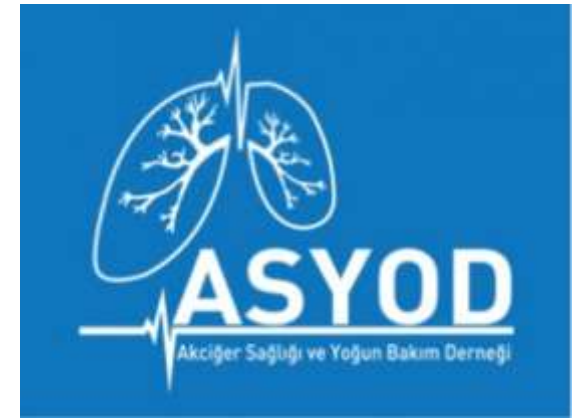




Interstitial Lung Disease - Case Discussion

Gamze KIRKIL

Firat University, Medicine Faculty

Chest Disease Department

Case-1

- 39 y, M
- Smoking history: 1 pack/day for 20 years, quit 2 years ago
- Occupation: Accountant
- Kept a budgerigar at home
- Medications: Lyrica
- Family history: Mother - breast cancer, father - prostate cancer

- He referred to our outpatient clinic after detecting pathology in the lungs on abdominal CT taken after gunshot in 2021
- No dyspnea, no cough

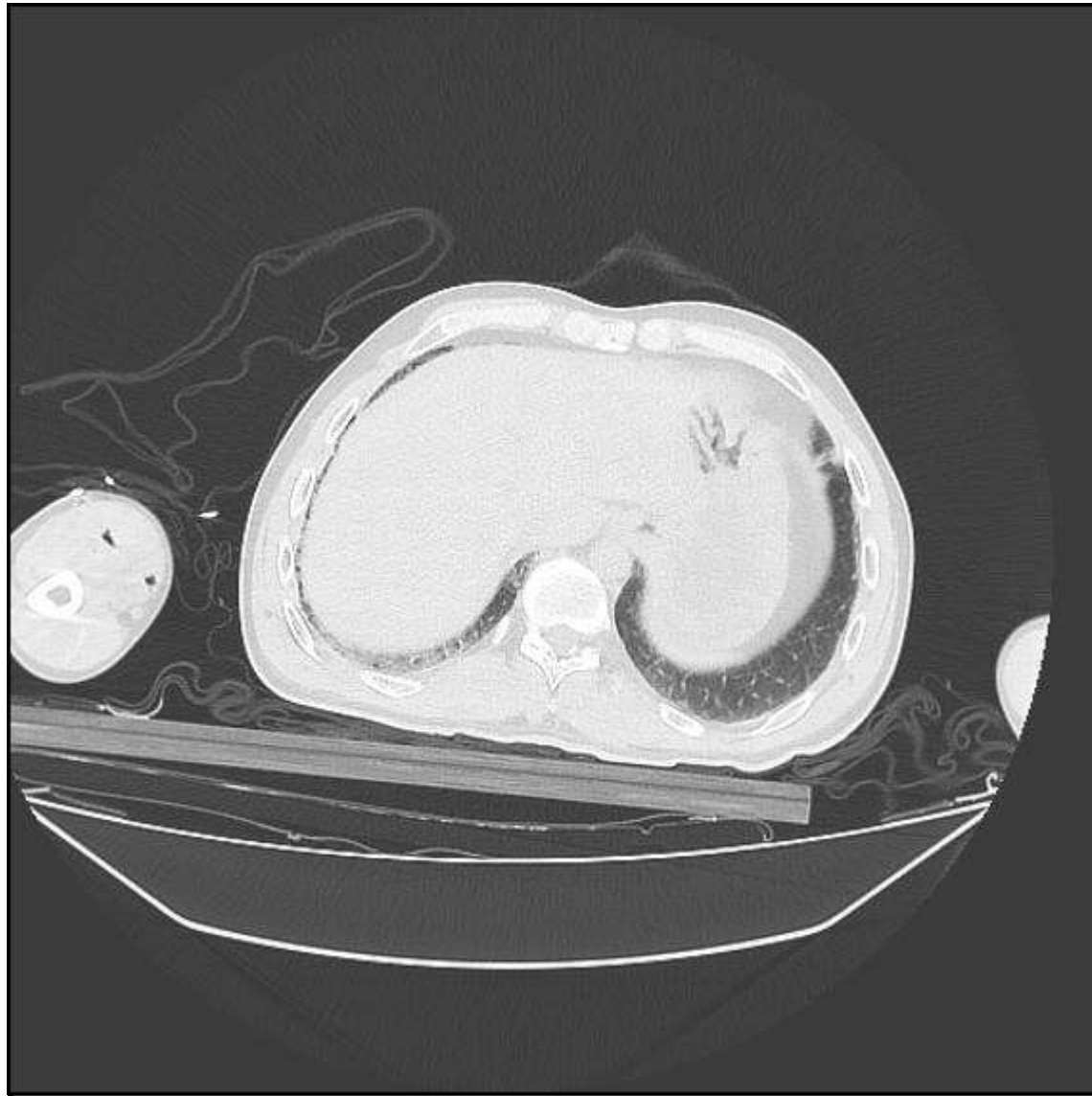
Physical examination

- TA: 120/80 mmHg, Temperature: 36.7 C, Pulse: 75/min, SpO2: %98
- Respiratory system examination is normal

10.02.2021



22.02.2021





T.C.
FIRAT ÜNİVERSİTESİ HASTANESİ
RADYOLOJİ RAPORU



Adı Soyadı :	Rapor Tarihi :	26.02.2021 10:38
T.C Kimlik No :	Dosya no :	1054964
Baba Adı : NİHAT	Başvuru No :	9879666
Kurumu : SSK SAĞLIK İŞLERİ MÜDÜRLÜĞÜ	Doğum Yeri - Tarih :	ELAZIĞ - 1985 Yaş: 35
İstem Tarihi : 22.02.2021(20984925)	İstem Kabul Tarihi :	22.02.2021(46261)
Hizmet Adı : BT, TORAKS	Cinsiyet :	E

Tanı :	Kodu	Adı
	E55.9	VİTAMİN D EKSİKLİĞİ, TANIMLANMAMIŞ
	K21	GASTRO-ÖZOFAJİYAL REFLÜ HASTALIĞI
	K58	İRRİTABİL BARSAK SENDROMU

ÇOK KESİTLİ B?LG?SAYARLI TOMOGRAF?
TORAKS

Teknik : 70 ml kontrast madde verilerek yapılan çok kesitli BT tetki?inde;

Brakiosefalik vasküler yapılar, trake ve ana bron?lar, özefagus normal görünümündedir.

Kalp ve ana vasküler yapılar normal boyutlarda olup patoloji izlenmemiştir.

Bilateral akci?er üst lob apikallerde plevral kal?nla?malar?n e?lik etti?i parankimal fibrotik de?i?iklikler izlenmektedir.

Bilateral akci?erlerde büllöz amfizematöz de?i?iklikler izlendi.

bilateral akci?er periferinde fibrotik de?i?iklikler buzlu cam görünümüleri ve bal pete?i görünümüleri izlendi (?nterstisiyel akci?er hastal???).

Sa? humerus ba?? ve sa? skapulada milimetrik alan izlendi (Kemik adac???).

Gö?üs duvar?, kemik yapılar ve yumu?ak dokular normal görünümündedir.

Thorax CT: Bilateral peripheral fibrotic changes, honeycomb and ground-glass opacities (ILD?)

Pulmonary Function Test

FEV1 pred: %75, FVC pred: %84, FEV1/FVC: %82

Dosya No	1054964				BUL	Başvuru Tarihi	Başvuru No	Alt Birim Adı
Başvuru No								Tüm Başvurular
Sonuç Durumu	☒ Bekleyenler	☒ Onaylanacaklar	☒ Tamamlanmışlar			24.09.2024 08:57	14434030	GÖĞÜS HASTALIKLARI POLİKLİNİ...
☐ Referans Aralığı Kontrol						02.07.2024 09:32	14136810	GÖĞÜS HASTALIKLARI POLİKLİNİ...
						12.02.2024 10:15	13645577	GÖĞÜS HASTALIKLARI POLİKLİNİ...

Barkod	Kabul Tarihi	N.K	N.K. Tarih	Test Adı	RF	Parametre ...	Sonuç	Birim	T.Sonuç	Durum	Alt Limit
00011128109	10.03.2021 10:50	+	10.03.2021 11:45	ANA 1/100 SERUM DIL...		ANA(HEP2) ...	Negatif				
00011096738	02.03.2021 09:47	+	02.03.2021 12:19	ANTI ENDOMİSYUM 1/...		ANTI ENDO...	Negatif				
00011128108	10.03.2021 10:50	+	10.03.2021 11:34	CRP	▼	CRP	<3.3	mg/L			0
00011128108	10.03.2021 10:50	+	10.03.2021 11:34	RF	▼	RF	<9.38	IU/mL			0
00011128106	10.03.2021 10:50	+	10.03.2021 11:36	CCP		CCP	< 0.5	u/mL			0
Barkod	Kabul Tarihi	N.K	N.K. Tarih	Test Adı	RF	Parametre ...	Sonuç	Birim	T.Sonuç	Durum	Alt Limit
00011128106	10.03.2021 10:50	+	10.03.2021 11:35	ANTI-SCL 70		ANTI-SCL 70	4.70	IU/ml		Negatif	0
00011128104	10.03.2021 10:50	+	10.03.2021 11:36	ANTI SM	▼	ANTI SM	<3.0	IU/ml		Negatif	0
00011128104	10.03.2021 10:50	+	10.03.2021 11:36	ANTI-DS DNA (ELISA)		ANTI-DS DN...	<10.0	IU/ml		Negatif	0
00011128104	10.03.2021 10:50	+	10.03.2021 11:36	ANTI U1 RNP		ANTI U1 RNP	12.40	IU/ml			0
00011128104	10.03.2021 10:50	+	10.03.2021 11:36	ANTI-SSB LA	▼	ANTI-SSB LA	<3.0	IU/ml		Negatif	0
00011128104	10.03.2021 10:50	+	10.03.2021 11:36	ANTI SENTROMER (ELI...	▼	ANTI SENTR...	<3.0	IU/ml		Negatif	0
00011096737	02.03.2021 09:47	+	02.03.2021 11:00	DOKU TRANSGLUTAMI...	▼	DOKU TRAN...	<3.0	U/ml		Negatif	0

Serologic markers are all negative

T.C
FIRAT ÜNİVERSİTESİ
PATOLOJİ LABORATUVARI
PATOLOJİ RAPORU
BİYOPSİ RAPORU

Hasta Adı Soyadı
Biyopsi/Sitoloji No **S-1736/21**
T.C. Kimlik No 3734*****
Yaş / Cinsiyeti 36 / E
DosyaNo 1054964

Biyopsi/Sitoloji No S-1736/21
İsteyen Bölüm GÖĞÜS HASTALIKLARI KLİNİĞİ
Tetkiki İsteyen Doktor MUTLU KULUÖZTÜRK
Rapor İlk Kayıt Tarihi

Tetkik İstem Zamanı	01.04.2021 11:27	Numune Kabul Zamanı	01.04.2021 13:58
Numune Alma Zamanı	01.04.2021 11:27	Uzman Onay Zamanı	13.04.2021 16:43
Rapor Onay Tarihi	12.04.2021 13:03	İstem Tarihi	01.04.2021 (21271564)
Rapor Kes. Tarihi	13.04.2021 16:43	İstem Kabul Tarihi	01.04.2021(909330)

KLİNİK ÖZET:

KLİNİK BİLGİ:

MAKROSKOB?: Kaptı gönderilen 20 cc berrak renkte mayı (2PAP,2MGG)

MİKROSKOB?:

- Bron? epitel hücreleri
- Alveolar makrofajlar
- Bu k?smi metaplazi de?i?likler gösteren skuamöz hücreler
- Yava?n bakteri kümeleri
- Lenfositler bask?n iltihap hücreleri

TANI:

AKC??ER, BRON? LAVAJ S?TOLOJ?S? VE HÜCRE BLO?U:
-AKT?F KRON?K ?LT?HAB? REAKS?YON



Bronchial lavage cytology: Lymphocyte-rich active chronic inflammatory reaction

- Patient was diagnosed ILD (HP???) based on radiological and bronchoscopic findings, and the steroid therapy is planned
- The patient did not want to use the drug because of side-effect profile
- Follow-up is recommended

2th visit: October 2022

- Shortness of breath and cough for 1 week

Physical Examination

- Left middle-lower zone, right lower zone inspiratory crackles (+)
- SpO₂: %96
- Clubbing (-), pretibial edema (-)

14.10.2022



Pulmonary function test:

FEV1 pred: %61, FVC pred: %68, FEV1/FVC: %80,
DLCO pred: %47

- Lung biopsy is recommended

TIBBİ PATOLOJİ ANABİLİM DALI
PATOLOJİ RAPORU

Hasta Adı Soyadı

T.C. Kimlik No 37348275616

Yaş / Cinsiyeti 38 / E

Dosya No 37348275616

Numune Türü

Tetkik İstem Zamanı 09.08.2023 11:28

Numune Alma Zamanı 09.08.2023 11:28

Eski Biyopsi No

Biyopsi/Sitoloji No

İsteyen Bölüm

Tetkiki İsteyen Doktor

B-16265-2023

GÖĞÜS CERRAHİ SERVİSİ

Numune Kabul Zamanı 09.08.2023 11:30

Uzman Onay Zamanı 18.08.2023 08:55

KLİNİK BİLGİ:

AC FİBROZİS ETY.

MAKROSKOPİ:

Kayıtsız poşette gönderilen büyüğü 0,8x0,4x0,4 cm küçüğü 0,3x0,3x0,3 cm ölçüsünde toplam 6 adet bej - kahverenkli nodüler dokunun tamamı 1-2,2 kasette takibe alındı.fs/ ega

MİKROSKOPİ:

Kesitlerde, bronş akciğer parankimi çok geniş kistik lezyonlar görülmüştür. İnterstisyel mesafeler kalın, alveoller makrofajla doludur. Bazı makrofajlarda multinükleer dev hücre oluşumu gözlenmiştir. İmmunohistokimyasal olarak CD34, Pan Keratin, Vimentin, P63, TTF-1, CD68, CD163, CD1a, S-100, Desmin ve Aktin uygulanmıştır. Kistik mesafelerin bülöz amfiyatöz değişim gösteren alveol alanları olduğu anlaşılmıştır. İnflamatuar reaksiyon son derece az olup, makrofajlardan oluşmakta ve alveol lumenine sınırlı kalmaktadır. Değişiklikler interstisyel akciğer hastalığı ve son dönem akciğer hastalığı - bal peteği akciğer görünümü ile uyumludur.

Lung Biopsy Pathology: Multinuclear giant cells in some macrophages, alveolar areas with bullous emphysematous changes, little inflammatory reaction with macrophages
Changes consistent with **honeycomb lung**

- Nintedanib prescribed to the patient with a diagnosis of **IPF**
- The patient, who did not want to use nintedanib, re-applied to our outpatient clinic

KULLANMA TALİMATI

OFEV® 150 mg yumuşak kapsül

Ağız yolu ile alınır.

- **Etkin madde:** Nintedanib. Her bir kapsül, 150 mg nintedanib içerir. Bu miktar 180,6 mg nintedanib esilata (etansulfonat) karşılık gelir.

- **Yardımcı maddeler:**

Kapsül içeriği: Orta zincirli trigliseridler, katı yağ (bitkisel kaynaklıdır), soya lesitini (E322),

Kapsül gövdesi: Jelatin (domuz derisi kaynaklı) gliserol (%85), titanyum dioksit (E171), kırmızı demir oksit (E172), sarı demir oksit (E172)

Baskı mürekkebi: şellak glaze (Coccus Lucca adlı böcekten elde edilir), siyah demir oksit (E172), propilen glikol (E1520)

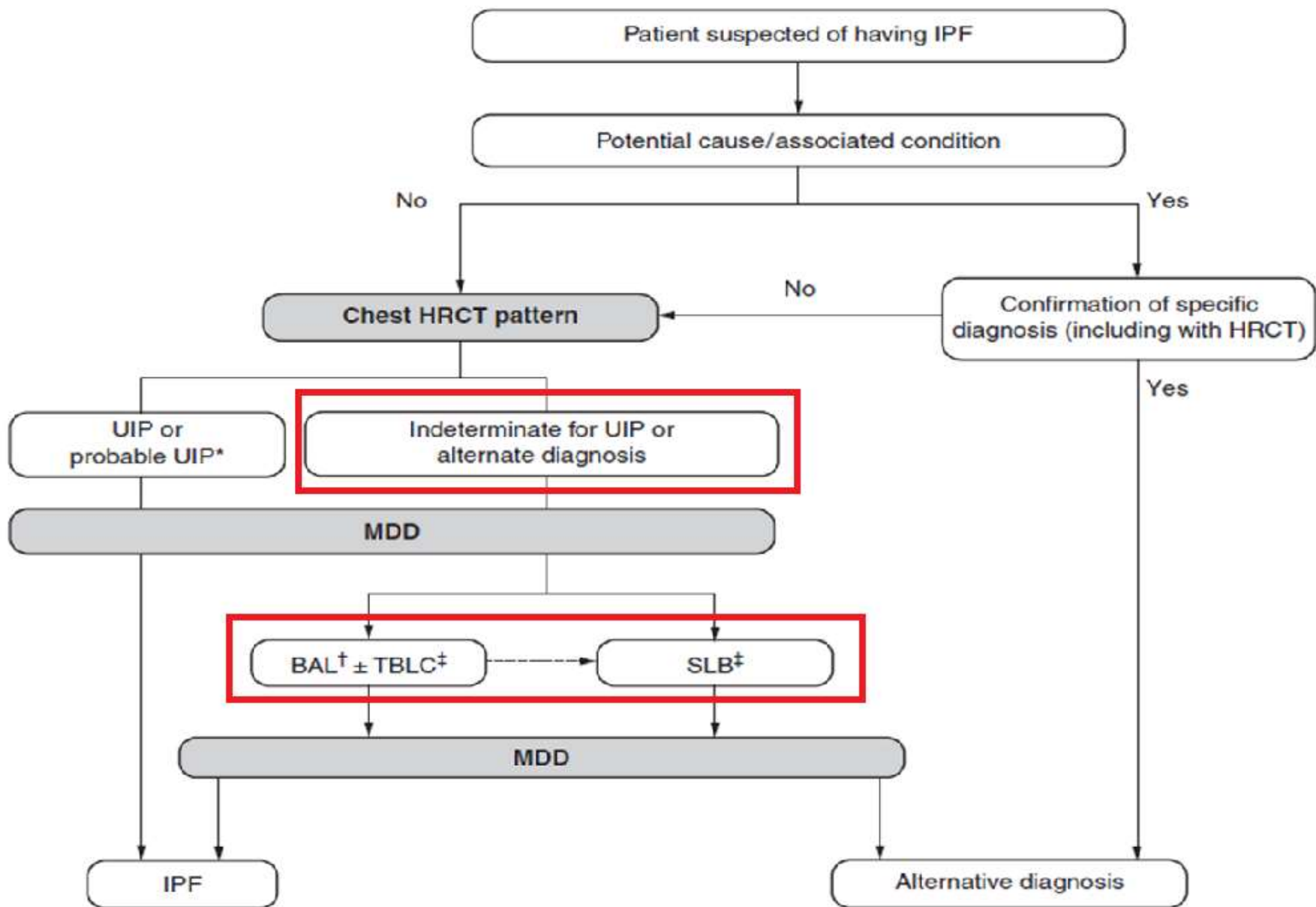
Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults

An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE WAS APPROVED BY THE AMERICAN THORACIC SOCIETY, EUROPEAN RESPIRATORY SOCIETY, JAPANESE RESPIRATORY SOCIETY, AND ASOCIACIÓN LATINOAMERICANA DE TÓRAX FEBRUARY 2022

Table 3. High-Resolution Computed Tomography Patterns in Idiopathic Pulmonary Fibrosis

	HRCT Pattern			CT Findings Suggestive of an Alternative Diagnosis
	UIP Pattern	Probable UIP Pattern	Indeterminate for UIP	
Level of confidence for UIP histology	Confident (>90%)	Provisional high confidence (70–89%)	Provisional low confidence (51–69%)	Low to very low confidence (≤50%)
Distribution	• Subpleural and basal predominant • Often heterogeneous (areas of normal lung interspersed with fibrosis) • Occasionally diffuse • May be asymmetric	• Subpleural and basal predominant • Often heterogeneous (areas of normal lung interspersed with reticulation and traction bronchiectasis/bronchiolectasis)	• Diffuse distribution without subpleural predominance	• Peribronchovascular predominant with subpleural sparing (consider NSIP) • Perilymphatic distribution (consider sarcoidosis) • Upper or mid lung (consider fibrotic HP, CTD-ILD, and sarcoidosis) • Subpleural sparing (consider NSIP or smoking-related IP)
CT features	• Honeycombing with or without traction bronchiectasis/bronchiolectasis • Presence of irregular thickening of interlobular septa • Usually superimposed with a reticular pattern, mild GGO • May have pulmonary ossification	• Reticular pattern with traction bronchiectasis/bronchiolectasis • May have mild GGO • Absence of subpleural sparing	• CT features of lung fibrosis that do not suggest any specific etiology	• Lung findings ◦ Cysts (consider LAM, PLCH, LIP, and DIP) ◦ Mosaic attenuation or three-density sign (consider HP) ◦ Predominant GGO (consider HP, smoking-related disease, drug toxicity, and acute exacerbation of fibrosis) ◦ Profuse centrilobular micronodules (consider HP or smoking-related disease) ◦ Nodules (consider sarcoidosis) ◦ Consolidation (consider organizing pneumonia, etc.) • Mediastinal findings ◦ Pleural plaques (consider asbestosis) ◦ Dilated esophagus (consider CTD)



AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis of Idiopathic Pulmonary Fibrosis An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

This official ATS/ERS/JRS/ALAT Clinical Practice Guideline was endorsed by the Pulmonary Pathology Society October 2018

Table 5. Histopathology Patterns and Features

UIP	Probable UIP	Indeterminate for UIP	Alternative Diagnosis
• Dense fibrosis with architectural distortion (i.e., destructive scarring and/or honeycombing) • Predominant subpleural and/or paraseptal distribution of fibrosis • Patchy involvement of lung parenchyma by fibrosis • Fibroblast foci • Absence of features to suggest an alternate diagnosis	• Some histologic features from column 1 are present but to an extent that precludes a definite diagnosis of UIP/IPF <i>And</i> • Absence of features to suggest an alternative diagnosis <i>Or</i> • Honeycombing only	• Fibrosis with or without architectural distortion, with features favoring either a pattern other than UIP or features favoring UIP secondary to another cause* • Some histologic features from column 1, but with other features suggesting an alternative diagnosis†	• Features of other histologic patterns of IIPs (e.g., absence of fibroblast foci or loose fibrosis) in all biopsies • Histologic findings indicative of other diseases (e.g., hypersensitivity pneumonitis, Langerhans cell histiocytosis, sarcoidosis, LAM)

IPF suspected*		Histopathology pattern†			
		UIP	Probable UIP	Indeterminate for UIP or biopsy not performed	Alternative diagnosis
HRCT pattern	UIP	IPF	IPF	IPF	Non-IPF dx
	Probable UIP	IPF	IPF	IPF (Likely)‡	Non-IPF dx
	Indeterminate	IPF	IPF (Likely)‡	Indeterminate§	Non-IPF dx
	Alternative diagnosis	IPF (Likely)‡	Indeterminate§	Non-IPF dx	Non-IPF dx

Re-evaluation of biopsy sample in a different hospital

+ Gönderilen Materyal : KONSÜLTASYON Materyallerin Alındığı Yer : AKCİĞER Materyalin Alınma Şekli : 5 Klinik Ön Tanı : İntersitisyel akciğer hastalığı son dönem bulguları ile uyumlu değişiklikler Makroskopi : Konsültasyon amacıyla gönderilen B- 16265-2023 nolu 14 adet lam+ 2 adet blok tarafımıza gönderilmiştir. Döküm, Kesit Tek: Simay Gök, Rapor Sek: Öznur Bozkurt Mikroskopi : Histokimyasal Boyama Panel Sonuçları : MTK uygulandı İmmunhistokimya Boyama Panel Sonuçları : Frozen Tanı : Histopatolojik Tanılar / Sitopatolojik Tanılar : Akciğer, Eksizyonel Biopsi; Konsültasyon: A- <u>Tip II pnömosit proliferasyonu,</u> <u>alveol septaları kalınlaştıran</u> <u>lenfoid proliferasyon, alveol</u> <u>boşluklarında makrofajlar, fibrozis,</u> <u>düz kas metaplazi odağı B- Tip II</u> pnömosit proliferasyonu, alveol septaları kalınlaştıran fibrozis,	01.09.2023	T.C. SAĞLIK BAKANLIĞI İSTANBUL YEDİKULE GÖĞÜS HASTALIKLARI VE GÖĞÜS CERRAHİSİ EAH	GÖĞÜS HASTALIKLARI	08.09.2023
---	------------	--	--------------------	------------

Pathology consultation at different center

Type 2 pneumocyte proliferation,
Lymphoid proliferation thickening the
alveolar septa

Macrophages in the alveolar spaces, fibrosis,
focus of smooth muscle metaplasia

Hastanın Adı Soyadı		Laboratuvar Kabul Tarihi/Saati	Eylül 01 2023, 11:50
Hasta T.C. Kimlik No		Patoloji Rapor Tarihi	Eylül 08 2023, 19:33
Doğum Tarihi, Cinsiyeti	20.03.1985 / E	Protokol No	
İsteyen Birim	4B.4 Göğüs Polikliniği D. TURAN	Rapordan Sorumlu I.Doktor	
İsteyen Hekim	DEMET TURAN	Raporlayan Sekreter	
İstemin Yapıldığı Tarihi/Saati	01.09.2023 11.03.40	Numune Alma Tarihi ve Saati	

Gönderilen Materyal KONSÜLTASYON

Materyallerin Alındığı Yer	AKCİĞER	Materyalin Alınma Şekli :	KONSÜLTASYON
-----------------------------------	---------	----------------------------------	--------------

Klinik Ön Tanı

İnterstitiyel akciğer hastalığı son dönem bulguları ile uyumlu değişiklikler

Makroskopi

Konsültasyon amacıyla gönderilen B- 16265-2023 nolu 14 adet lam+ 2 adet blok tarafımıza gönderilmiştir.

Döküm, Kesit Tek: Simay Gök, Rapor Sek: Öznur Bozkurt

TIBBİ LABORATUVAR YORUMU

Bulgular fibrotik tip Nonspesifik İnterstitiyel Pnömoni paterni ile uyumludur. Olgunun kollagen doku hastalıkları yönünden tetkiki önerilir

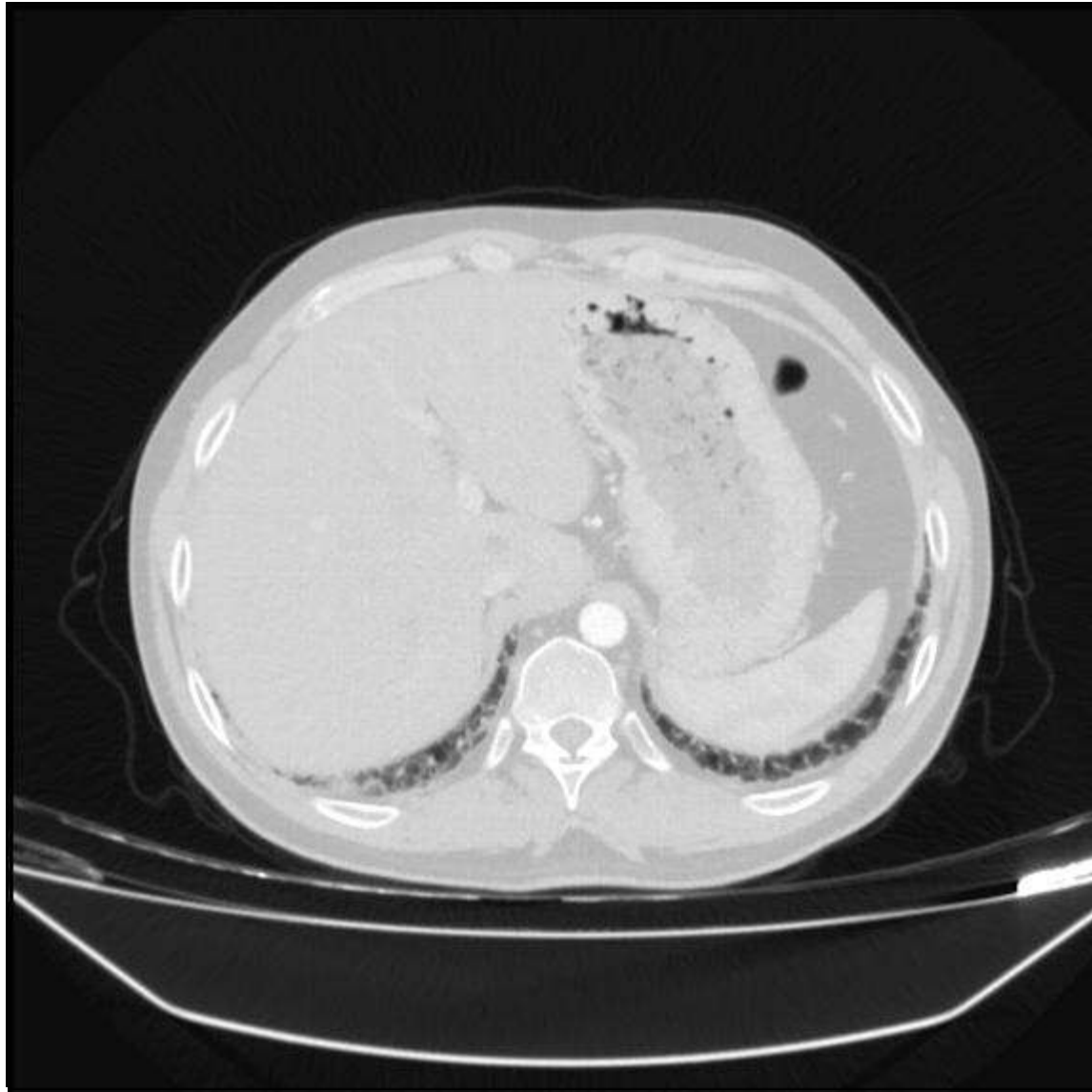
The findings are compatible with **fibrotic-type NSIP**, evaluation of the patient for collagen vascular diseases is recommended

- No pathology was detected after Rheumatology consultation
- Steroids were prescribed

At the 6th month of treatment

- Worsening shortness of breath; dyspnea when climbing one flight of stairs or walking quickly
- PE: Bilateral middle and lower zone inspiratory crackles (+), HR: 103/min, SpO₂: %91
- FEV₁pred: %48, FVCpred: %45, FEV₁/FVC: %84
- DLCO could not be performed

13.02.2024



FIRAT UNIVERSİTESİ HASTANESİ
RADYOLOJİ RAPORU



Adı Soyadı :	Rapor Tarihi :	14.02.2024 13:47
T.C Kimlik No :	Dosya no :	1054964
Baba Adı :	Başvuru No :	13645577
Kurumu :	Doğum Yeri - Tarih :	SSK SAĞLIK İŞLERİ MÜDÜRLÜĞÜ ELAZIĞ - 1985 Yaş: 38
İstem Tarihi :	İstem Kabul Tarihi :	13.02.2024(29725199) 13.02.2024(R100460)
Hizmet Adı :	Cinsiyet :	BT, TORAKS, KONTRASTLI E

Tanı :	Kodu	Adı
	R05	ÖKSÜRÜK
	R05	ÖKSÜRÜK

**ÇOK KESİTLİ BİLGİSAYARLI TOMOGRAFİ
TORAKS**

Teknik : Kontrast madde verilmeden yapılan çok kesitli BT tetkikinde;

Trakea ve ana bronşlar, özofagus normal görünümündedir.

Bilateral akciğerlerde orta- alt lobda daha belirgin periferik retikülasyon artışı periferik ve paramediastinal subplevral hava kistleri-amfizematöz değişiklikler izlendi. Her iki akciğerde yer yer traksiyon bronkiektazileri izlenmektedir (Olası UIP ?).

Bilateral akciğerde paraseptal amfizematöz değişiklikler izlendi. Orta lobda bant atelektaziler izlendi.

Bilateral akciğer üst lob apikallerde plevroparankimal fibröz kep izlenmektedir.

Prominent peripheral reticulation in the middle and lower lobes of both lungs, areas of paramediastinal paraseptal emphysema, and traction bronchiectasis= **Probable UIP**

ORIGINAL ARTICLE

 OPEN ACCESS  Check for updates

Progressive fibrosing interstitial lung diseases: current practice in diagnosis and management

Marlies Wijisenbeek^a , Michael Kreuter^b, Amy Olson^c, Aryeh Fischer^d , Elisabeth Bendstrup^e , Christopher D. Wells^f, Christopher P. Denton^g, Baher Mounir^h, Leila Zouad-Lejour^h, Manuel Quaresma^h and Vincent Cottinⁱ 

Table 1. Percentage of US patients who received treatment for non-IPF ILDs in 2016.

	Any treatment ^a	Corticosteroids	Mycophenolate mofetil	Azathioprine	Cyclosporine	Tacrolimus	Cyclophosphamide
RA-ILD	72	69	7	9	5	3	0
SSc-ILD	74	59	29	15	5	4	1
Other CTD-ILDs	67	61	21	15	7	4	0
iNSIP	71	62	15	6	3	3	0
HP	75	74	6	8	2	1	0
Sarcoidosis-ILD	63	62	3	3	2	2	0
Other specified non-IPF ILDs ^b	50	49	3	2	2	1	0
Non-specified ILDs ^c	52	51	3	2	2	2	0

- MMF 500 mg 2x2 was added to the treatment because of radiological, clinical and functional impairment

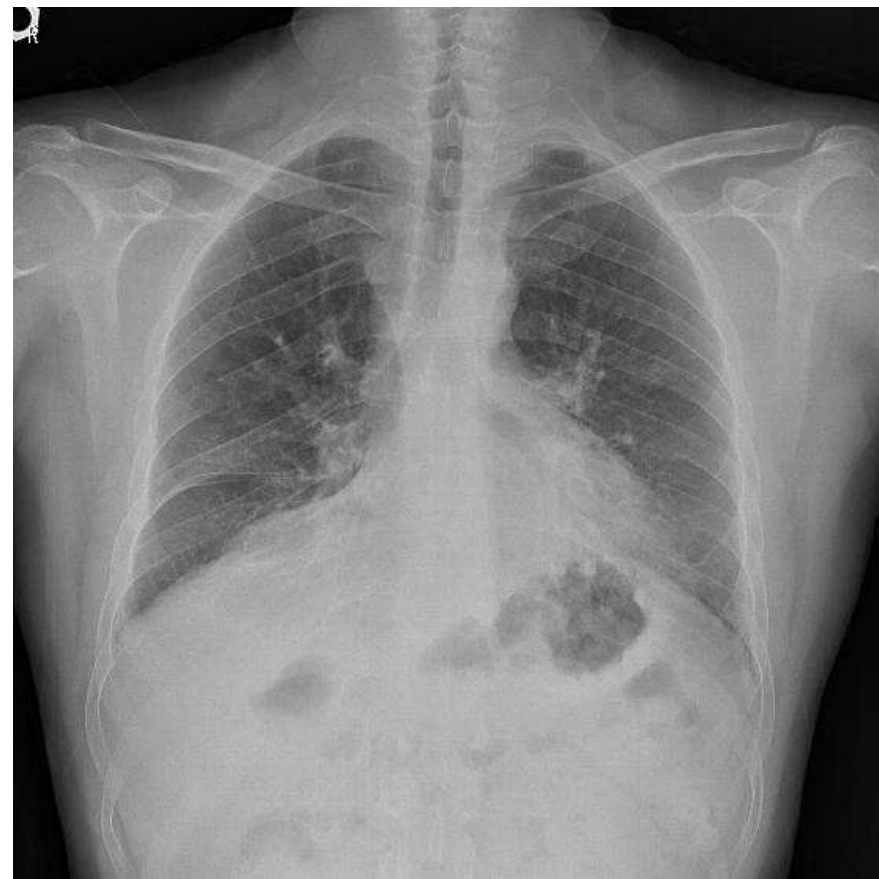
September 2024

- Worsening symptoms
- PE: Bilateral middle and lower zone inspiratory crackles (+), clubbing (+), SpO2: %90
- FEV1pred: %42, FVCpred: %38, FEV1/FVC: %88
- DLCOpred: %23

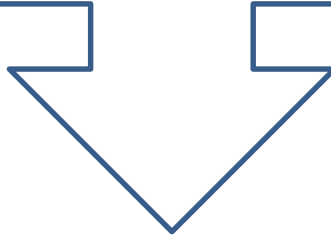
13.02.2024



24.09.2024



**The patient is considered to be progressing
radiologically, functionally, and clinically**



**PROGRESSIVE PULMONARY
FIBROSIS**

Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults

An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

Ganesh Raghu, Martine Remy-Jardin, Luca Richeldi, Carey C. Thomson, Yoshikazu Inoue, Takeshi Johkoh, Michael Kreuter, David A. Lynch, Toby M. Maher, Fernando J. Martinez, Maria Molina-Molina, Jeffrey L. Myers, Andrew G. Nicholson, Christopher J. Ryerson, Mary E. Strek, Lauren K. Troy, Marlies Wijsenbeek, Manoj J. Mammen, Tanzib Hossain, Brittany D. Bissell, Derrick D. Herman, Stephanie M. Hon, Fayez Kheir, Yet H. Khor, Madalina Macrea, Katerina M. Antoniou, Demosthenes Bouros, Ivette Buendia-Roldan, Fabian Caro, Bruno Crestani, Lawrence Ho, Julie Morisset, Amy L. Olson, Anna Podolanczuk, Venerino Poletti, Moisés Selman, Thomas Ewing, Stephen Jones, Shandra L. Knight, Marya Ghazipura, and Kevin C. Wilson; on behalf of the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Asociación Latinoamericana de Tórax

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE WAS APPROVED BY THE AMERICAN THORACIC SOCIETY, EUROPEAN RESPIRATORY SOCIETY, JAPANESE RESPIRATORY SOCIETY, AND ASOCIACIÓN LATINOAMERICANA DE TÓRAX FEBRUARY 2022

Table 4. Definition of Progressive Pulmonary Fibrosis

Definition of PPF

In a patient with ILD of known or unknown etiology other than IPF who has radiological evidence of pulmonary fibrosis, PPF is defined as at least two of the following three criteria occurring within the past year with no alternative explanation*:

- 1 Worsening respiratory symptoms
- 2 Physiological evidence of disease progression (either of the following):
 - a. Absolute decline in FVC $\geq 5\%$ predicted within 1 yr of follow-up
 - b. Absolute decline in DL_{CO} (corrected for Hb) $\geq 10\%$ predicted within 1 yr of follow-up
- 3 Radiological evidence of disease progression (one or more of the following):
 - a. Increased extent or severity of traction bronchiectasis and bronchiolectasis
 - b. New ground-glass opacity with traction bronchiectasis
 - c. New fine reticulation
 - d. Increased extent or increased coarseness of reticular abnormality
 - e. New or increased honeycombing
 - f. Increased lobar volume loss

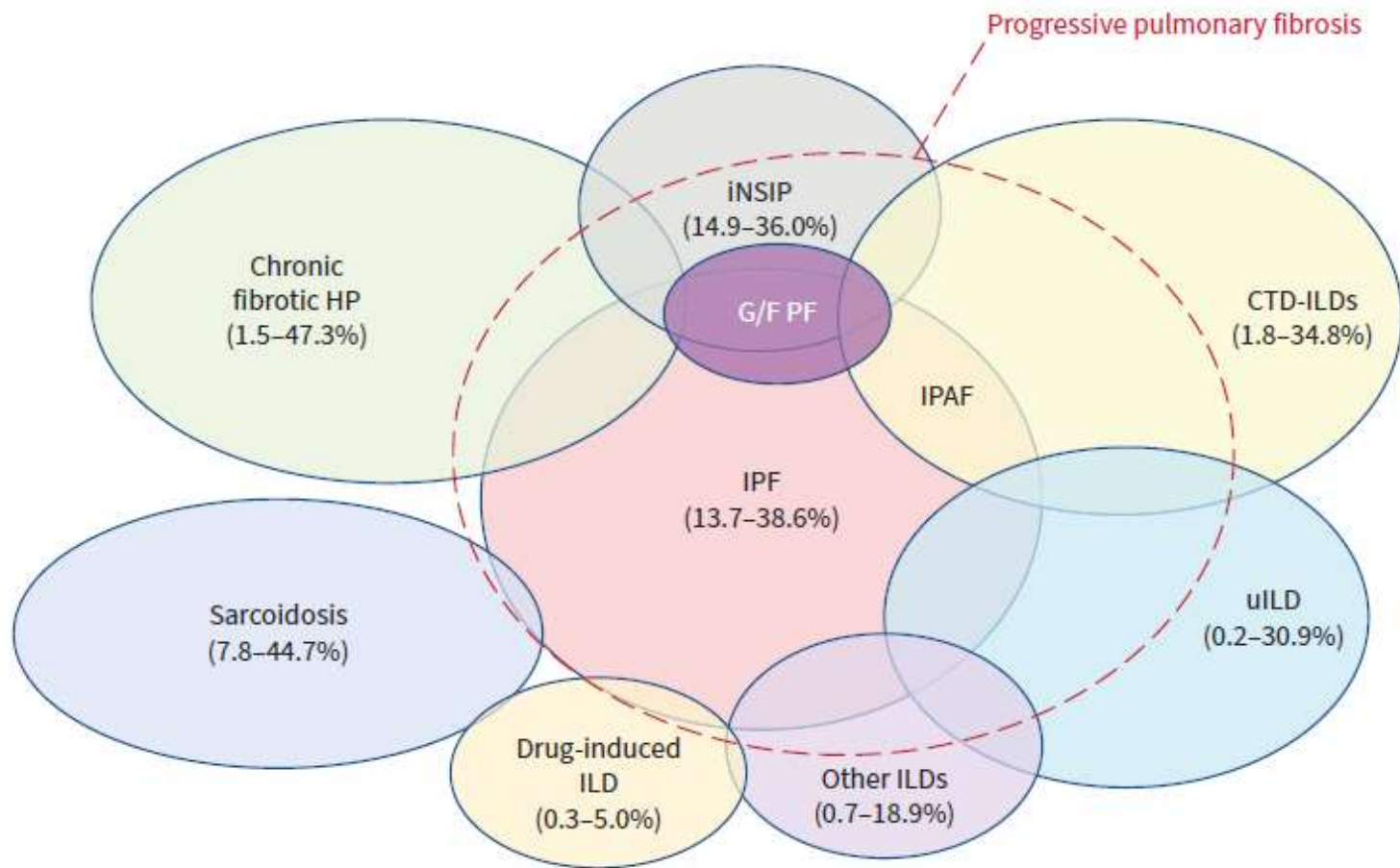


FIGURE 1 Schematic representation of the prevalent spectrum of interstitial lung diseases (ILDs) that may be associated with “progressive pulmonary fibrosis (despite management)”. The lowest and highest prevalences across different countries are shown in brackets [14]. CTD: connective tissue disease; G/F PF: genetic and/or

AMERICAN THORACIC SOCIETY DOCUMENTS

Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults

An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

8 Ganesh Raghu, Martine Remy-Jardin, Luca Richeldi, Carey C. Thomson, Yoshikazu Inoue, Takeshi Johkoh, Michael Kreuter, David A. Lynch, Toby M. Maher, Fernando J. Martinez, Maria Molina-Molina, Jeffrey L. Myers, Andrew G. Nicholson, Christopher J. Ryerson, Mary E. Strek, Lauren K. Troy, Marlies Wijsenbeek, Manoj J. Mammen, Tanzib Hossain, Brittany D. Bissell, Derrick D. Herman, Stephanie M. Hon, Fayez Kheir, Yet H. Khor, Madalina Macrea, Katerina M. Antoniou, Demosthenes Bouros, Ivette Buendia-Roldan, Fabian Caro, Bruno Crestani, Lawrence Ho, Julie Morisset, Amy L. Olson, Anna Podolanczuk, Venerino Poletti, Moisés Selman, Thomas Ewing, Stephen Jones, Shandra L. Knight, Marya Ghazipura, and Kevin C. Wilson; on behalf of the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Asociación Latinoamericana de Tórax

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE WAS APPROVED BY THE AMERICAN THORACIC SOCIETY, EUROPEAN RESPIRATORY SOCIETY, JAPANESE RESPIRATORY SOCIETY, AND ASOCIACIÓN LATINOAMERICANA DE TÓRAX FEBRUARY 2022

Evidence-based Recommendations for Treatment of PPF, Other than IPF

Pirfenidone. *We recommend further research into the efficacy, effectiveness, and safety of pirfenidone in both 1) non-IPF ILD manifesting PPF in general and 2) specific types of non-IPF ILD manifesting PPF.*

Nintedanib.

We suggest nintedanib for the treatment of PPF in patients who have failed standard management for fibrotic ILD, other than IPF (conditional recommendation, low-quality evidence). Remarks: Standard We recommend research into the efficacy, effectiveness, and safety of nintedanib in specific types of non-IPF ILD manifesting PPF.



Progressive pulmonary fibrosis: an expert group consensus statement

Sujeet K. Rajan ¹, Vincent Cottin ², Raja Dhar³, Sonye Danoff⁴, Kevin R. Flaherty⁵, Kevin K. Brown⁶, Anant Mohan⁷, Elizabeth Renzoni⁸, Murali Mohan⁹, Zarir Udwadia¹⁰, Padmanabha Shenoy¹¹, David Currow¹², Anand Devraj¹³, Bhavin Jankharia¹⁴, Ritu Kulshrestha¹⁵, Steve Jones¹⁶, Claudia Ravaglia¹⁷, Silvia Quadrelli¹⁸, Rajam Iyer¹⁹, Sahajal Dhooria ²⁰, Martin Kolb ^{21,23} and Athol U. Wells^{22,23}

¹Bombay Hospital Institute of Medical Sciences and Bhatia Hospital, Mumbai, India. ²National French Reference Coordinating Center for Rare Pulmonary Diseases, Louis Pradel Hospital Hospices Civils de Lyon, Université Claude Bernard Lyon 1, INRAE, Member of ERN-LUNG, Lyon, France. ³CK Birla Hospitals, Kolkata, India. ⁴Johns Hopkins School of Medicine, Baltimore, MD, USA. ⁵University of Michigan, Ann Arbor, MI, USA. ⁶Department of Medicine, National Jewish Health, Denver, CO, USA. ⁷All India Institute of Medical Sciences, New Delhi, India. ⁸Royal Brompton Hospital/Imperial College London, London, UK. ⁹Narayana Health, Bengaluru, India. ¹⁰Breach Candy Hospital, Mumbai, India. ¹¹Department of Rheumatology, Centre for Arthritis and Rheumatism Excellence, Kochi, India. ¹²University of Technology, Sydney, Australia. ¹³Department of Radiology, Royal Brompton Hospital, London, UK. ¹⁴Picture This by Jankharia, Mumbai, India. ¹⁵Department of Pathology, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi, India. ¹⁶European Idiopathic Pulmonary Fibrosis Federation (EU-IPFF), Peterborough, UK. ¹⁷Pulmonology Unit, GB Morgagni Hospital/University of Bologna, Forlì, Italy. ¹⁸Hospital Británico de Buenos Aires, Buenos Aires, Argentina. ¹⁹Bhatia Hospital and PD Hinduja Hospital, Mumbai, India. ²⁰Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India. ²¹Firestone Institute for Respiratory Health, St Joseph's Healthcare and McMaster University, Hamilton, ON, Canada. ²²Interstitial Lung Disease Unit, Royal Brompton and Harefield NHS Foundation Trust, London, UK. ²³Co-senior authors.

Corresponding author: Sujeet K. Rajan (skrajan@hotmail.com)



Shareable abstract (@ERSpublications)

Progressive pulmonary fibrosis (PPF) explains what clinicians increasingly face in practice. Assessing ILD progression, its risk and improved treatments based on current evidence for PPF (despite initial management) form the mainstay of this document. <http://bit.ly/3GLdqfs>

Cite this article as: Rajan SK, Cottin V, Dhar R, et al. Progressive pulmonary fibrosis: an expert group consensus statement. *Eur Respir J* 2023; 61: 2103187 [DOI: 10.1183/13993003.03187-2021].

Key conclusions

- 1) The long-term side effects with systemic corticosteroid therapy are a cause for concern in the treatment of PPF; alternative long-term immunosuppressive agents may be associated with less side effects [77].
- 2) A case-by-case and disease-by-disease approach and review are required to assess the added effectiveness of immunosuppressants to the baseline steroid treatment.

Key conclusions

- 1) Initial treatment should be based on the precise primary diagnosis.
- 2) Apart from IPF, SSc-ILD and, possibly, rheumatoid arthritis-associated ILD (UIP), antifibrotic medication should not be considered as a first-line therapy.
- 3) In PPF, there is growing evidence that antifibrotic therapy reduces lung function decline, regardless of background immunosuppressive therapy.
- 4) Careful monitoring for adverse events in the patient subgroup treated with combination therapy is advised.

Key conclusions

- 1) The group does not advise general upfront combination therapy.
- 2) Antifibrotics may be administered sequentially in the context of PPF.

Pharmacological Treatment of Idiopathic Pulmonary Fibrosis (Update) and Progressive Pulmonary Fibroses: S2k Guideline of the German Respiratory Society

Respiration 2024;103:782–810

DOI: 10.1159/000540856

Jürgen Behr^a Francesco Bonella^b Björn Christian Frye^c Andreas Günther^d
Lars Hagmeyer^e Jörg Henes^f Philipp Klemm^g Dirk Koschel^h
Michael Kreuter^{i,j} Gabriela Leuschner^a Dennis Nowak^k Antje Prasse^l
Bernd Quadder^m Helmut Sitterⁿ Ulrich Costabel^b

R15 Recommendation

↑ PPF patients should be treated with pirfenidone if antifibrotic therapy with nintedanib was not sufficiently effective or has been discontinued due to side effects

↑ ↑ A therapy switch shall be determined in the context of an ILD MDD (ILD Board)

Consensus strength: 100%

R30 Recommendation

↓ ↓ Outside of controlled clinical trials, IPF or PPF patients shall not be treated with a combination of pirfenidone and nintedanib

Consensus strength: 100%

Pirfenidone was started after obtaining approval for off-label use with the diagnosis of **PPF**

Tanı ve İlaç Bilgileri

Tanı Kodu	Tanı Adı	Alt Tanı	Tanı Tarihi
J84.1	İntersitisyel akciğer hastalığı, diğer, fibrozisli	fibrotik NSİP	24.09.2024

Etkin Madde	Miktarı	Doz 1	X	Doz 2	Periyodu	K. Şekli	Rapor Süresi
PIRFENIDON	600 mg	4	X	1	1 Gün	Ağızdan(Oral)	1 Yıl

Açıklama

İlgili etkin maddeli ilacın kullanımı, Kısa Ürün Bilgisi (KÜB) dahilinde olup, 1 (bir) yıllık dozda kullanımı uygundur.

Karar

Uygun görülmüştür

Karar Tarihi

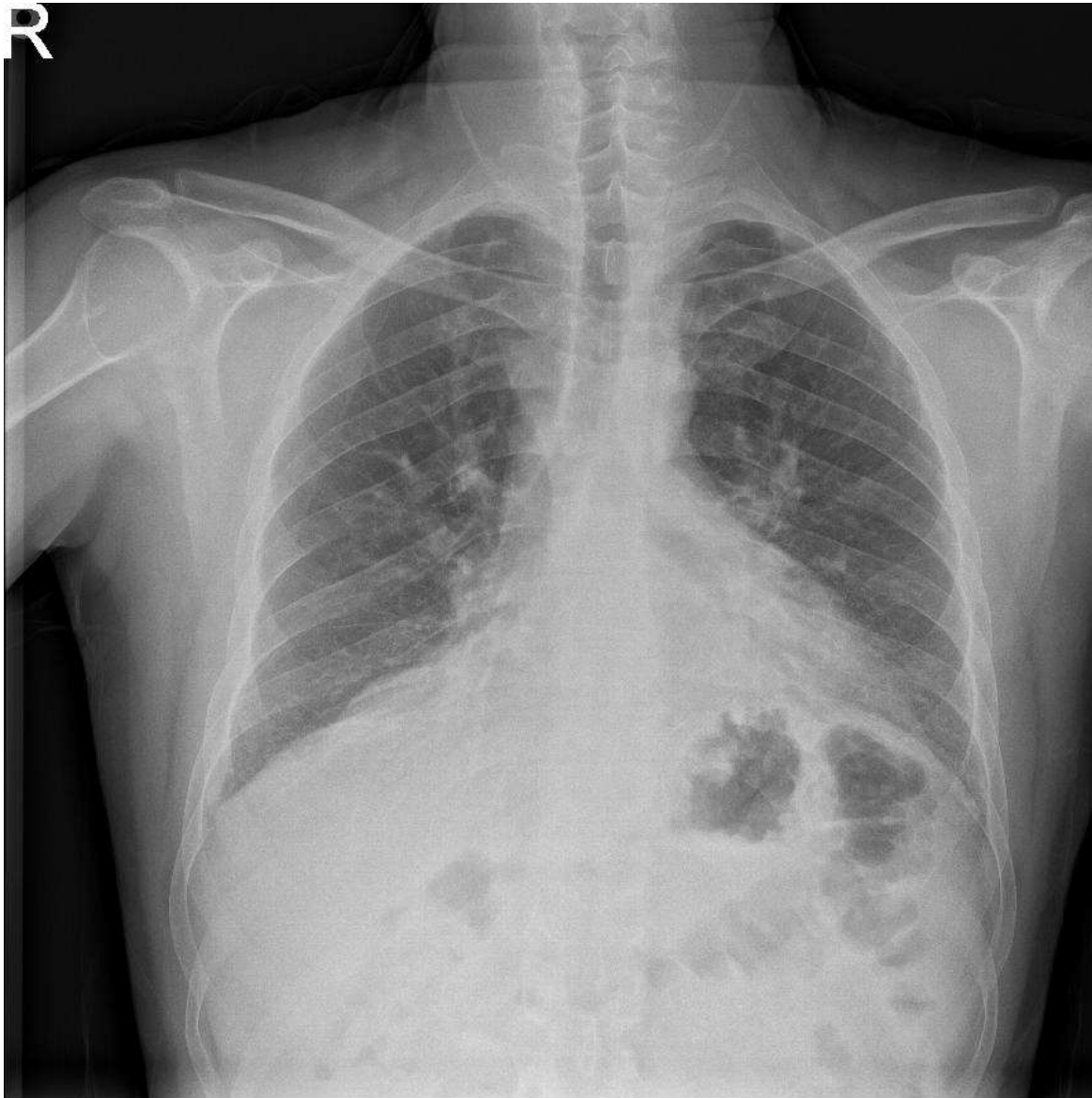
26.09.2024

2nd year of Pirfenidone treatment

03.06.2026

- Dyspnea persists
- SpO2:%90
- FVC pred: % 37
- FEV1pred: %40
- FEV1/ FVC: %87
- DLCOpred: %24
- No drug side effect

03.06.2026





Management of PF-ILD

INITIAL COMPREHENSIVE EVALUATION

History and Physical Exam (r/o identifiable causes, AEx history)
Symptom Assessment (questionnaires e.g. SGRQ, K-BILD)
Pulmonary function test
Quantification of lung fibrosis on HRCT
± Biopsy

MILD DISEASE

Asymptomatic

FVC decline <5% predicted at 12 months
<10% of lung fibrosis **OR**
CT features not consistent with UIP

Pulmonary function test
Exercise capacity (6-MWT)
Every 6-12 months
HRCT every 12 months

Remove offending agent
Smoking cessation
Close observation
Treat underlying cause (immunosuppression for autoimmune disease)

MODERATE DISEASE

Mild symptoms

FVC decline ≥5 – <10% predicted at 12 months
>10% of lung fibrosis on HRCT **OR**
Indeterminate UIP

Pulmonary function test
Exercise capacity (6-MWT)
Every 3-6 months
HRCT 6-12 months

Multidisciplinary discussion
May require tissue diagnosis
Immunosuppression therapy
Consider initiation of antifibrotic therapy
Pulmonary rehabilitation

SEVERE DISEASE

Symptomatic with decrease QoL ± frequent AEx
FVC decline ≥10% predicted at 12 months
>10% of lung fibrosis on HRCT
Probable or typical UIP on HRCT **OR**
Definite UIP on histopathology

Pulmonary function test
Exercise capacity (6-MWT)
Every 3-6 months
HRCT 6-12 months

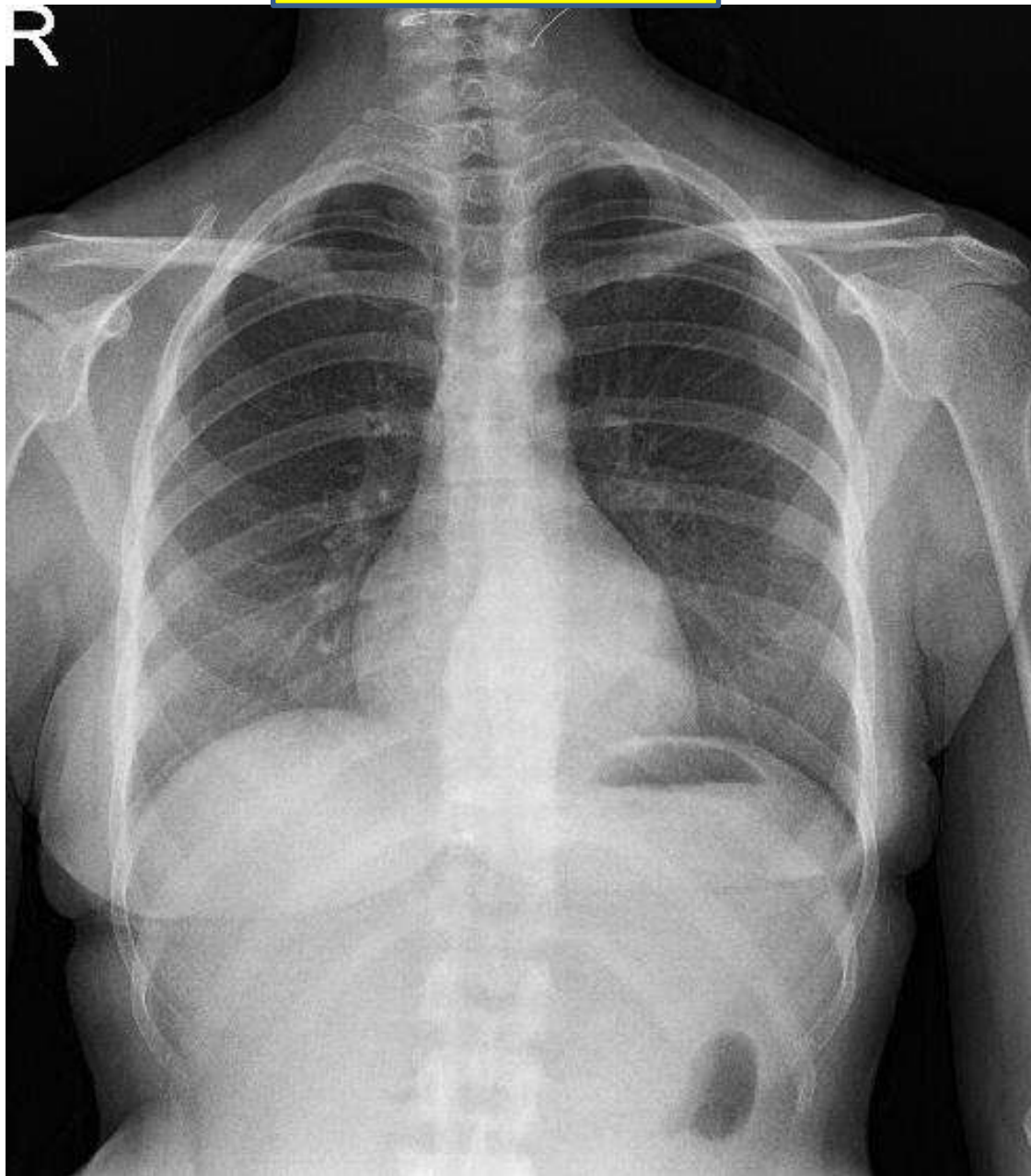
Multidisciplinary discussion
Consider antifibrotic therapy as first-line treatment
Continuation of immunosuppression if evidence of active inflammation (serologic, inflammatory markers, GGO on HRCT)
Pulmonary rehabilitation
Early lung transplant evaluation
Palliative care consultation

Gibson CD, et al. Lung 2020

Case-2

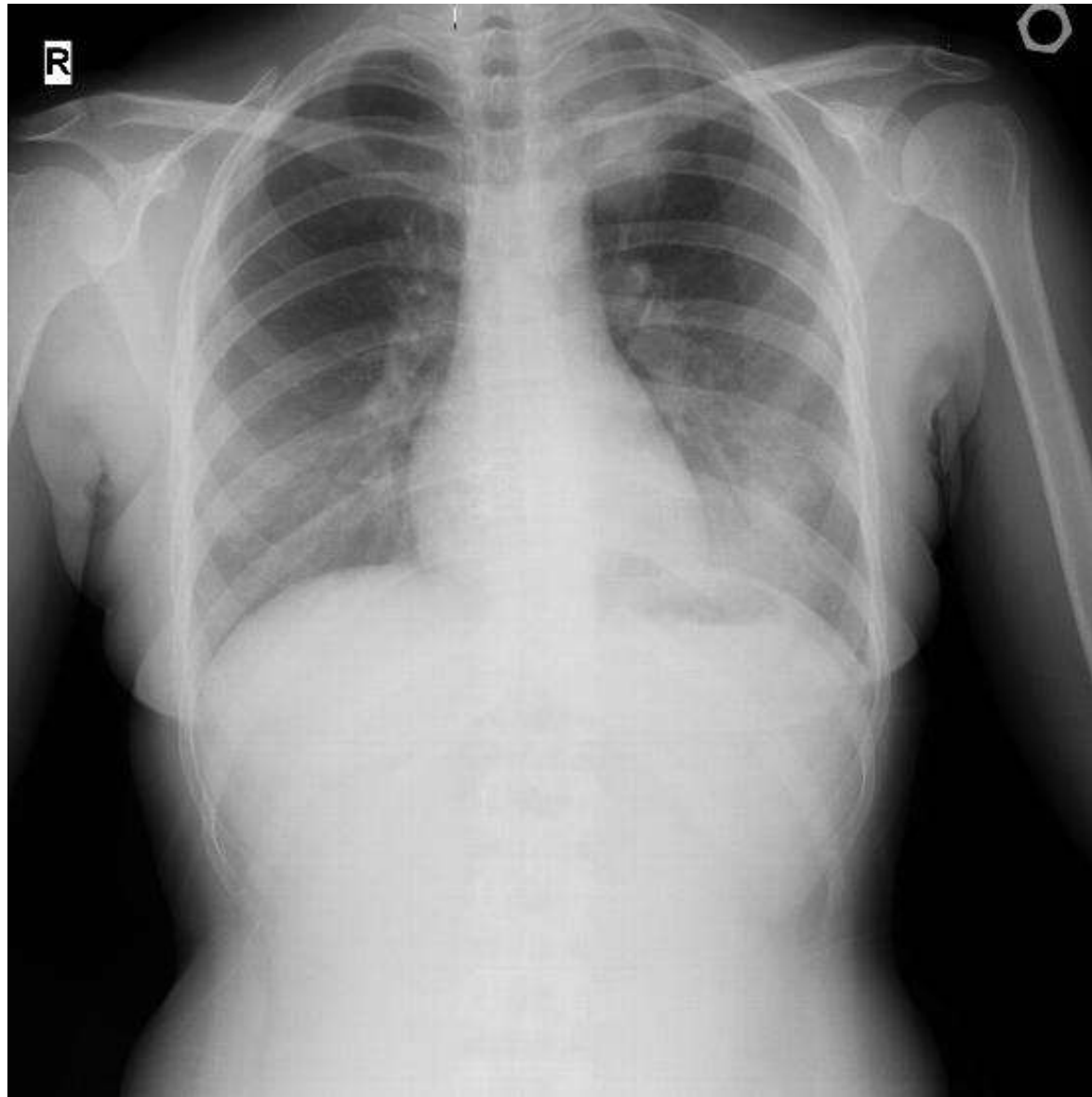
- 34 y, F
- She applied to the Rheumatology outpatient clinic 5 years ago due to joint pain
- PE: Normal
- No laboratory tests performed

01.07.2019



- Anti-inflammatory treatment prescribed
- Re-applied to the Rheumatology outpatient clinic after 3 months because of persistent joint pain

23.10.2019



Laboratory

➤ CBC

✓ WBC: 8340/ μ L

✓ **Hb: 10.7 g/dL**

✓ **Hct: % 32**

✓ Plt: 435000/ μ L

✓ **CRP: 200 mg/L (0-5)**

✓ **RF: 104IU/ml (0-15)**

➤ Biochemistry

✓ Urea: 29 mg/dl

✓ Creatinine: 0.58 mg/dl

✓ AST: 37 U/L

✓ **ALT: 76 U/L**

✓ Urinalysis

• **+++ RBC/uL**

Reçete İçin Seçilmiş ICD 10 Tanıları

Tanı Kodu	Tanı Adı
M36.8	BAĞ DOKUSUNUN SİSTEMİK BOZUKLUKLARI, BAŞKA YERDE SINIFLANMIŞ DİĞER
K21.9	GASTRO-ÖZOFAJİAL REFLÜ HASTALIĞI, ÖZOFAJİTSİZ
M79.7	FIBROMİYALJİ

Hasta Adı :	Reçete Tarih : 23.10.2019 00:00:00
TC Kimlik No :	Reçete Türü : Normal
Reçete S.No : 2075131	Reçete Tipi : Ayaktan Reçetesi
Takip No : 31GBB9L	Reçete No : 18B3VTL
Reçeteyi Yazan Doktor	
Branş Kodu : ROMATOLOJİ	

Barkod	İlaç Adı	Adet	Doz	Periyodu	Periyot Birim	Kullanım Sekli
8699638012053	EMTHEXATE 2.5 MG 100 TB.	1,0	1,00 X 6,00	1,00	Hafta	Ağızdan(Oral)
8699532010865	DELTACORTIL 20 TABLET	5,0	1,00 X 3,00	1,00	Gün	Ağızdan(Oral)

MTX+Deltacortil prescribed with the diagnosis of **Systemic disorders of connective tissue**

- Two weeks later, the patient presented to the emergency department with shortness of breath and hemoptysis
- PE: General condition moderate, conscious, cooperative, oriented
- Bilateral diffuse inspiratory crackles (+),
- **SpO2: %90** (room air), TA: 110/70 mmHg, HR: **134/min**, RR: 26/min, Temperature: 37.2 C

Laboratory

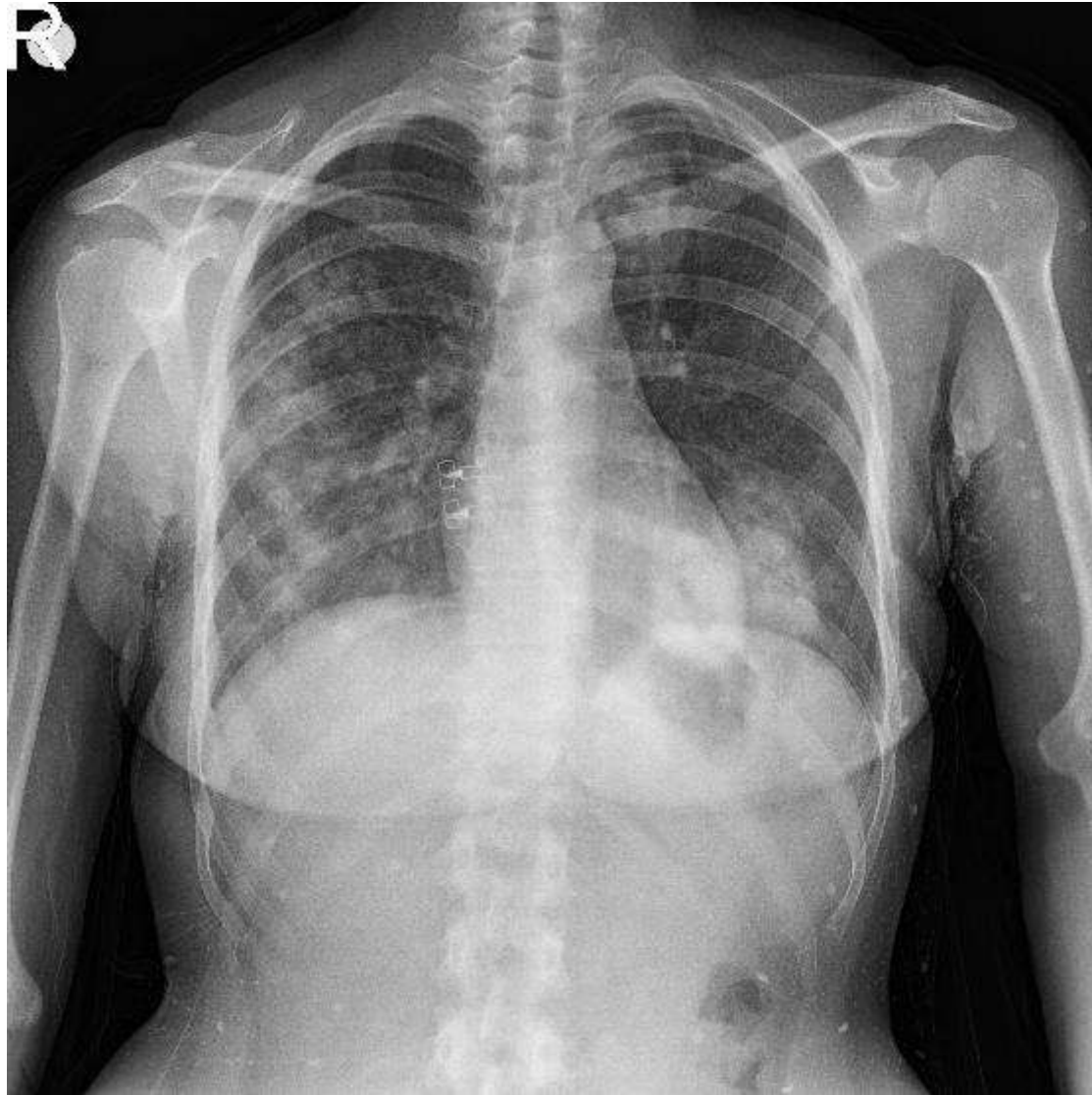
➤ CBC

- ✓ WBC: 9410/ μ L
- ✓ Hb: 8.5 g/dL
- ✓ Hct: 26.6 %
- ✓ Plt: 374000/ μ L
- ✓ CRP: 145 mg/L (0-5)

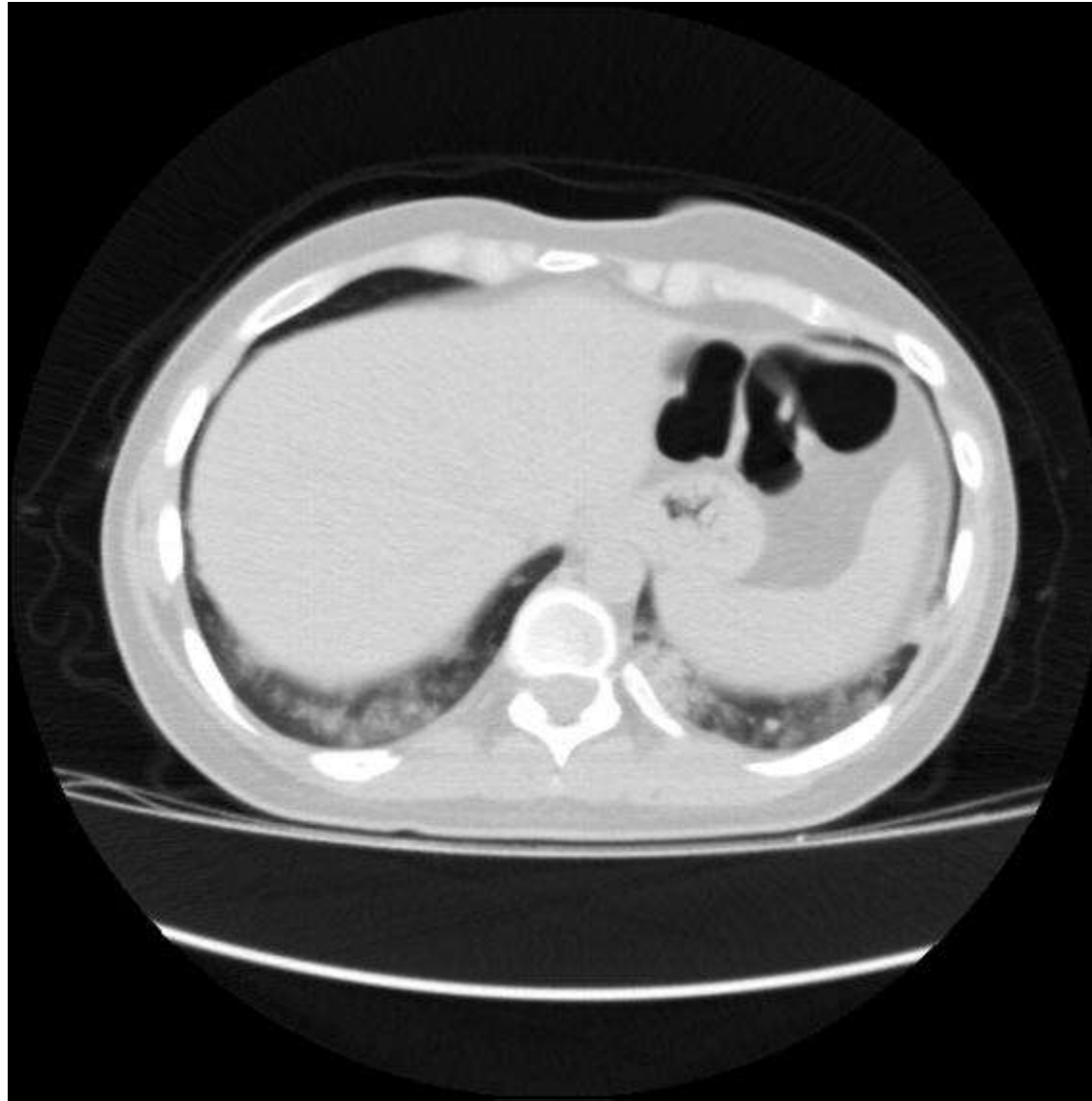
➤ Biochemistry

- ✓ Urea: 52 mg/dl
- ✓ Creatinine: 0.58 mg/dl
- ✓ AST: 37 U/L
- ✓ ALT: 49 U/L
- ✓ Urinalysis
 - +++ RBC/uL

09.11.2019



12.11.2019





F.C.
FIRAT ÜNİVERSİTESİ HASTANESİ
RADYOLOJİ RAPORU



Adı Soyadı :	Rapor Tarihi :	12.11.2019 01:20
T.C Kimlik No :	Dosya no :	809719
Baba Adı : ŞÜKRÜ	Başvuru No :	8673281
Kurumu : SSK SAĞLIK İŞLERİ MÜDÜRLÜĞÜ	Doğum Yeri - Tarih :	ELAZIĞ - 1990 Yaş:29
İstem Tarihi : 12.11.2019(18295976)	İstem Kabul Tarihi :	12.11.2019(46261)
Hizmet Adı : BT, TORAKS	Cinsiyet :	K

Tanı :	Kodu	Adı
	R07.4	GÖĞÜS AĞRISI, TANIMLANMAMIŞ
	R06.0	DİSPNE
	M79.7	FİBROMİYALJİ
	D64	ANEMİ, DİĞER
	R06	SOLUNUM ANORMALLİKLERİ
	M25.5	EKLEM AĞRISI
	M79.9	YUMUŞAK DOKU BOZUKLUĞU, TANIMLANMAMIŞ
	R77.0	ALBÜMIN ANORMALLİĞİ
	M31.3	WEGENER GRANÜLOMATOZU

AC?L ÇOK KES?TL? B?LG?SAYARLI TOMOGRAF?
TORAKS

Teknik : Kontrast madde verilmeden yapılan 64-ÇKBT incelemesinde:

**Bilateral akci?erde yayg?n yamal? konsolidasyon alanlar?, tomurcuklanm?? a?aç
görünümleri ve yer yer kavitelerinde izlendi?i görünüm dikkati çekmektedir (Akci?er
tüberkülozu ?Vaskülit ?).**

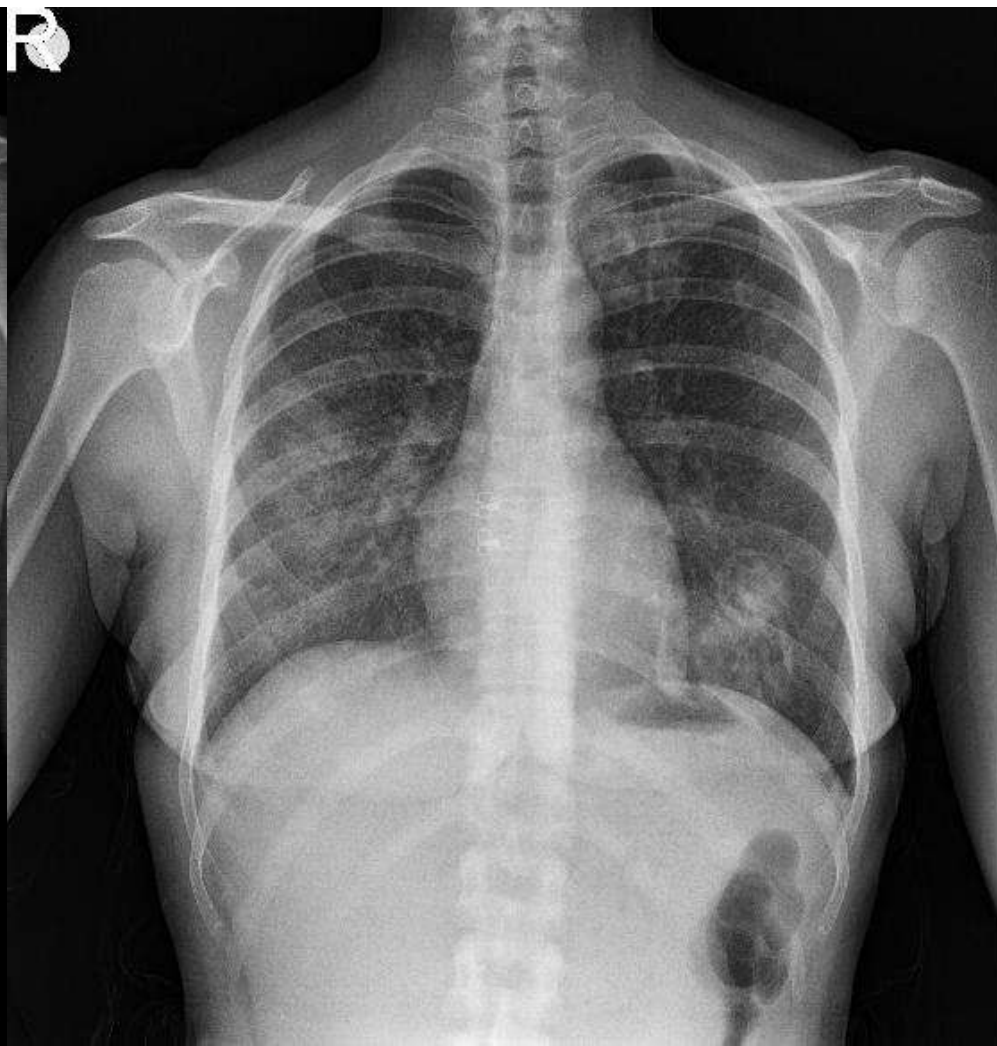
Thorax CT: Bilaterally widespread areas of patchy consolidation, "budding tree" appearances, and cavities (Tuberculosis? Vasculitis?)

- The patient was hospitalized to the ICU with a diagnosis of **alveolar hemorrhage**
- Methylprednisolone 1 g for 3 days, followed by 1 mg/kg (IV)
- Cyclophosphamide 500 mg IV
- Plasmapheresis
- Rituximab prescribed after 2 weeks

13.11.2019



18.11.2019



12.11.2019 09:04	-		ANCA-C	▲	ANCA C	37,9	U/ml	Pozitif
12.11.2019 09:04	-		ANTI-DS DNA (ELISA)		ANTI-DS DN...	<10,0	IU/ml	Negatif
12.11.2019 09:04	-		ANCA-P	▼	ANCA P	<3,0	IU/ml	Negatif

07.09.2017 08:15	H62.2 - OTİTİS EKSTERNA, MANTARLARDA H60.9 - OTİTİS EKSTERNA, TANIMLANMAMIŞ	KULAK BURUN BOĞAZ HASTALIKLARI
31.01.2018 14:57	H66.0 - AKUT SÜPÜRATİF OTİTİS MEDİA	KULAK BURUN BOĞAZ HASTALIKLARI
13.02.2018 10:10	H91.9 - İŞİTME KAYBI, TANIMLANMAMIŞ H66.3 - KRONİK SÜPÜRATİF OTİTİS MEDİA, DİĞER H62.2 - OTİTİS EKSTERNA, MANTARLARDA	KULAK BURUN BOĞAZ HASTALIKLARI

A review of past e-Nabız data revealed repeated visits to the ENT outpatient clinic



T.C.
FIRAT ÜNİVERSİTESİ HASTANESİ
RADYOLOJİ RAPORU



Adı Soyadı :		Rapor Tarihi :	14.11.2019 14:48
T.C Kimlik No :		Dosya no :	809719
Baba Adı :		Başvuru No :	8673281
Kurumu :	SSK SAĞLIK İŞLERİ MÜDÜRLÜĞÜ	Doğum Yeri - Tarih :	ELAZIĞ - 1990 Yaş: 29
Istem Tarihi :	12.11.2019(18301962)	Istem Kabul Tarihi :	12.11.2019(46255)
Hizmet Adı :	BT, PARANAZAL SINÜS	Cinsiyet :	K

Tanı :	Kodu	Adı
	R07.4	GÖĞÜS AĞRISI TANIMLANMAMIŞ
	R06.0	DİSPNE
	M79.7	FİBROMİYALJİ
	D64	ANEMİ, DİĞER
	R08	SOLUNUM ANORMALLİKLERİ
	M25.5	EKLEM AĞRISI
	M79.9	YUMUŞAK DOKU BOZUKLUĞU, TANIMLANMAMIŞ
	R77.0	ALBÜMİN ANORMALLİĞİ
	M31.3	WEGENER GRANÜLOMATOZU

KL?N?K: Wegener vaskülit

PARANAZAL SİNÜS BT NCELEMESİ

Koronal planda alınan kesitlerin değerlendirilmesinde

Bilateral orta konkada konka bülloza ile uyumlu görünüm izlendi.
Sağ maksiller sinüste ve sfenoid sinüs sol komponentte mukozal kalınlaşmalar izlenmektedir (inflamatuar Sinüs Hastalığı?).
Sol maksiller sinüsün aerasyonları tabiidir

Paranasal sinus CT: Mucosal thickening was observed in the right maxillary sinus and the left component of the sphenoid sinus; **Inflammatory sinus disease?**

**T.C
FIRAT ÜNİVERSİTESİ
PATOLOJİ LABARATUVARI
PATOLOJİ RAPORU**

BİYOPSİ RAPORU

Hasta Adı Soyadı		Biyopsi/Sitoloji No	B-16164/19
Biyopsi/Sitoloji No	B-16164/19	İsteyen Bölüm	ROMATOLOJİ YOĞUN BAKIM ÜNİTESİ
T.C. Kimlik No	4562*****	Tetkiki İsteyen Doktor	SÜLEYMAN SERDAR KOCA .
Yaş / Cinsiyeti	29 / K	Rapor İlk Kayıt Tarihi	
DosyaNo	809719		

Tetkik İstem Zamanı	21.11.2019 11:04	Numune Kabul Zamanı	21.11.2019 11:08
Numune Alma Zamanı	21.11.2019 11:04	Uzman Onay Zamanı	02.01.2020 09:54
Rapor Onay Tarihi	30.12.2019 10:25	İstem Tarihi	21.11.2019(18380092
Rapor Kes. Tarihi	02.01.2020 09:54	İstem Kabul Tarihi	21.11.2019(909520)

KLİNİK ÖZET:

KLİNİK BİLGİ:

KL?N?K ÖN TANI: Wegener granülomatozu?

MAKROSKOB?: Formol tespitli 0,3-0,2 cm çap?nda kirli beyaz renkli düzensiz ?ekli 2 adet materyalin tümü takibe al?nd? (2P-1K)

H?STOK?MYASAL BOYALAR:

PAS:Ola?an

GMS:Ola?an

TANI:

BURUN SA? SEPTUM MUKOZASI, PUNCH B?YOPS?:

-ÜLSER, ?LT?HAB? GRANÜLASYON DOKUSU VE AKT?F KRON?K ?NFLAME MUKOZAL DOKU FRAGMANLARI

Yorum: Gönderilen biyopsi örnekleri nonspesifik ülsere yüzeysel mukozal doku fragmanlar?ndan ibaret olup mevcut biyopsiyle klinik ön tan?ya yönelik daha ileri yorum yap?lamam??t?r. Klinik korelasyon önerilir.

Right nasal septal mucosa biopsy: Ulcer, inflammatory granulation tissue, active chronic inflamed mucosal tissue

Our patient has;

- Bilaterally widespread areas of patchy consolidation, "budding tree" appearances, and cavities on Thorax CT
- Hematuria
- Inflammatory granulation tissue on nasal septal mucosa
- c-ANCA (+)

VASCULITIS

THE AMERICAN COLLEGE OF RHEUMATOLOGY 1990 CRITERIA FOR THE CLASSIFICATION OF WEGENER'S GRANULOMATOSIS

**RANDI Y. LEAVITT, ANTHONY S. FAUCI, DANIEL A. BLOCH, BEAT A. MICHEL,
GENE G. HUNDER, WILLIAM P. AREND, LEONARD H. CALABRESE, JAMES F. FRIES, J. T. LIE,
ROBERT W. LIGHTFOOT, JR., ALFONSE T. MASI, DENNIS J. McSHANE, JOHN A. MILLS,
MARY BETTY STEVENS, STANLEY L. WALLACE, and NATHAN J. ZVAIFLER**

Arthritis and Rheumatism, Vol. 33, No. 8 (August 1990)

Table 3. 1990 criteria for the classification of Wegener's granulomatosis (traditional format)*

Criterion	Definition
1. Nasal or oral inflammation	Development of painful or painless oral ulcers or purulent or bloody nasal discharge
2. Abnormal chest radiograph	Chest radiograph showing the presence of nodules, fixed infiltrates, or cavities
3. Urinary sediment	Microhematuria (>5 red blood cells per high power field) or red cell casts in urine sediment
4. Granulomatous inflammation on biopsy	Histologic changes showing granulomatous inflammation within the wall of an artery or in the perivascular or extravascular area (artery or arteriole)

* For purposes of classification, a patient shall be said to have Wegener's granulomatosis if at least 2 of these 4 criteria are present. The presence of any 2 or more criteria yields a sensitivity of 88.2% and a specificity of 92.0%.

2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for granulomatosis with polyangiitis

Joanna C Robson ¹, Peter C Grayson ², Cristina Ponte ³, Ravi Suppiah ⁴, Anthea Craven ⁵, Andrew Judge ^{6 7}, Sara Khalid ⁵, Andrew Hutchings ⁸, Richard A Watts ^{5 9}, Peter A Merkel ¹⁰, Raashid A Luqmani ⁵; DCVAS Investigators

- Bloody nasal discharge, nasal crusting, or sinonasal congestion (+3)
 - Cartilaginous involvement (+2)
 - Conductive or sensorineural hearing loss (+1)
 - Cytoplasmic ANCA or anti-PR3 ANCA positivity (+5)
 - Pulmonary nodules, mass, or cavitation on chest imaging (+2)
 - Granuloma or giant cells on biopsy (+2)
 - Inflammation or consolidation of the nasal/paranasal sinuses on imaging (+1)
 - Pauci-immune glomerulonephritis (+1)
 - Perinuclear ANCA or anti-MPO ANCA positivity (-1)
 - Eosinophil count more than 1×10^9 cells/L (-4)
- Total score: 10

After excluding mimics of vasculitis, a patient diagnosed with small- or medium-vessel vasculitis could be classified as having GPA if the cumulative score is 5 or more points. When these criteria were tested in the validation dataset, the sensitivity was 93%, and the specificity was 94%.^[28]

EULAR/ERA-EDTA recommendations for the management of ANCA-associated vasculitis

M Yates,^{1,2} R A Watts,^{2,3} I M Bajema,⁴ M C Cid,⁵ B Crestani,⁶ T Hauser,⁷ B Hellmich,⁸ J U Holle,⁹ M Laudien,¹⁰ M A Little,¹¹ R A Luqmani,¹² A Mahr,¹³ P A Merkel,¹⁴ J Mills,¹⁵ J Mooney,¹ M Segelmark,^{16,17} V Tesar,¹⁸ K Westman,¹⁹ A Vaglio,²⁰ N Yalçındağ,²¹ D R Jayne,²² C Mukhtyar¹

Ann Rheum Dis 2016;75:1583–1594. doi:10.1136/annrheumdis-2016-209133

Table 1 Recommendation statements

Statement	Level of evidence	Grade of recommendation
1. We recommend that patients with AAV are managed in close collaboration with, or at, centres of expertise.	3	C
2. A positive biopsy is strongly supportive of a diagnosis of vasculitis and we recommend biopsies to assist in establishing a new diagnosis and for further evaluation for patients suspected of having relapsing vasculitis.	3	C
3. For remission-induction of new-onset organ-threatening or life-threatening AAV we recommend treatment with a combination of glucocorticoids and either cyclophosphamide OR rituximab.	1 for GPA/MPA, 3 for EGPA	A for GPA/MPA, C for EGPA
4. For remission-induction of non-organ-threatening AAV we recommend treatment with a combination of glucocorticoids and either methotrexate or mycophenolate mofetil*.	1B	B for MTX, C for MMF
5. For a major relapse of organ-threatening or life-threatening disease in AAV we recommend treatment as per new disease with a combination of glucocorticoids and either cyclophosphamide OR rituximab.	1 for GPA/MPA, 3 for EGPA and CYC, 4 for EGPA and RTX	A for GPA/MPA, C for EGPA and CYC, C for EGPA and RTX
6. (i) Plasma exchange should be considered for patients with AAV and a serum creatine level of ≥ 500 $\mu\text{mol/L}$ (5.7 mg/dL) due to rapidly progressive glomerulonephritis in the setting of new or relapsing disease.	1B	B
6. (ii) Plasma exchange can also be considered for the treatment of severe diffuse alveolar haemorrhage.	3	C

EULAR recommendations for the management of ANCA-associated vasculitis: 2022 update

Bernhard Hellmich ¹, Beatriz Sanchez-Alamo,² Jan H Schirmer,³ Alvise Berti ^{4,5}, Daniel Blockmans,⁶ Maria C Cid ⁷, Julia U Holle,⁸ Nicole Hollinger,¹ Omer Karadag,⁹ Andreas Kronbichler,^{10,11} Mark A Little,¹² Raashid A Luqmani,¹³ Alfred Mahr,¹⁴ Peter A Merkel ¹⁵, Aladdin J Mohammad ^{11,16}, Sara Monti ^{17,18}, Chetan B Mukhtyar ¹⁹, Jacek Musial,²⁰ Fiona Price-Kuehne,¹¹ Mårten Segelmark,²¹ Y K Onno Teng ²², Benjamin Terrier ²³, Gunnar Tomasson ^{24,25}, Augusto Vaglio ²⁶, Dimitrios Vassilopoulos ²⁷, Peter Verhoeven,²⁸ David Jayne ¹¹

Hellmich B, et al. *Ann Rheum Dis* 2024;**83**:30–47. doi:10.1136/ard-2022-223764

Table 2 Examples of organ/life-threatening and not organ/life-threatening manifestations in patients with AAV

Examples of potentially organ/life-threatening manifestations*

Glomerulonephritis

Pulmonary haemorrhage

Meningeal involvement

Central nervous system involvement

Retro-orbital disease

Cardiac involvement

Mesenteric involvement

Mononeuritis multiplex

Examples of manifestations that are not ultimately organ/life-threatening*

Nasal and paranasal disease without bony involvement (erosion) or cartilage collapse or olfactory dysfunction or deafness

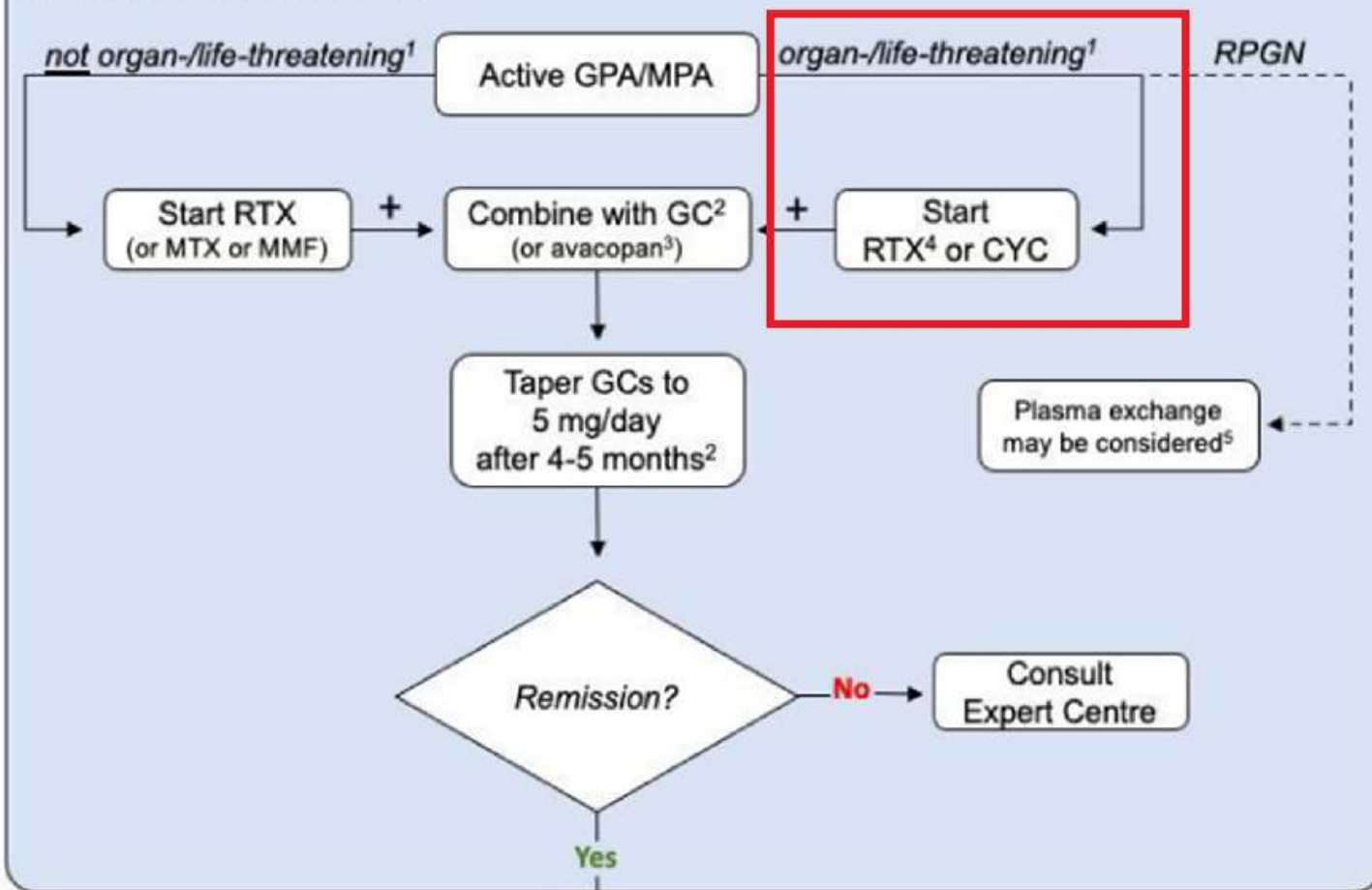
Skin involvement without ulceration

Myositis (skeletal muscle only)

Non-cavitating pulmonary nodules

Episcleritis

Induction of Remission



As part of regimens for induction of remission in GPA or MPA, we recommend treatment with oral glucocorticoids at a starting dose of 50–75 mg prednisolone equivalent/day, depending on body weight. We recommend stepwise reduction in glucocorticoids according to [table 4](#) and achieving a dose of 5 mg prednisolone equivalent per day by 4–5 months.

Plasma exchange may be considered as part of therapy to induce remission in GPA or MPA for those with a serum creatinine >300 µmol/L due to active glomerulonephritis.*

Routine use of plasma exchange to treat alveolar haemorrhage in GPA and MPA is not recommended.†

At 6th month of induction treatment

- No symptom
- PE: No pathological sign
- Lab: Hb: 13 gr/dl, Hct: %35
- Urine analysis: N
- Treatment with Rituximab every 6 months planned

Maintenance of Remission

Continue or switch to RTX for 24-48 months
(or AZA or MTX)
continue GC taper / stop avacopan⁶

Induction of remission
(see upper panel)

Sustained
Remission?

No

Relapse

Yes

GC/avacopan⁶
stopped?

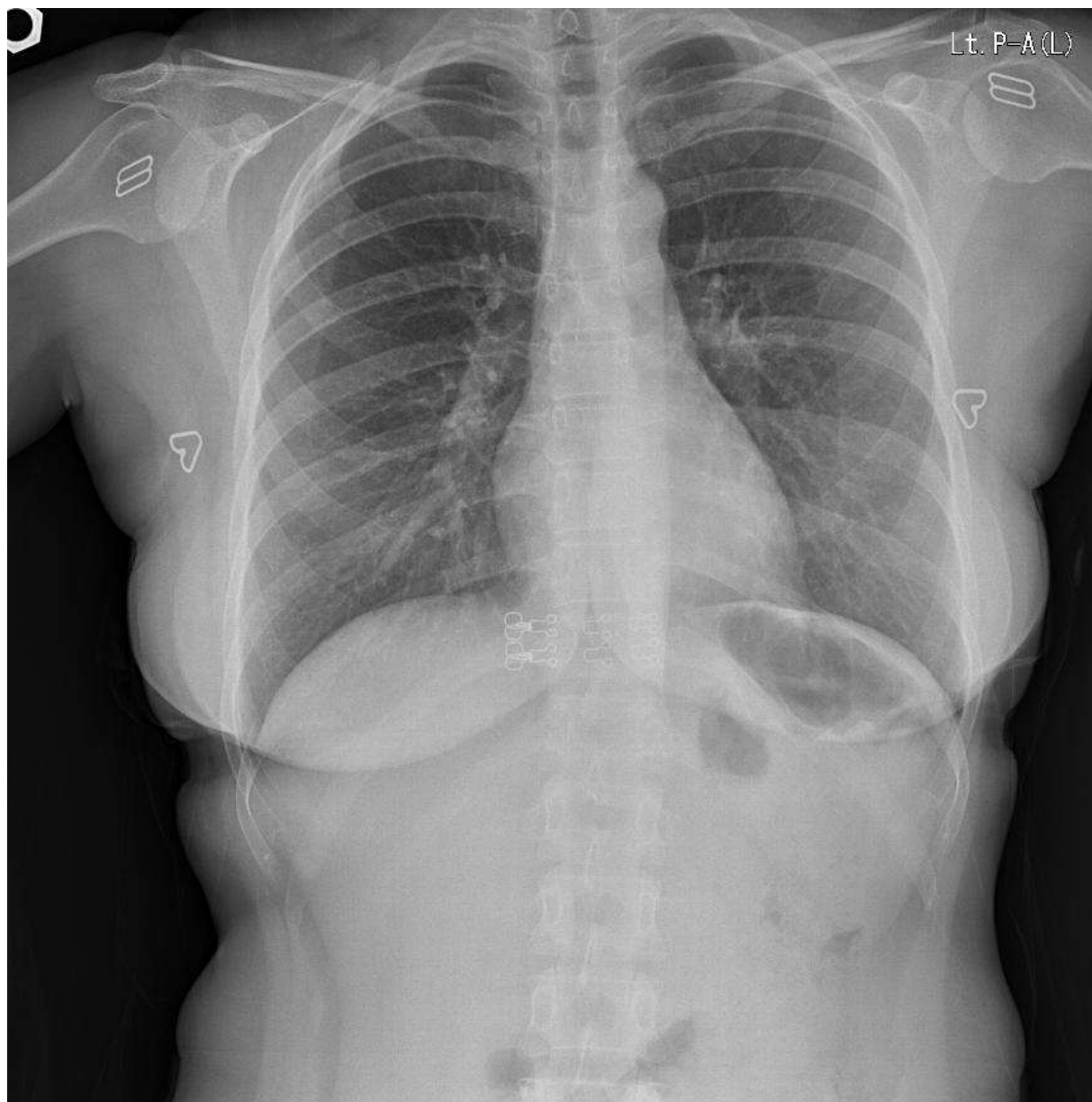
Yes

Assess individual relapse risk,
comorbidities and patient preferences

Continue or stop
maintenance treatment

We recommend that therapy to maintain remission for GPA and MPA be continued for 24–48 months following induction of remission of new-onset disease.* Longer duration of therapy should be considered in relapsing patients or those with an increased risk of relapse, but should be balanced against patient preferences and risks of continuing immunosuppression.†

Last visit 09.04.2026



Laboratory

➤ CBC

- ✓ WBC: 8300/ μ L
- ✓ Hb: 13.8 g/dL
- ✓ Hct: 41.2 %
- ✓ Plt: 374000/ μ L
- ✓ CRP: 4.5 mg/L

➤ Biochemistry

- ✓ Urea: 25 mg/dl
- ✓ Creatinine: 0.58 mg/dl
- ✓ AST: 15 U/L
- ✓ ALT: 18 U/L

✓ Urinalysis

- +/- RBC/uL

- The case remains stable in the 7th year of maintenance therapy...

Case-3

- 50 y, F
- Complaints: Cough, sputum
- Receiving IVIG (30 g/month) for 1 year with a diagnosis of CVID
- Allergic rhinitis (+), Asthma (+)
- Skin lesions (-)
- Joint findings (-)

CURRENT
AKIN GER GRAFI PA (TEK YON)
12.05.2021 15:56
Name : ATEŞ FILİZ
7/09/2021
Accession Number: 6002661021
Birth Date : 1.09.1973
F/50Y
Acc. No : 6002661021

JPEG
Img 1/1 Srs 1/1
DX: CHEST
Step : Chest PA

10mm

DL%100 Vw%100
MagP:0.3 MagA%25.3

110

Performing Physician : COLAK SEVGİ UZM.DR.



- Sputum ARB x3 (-), no growth in culture (-)

FOB

- Lavage ARB (-), no growth in culture (-)
- BAL: % 11 lymphocytes, % 54 macrophages, % 35 neutrophils, CD4/CD8: 1.7
- Cytology: Marked neutrophil leukocyte increase, benign in nature, inflammatory BAL findings
- Tru-cut biopsy: Findings of fibrosis and inflammation

- **EBUS:** 4R, 7, 11L, 11R lymph nodes were sampled
- TBB applied
- Diagnosis: **Granulomatous inflammation**

TANI

GRANÜLOMATÖZ İNFLAMASYON BULGULARI, BRONŞ BİYOPSİSİ.

YORUM

Olgunun, sarkoidozis ve tbc başta olmak üzere olası granülomatöz inflamasyon etyolojileri yönünden araştırılması önerilir

- Lavage ARB (-)
- TB PCR (-)
- *Mycobacterium Tuberculosis* culture (-)
- TST: 4 mm
- IGRA: (-)
- Given the diagnosis of CVID,
- **The patient was diagnosed with GLILD**

Granulomatous and Lymphocytic Interstitial Lung Disease

- GLILD is a severe non-infectious complication of CVID
- GLILD develops in 8-20% of CVID patients
- GLILD is a significant cause of morbidity and premature mortality among patients with CVID
- GLILD has been defined as “a distinct **clinico-radio-pathological ILD** occurring in patients with CVID, associated with a **lymphocytic infiltrate and/or granuloma** in the lung, and in whom other conditions have been considered and where possible excluded”

Hurst JR, et al. British lung foundation/United Kingdom primary immunodeficiency Network consensus statement on the definition, diagnosis, and management of granulomatous-lymphocytic interstitial lung disease in common variable immunodeficiency disorders. J Allergy Clin Immunol Pract. 2017;5(4):938–945

Predictors for GLILD diagnosis

- Splenomegaly
- Autoimmune cytopenias
- Low IgG, IgM and IgA levels
- Increased CD21^{lo} B cells percentage
- Lower percentage of switched-memory B cells and marginal zone B cells
- Low TLC, FVC, and DLCO %pred

Clinical manifestation

- 20-50 years
- Higher prevalence among females
- 15% of patients may be asymptomatic
- Symptoms; exertional dyspnea and nonproductive cough
- Production of sputum, wheezing can be seen in patients with concomitant bronchiectasis
- PE: Inspiratory crackles, wheezing, splenomegaly, lymphadenopathy

Approach to diagnosing and managing granulomatous-lymphocytic interstitial lung disease



eClinicalMedicine
2024;75: 102749



Jessica Galant-Swofford,^a Jason Catanzaro,^b Rosane Duarte Achcar,^c Carlyne Cool,^d Tilman Koelsch,^e Tami J. Bang,^e David A. Lynch,^e Rafeul Alam,^a Rohit K. Katial,^a and Evans R. Fernández Pérez^{f,*}

HRCT Pattern^a

Typical GLILD

Distribution

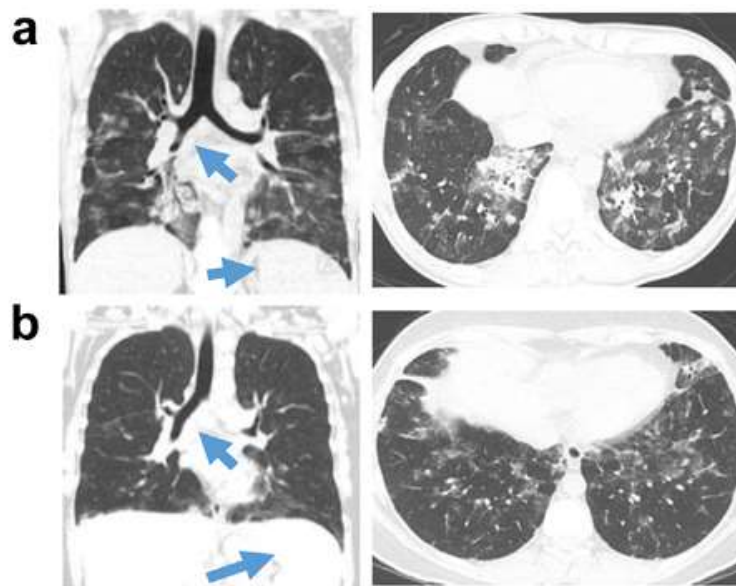
- Axial: peribronchovascular predominance
- Craniocaudal: lower lung zones

Features

- All of the following features: nodularity, ground-glass opacity, consolidation

Other findings

- Hilar, mediastinal lymphadenopathy, splenomegaly



Approach to diagnosing and managing granulomatous-lymphocytic interstitial lung disease

Jessica Galant-Swafford,^a Jason Catanzaro,^b Rosane Duarte Achcar,^c Carlyne Cool,^d Tilman Koelsch,^e Tami J. Bang,^e David A. Lynch,^e Rafeul Alam,^a Rohit K. Katial,^a and Evans R. Fernández Pérez^{f,*}



eClinicalMedicine
2024;75: 102749



Histopathological Pattern^b

Typical GLILD

Major features

- Presence of two major features in at least one of the sampled lobe(s) of the lung (surgical lung biopsy):
 1. Pulmonary lymphoid hyperplasia with reactive germinal centers in the form of:
 - Follicular bronchiolitis, And/or
 - Nodular lymphoid hyperplasia, And/or
 - Any interstitial lymphocytic infiltrates
 2. Granulomas (well, moderately, or poorly-formed)

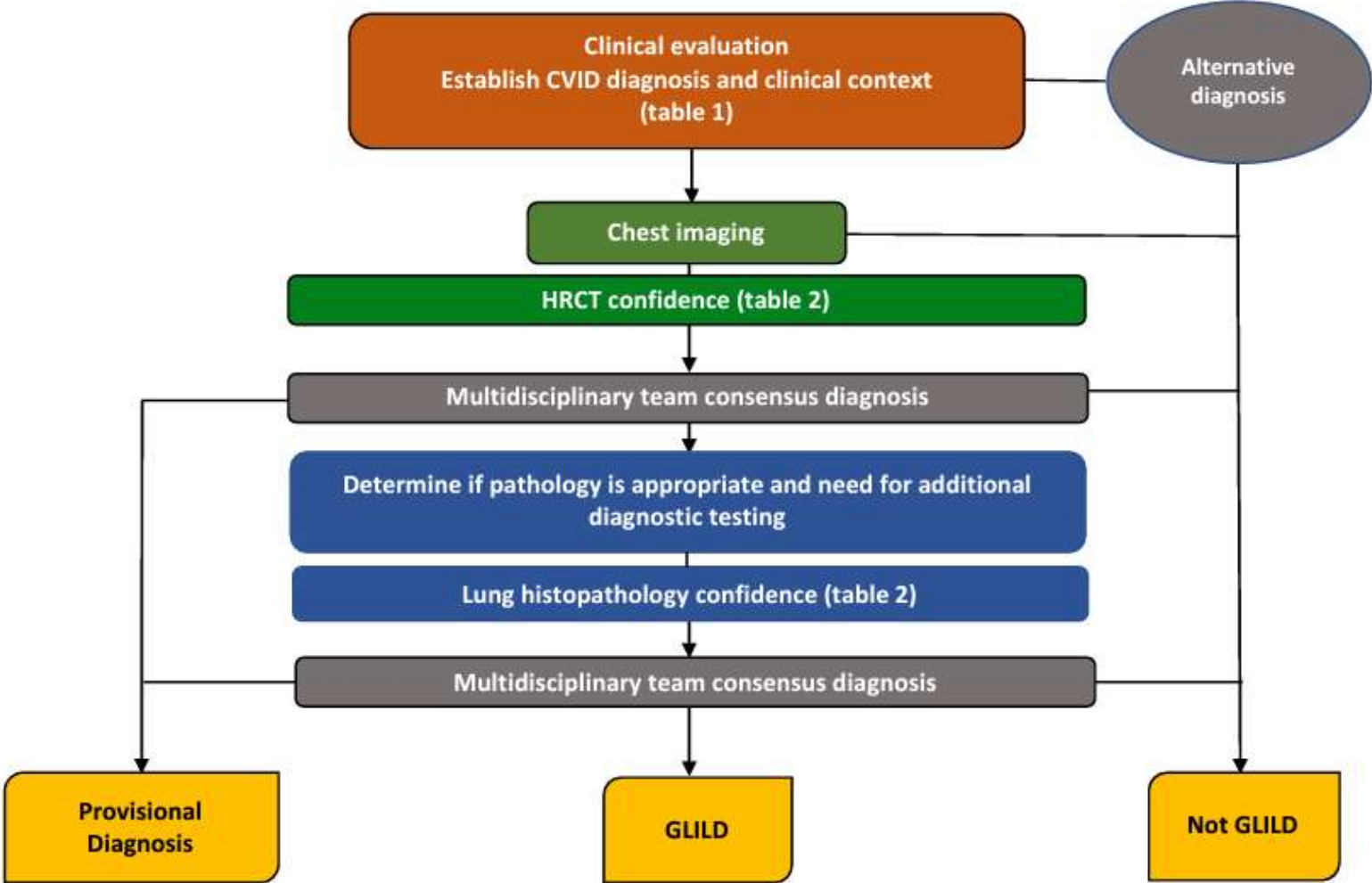
Secondary features

1. Organizing pneumonia
2. Interstitial scarring
 - Lack of features of an alternative diagnosis

Approach to diagnosing and managing granulomatous-lymphocytic interstitial lung disease



Jessica Galant-Swofford,^a Jason Catanzaro,^b Rosane Duarte Achcar,^c Carlyne Cool,^d Tilman Koelsch,^e Tami J. Bang,^e David A. Lynch,^e Rafeul Alam,^a Rohit K. Katial,^a and Evans R. Fernández Pérez^{f,*}



GRANULOMATOUS-LYMPHOCYTIC INTERSTITIAL LUNG DISEASE MIMICKING SARCOIDOSIS

*David M Perlman¹, Muthya Tejasvini Sudheendra¹, Emilian Racila², Tadashi L Allen³, Avni Joshi⁴,
Maneesh Bhargava¹*

Table 1. Differences in Granulomatous lymphocytic interstitial lung disease and sarcoidosis

Feature	GLILD	Sarcoidosis
Organ system involvement (22, 55)		
Pulmonary	51%	95%
Spleen	46%	6.7
Lymph node		15.2
Liver	41%	11.5
Skin	7%	15.9
Bone marrow	8%	3,9%
CNS	5%	4.6%
GI tract	15%	Rare
Recurrent infections	Common	May occur if architectural distortion of lung
Autoimmunity	Frequently report	Not seen
Immunoglobulin levels	Low	Normal or high. May be low in patients on long term steroids
Chest CT		
Distribution	Could have lower lobe disease	Upper lobe predominant disease
Common finding	Larger nodule with random or perilymphatic distribution	Perilymphatic micronodular infiltrate in bronchovascular distribution
Flame shape hemorrhage, 'halo' sign (16)	More common than sarcoidosis	Could be seen
Bronchiectasis	Common due to recurrent infections	Cicatricial bronchiectasis in setting of architectural distortion
Mediastinal / hilar adenopathy	Present	More prominent
Bronchoalveolar fluid findings		
Cultures	Rules out infection in cases of CVID (42)	Usually negative. Must rule out etiologies that may mimic clinical or radiologic manifestations of sarcoidosis such as histoplasma or tuberculosis
CD4: CD8 ratio	Usually, normal	High (> 3.5)

Treatment

- IGRT should be optimized before the initiation of immunosuppressive therapy
- Immunosuppressive treatment (steroid, MMF, AZA), rituximab
- Hematopoietic stem cell transplantation (HSCT) is a potential definitive therapy

Thank you for your attention...