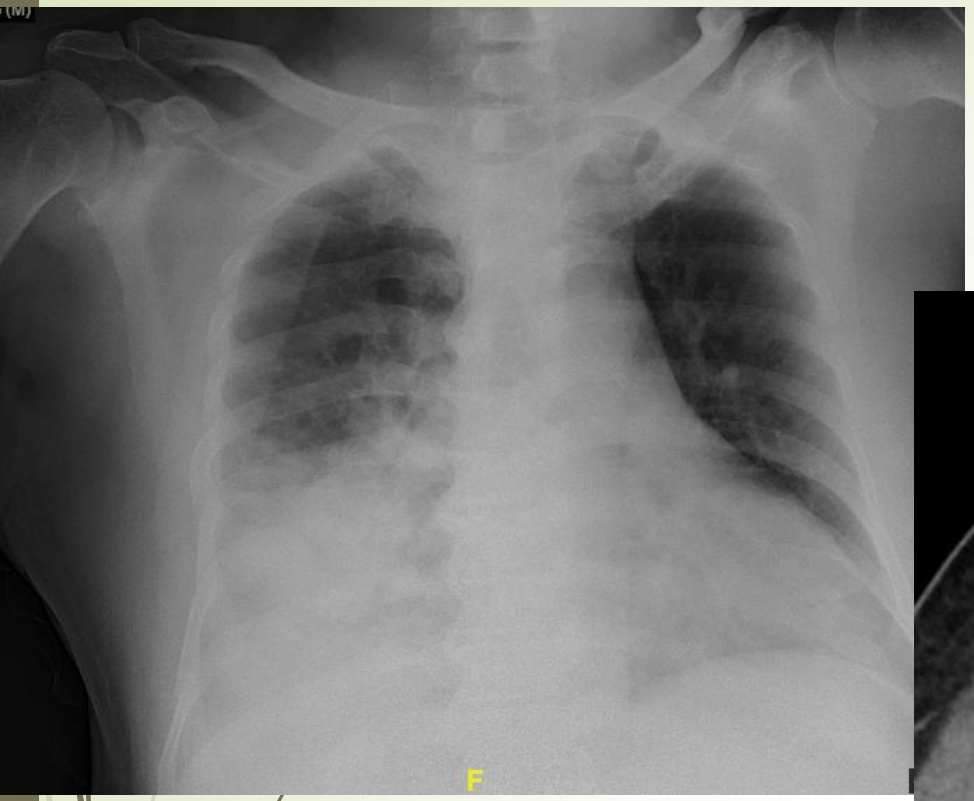

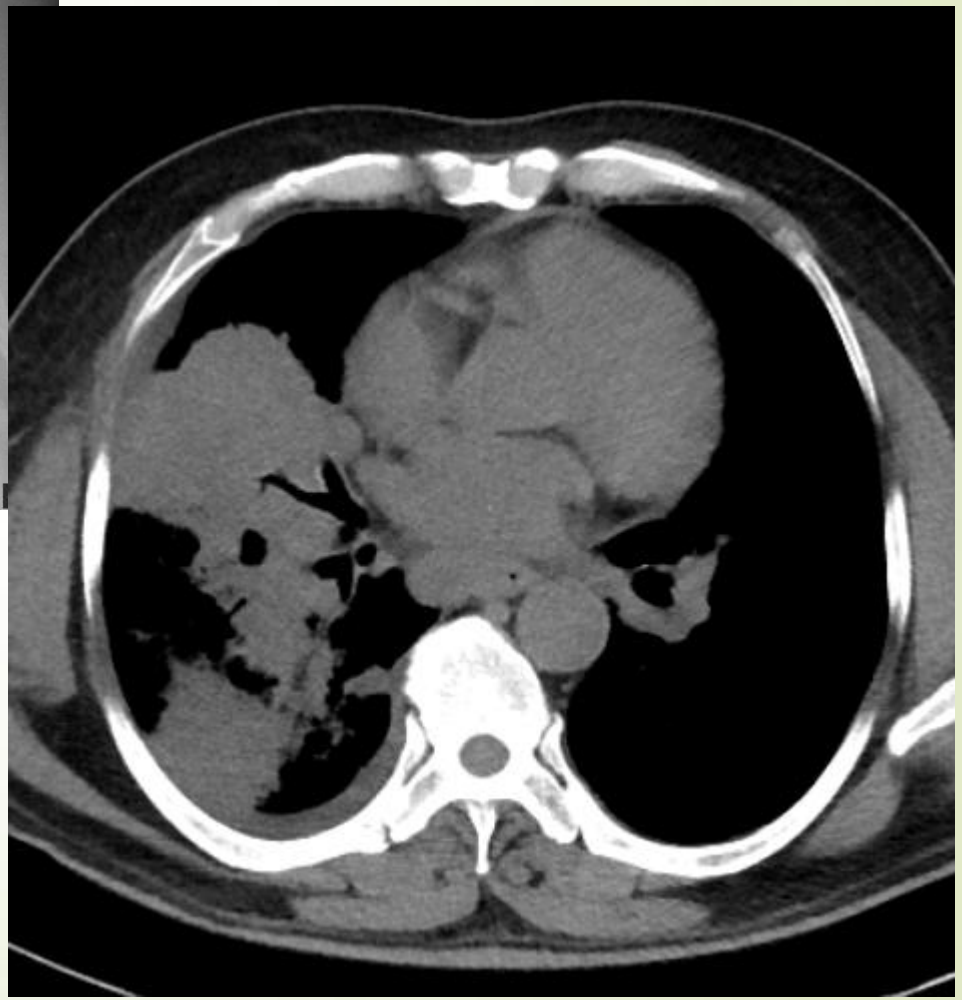

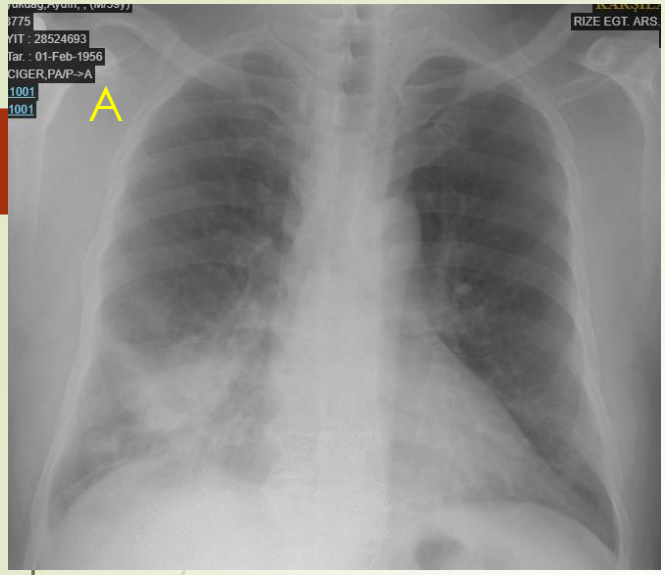
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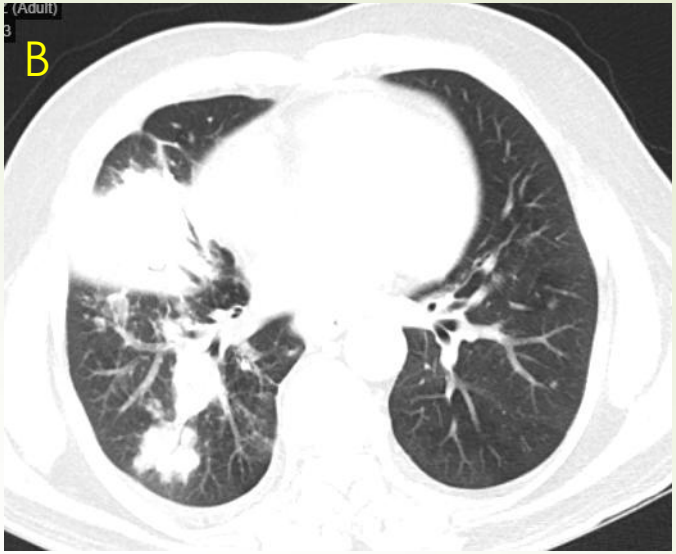
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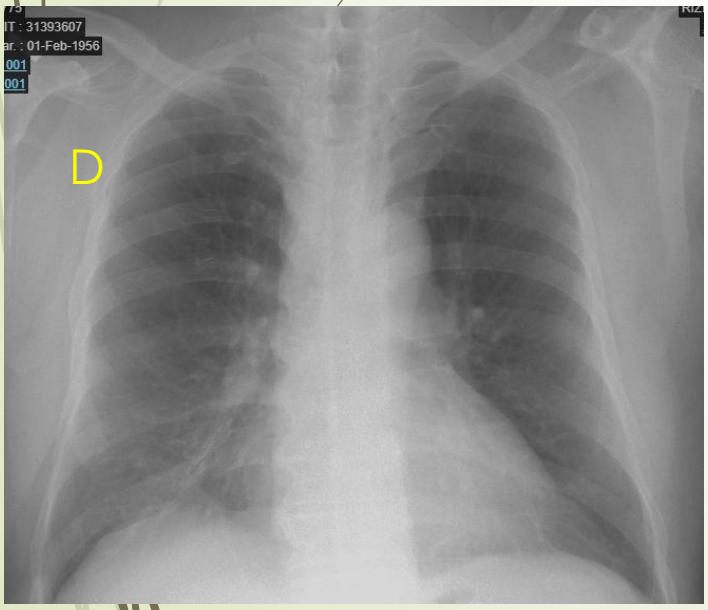
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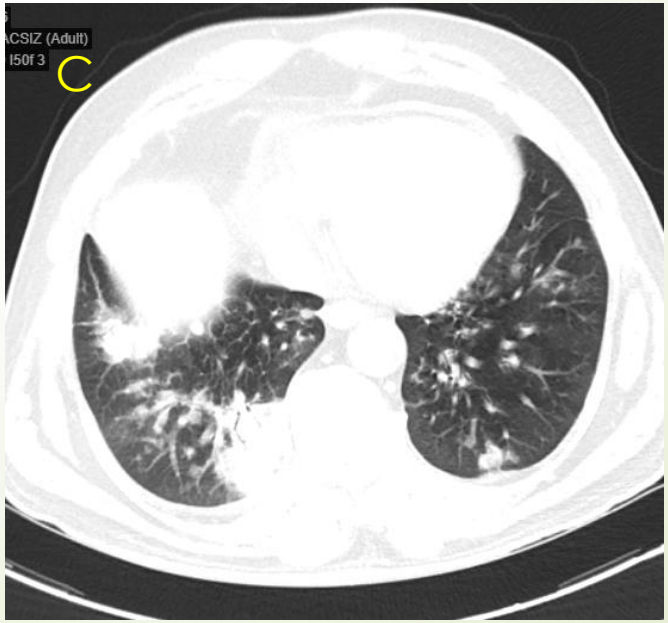
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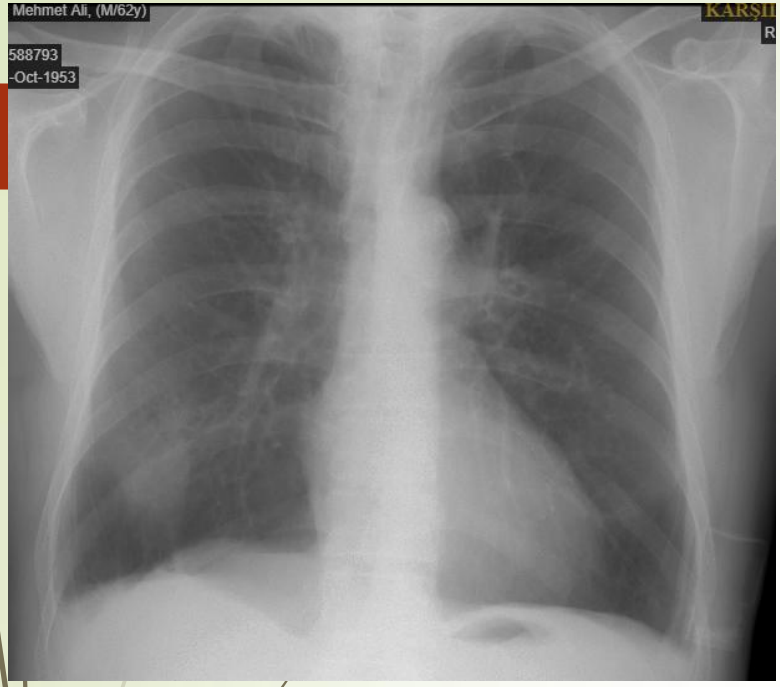
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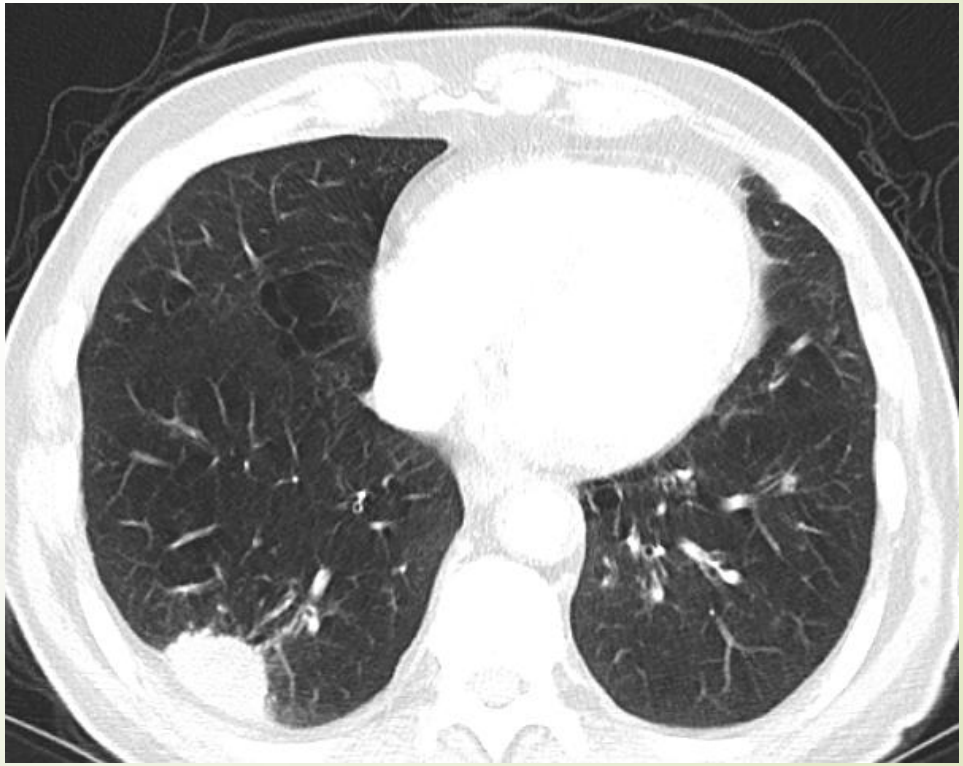

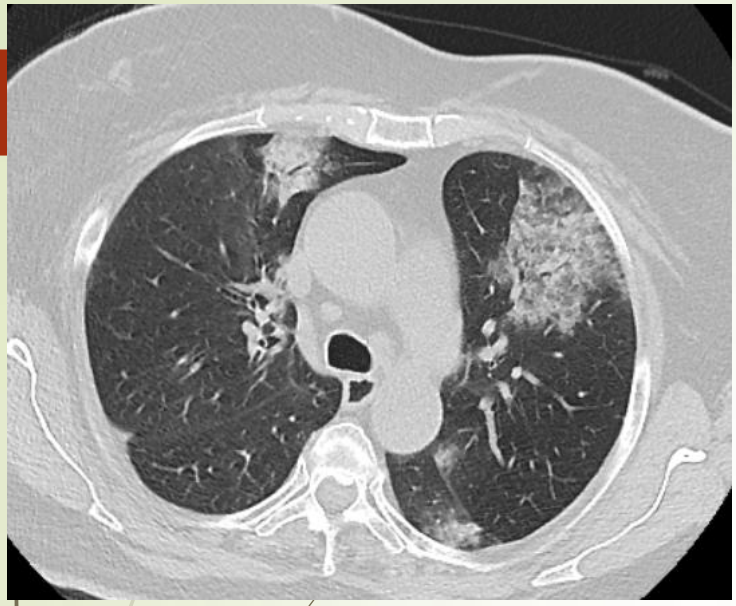

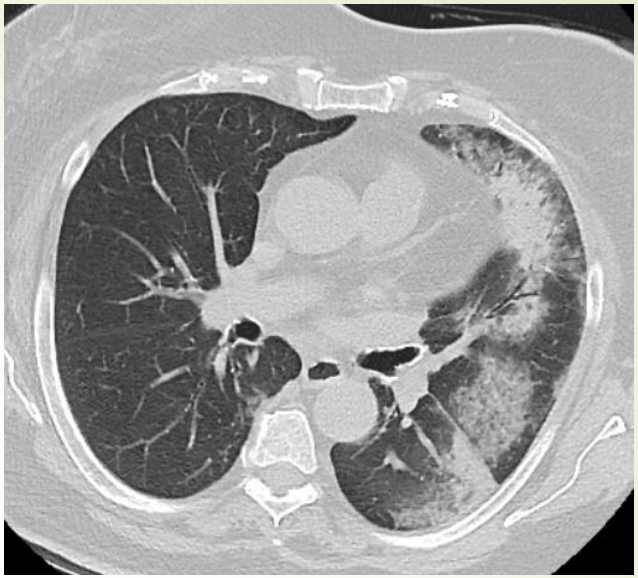

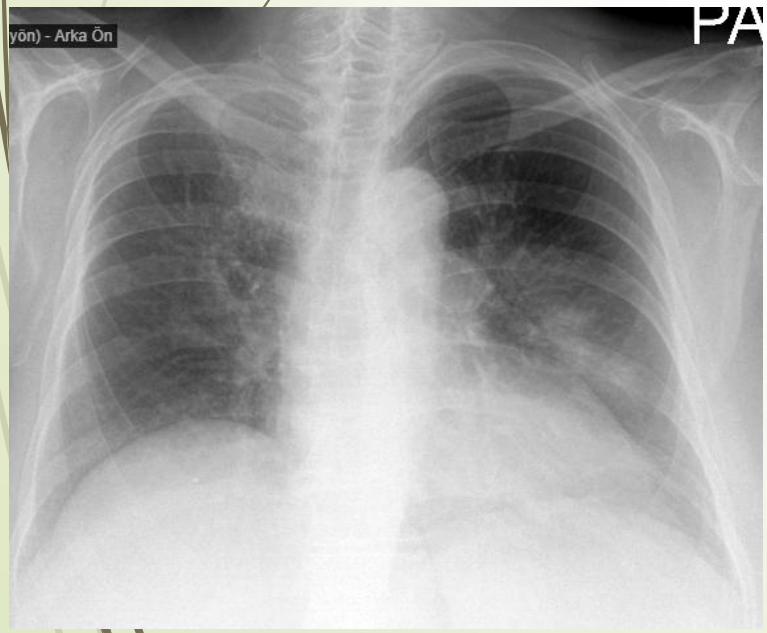
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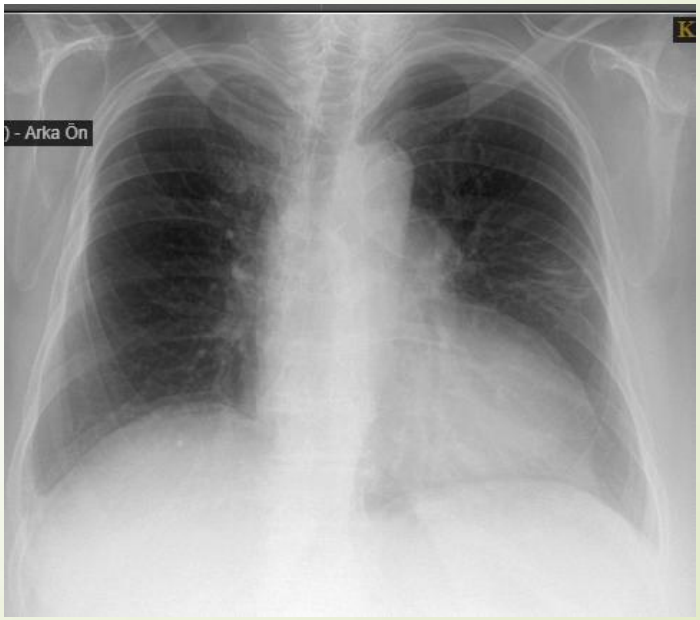
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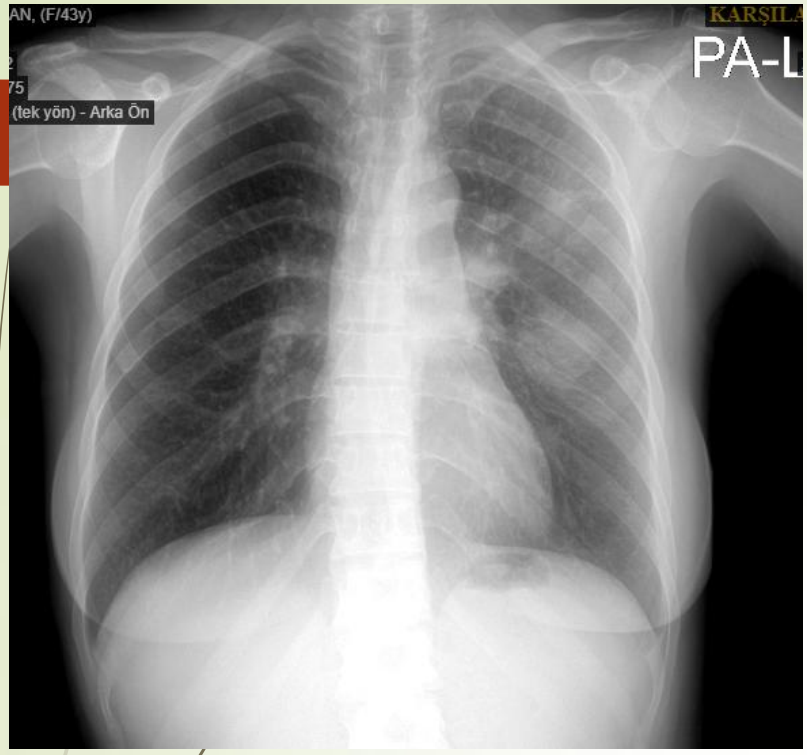
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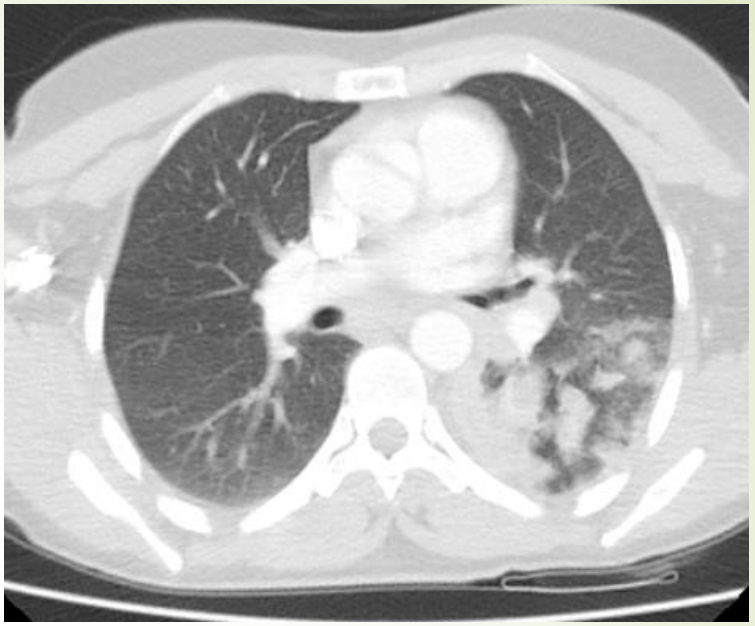

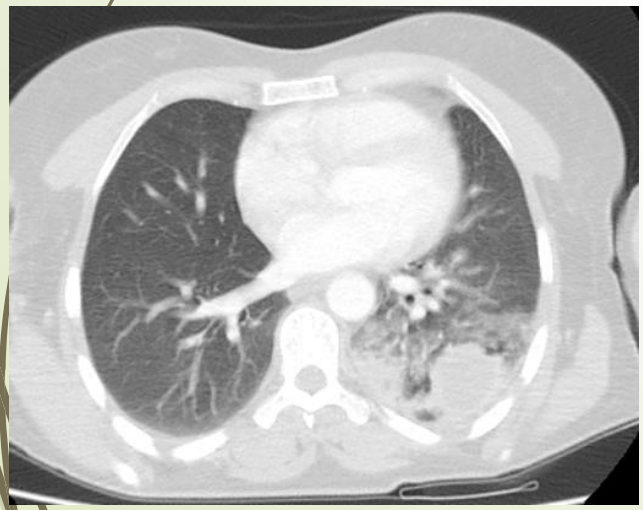

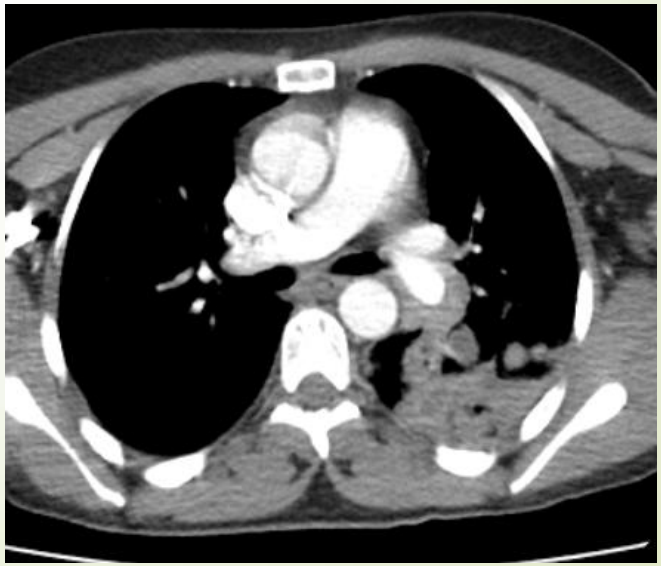

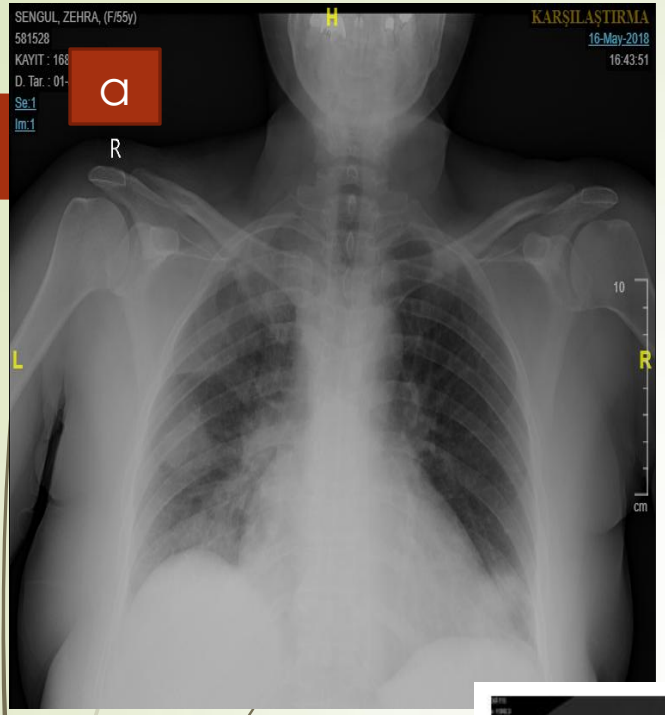
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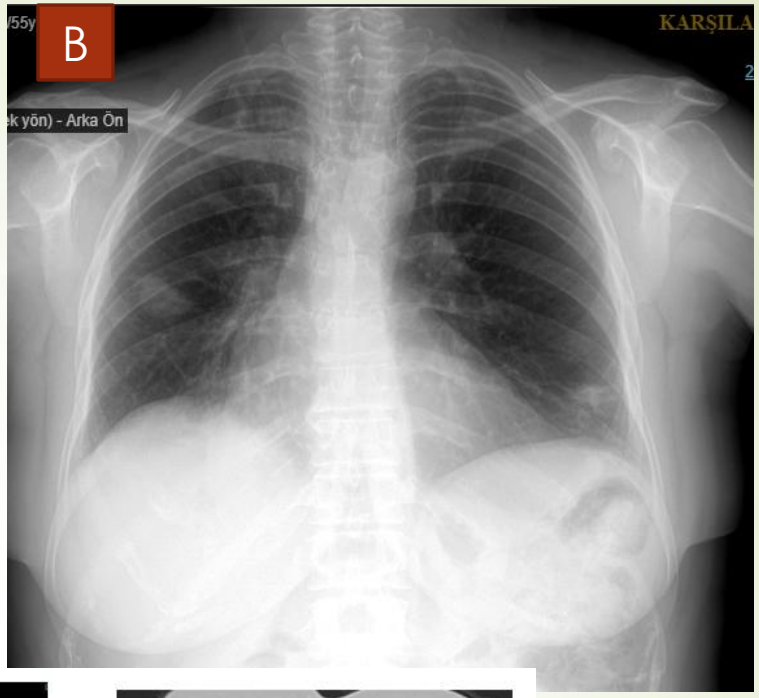
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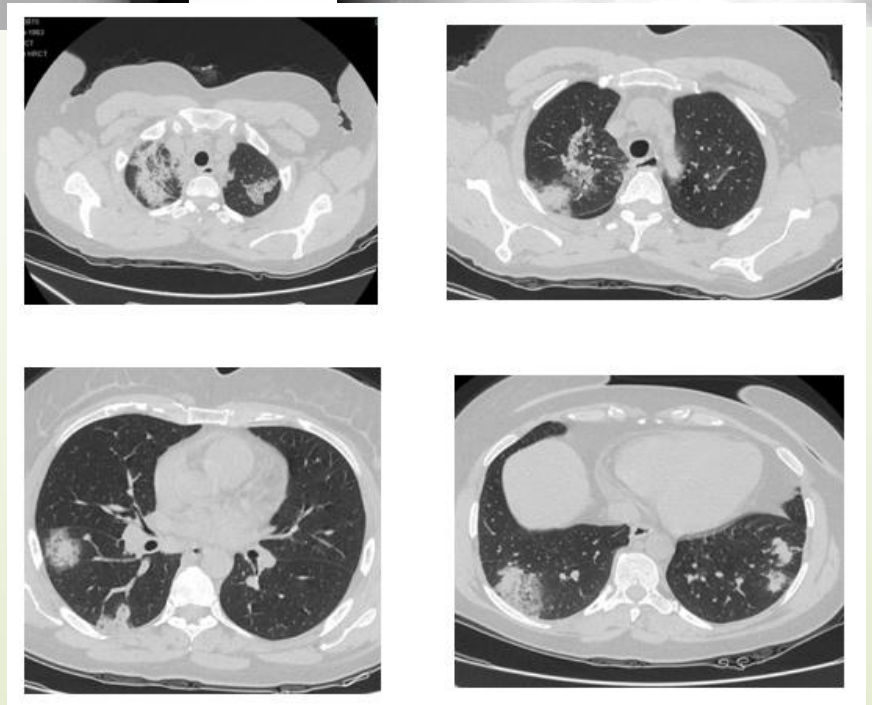

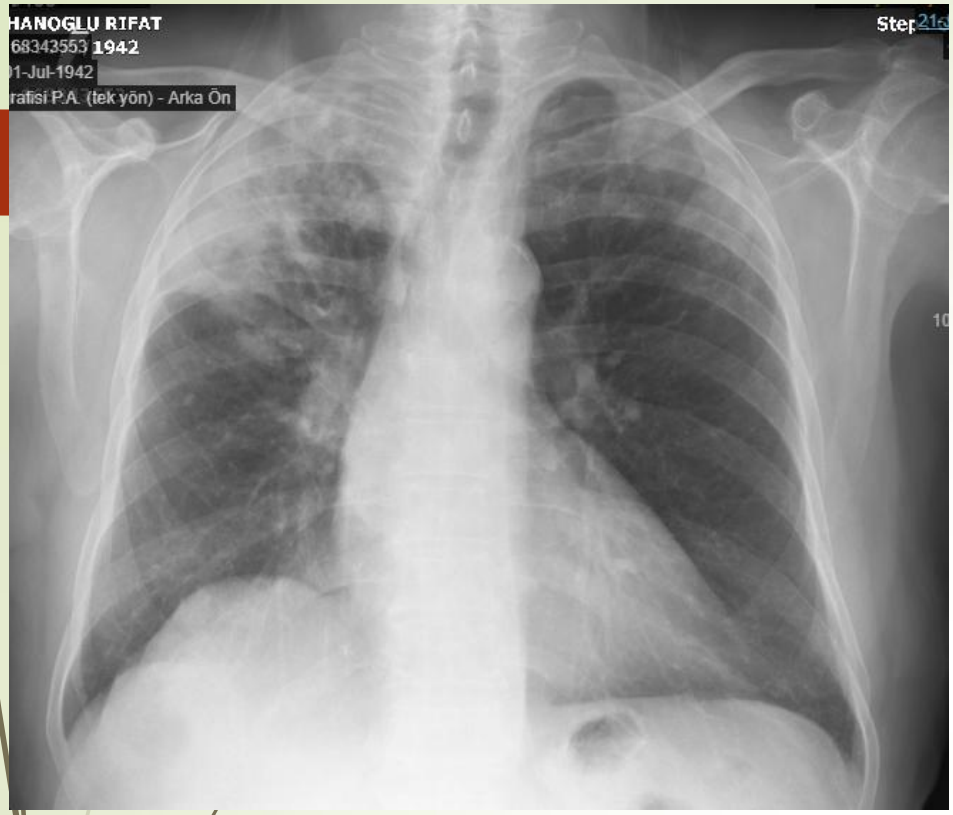
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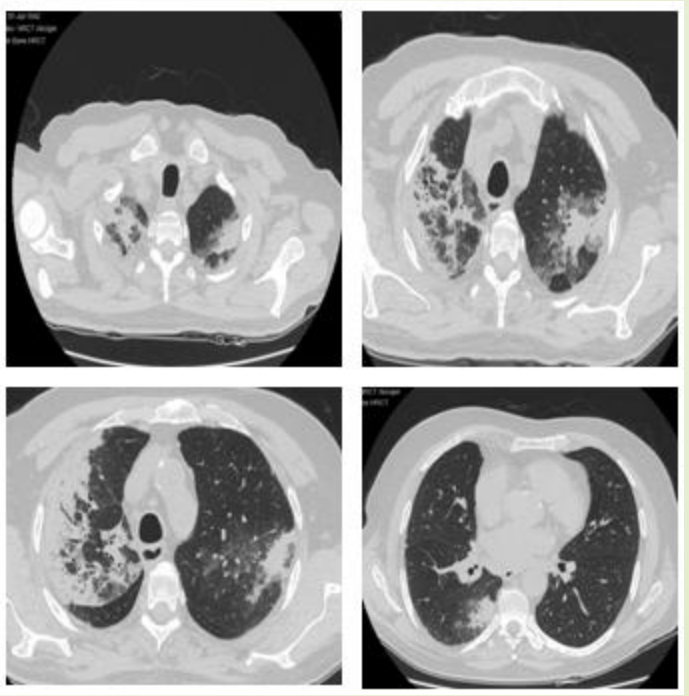

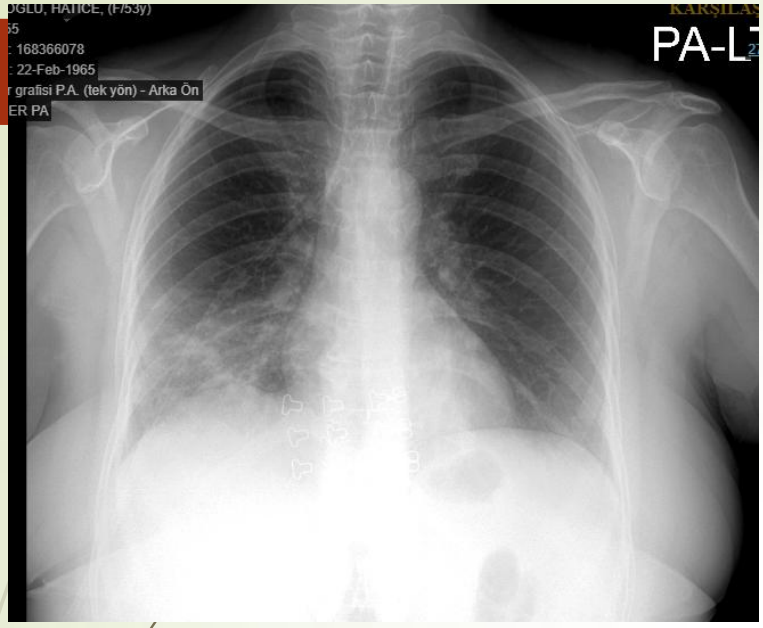
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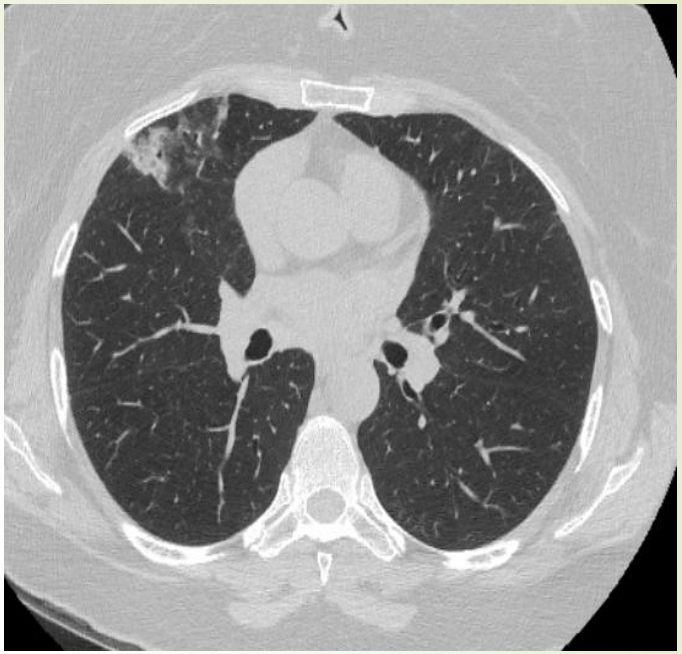

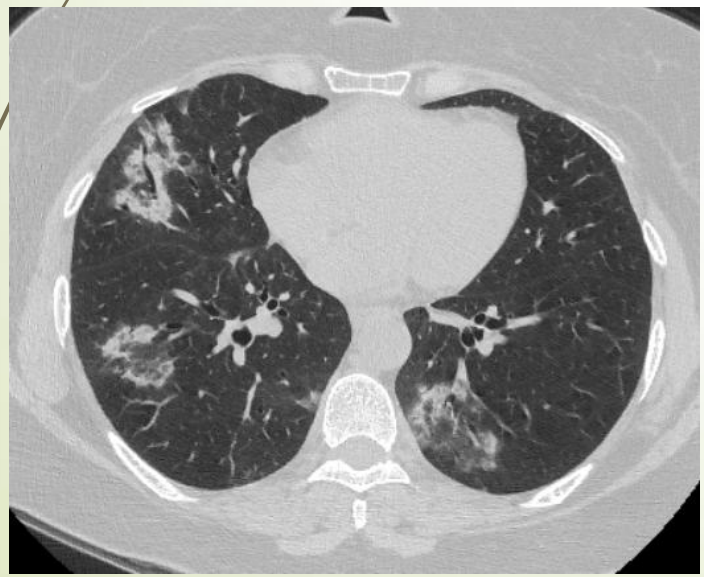

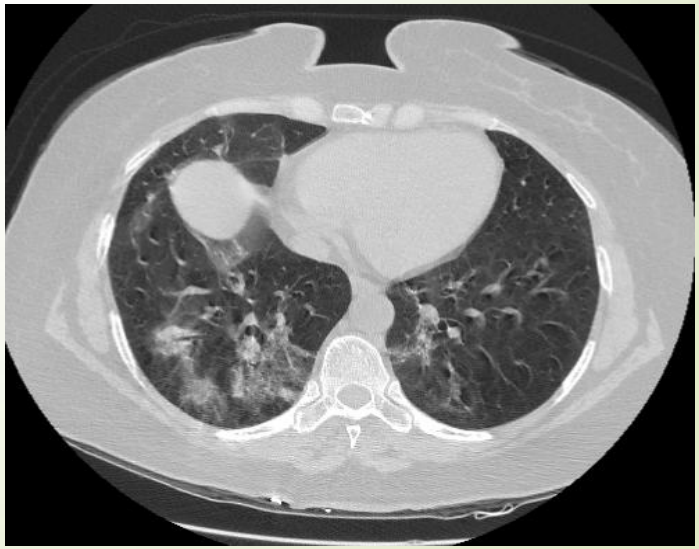

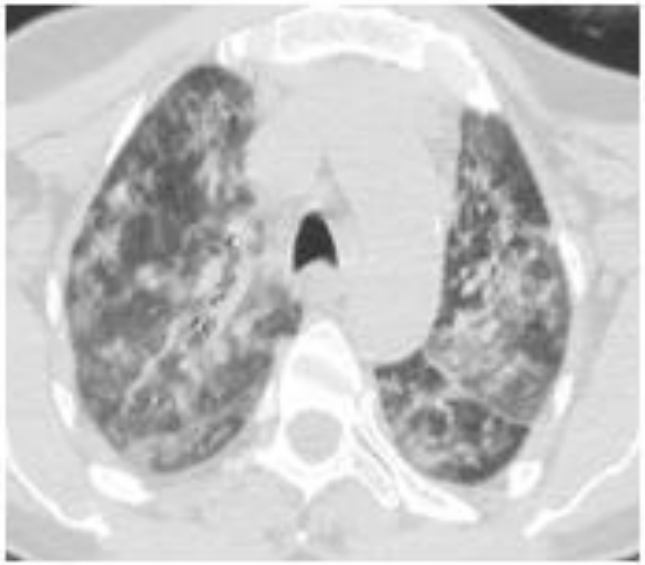

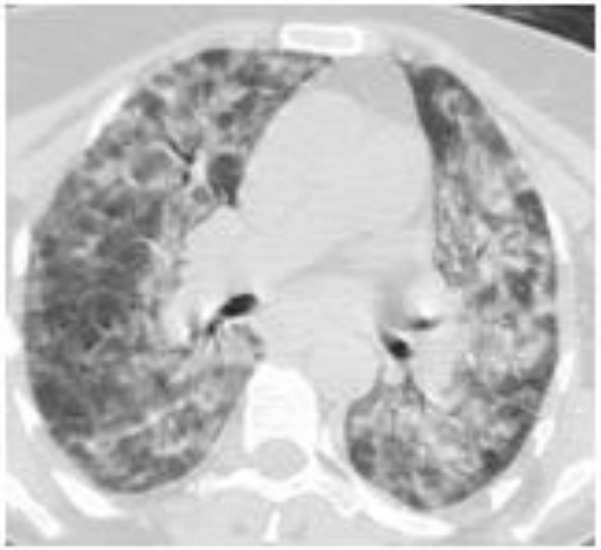

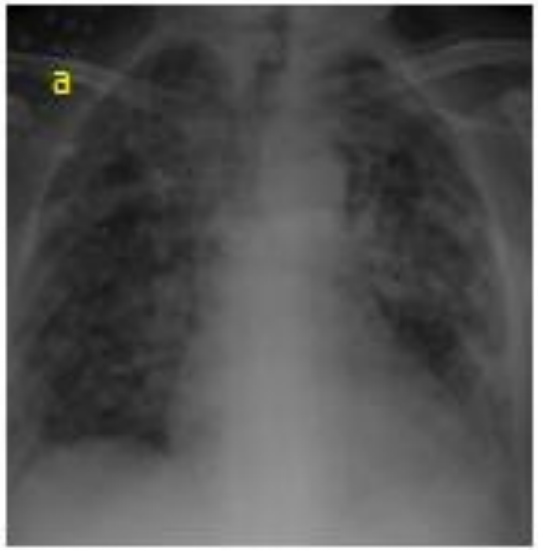
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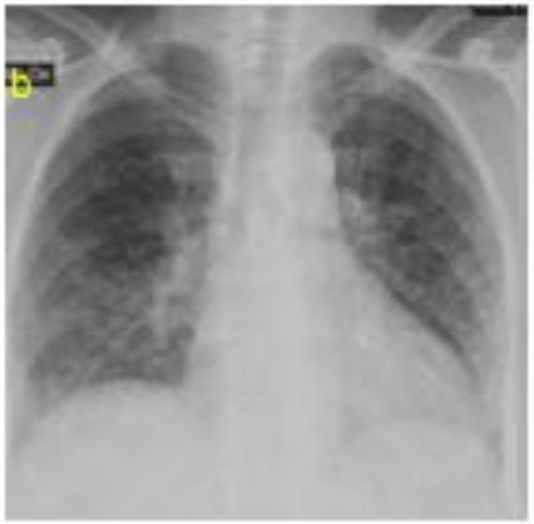

b

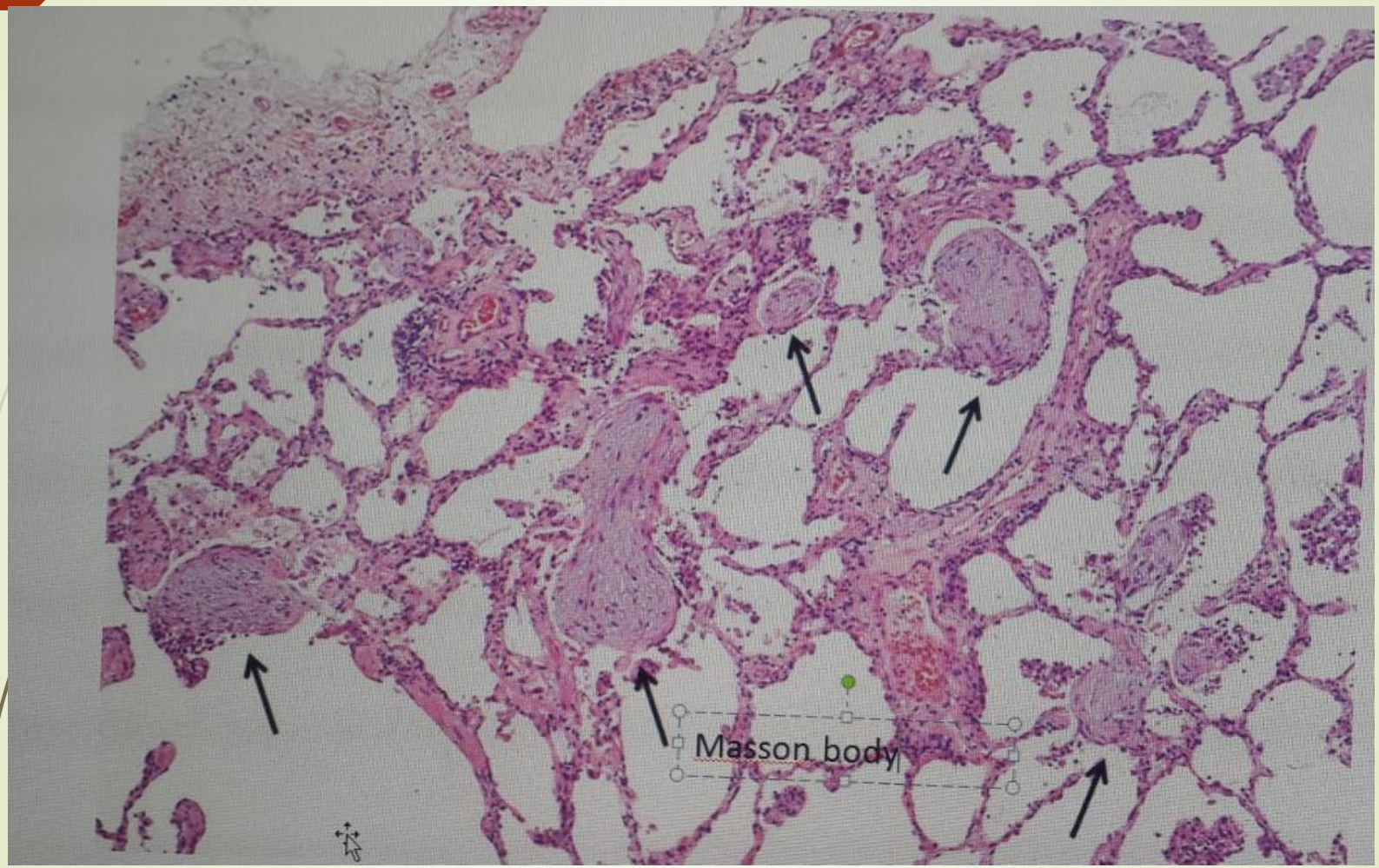
- SFT Diffüz KOP'lu hastalarda restriktif paternde
- Diffüzyon kapasitesinde genellikle azalma izlenir
- 6 dk yürüme testinde desatürasyon görülür
- Semptomatik olguların hemen hepsinde arteriyel hipoksemi mevcuttur

- FOB-BAL'da "mixed-patern": lenfositte artış (%20-40), nötrofil (%10), eozinofil (%5-10)
- FOB-BAL ile diğer hastalıkların dışlanması için gereklidir (enfeksiyon, malignite, alveoler hemoraji….)
- CD4/CD8 oranı azalır (CD8 artar)
- BAL'da lenfosit azlığı kötü prognoz kriteridir

Handra D, Hershberger DM. Pneumonia, Cryptogenic Organizing. 2018 Oct 27.StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-.Available from http://www.ncbi.nlm.nih.gov/books/NBK507874

- Tanıda akciğer biyopsisi altın standarttır
- Ancak yüksek HRCT destekli transbronşiyal biyopsiyle de tanısal örnek elde etme şansı yüksek
- Periferik lezyonlarda BT eşliğinde biyopsi de uygun tanısal yaklaşımdır

- Akciğer biyopsisinde, alveol yapısı korunmuş olmasına karşılık alveol duvarı lenfosit, makrofaj, plasma hücresi, nötrofil , eozinofil gibi çeşitli hücrelerle infiltre olabilir
- Fibroblastlar, kollajen ve fibrinli eksudanın oluşturduğu granülasyon dokusu tomurcuklarının görülmesi ile tanı konmaktadır (Masson bady)


Masson body

TEDAVİ:

- Standart tedavi: 6-12 ay süre ile kortikosteroiddir
- Bazı hastalar birbirini izleyen relapslar gösterdikleri için daha uzun tedaviye gereksinim duyabilmektedir.
- Klinik birkaç gün içinde düzelirken radyolojik düzelme birkaç haftada ortaya çıkar

Proposed Therapeutic Regimen for Typical Cryptogenic Organizing Pneumonia

Step	Duration (weeks)	Doses of Prednisone
Treatment of initial episode		
1	4	0.75 mg/kg/d
2	4	0.5 mg/kg/d
3	4	20 mg/d
4	6	10 mg/d
5	6	5 mg/d
Treatment of relapse		
1	12	20 mg/d
2	6	10 mg/d
3	6	5 mg/d

Cottin V, Cordier JF. Cryptogenic organizing pneumonia. Semin Respir Crit Care Med. 2012 Oct;33(5):462-75. Epub 2012 Sep 21

- Spontan remisyon hafif vakaların yaklaşık % 50'sinde görülür
- Hastalar tedaviye hızlı semptomatik yanıt gösterir ve % 80'e kadar tam iyileşme sağlanır
- Nüksler yaygındır ancak morbidite ve mortalite açısından önemli değildir

Nüks için risk fatörleri:

- Bilateral yaygın olması
- Traksiyon bronşektazi olması
- Steroide yanıtın yavaş yada parsiyel olması

Saito Z, Kaneko Y, Hasegawa T, Yoshida M, Odashima K, Horikiri T, Kinoshita A,Saitoh K, Kuwano K. Predictive factors for relapse of cryptogenic organizing pneumonia. BMC Pulm Med. 2019 Jan 9;19(1):10. doi: 10.1186/s12890-018-0764-8

- KOP nadiren ciddi ya da hızlı ilerler
- MV gereksinimi gösteren bazı ağır olguların kortikosteroid tedavisiyle tamamen düzelebildiği gösterilmiştir

Kötü prognostik özellikler:

- Radyolojik olarak interstisyel fibrozis bulgularının olması
- Eşlik eden hastalık varlığı
- Histopatolojik bulgular arasında organize pnömoni yanında akciğer parankiminde skar ve yeniden yapılanmanın görülmesidir

Cottin V, Cordier JF. Cryptogenic organizing pneumonia. Semin Respir Crit Care Med. 2012 Oct;33(5):462-75

PLoS One. 2017 Sep 25;12(9):e0184739. doi: 10.1371/journal.pone.0184739. eCollection 2017.

Cryptogenic organizing pneumonia-Results of treatment with clarithromycin versus corticosteroids-Observational study.

Radzikowska E[1], Wiatr E[1], Langfort R[2], Bestry I[3], Skoczylas A[4], Szczepulska-Wójcik E[2], Gawryluk D[1], Rudziński P[5], Chorostowska-Wynimko J[6], Roszkowski-Śliż K[1].

Author information

Abstract

BACKGROUND: Cryptogenic organizing pneumonia (COP) is a clinicopathological syndrome of unknown origin. Corticosteroids are the standard treatment, but clarithromycin (CAM) is also effective. The aim of this observational retrospective study was to compare the results of CAM versus prednisone (PRE) treatment in patients with biopsy-proven OP without respiratory insufficiency.

MATERIAL AND METHODS: In a 15-year period, 40 patients were treated with CAM (500 mg twice daily orally for 3 months) and 22 with PRE (mean initial dose of 0.67 ± 0.24 mg/kg/d for a mean of 8.59 ± 3.05 months).

RESULTS: The clinical presentation, laboratory, and radiological findings did not differ markedly between patients treated with CAM and PRE, with the exception of a higher frequency of sweats (55% vs. 23%; $p < 0.015$), ground glass opacities (95% vs. 50%; $p < 0.0001$) and nodular lesions (45% vs. 18%; $p = 0.036$) in the CAM group. A complete response was achieved in 35(88%) patients treated with CAM and in all treated with PRE. Patients treated with PRE relapsed more frequently than those treated with CAM (54.5% vs. 10%; $p < 0.0001$). Corticosteroid-related adverse events were noticed in 8(6.5%) patients (with one death), but CAM caused only one (2.5%) allergic reaction. A FVC >80% identified patients who might be successfully treated with CAM with a sensitivity of 60% and a specificity of 88.57% (AUC 0.869; 95% CI 0.684-1; $p = 0.008$); the figures for the FEV1 were >70%, a sensitivity of 60%, and a specificity of 91.43% (AUC 0.809; 95%CI 0.609-1; $p = 0.027$).

CONCLUSIONS: CAM can be used to treat COP patients in whom the pulmonary function parameters are within normal limits. Such therapy is shorter, better tolerated, and associated with fewer adverse events and relapses than is PRE. However, the therapy is ineffective in some patients.

Sonuç

- Antibiyotik tedavisine rağmen iyileşmeyen pnömoni semptomları ile birlikte kalıcı pulmoner opasiteler, KOP için şüphe uyandırmalıdır
- COP tanısı konmadan önce sekonder nedenlerin kesin araştırması yapılmalıdır

AYIRICI TANI

Multiple patchy alveolar opacities (typical COP)	Eosinophilic pneumonia (especially chronic idiopathic) Pneumonic-type alveolar cell adenocarcinoma of the lung Primary pulmonary lymphoma (low-grade B cell lymphoma of the mucosa-associated lymphoid tissue) Aspiration pneumonia Others: infectious pneumonia; tuberculosis or nontuberculous mycobacterial infection; granulomatosis with polyangiitis (Wegener's); diffuse alveolar hemorrhage; multiple infarction
Solitary focal nodule or mass (focal COP)	Lung carcinoma Round pneumonia or abscess Inflammatory pseudotumors Others: all causes of coin lesions or masses
Diffuse infiltrative opacities (progressive/fibrosing COP)	Idiopathic interstitial pneumonias, especially nonspecific interstitial pneumonia and acute exacerbation of idiopathic pulmonary fibrosis Interstitial pneumonias overlapping with organizing pneumonia Others: all causes of infiltrative opacities especially of infectious or neoplastic origin

TEŞEKKÜRLER