Sjogren Sendromu: Pulmoner Tutulum

Dr. Gökhan Keser

Ege İç Hastalıkları Romatoloji

VII. Aydın Romatoloji Günleri

15 Ekim 2022

Bu sunumla ilgili olarak,
herhangi bir çıkar çatışmam yoktur.

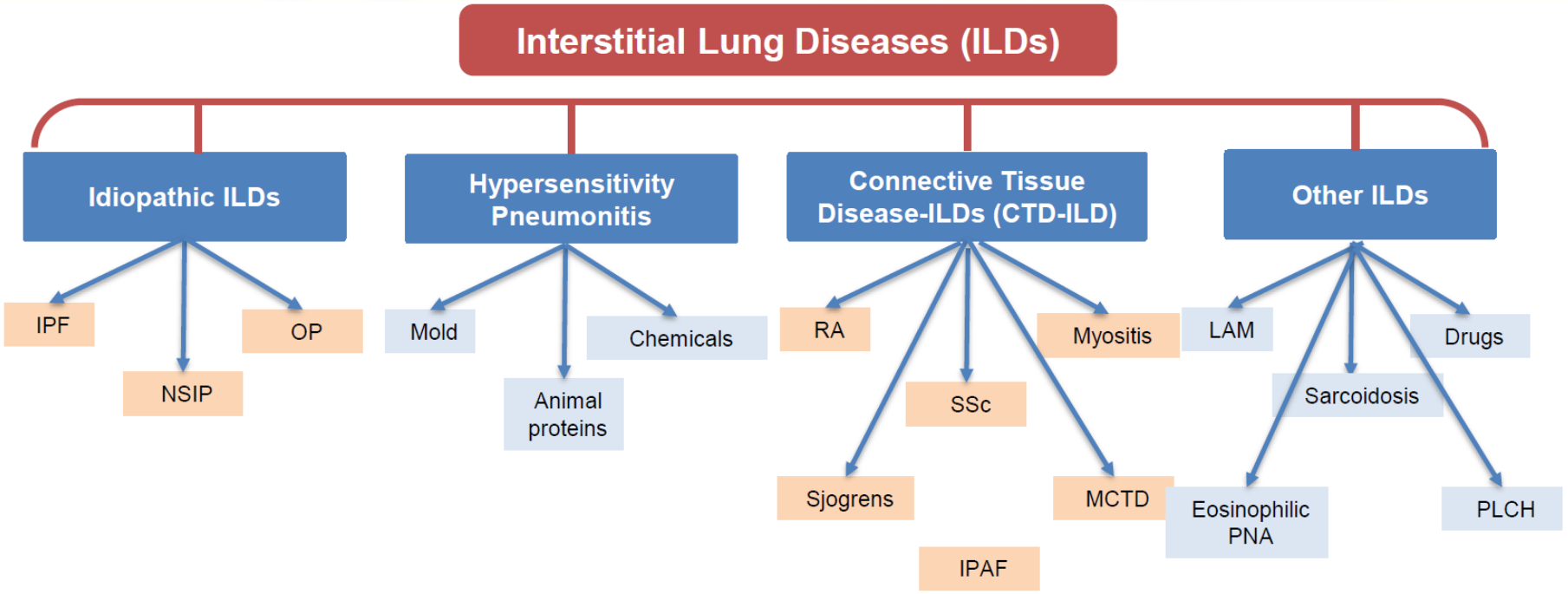
BDH seyrinde pulmoner etkilenme nasıl olabilir?

- **İmmun mekanizmalar üzerinden doğrudan akciğer tutulabilir**
  - Plevral tutuluş, kalınlaşma, plörezi
  - Havayolu tutuluşu
    - Üst hava yolları (krikoaritenoid ve trakeal etkilenme)
    - Alt hava yolları (bronşiyektazi, bronşiyolit)
  - Vasküler (Pulmoner Arteriyel Hipertansiyon, Vaskülit
  - Pulmoner parankim tutuluşu
    - **İntersisyel Akciğer Hastalığı (ILD)**
    - Diffüz Alveolar Hemoraji
    - Akut pneumonitis
    - Romatoid Nodül
- **Tedavide kullanılan ilaçlara bağlı pulmoner toksisite gelişebilir**
- **İS tedavi zemininde enfeksiyonlar akciğeri tutabilir.**
- **Diğer mekanizmalar**
  - Miyopati zemininde hipoventilasyon
  - Kardiyak tutuluşa (KAH, kardiyomiyopati…) sekonder pulmoner etkilenme
  - Pulmoner tromboemboli (aFL sendromu….)
  - Sekonder malignite

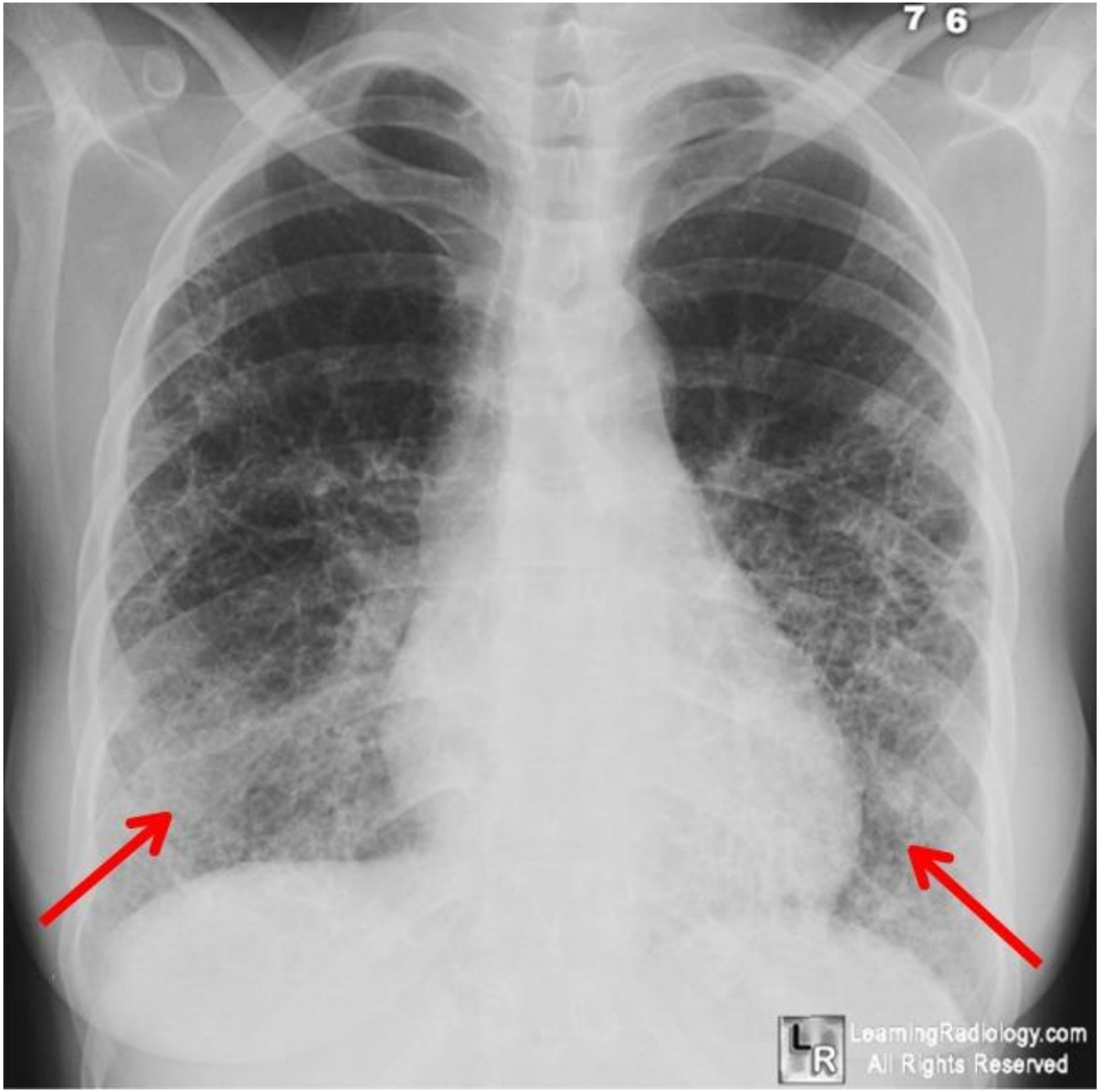
De Lauretis A, et al: *Chronic Respiratory Disease 2011 8: 53*

- Pulmoner intersisyum
- Büyük ve küçük hava yolları
- Plevra
- Pulmoner damarlar

Birden fazla kompartmanda tutuluş olması, BDH pulmoner tutuluş için bir ip ucu olabilir.



Travis WD et al. *Am J Respir Crit Care Med.* 2013;188(6):733-748.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BDH zemininde en sık görülen pulmoner tutuluş örnekleri

Table 1. Pattern of respiratory involvement in connective tissue disease

	Airways	Pleura	PAH	Muscle	ILD	ILD pattern
SSc	−/+	−/+	+++	−	+++++	NSIP>>>UIP
RA	++++	+++	−/+	−	++	UIP>NSIP>OP=DAD
PM/DM	−/+	−	−/+	++	++++	NSIP=OP>DAD>UIP
Sjögren's	+++++	−/+	+	−/+	+++	NSIP>LIP>OP=UIP=DAD
SLE	−/+	++++	++	+	+	NSIP>DAD=LIP=OP=UIP

Abbreviations: SSc: systemic sclerosis, RA: rheumatoid arthritis, PM/DM: polymyositis/dermatomyositis, SjS: Sjögren's syndrome, SLE: systemic lupus erythematosus, NSIP: non-specific interstitial pneumonia, UIP: usual interstitial pneumonia, OP: organizing pneumonia, DAD: diffuse alveolar damage, LIP: lymphocytic interstitial pneumonia.

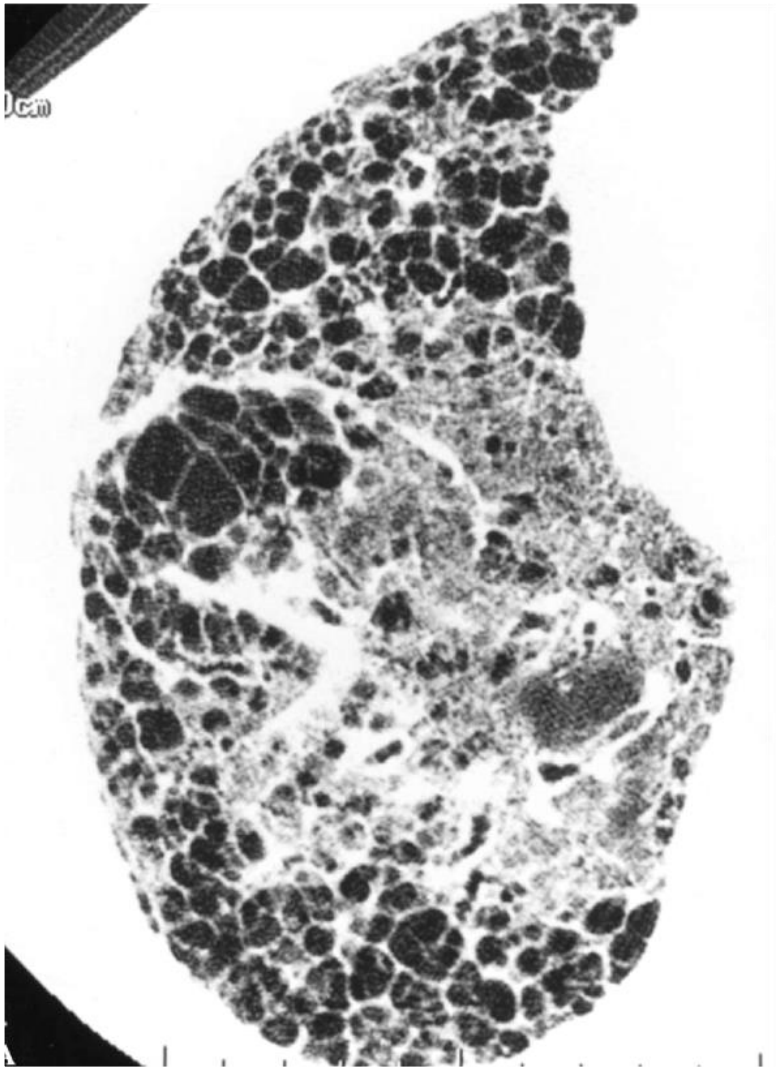
de Lauretis A et al: *Chronic Respiratory Disease 2011 8: 53*

- Rheumatoid arthritis (RA): 10-58%
- Systemic sclerosis (SSc): >65%
- Sjogren's syndrome: 25%
- Dermatomyositis/Polymyositis: 23-65%
- Systemic lupus erythematosus (SLE): 3-13%
- Mixed connective tissue disease (MCTD): 18-66%

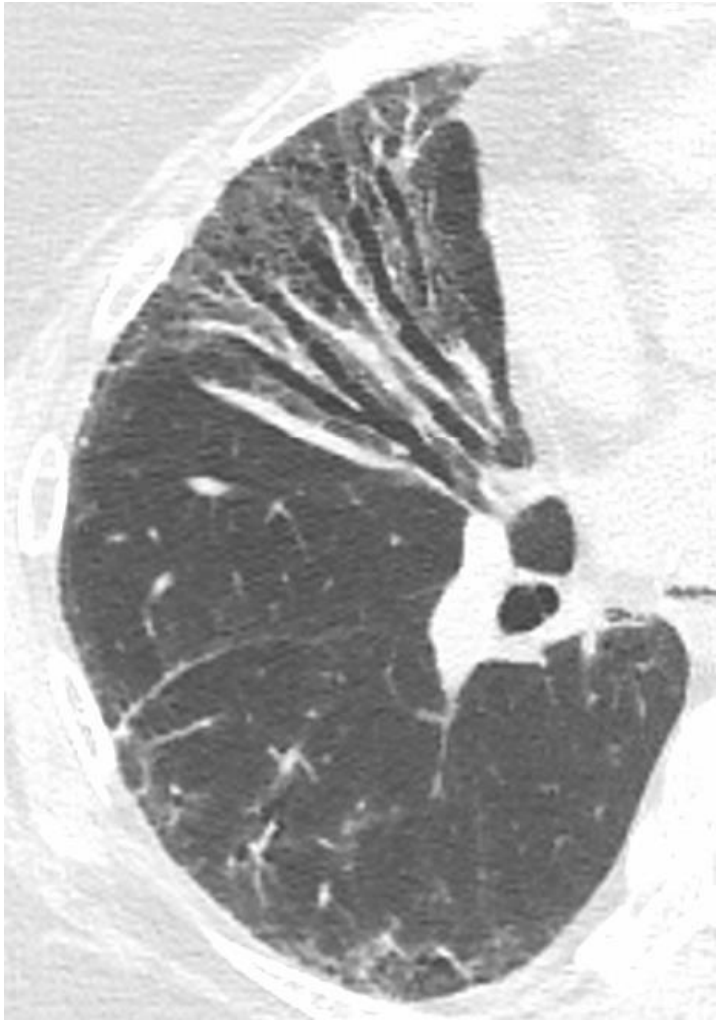
NSIP versus UIP

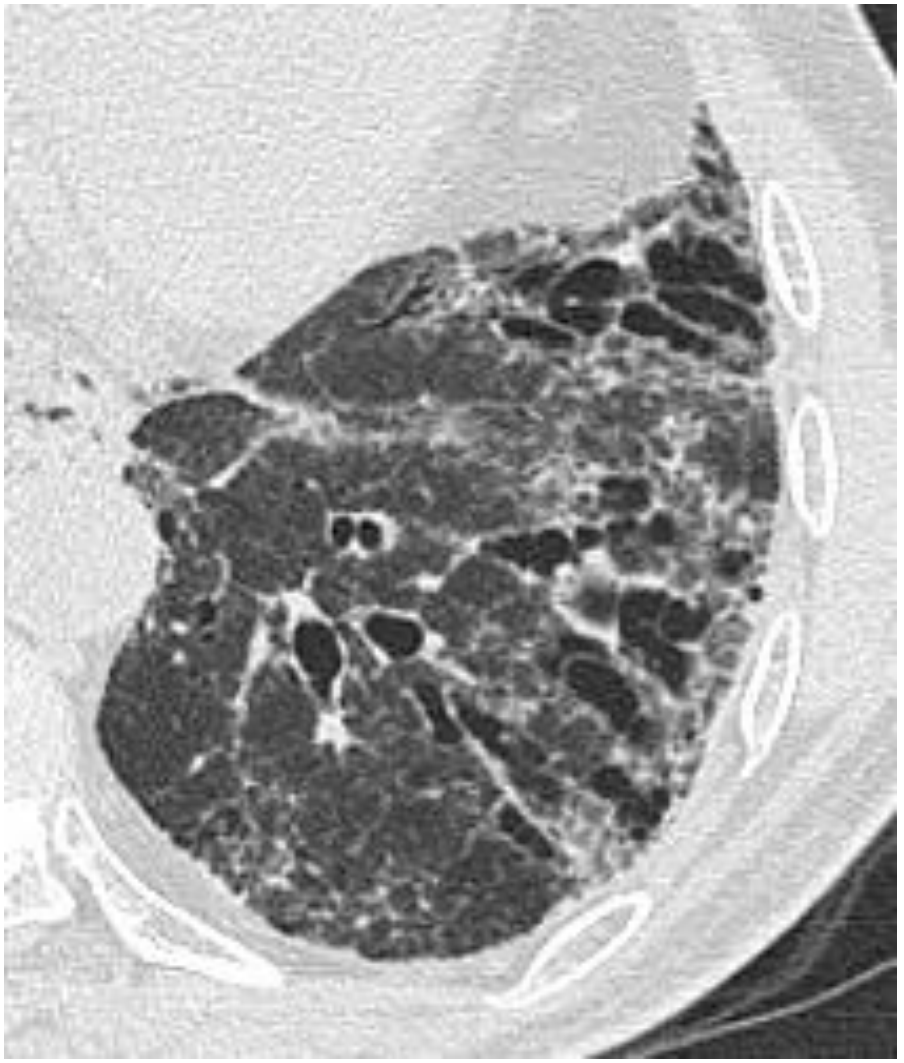
- **Non-Spesifik İntersisyel Pnömoni (NSIP)**
  - RA dışında tüm BDH'larında en sık görülen tip
  - Tipik özellik buzlu cam manzarası
  - Bal peteği görünümü az veya yok.
- **"Usual Interstitial Pneumonia" (UIP)**
  - IPF'in tipik histolojisi
  - RA'te en sık görülen tip
  - Tipik özellik bal peteği akciğer; buzlu cam manzarası yok;
  - Genelde kötü prognoz; ancak BDH zemininde ise daha iyi prognoz

Balpeteği nedir?

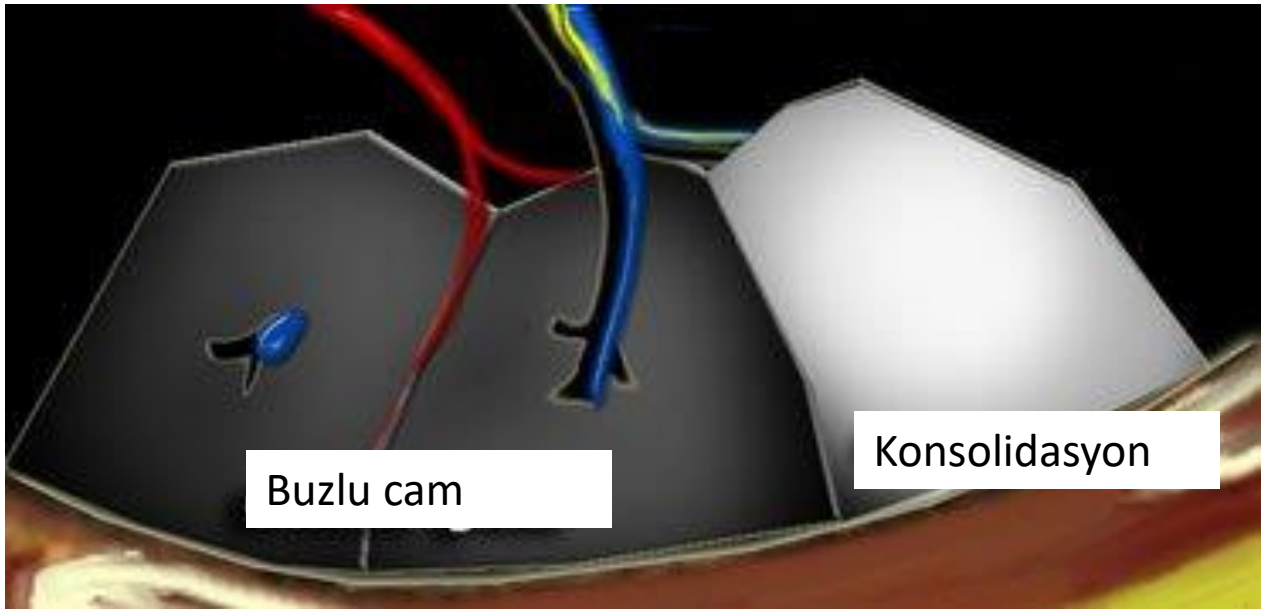


Traksiyon Bronşektazisi nedir?





Buzlu cam nedir?

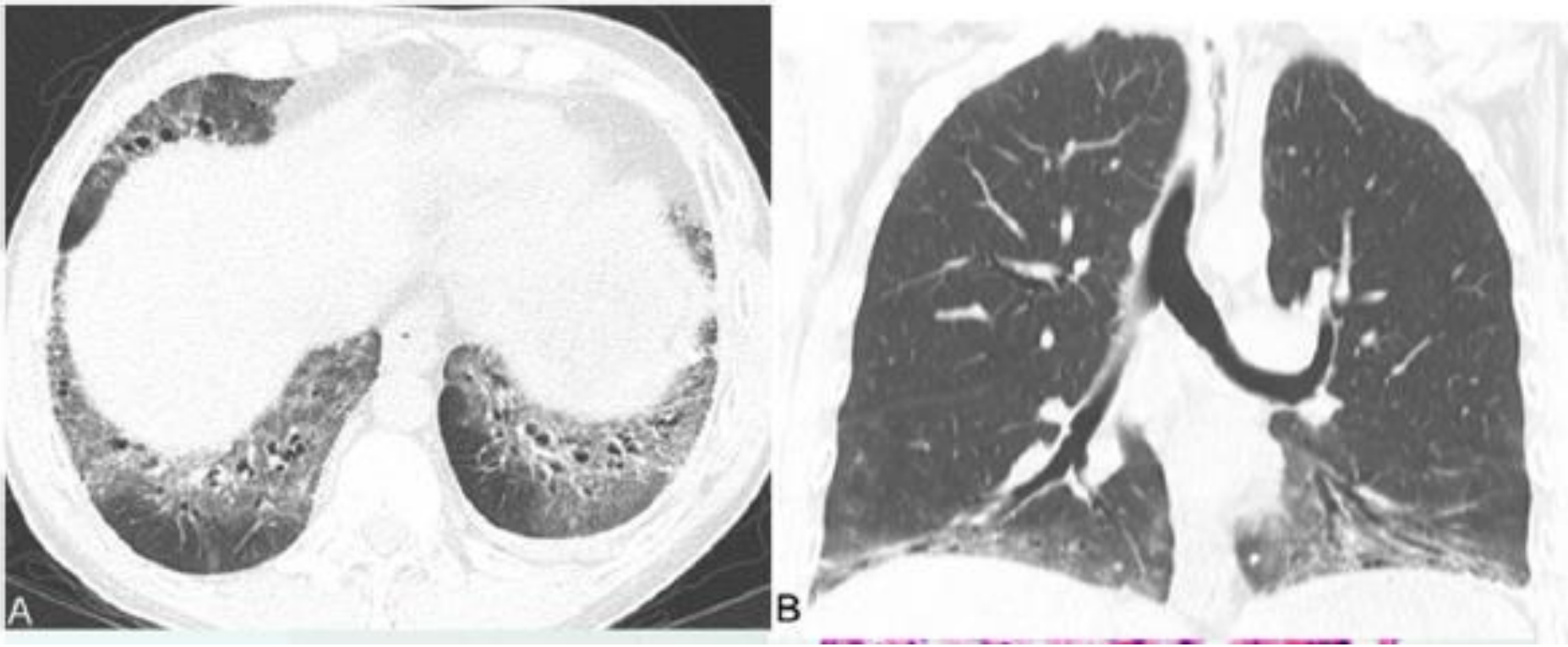


BUZLU CAM İLE KONSOLİDASYONUN FARKI ?

Buzlu cam dansitesinde artan dansite normal anatomiyi tamamen silmez ve içinde vasküler yapılar seçilebilir. Konsolidasyon ise normal anatomiyi tamamen siler

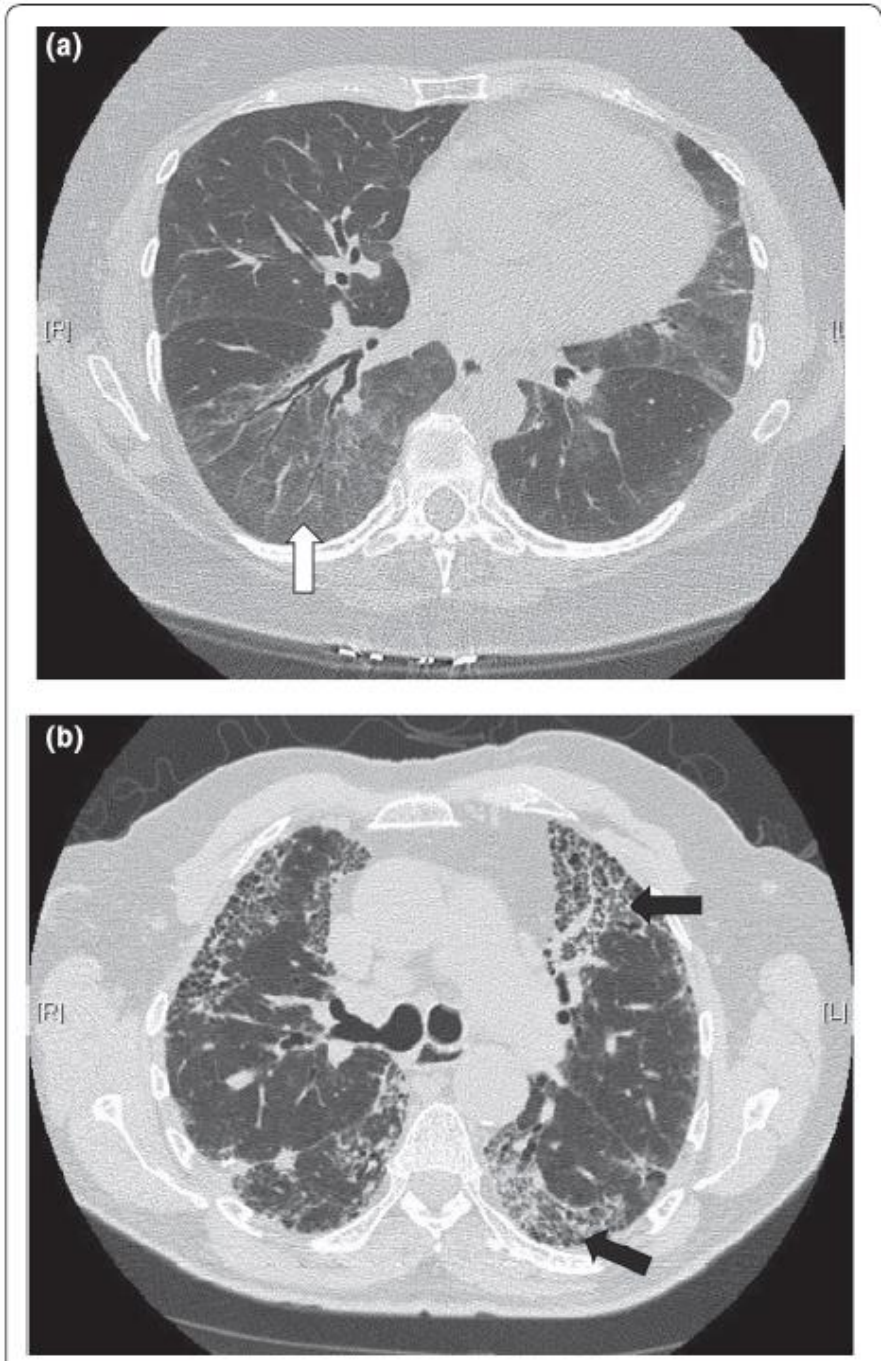
NSIP

RA dışında tüm BDH'larında en sık görülen tip



Yaygın bilateral alt lob buzlu cam opasiteleri ve belirgin traksiyon bronşiyektazileri; subplevral alan korunmuş; peribronkovasküler yerleşim ön planda
Diffüz alveoler duvar kalınlaşması ve fibrozis; alveoler mimari korunuyor; balpeteği ve fibroblastik foküs yok; intersisyel inflamasyon hafif

Travis WD, et al. Am J Respir Crit Care Med, 2013



NSIP

NSIP traksiyon bronşyektazileri , bal peteği AC görünümü ile karışmamalı !

UIP

Castelino FV, Varga J: *Arthritis Research & Therapy 2010, 12:213.*

LIP

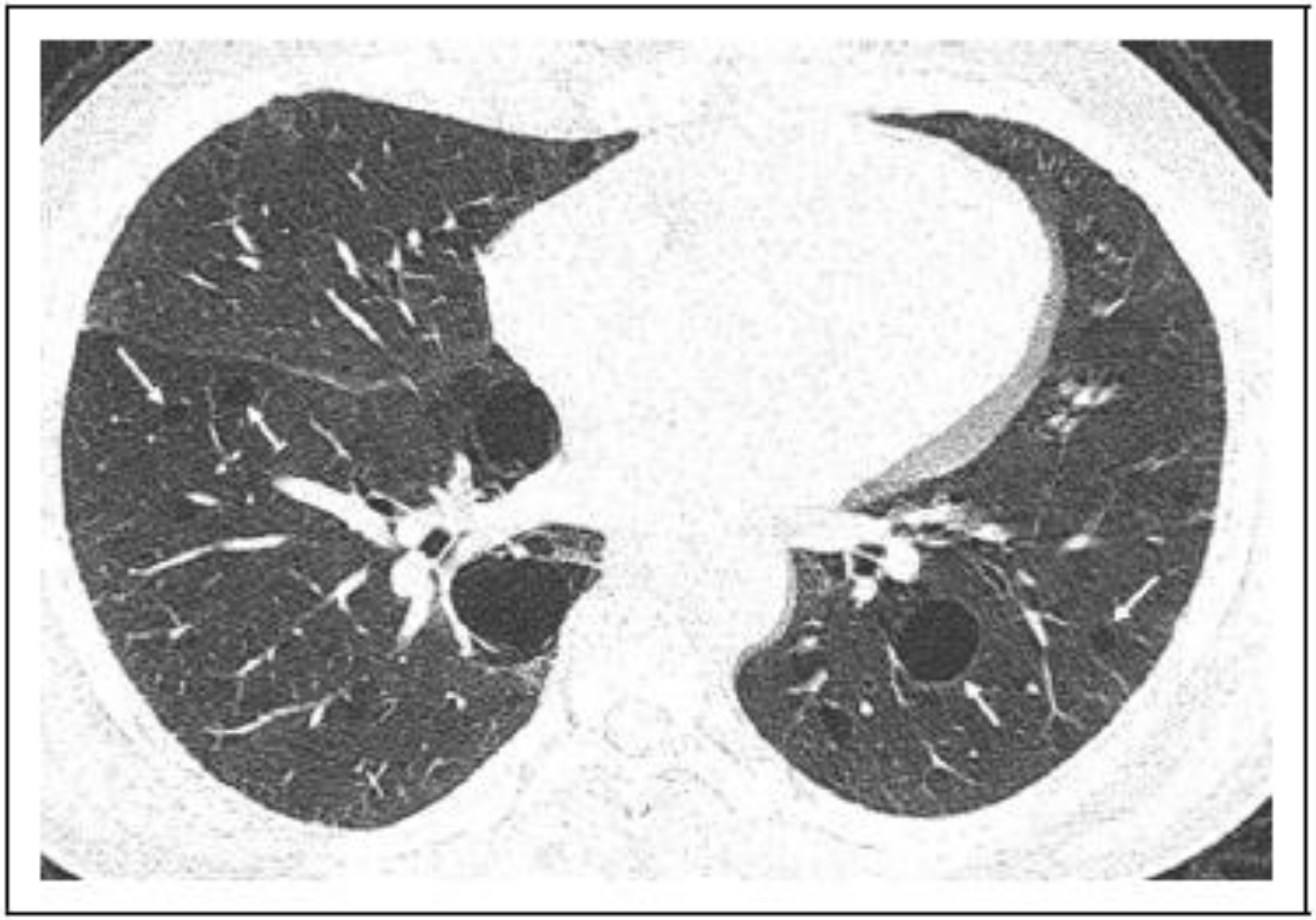


Figure 5. CT of a 51-year-old patient with Sjögren's syndrome showing scattered cysts of varying sizes (arrows) and the suggestion of a mild increase in background attenuation consistent with lymphocytic interstitial pneumonia.

Lauretis et al: ***Chronic Respiratory Disease, 2011***

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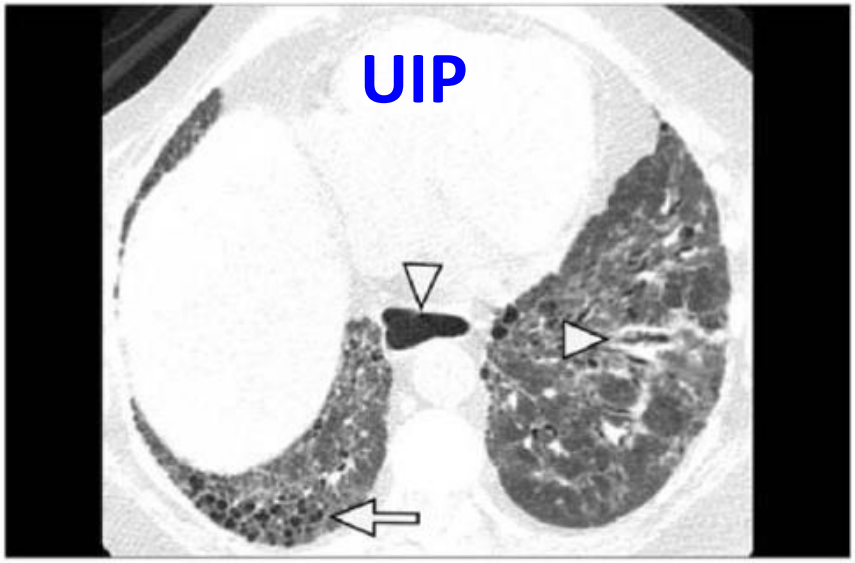
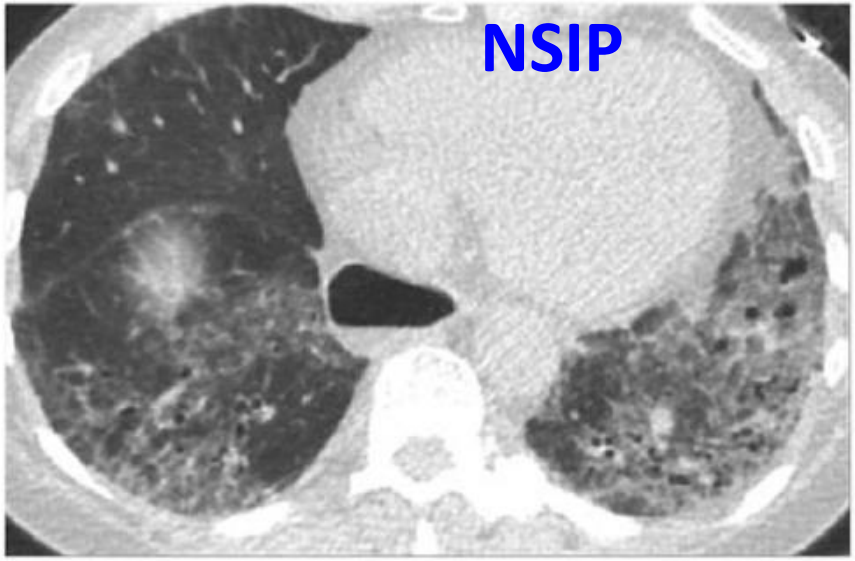
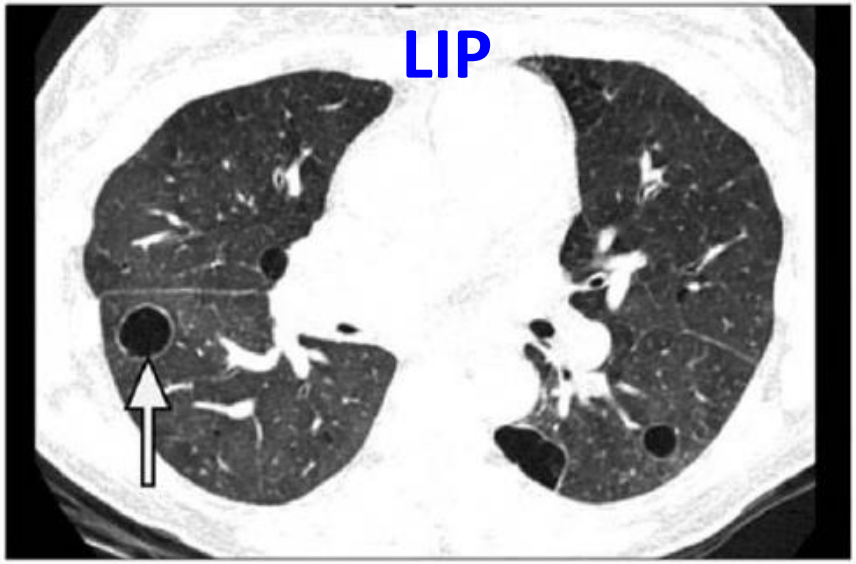


A



B



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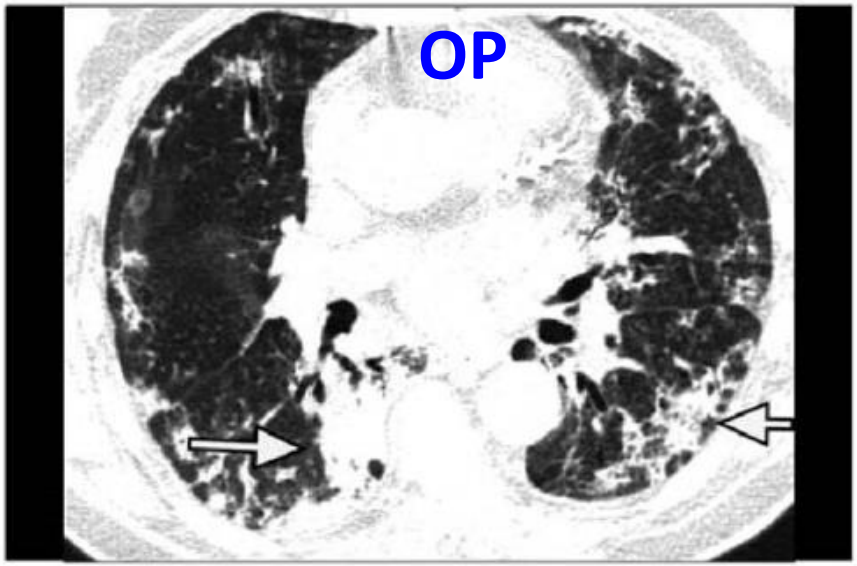

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Wallace et al, Curr Opin Rheumatol 2016

Lin et al. BMC Pulmonary Medicine (2022) 22:73
https://doi.org/10.1186/s12890-022-01868-5

BMC Pulmonary Medicine

RESEARCH Open Access

Interstitial lung disease in Primary Sjögren's syndrome

Wei Lin[1†], Zhifei Xin[2†], Jianlong Zhang[3†], Ning Liu[1], Xiuying Ren[1], Meilu Liu[1], Yashuang Su[1], Yixuan Liu[1], Liu Yang[1], Shaoying Guo[1], Yupeng Yang[4], Yang Li[5], Jingjing Cao[1], Xiaoran Ning[1], Jingjing Li[1], He Xue[1], Nannan Niu[1], Yingmin Chen[3], Fang Li[1], Lijun Sun[1*], Xiaopeng Zhang[2*], Fengxiao Zhang[1] and Wen Zhang[6]

- 333 pSjS olgusu; retrospektif analiz; 66 olguda İAH (%19.82)
- En sık AC HRCT bulguları: Buzlu cam (%87.9) ve septal/sub pleval çizgi (%81.8)
- NSIP (n = 42), UIP (n = 20), LIP (n = 3), Kriptojenik organize pnömoni (n = 1)
- Sedim/CRP ile HRCT skoru korele
- İAH Risk Faktörleri:
  - Yaş, Raynaud, lenfopeni, öksürük, dispne, diş çürükleri

frontiers in Immunology

REVIEW
published: 12 June 2019
doi: 10.3389/fimmu.2019.01327

Pulmonary Manifestations of Primary Sjögren's Syndrome: Underlying Immunological Mechanisms, Clinical Presentation, and Management

*Sarthak Gupta†, Marcela A. Ferrada† and Sarfaraz A. Hasni**

- pSjS klinik anlamlı pulmoner tutuluş prevalansı %9-20
- Çok kapsamlı incelemeler: %43-75 !!!
- AC BT taraması: %34-50 olguda pozitif bulgu
- Tanı sonrası 1 yıl içinde %10 olguda; 5 yıl içinde %20 olguda

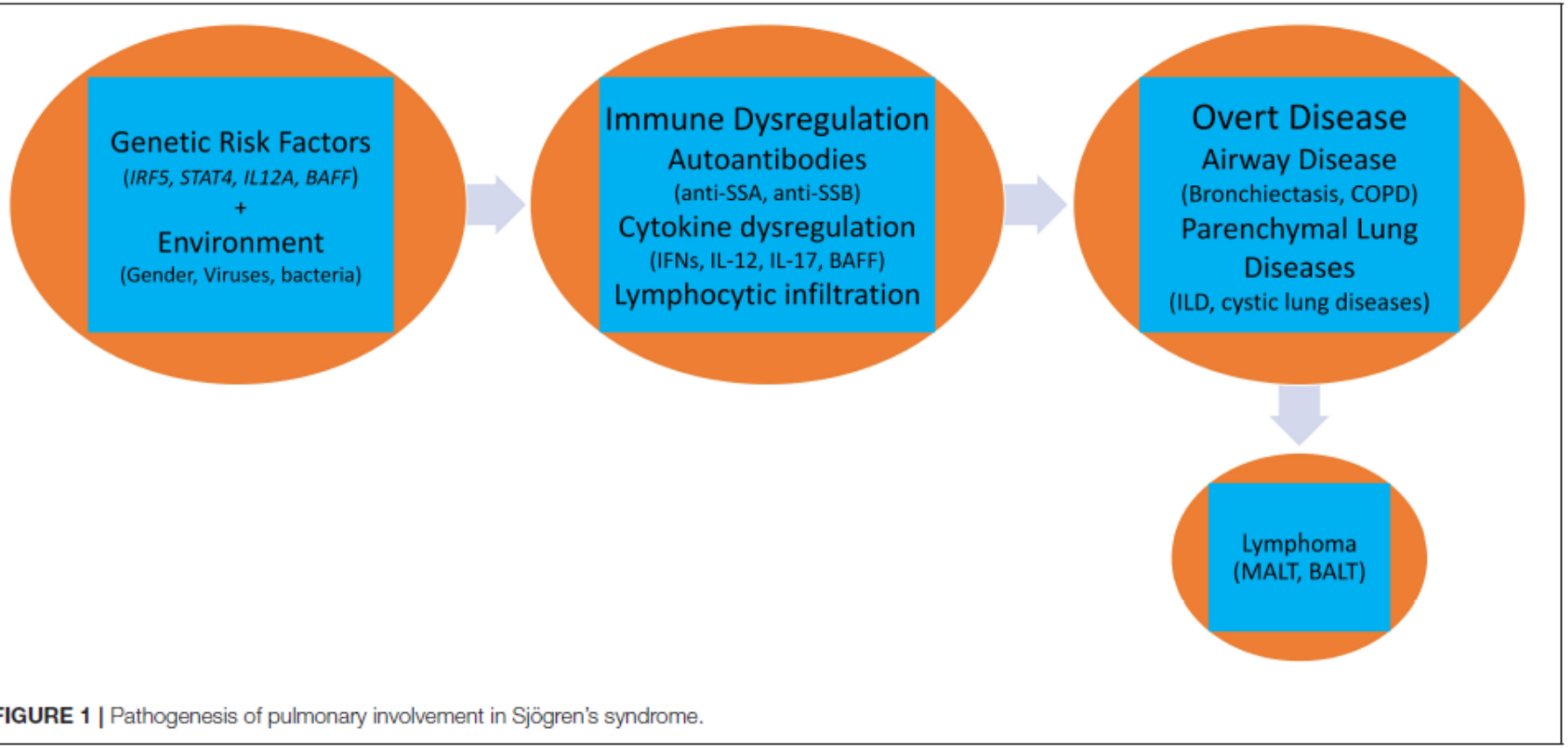


FIGURE 1 | Pathogenesis of pulmonary involvement in Sjögren's syndrome.

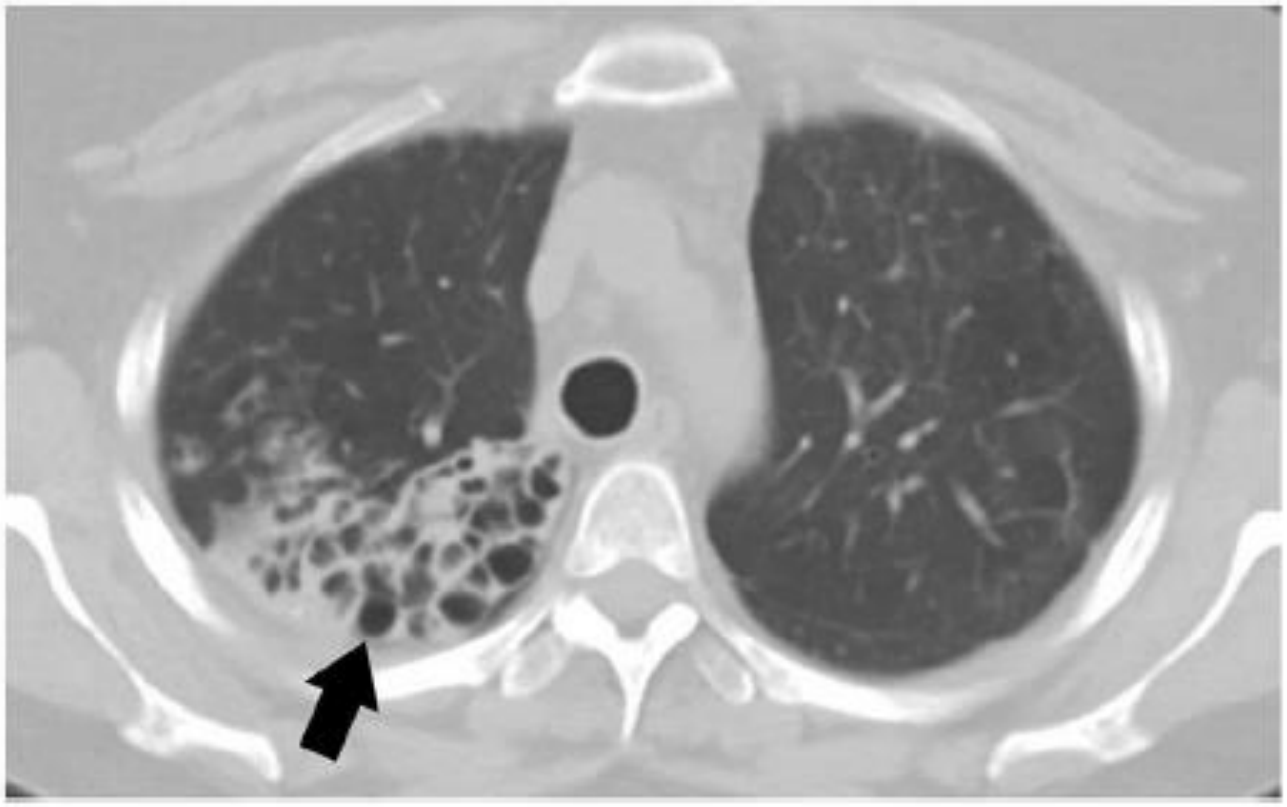


FIGURE 2 | CT scan of a 44-year-old female with primary Sjögren's syndrome demonstrating bronchiectasis on the right lower lobe.

Pulmonary manifestations of Sjögren's syndrome

Thomas Flament[1], Adrien Bigot[2], Benjamin Chaigne[2], Helene Henique[1,2,3,4], Elisabeth Diot[2] and Sylvain Marchand-Adam[1,3,4]

Thoracic manifestations	Prevalence	Peculiar aspects in Sjögren's syndrome	Treatment
Airway disease			
Cough	41–61%#		Secretagogues (pilocarpine) Nebulised saline solution
BHR	42–60%#		Inhaled corticosteroids
Bronchiolitis	12–24%#	Mainly follicular bronchiolitis	Steroids Rituximab Macrolides
Bronchiectasis	7–54%#	Mainly cylindrical bronchiectasis	
Pulmonary infections	10–35%#		

Flament T, et al. Eur Respir Rev 2016; 25: 110–123

Interstitial lung disease			
Nonspecific interstitial pneumonia	45%[¶]		Steroids Hydroxychloroquine Azathioprine Cyclophosphamide Rituximab
Usual interstitial pneumonia	16%[¶]		No benefit of immunosuppressive drugs
Lymphocytic interstitial pneumonitis	15%[¶]		Steroids Azathioprine Cyclophosphamide Chlorambucil Rituximab
Organising pneumonitis	11%[#]		Steroids Azathioprine Cyclosporine Infliximab Rituximab Tocilizumab
Others pulmonary manifestations in Sjögren's syndrome			
Pulmonary amyloidosis	Rare	96.5% female	Steroids
Pulmonary lymphoma	2%[¶]		Specific haematological treatment
Pulmonary embolism and pulmonary hypertension	Rare	Risk of venous thrombosis or pulmonary embolism in Sjögren's syndrome patients is greater than in the general population	

Flament T, et al. Eur Respir Rev 2016; 25: 110–123

frontiers in Medicine

BRIEF RESEARCH REPORT
published: 16 July 2020
doi: 10.3389/fmed.2020.00332

!!!!!!!!

Lung Involvement in Primary Sjögren's Syndrome—An Under-Diagnosed Entity

Georgios Sogkas[1†], Stefanie Hirsch[1†], Karen Maria Olsson[2,3], Jan B. Hinrichs[4], Thea Thiele[1], Tabea Seeliger[5], Thomas Skripuletz[5], Reinhold Ernst Schmidt[1], Torsten Witte[1], Alexandra Jablonka[1†] and Diana Ernst[1†]*

and non-specific-ILD. Lung involvement was confirmed in 31/268 pSS patients (13%). One-third (10/31) of pSS-ILD patients were Ro/SSA antibody negative. ILD at pSS diagnosis was present in 19/31 (61%) patients. The commonest phenotype was UIP $n = 13$ (43%), followed by NSIP $n = 9$ (29%), DIP $n = 2$ (6 %), CPFE $n = 2$ (6 %), and non-specific-ILD $n = 5$ (16%). Forced vital capacity (FVC) and carbon monoxide diffusion capacity (D_{LCO}) appeared lower in UIP and DIP, without reaching a significant difference.

BDH Olgusunda Pulmoner Tutuluş Tanısı

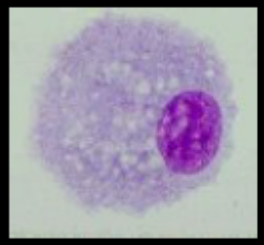
- Öykü ve FB
- PA AC grafisi
- DLco
- AC HRCT
- BAL ?

Erken Dönemde Tanı:

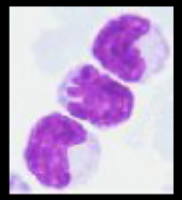
- AC HRCT bulguları
- Efor dispnesi
- DLCo bozukluğu
- Spirometrik anormallikler
- Direk grafi
- Semptomlar

- Surfactant protein D (SP-D) ve Krebs von den Lungen-6 (KL-6), tip II alveoler hc.lerde sunulan AC epitel hasarının göstergesi olan glikoproteinlerdir. Serum düzeylerine bakılabilir.
- İnhale 99mTc-DTPA'nın klirensi, epitel hasarı ve geçirgenliği hakkında fikir verebilir.

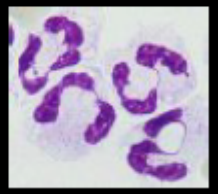
Cells normally present in BAL fluid



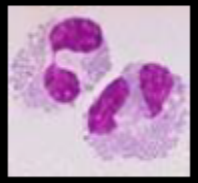
Alveolar macrophages (AMs): 80-90%



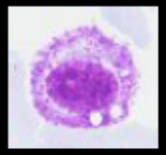
Lymphocytes (Lym): 5-15%



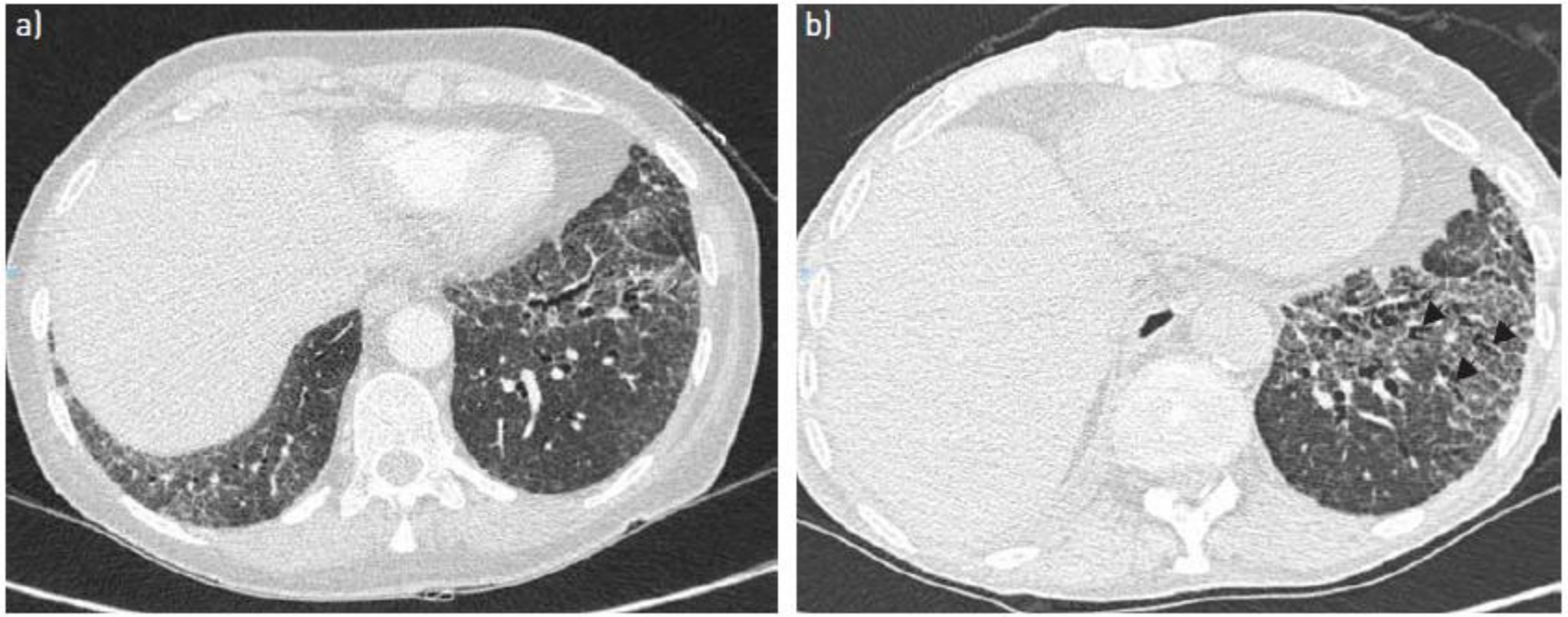
Neutrophils (PMNs): 1-4%



Eosinophils (Eos): < 3%



Mast cells (MC): < 1%



NSIP yeni tanı almış pSjS olgusunda ve üç yıl sonra

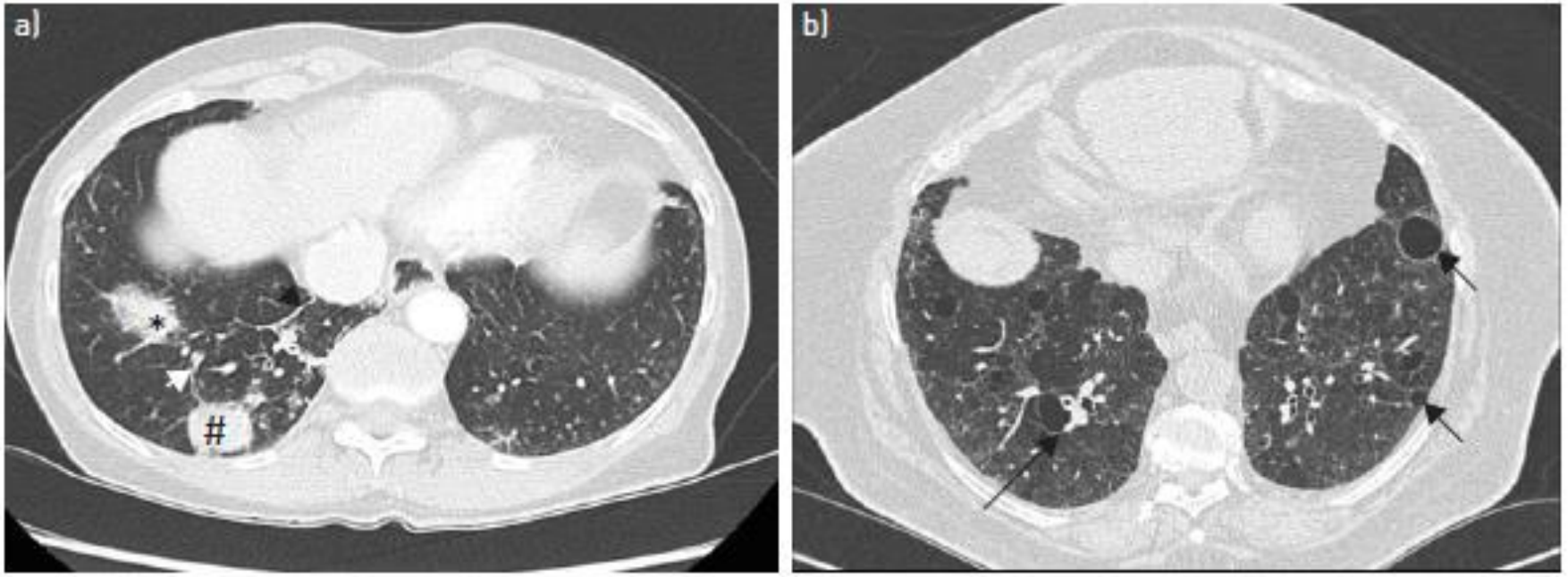


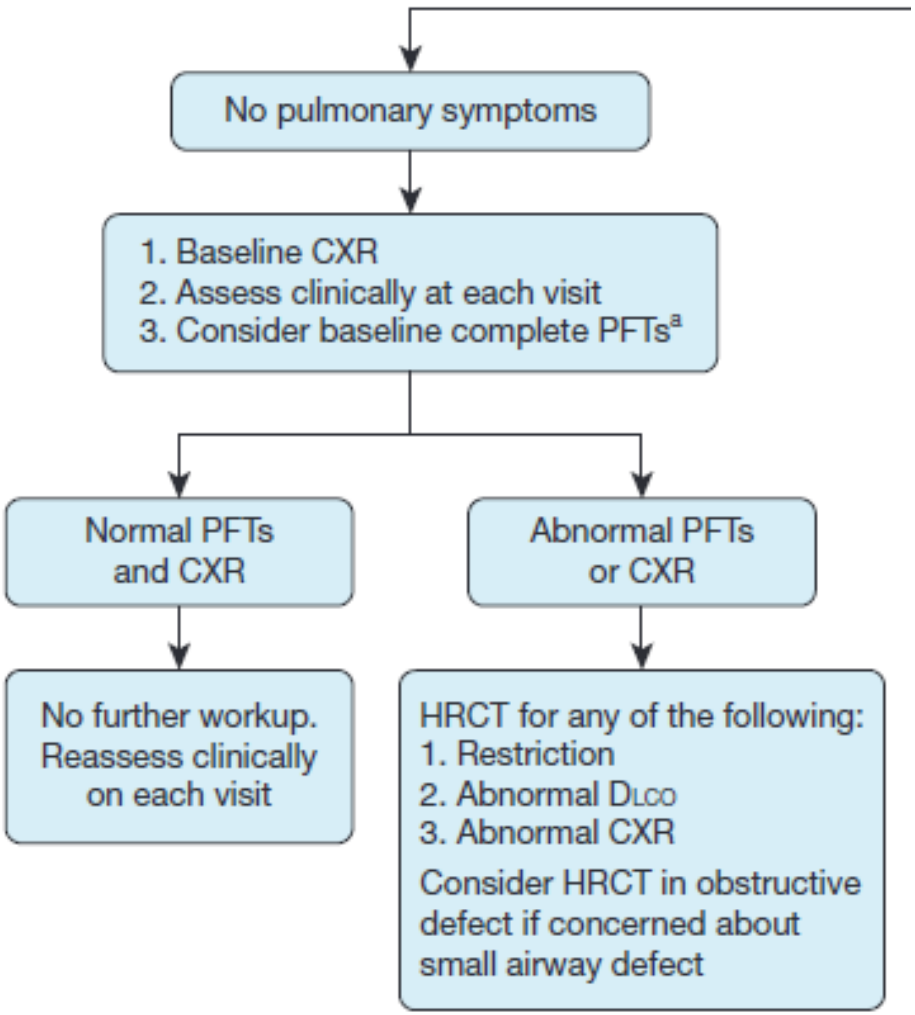
FIGURE 4 a) Mucosa-associated lymphoid tissue lymphoma in a 45-year-old woman with primary Sjögren's syndrome. High-resolution computed tomography (CT) shows air space consolidation (*), mass (#) and interlobular septal thickening (arrowheads) in the right lower lobe. b) High-resolution CT obtained in a 64-year-old woman with lymphocytic interstitial pneumonitis and primary Sjögren's syndrome shows well-defined, round, thin-walled air cysts in the peribronchovascular regions (arrows), and areas of ground-glass and reticular attenuation.

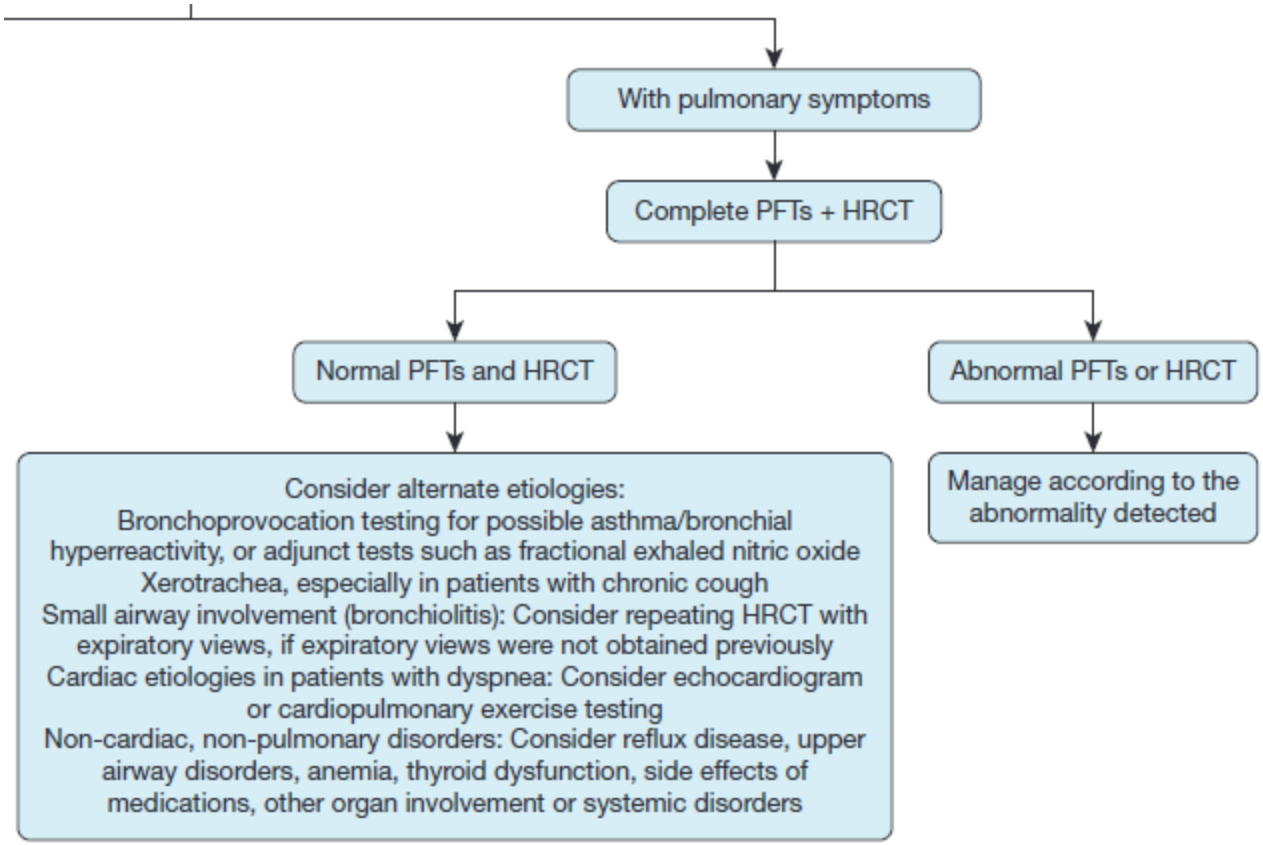
Flament T, et al. Eur Respir Rev 2016; 25: 110–123

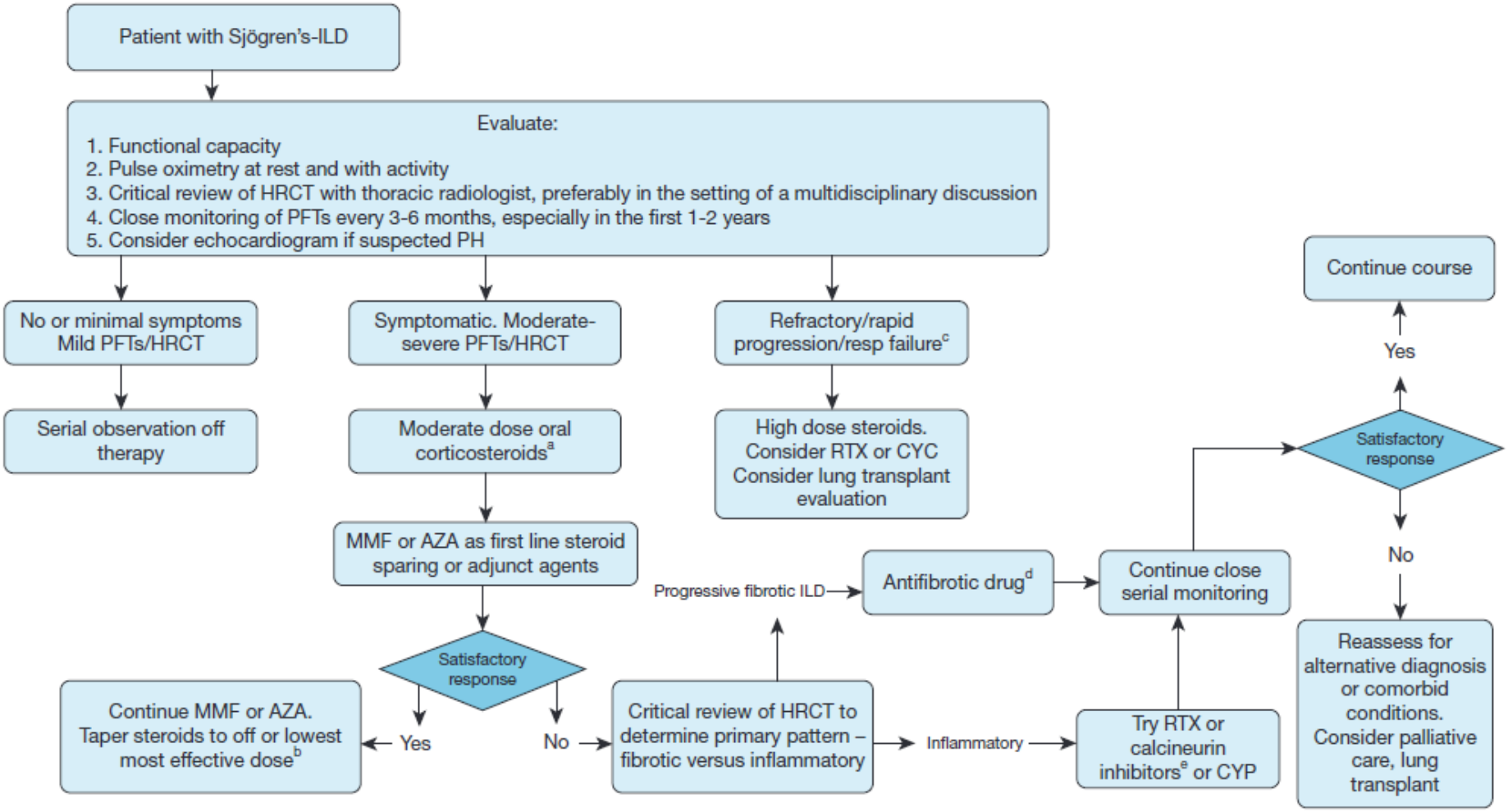
CHEST

Consensus Guidelines for Evaluation and Management of Pulmonary Disease in Sjögren's

*Augustine S. Lee, MD; R. Hal Scofield, MD; Katherine Morland Hammitt, MA; Nishant Gupta, MD; Donald E. Thomas, MD; Teng Moua, MD; Kamonpun Ussavarungsi, MD; E. William St Clair, MD; Richard Meeh Kieron Dunleavy, MD; Matt Makara, MPH; Steven E. Carsons, MD; Nancy L. Carteron, MD, in collaboration wit Consensus Expert Panel (CEP) Members**

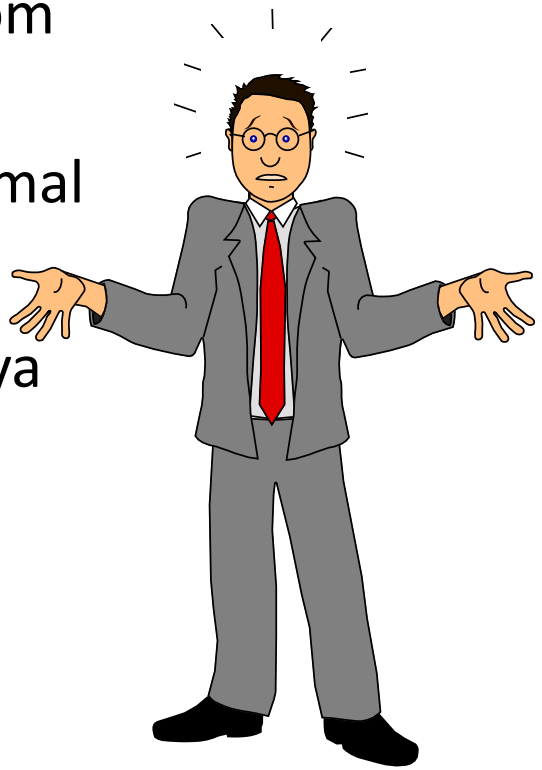



With pulmonary symptoms
Complete PFTs + HRCT
Normal PFTs and HRCT
Abnormal PFTs or HRCT
Consider alternate etiologies:
Bronchoprovocation testing for possible asthma/bronchial hyperreactivity, or adjunct tests such as fractional exhaled nitric oxide
Xerotrachea, especially in patients with chronic cough
Small airway involvement (bronchiolitis): Consider repeating HRCT with expiratory views, if expiratory views were not obtained previously
Cardiac etiologies in patients with dyspnea: Consider echocardiogram or cardiopulmonary exercise testing
Non-cardiac, non-pulmonary disorders: Consider reflux disease, upper airway disorders, anemia, thyroid dysfunction, side effects of medications, other organ involvement or systemic disorders
Manage according to the abnormality detected


Patient with Sjögren's-ILD
Evaluate:
1. Functional capacity
2. Pulse oximetry at rest and with activity
3. Critical review of HRCT with thoracic radiologist, preferably in the setting of a multidisciplinary discussion
4. Close monitoring of PFTs every 3-6 months, especially in the first 1-2 years
5. Consider echocardiogram if suspected PH
No or minimal symptoms Mild PFTs/HRCT
Symptomatic. Moderate-severe PFTs/HRCT
Refractory/rapid progression/resp failure[c]
Serial observation off therapy
Moderate dose oral corticosteroids[a]
High dose steroids. Consider RTX or CYC Consider lung transplant evaluation
MMF or AZA as first line steroid sparing or adjunct agents
Satisfactory response
Yes
No
Continue MMF or AZA. Taper steroids to off or lowest most effective dose[b]
Critical review of HRCT to determine primary pattern – fibrotic versus inflammatory
Progressive fibrotic ILD
Antifibrotic drug[d]
Inflammatory
Try RTX or calcineurin inhibitors[e] or CYP
Continue close serial monitoring
Satisfactory response
Yes
Continue course
No
Reassess for alternative diagnosis or comorbid conditions. Consider palliative care, lung transplant

Göğüs Hastalıkları'ndan Konsültasyon:

- Efor dispnesi ile gelen 55 yaşında kadın hastada, NSIP ile uyumlu AC HRCT bulguları var.
- Öyküde, fizik bakıda ve sistem sorgulamasında romatolojik bir hastalık ile uyumlu bir semptom veya bulgu yok.
- Biyokimya, hemogram, rutin idrar ve AFY normal
- Sadece ANA 1/320 titrede granüler pozitif
- Bu hastada SSc, SLE, AAV, RA, SjS, DM/PM veya MBDH tanısı konulamıyor.
- Yaklaşım ?



ERS/ATS TASK FORCE
INTERSTITIAL LUNG DISEASE

Eur Respir J 2015

An official European Respiratory Society/ American Thoracic Society research statement: interstitial pneumonia with autoimmune features

Aryeh Fischer[1,17,18], Katerina M. Antoniou[2], Kevin K. Brown[3], Jacques Cadranel[4], Tamera J. Corte[5,18], Roland M. du Bois[6], Joyce S. Lee[7,18], Kevin O. Leslie[8], David A. Lynch[9], Eric L. Matteson[10], Marta Mosca[11], Imre Noth[12], Luca Richeldi[13], Mary E. Strek[12,18], Jeffrey J. Swigris[3,18], Athol U. Wells[14], Sterling G. West[15], Harold R. Collard[7,18,19] and Vincent Cottin[16,18,19], on behalf of the "ERS/ATS Task Force on Undifferentiated Forms of CTD-ILD"

"autoimmune featured interstitial lung disease"
"undifferentiated connective tissue disease associated interstitial lung disease"
"lung-dominant connective tissue disease"

İlginiz için teşekkür ederim