INTERSTITIAL LUNG DISEASES

By

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- **General features of ILDs**
- **Idiopathic Pulmonary Fibrosis (IPF)**
- **Sarcoidosis**

INTERSTITIAL LUNG DISEASES

- They are also called Diffuse Parenchymatous lung diseases which are heterogenous groups of diseases characterized by diffuse inflammation of the interstitium with alveoli (alveolo-interstitial affection) and they are are sharing certain similar features clinically , pathologically and radiologically but they are completely different regarding the etiologic cause

- **ILDs might be :**

A) Primary (I.e group which is idiopathic in etiology called "Idiopathic interstitial pneumonias or pneumonitis"

B) Secondary to either

☞ ***Certain etiologic cause***

- Drugs: eg methotrexate & amiodarone etc
- Collagen diseases E.g Scleroderma , etc
- radiation E.g Radiation pneumonitis
- hypersensitivity E g hypersensitivity pneumonitis (HSP)
- occupational as in chronic exposure to inorganic dust like pneumoconiosis & asbestosis

☞ ***Granulomatous disease*** such as Sarcoidosis (multisystem affection)

☞ ***Rare forms of ILDs***

- Pulmonary Langerhans cell histeocytosis (PLCH)
- Eosinophilic pneumonia
- Lymphangio- leiomyomatosis

optional امراض صعبة الاسم ونادره معرفتها

General features of ILDs (DPLDs)

➢ Pathophysiology

بعض هذة الأمراض تتميز بأن التهاب ال interstial tissue يؤدى إلى

Activation of fibroblasts (main cell in the interstium)

To produce excess collagen mediated certain chemicals (mediators) e.g TGF B1

---> Fibrosis --> fibrotic lung diseases

تكون هذة التغيرات شديده جدااا وتصل لأقصى درجه لها فى مرض يسمى

Idiopathic pulmonary fibrosis

These fibrotic changes will lead to the following

- Alveolar affection leads to defect in gas exchange unit (hypoxia = low O2 sat + low PaO2)
- changes in lung volumes, mechanics and function
- Fibrous tissue as it is retractile ---> leads to marked decrease in FVC and mild decrease in FEV1... So

المحصله إن ال

FEV1/FVC > 70 %

+

Diffusion defect (Alveolar damage) --> low DLCO or TLCO

Also decrease in KCO

➢ Clinical presentation

All ILDs present with

- Dyspnea on exertion
- Dry cough
- Inspiratory crackles (Velcro type) not altered by cough
- Fibrosis might be apical in location (insp crackles are heard on the apical regions) like in ankylosing spondylitis, Pneumoconiosis

  Or

  Might be basal, so inspiratory crackles are heard on the basal lung regions like IPF, Collagen diseases-associated fibrosis

- Some diseases present with finger clubbing e.g IPF & asbestosis
  Finger clubbing is due to chronic hypoxemia
- every chronic ILD might be complicated é Pulmonary HTN (LL edema , increased JVP , accentuated P2 and left parasternal pulsations & heave)
- Occasional Wheezes might be heard in some ILD

Presentation in ILDs might be either

- gradual as in most of ILDs (over months to years)
- Acute (over days to weeks) rapid progressive dyspnea with development of respiratory failure with great similarly to ARDS as in Acute interstitial pneumonia (AIP) (it is one of idiopathic interstitial pneumonitis)
- Subacute (over weeks to months) such as (Cryptogenic organizing pneumonia COP)

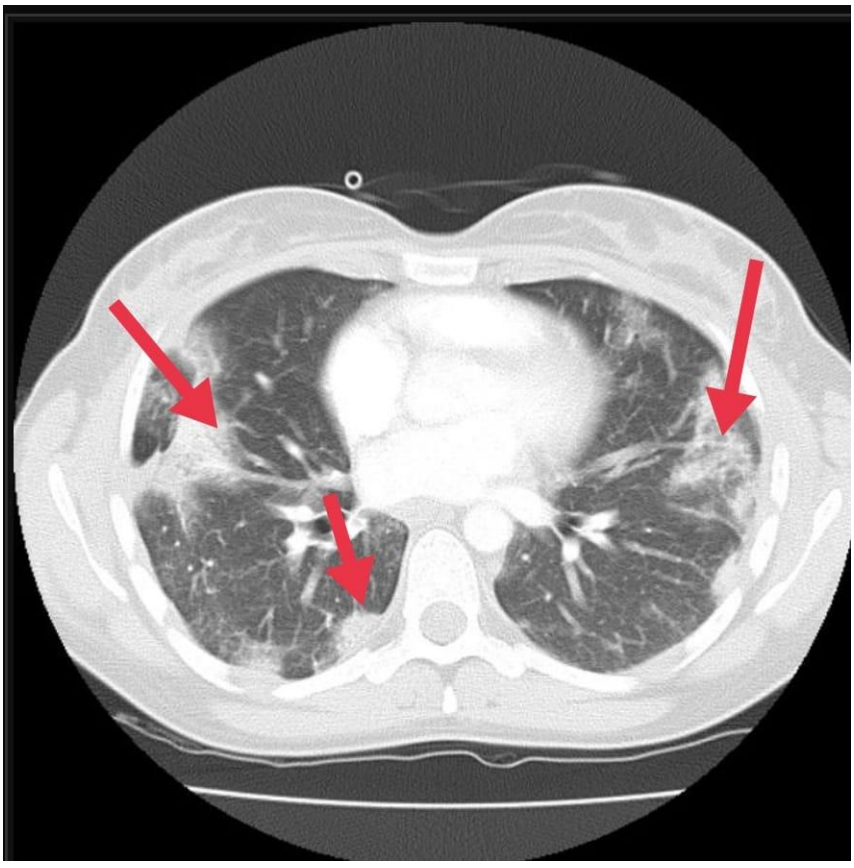
➢ Imaging

ILDs have certain characteristic features

I. Ground glass opacities

Ground-glass opacification/opacity (GGO) is referring to an area of increased attenuation in the lung on computed tomography (CT) with preserved bronchial and vascular markings.

It is (((a non-specific sign))) with a wide etiology including infections including COVID19 & other viral infections, chronic interstitial disease and acute alveolar disease

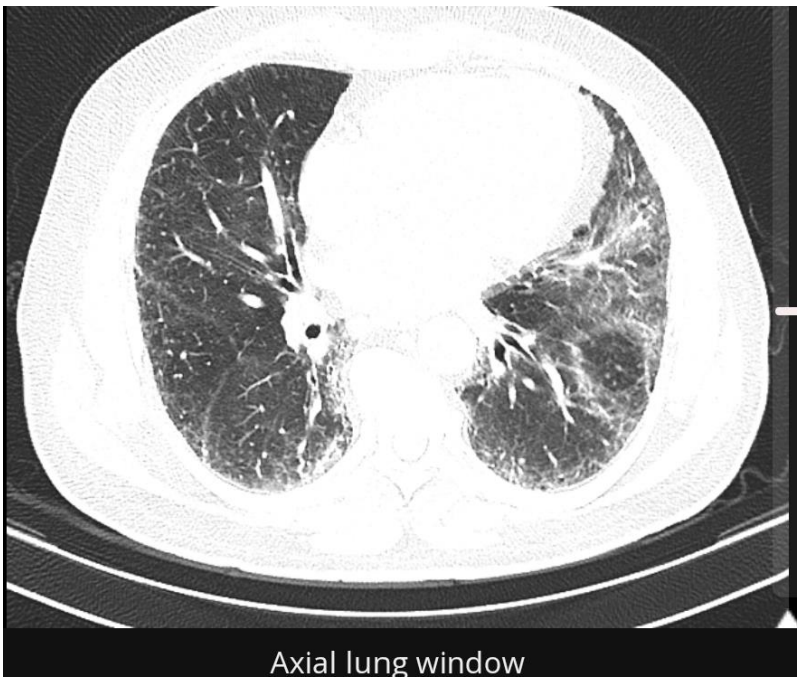


ملحوظه هاامه

1- IF Main widespread radiologic feature in ILD is GGOs --> this means the outcome is good & favourable (.ie responsive for ttt & reversible)
2- GGOs can't be evaluated in Chest X ray (just finding in High resolution CT chest (HRCT)

II. Reticular Opacities

Reticular opacities seen on HRCT in patients with diffuse lung disease can indicate lung infiltration with interstitial thickening or fibrosis.

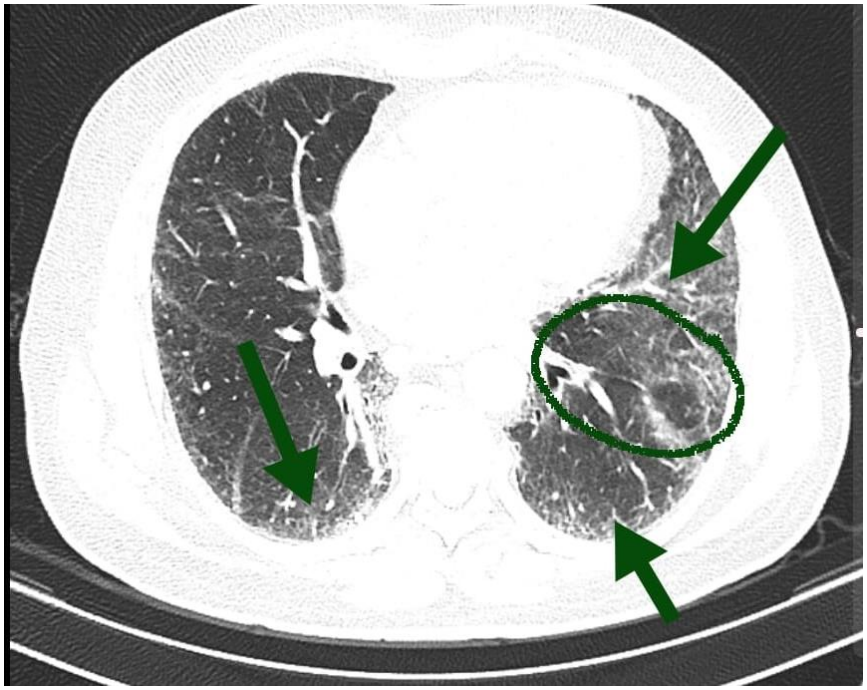

Axial lung window

Three principal patterns of reticulation may be seen.

1) Reticular pattern

These are Interlobular septal thickening and irregular reticulation

خطوط كثيره متقاطعه بتدى منظر الشبكه



ملحوظه هامة :

الخطوط نفسها لا تؤدى إلى تغيير فى ال transparency فى ال lung field ولكن قد تلاحظ Haziness كخلفيه للreticularations كما هو واضح فى الصورة

This haziness = GGOs يبقى غالبا ما يكون ال Reticularations are present on background of GGOs

☞ **Reticular pattern in CXR**

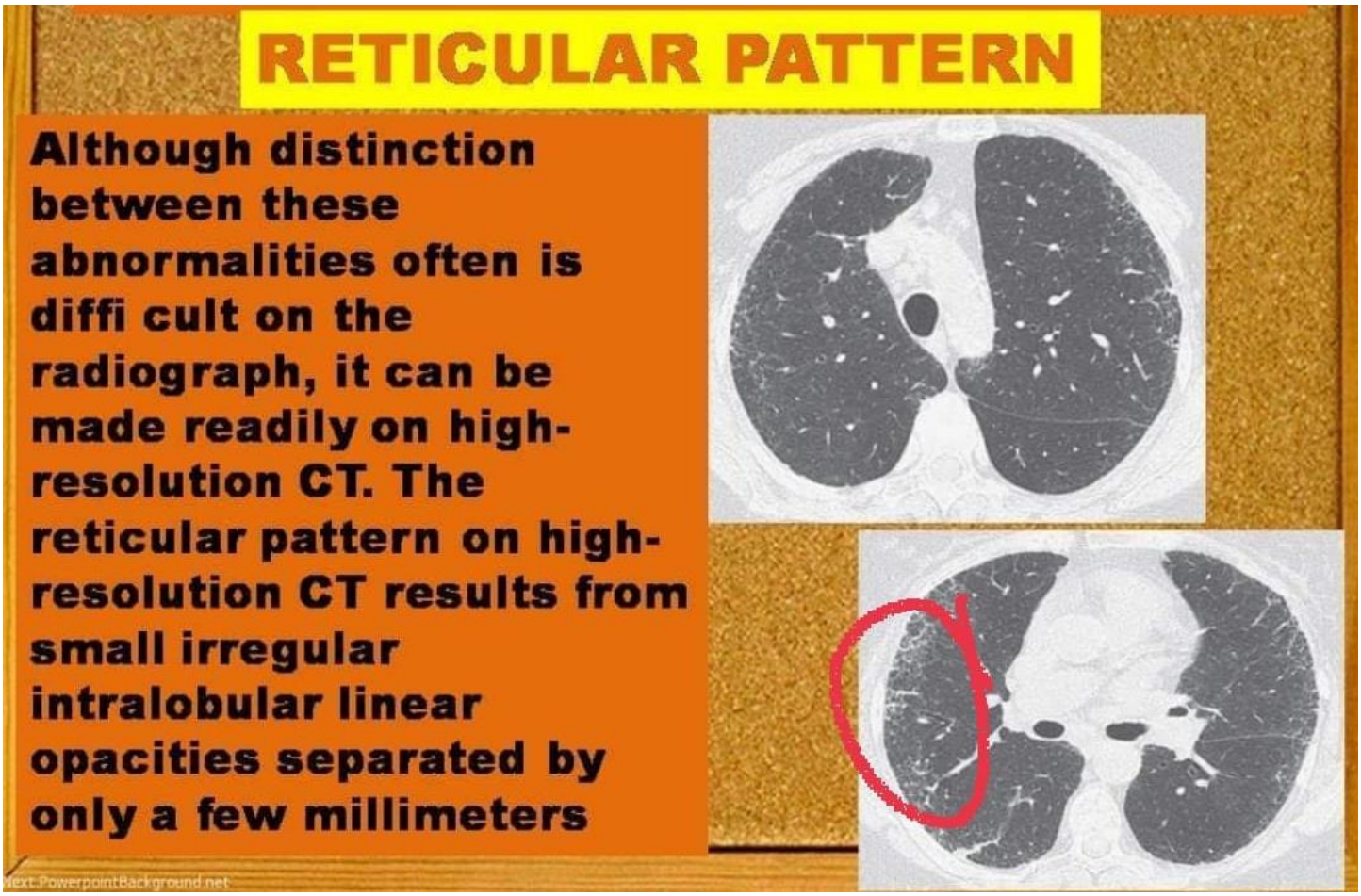
Interstitial Pattern

RETICULAR PATTERN

A reticular pattern is characterized by innumerable, interlacing line shadows that suggest a mesh. On the chest radiograph, the pattern may be the result of summation of smooth or irregular linear opacities, cystic spaces, or both

Common causes of a reticular pattern include idiopathic interstitial fibrosis, nonspecific interstitial pneumonia, fibrosis associated with collagen vascular disease, chronic hypersensitivity pneumonitis, sarcoidosis, and asbestosis.

☞ **Reticular pattern in CT**



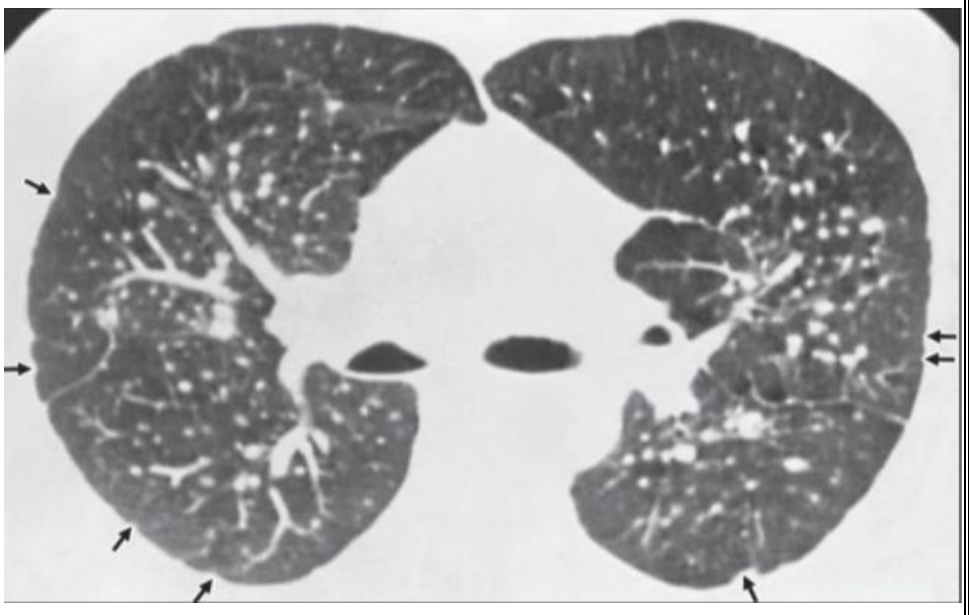
2) Nodular pattern

Some ILDs like Sarcoidosis, hypersensitivity pneumonitis and Respiratory bronchiolitis related ILD have nodular pattern in HRCT

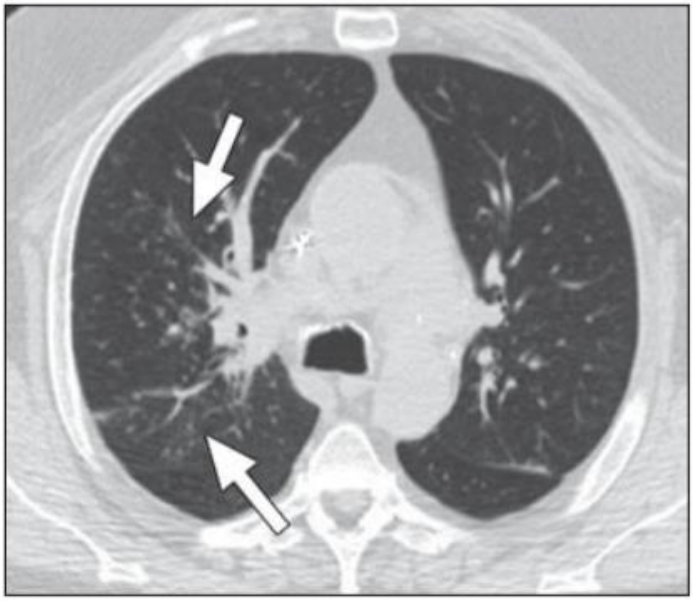
Nodules are well defined dot like lesions

Example

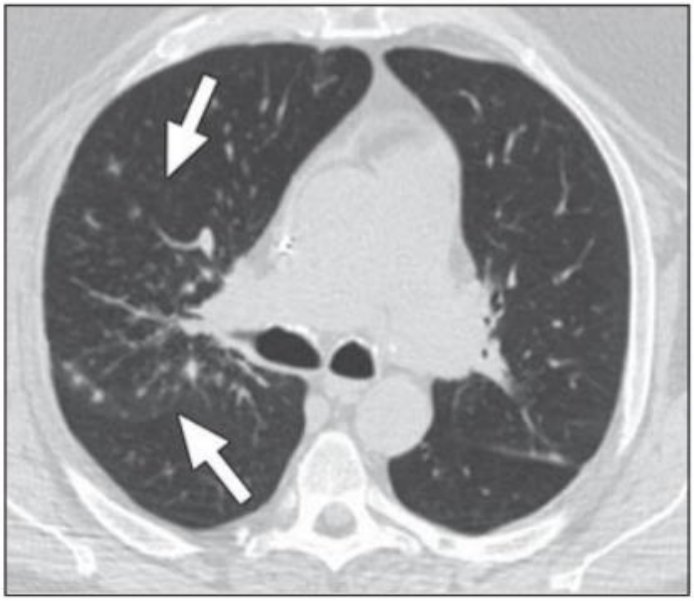
- Silicosis →



- Perihilar interstitial nodules in Sarcoidosis



A



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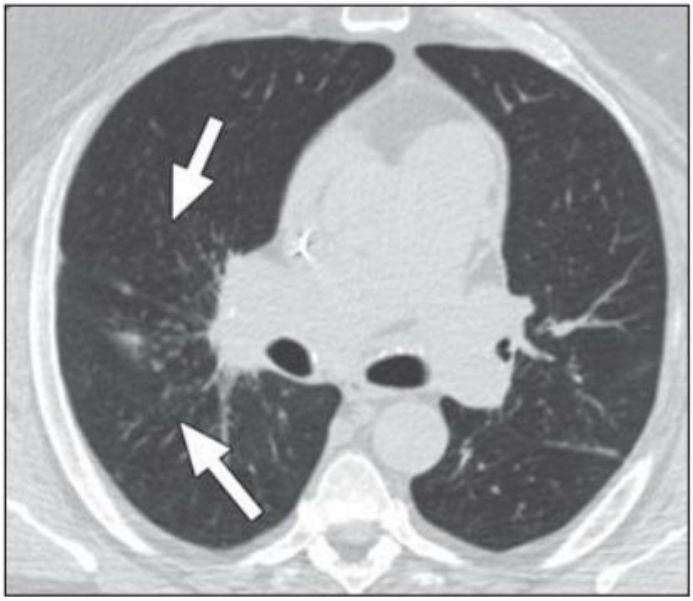


C

Fig. 5—Sarcoidosis.
A–C, CT images at various anatomic levels show primarily perihilar interstitial nodules (*arrows*) in typical distribution.

- Ill defined small nodules that surround the emphysematous lesions in disease called Respiratory bronchiolitis -associated ILD (smoking related disease)

A

B

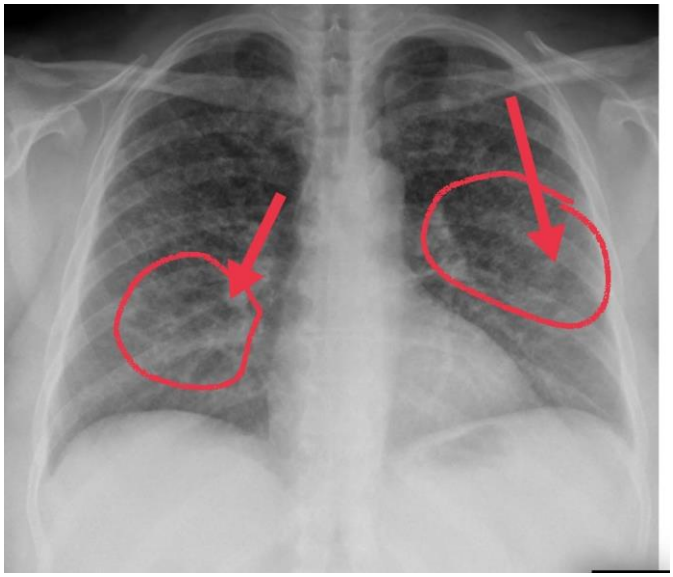
C

Fig. 12—Respiratory bronchiolitis.
A–C, CT images obtained at various levels of right upper lobe show centrilobular emphysema (*white arrows*). Emphysematous lesions are surrounded by subtle, ill-defined airspace nodules, typical of disease (*black arrows*).

3) reticulo-nodular

Some ILD might present e' reticulo-nodular shadow in CXR

Reticulo-nodular shadow in CXR as in Pulmonary Lungerhans Cell histeocytosis (PLCH) that appears as multiple small sized cysts surrounded by nodules + GGOs



- In Some ILDs like Idiopathic pulmonary fibrosis (IPF) diffuse reticular show might be associated more severe radiologic fibrotic changes like

Honeycomb منظر خلية النحل

and **Traction bronchiectasis** منظرقضيب القطر

Fibrotic changes نتيجة

☞ This is a case of

Idiopathic Pulmonary Fibrosis {IPF}

الدائره الحمراء معلمه على منظر خلية النحل

(honeycomb) ال

والسهم بيشير لمنظر يشبة قضيب القطر أو الترام

Tram track

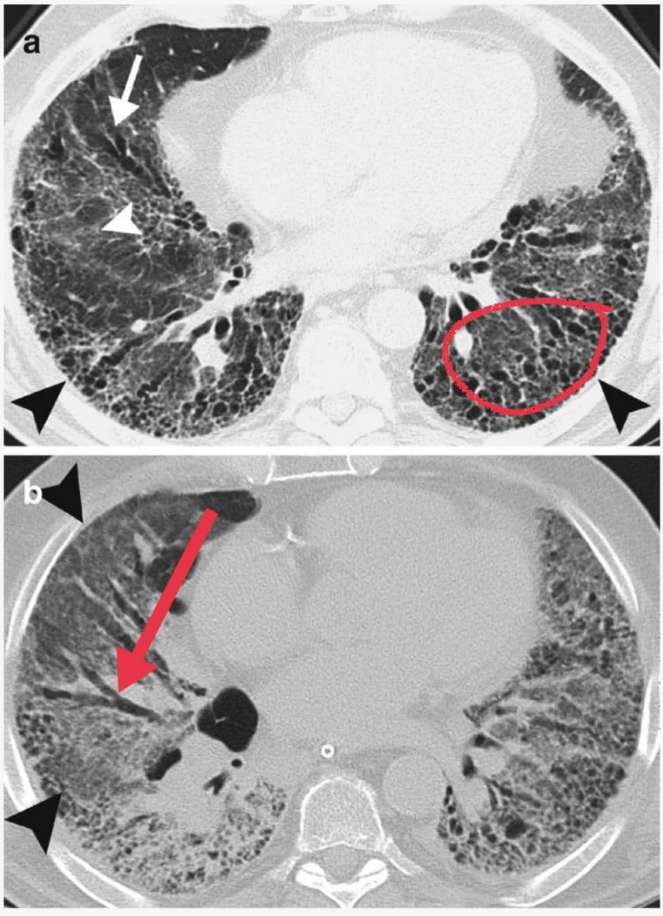
طبعا على خلفية متليفه

Tram track appearance + Honeycomb + GGOs + reticulations

Tram track فى الحالة دى ال

ده اسمه

TRACTION BRONCHIECTASIS



ملحوظة اولى :

دائما هتلاقى ال

Honeycomb: peripheral and subpleural

ملحوظة تانية :

Honeycomb = advanced fibrosis = bad prognosis & poor response to treatment particularly steroids and often it is irreversible

ملحوظة تالتة: غالبا ال honeycomb ده بنشوفه فى مرض الIPF

➢ SPIROMETRY

على مستوىspirometry

ILDs cause Restrictive pattern

FEV1 /FVC ≥ 70%

Marked ↓ in FVC

Mild ↓ in FEV1

Low DLCO or TLCO

Low KCO

Idiopathic pulmonary fibrosis IPF

- One of commonest interstitial lung diseases احد اشهر أمراض التليف الرئوى
- And it is one of the idiopathic interstitial pneumonitis
- previously called cryptogenic fibrosis Alveolitis

طب تحت الميكروسكوب لو اخدنا عينه من الرئه المصابه هيبان ايه ؟

Histopathologically = Usual interstitial pneumonitis

➢ Risk factors

- Age > 50 (middle & old patients
- M > F
- Associated GERD
- Smoking

➢ Pathophysiology

Activation of fibroblasts in the interstitial tissue of the lungs

⬇⬇⬇

Which lead to increased deposition of Excess Collagen

Through stimulation of transforming growth factor Beta 1{TGF beta 1}

⬇⬇⬇

--> Progressive fibrotic changes

⬇⬇⬇

Alveolar damage

⬇⬇⬇

Hypoxemia (low O2 saturation + low PaO2)

+

Restrictive pattern in SPIROMETRY

If not treated ➔➔Complications

➢ Complications

- ♦ Cor pulmonale (right sided heart failure + Pulmonary HTN due to chronic hypoxia
- ♦ Respiratory failure
- ♦ Acute exacerbation of IPF

➢ ما هى اعراض مرض ال IPF ؟

Symptoms (Non specific)

- Gradual dyspnea on exertion
- Dry cough

Signs

- Finger clubbing (25 - 50%)
- Bibasal inspiratory crackles not changed with cough
- Features of Pulmonary HTN (might be present)
  - Palpable & accentuated P2
  - High JVP
  - LL edema
  - Lt Parasternal heave

ملحوظة : لا تنسى أن التليف موجود فى ال (lower lung lobes) Basal lung lobes

➢ DD

Other idiopathic interstitial pneumonitis

- Non specific interstitial pneumonitis
- Desquamative interstitial pneumonitis DIP
- Lymphocytic I P
- Respiratory bronchiolitis Related ILD
- Acute interstitial pneumonitis AIP

Other causes of ILD

- Drugs
- Occupational causes
- Collagen diseases

هل هناك معايير عالمية حاسمة لتشخيص ال IPF ؟

الجواب : يوجد

ATS American Thoracic Society **/ ERS** European Respiratory Society

Diagnostic criteria for IPF

- **Major Criteria**

- Exclusion of other known causes of ILDs such as certain drug toxicities, environmental exposures, and connective tissue diseases
- Abnormal pulmonary function tests study showing evidence of restriction (high FEV1/FVC , + impaired gas exchange { low PaO2 or low TLCO}
- Bibasal reticular abnormalities with minimal ground glass opacities on HRCT
- Transbronchial lung biopsy or BAL showing no features supporting alternative diagnosis

- **Minor Criteria**

- Age > 50 yrs old
- evidence of bibasal inspiratory crackles (dry or Velcro type in quality
- insidious onset of otherwise unexplained dyspnea on exertion
- duration of illness > 3 months

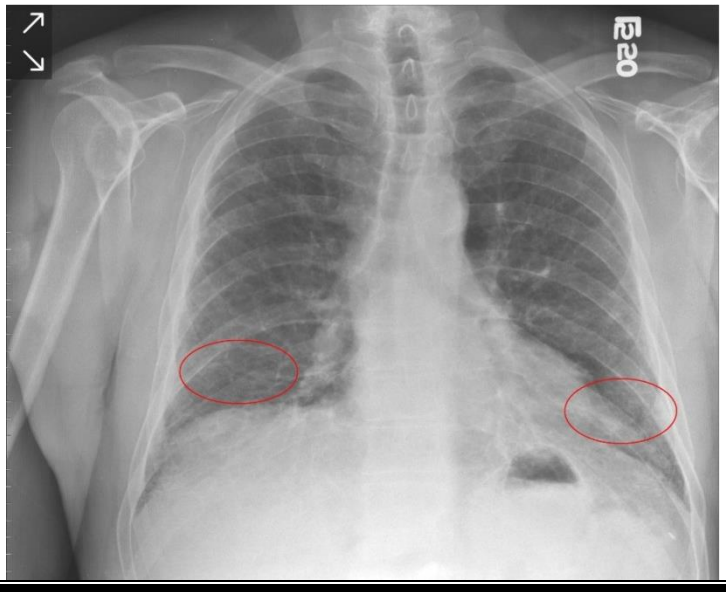
➢ من خلال المعايير السابقه يتبين لنا أن مرض ال IPF هو مرض متشابه مع أمراض تليّفيه أخرى ولكن تشخيصه يعتمد أكثر على استبعاد كل الاحتمالات الأخرى للتليف بالاضافه الى العلامات الأخرى

➢ ايه هيا الفحوصات اللى تعملها عشان تشخص ال IPF ؟

IMAGING

- **CXR:**

Show bi-basal reticular shodows



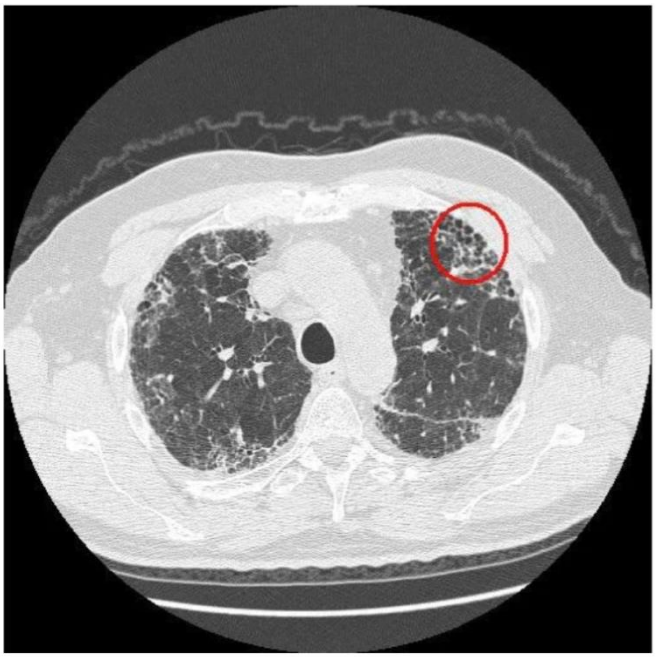
- **High Resolution CT chest**

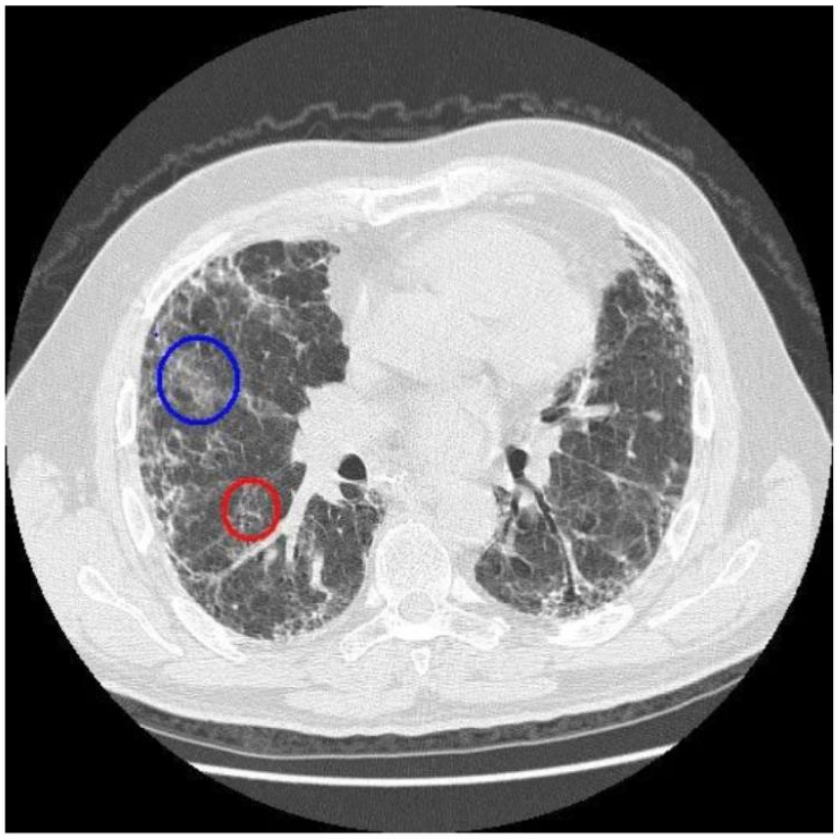
  It is more specific than CXR

  Diffuse basal reticular opacities with minimal GGOs with pathognomonic Subpleural Honeycomb (red circle)

  +

  TRACTION Bronchiectasis





A patient with IPF and a confirmed histologic diagnosis of usual interstitial pneumonia. Note the reticular opacities (red circle) distributed in both lung bases and the minimal ground-glass opacities (blue circle).

BIOPSY

- Sure diagnostic tool is Biopsy either taken by bronchoscopy {Transbronchial biopsy} Or By VATS (thoraco-scopic Guided biopsy)
- Histopathology shows Usual Interstitial Pneumonia UIP مهمه جداا
- Broncho-Alveolar Lavage {BAL} shows 75 - 90% neutrophils and also to exclude lymphocytes & other cells like eosinophils

SPIROMETRY

Restrictive pattern

High FEV1/FVC > 70%

+ Low PaO2

+ Low TLCO

N.B: You should do ECHO to exclude Associated pulmonary Hypertension

- TREATMENT

Non pharmacological

- Stop smoking if smoker
- Vaccination (yearly influenza vaccine + pneumococcal vaccine every 3 - 5 years)

  Influenza vaccines (Vaxigrip, Influvac)

  Pneumococcal vaccines (Prevenar 13)
- if significant Hypoxia

  PaO2 < 55

  Or PaO2: 55 – 60

  +

  Pulmonary HTN

  Polycythemia

  Nocturnal hypoxemia

المريض لازم يوضع على

Long term Oxygen Therapy {LTOT}

Pharmacological treatment

- Steroids, steroid sparing drugs and N acetylcysteine are NO longer recommended by the American Thoracic Society / European Respiratory Society

I. First line become

Pirfenidone (anti-fibrotic agent through inhibition of TGF B1

(Provided that FEV1 > 50)

E.g Pirfenex 200

II. Second line therapy

Nintedanib (Tyrosine kinase inhibitor TKI) is used when the pirfenidone is not effective or there is contra-indication for its use

E.g Ofev

- In refractory IPF ➪ Lung transplantation
- If associated pulmonary HTN ➪ Heart /Lung transplantation

SARCOIDOSIS

- A multi-system disease characterized by formation of granulomas in many organs of the body such as lungs , Skin , Eyes , and less often heart , CNS , kidneys and liver

Pathophysiology

There is a problem in cell mediated immunity with reduction of CD8 lymphocytes with increased CD4/CD8 ratio leading to Granulomatous inflammation

The granuloma is formed of multi-nucleated giant cells without caseation (to differentiate it from TB)

Prevalence & incidence

الاحصائيات الغربيه متمثله فى الولايات المتحده الامريكيه بتقول إن ال

Prevalence: 10 - 20 patients in 100,000

كمان هو مشهور الحدوث فى المرضى ذوو البشره السوداء

Black patients (certain racial prevalence)

كما أنه مشهور فى بعض الدول اللى فيها black population
طبعا زى دول افريقيا وكمان ال Afro-americans in USA

What is the Clinical features?

Sarcoidosis might be ACUTE or CHRONIC or present as certain syndromes

I. ACUTE SARCOIDOSIS

- Called **{Lofgren's Syndrome}**
- Rare disease **characterized by**

- Fever, polyarthritis, cough
- Skin rash called " Erythema Nodosum "

وده طفح جلدي لونه احمر بيبقى على ال chins of tibia ،، وكمان مؤلم مع الضغط عليه

- CXR : shows bilateral hilar lymphadenopathy (BHL)

المرض ده نادر والغريب أنه مشهور فى المنطقه الاسكندنافيه الاوربيه عكس ال chronic sarcoid والمشهور فى السود !!

♦ **Treatment**

- Prognosis is often good
- The disease may resolve over 2 weeks
    - First line ttt (most patients improve with such ttt) … >> NSAIDs ± colchicine
    - If refractory …>> Oral steroids untill full improvement

II. CHRONIC SARCOIDOSIS

Most cases are chronic

Pulmonary features:

90% of cases have pulmonary affection

The Classic Pulmonary Sarcoidosis is in the form of interstitial lung disease {ILD}

Symptoms:
- Dry cough
- Dyspnea (chronic)
- Hemoptysis is rare in sarcoidosis

Signs: Picture of upper lobe fibrosis

{Bilateral inspiratory crackles heard in upper lung zones which are not changed with cough}

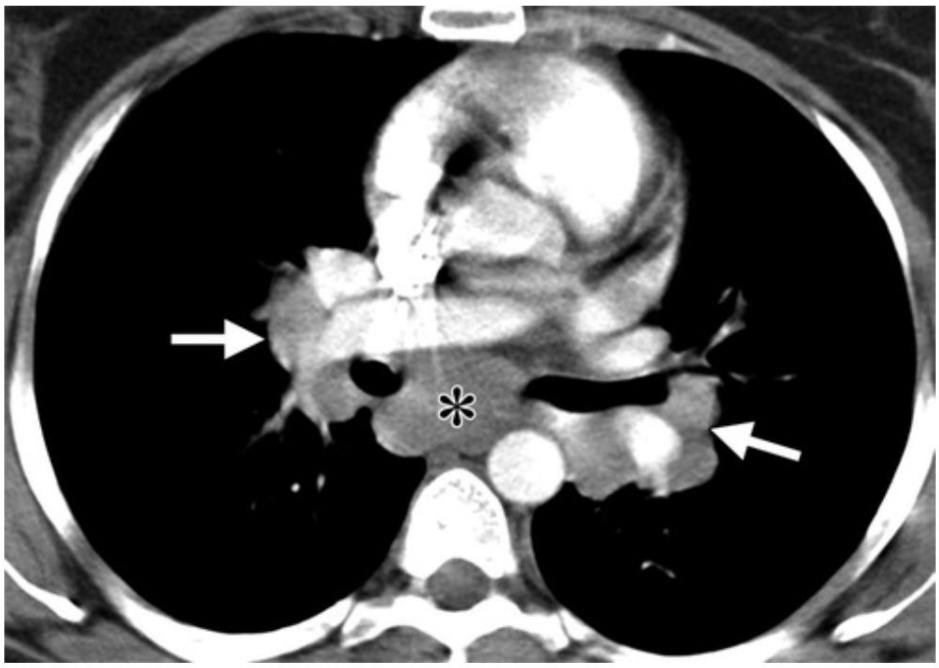
Imaging

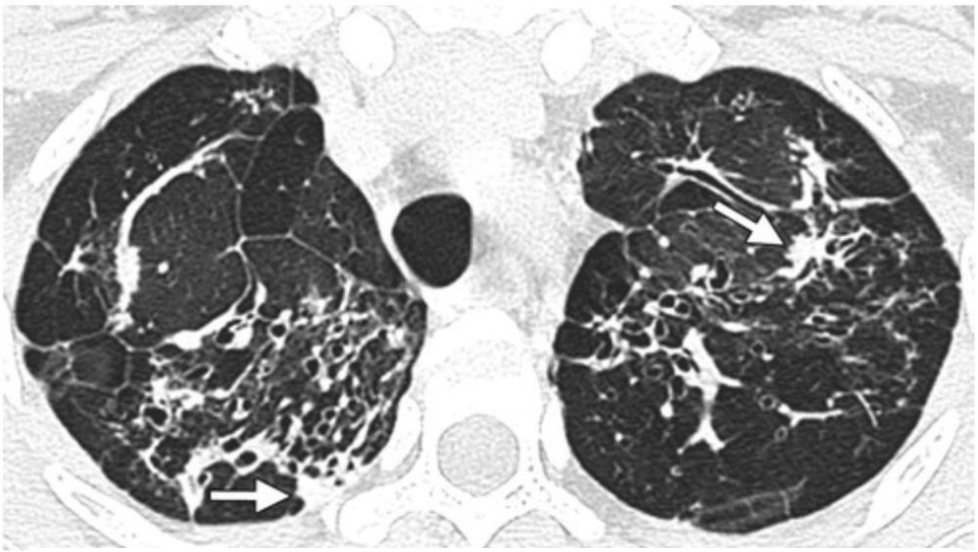
- **CXR:**

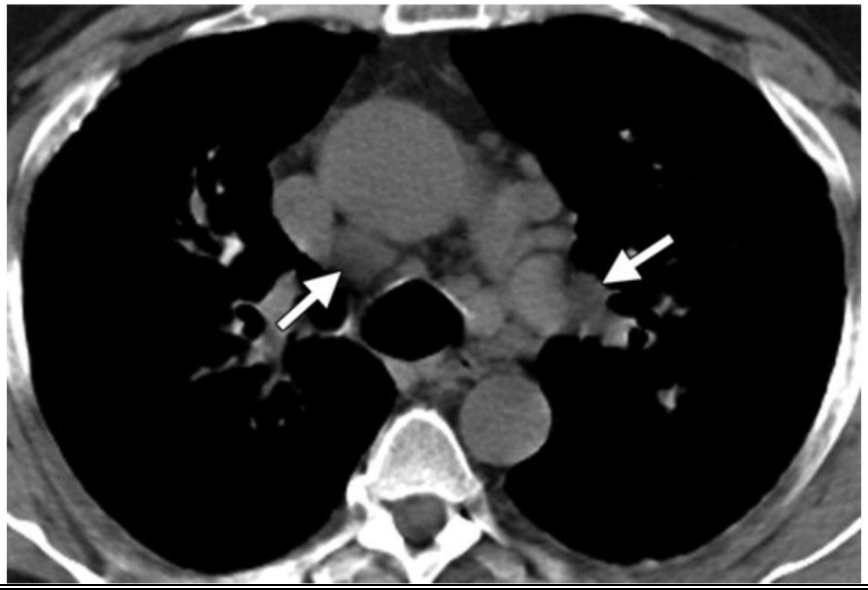
  May show Bilateral hilar lymphadenopathy {BHL} ± bilateral interstitial shadow

- **CT chest:**

May show variable appearences







- **Pulmonary Sarcoidosis is classified according to imaging into**

5 stages (***Siltzbach's classification System***)

Stage 0: normal

Stage 1: BHL

Stage 2: BHL + bilateral upper lobes interstitial/nodular shadow

Stage 3: bilateral interstitial upper lobes interstitial/nodular shadows

Stage 4: advanced fibrosis

Staging of Sarcoidosis on the Basis of Chest Radiographs

STAGE 0	No abnormalities	5%–10%
STAGE 1	Lymphadenopathy (fig. A)	50%
STAGE 2	Lymphadenopathy + pulmonary infiltration (fig. B)	25%–30%
STAGE 3	Pulmonary infiltration (fig. C)	10%–12%
STAGE 4	Fibrosis	5% (up to 25% during the course of the disease)

- Parenchymal lung affection (interstitial shows in imaging) in patients with Sarcoidosis needs <u>2 important investigations</u>
  - **Spirometry**: looking for Restrictive pattern with early low DLCO
  - **Transbronchial biopsy:** Which reveals?

    "Non Caseating Granuloma"

- Other rare lung **complications** in sarcoidosis
  - Chylothorax
  - Pneumothorax

- Other atypical features of sarcoidosis in imaging { rare}

✓ Cysts

✓ Effusion

✓ Consolidations

✓ Pleural thickening

✓ Aspergilloma (fungal ball) on top of sarcoid lesions

N.B: PULMONARY HYPERTENSION may occur in somes cases of Sarcoidosis

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EXTRA - PULMONARY SARCOIDOSIS

Sarcoidosis also affects other organs like

✓ Skin: 20 - 35%

✓ Eyes: 20 - 30%

✓ Liver: 30 - 40%

✓ Heart: 5 - 25%

✓ Nervous System: 1 - 5%

✓ Musculo-skeletal system (Joints) : 2 - 38%

Others

✓ Hypothalamo-pituitary Affection

✓ Kidney affection

I. Cutaneous Sarcoidosis

➢ Sarcoidosis commonly affects the SKIN with certain characteristic skin lesions such as

- ERYTHEMA NODOSUM
- LUPUS PERNIO
- Nummular eczema
- Erythema multiform
- Skin plaques
- Maculo-papular eruption
- subcutaneous nodules

- The most important skin lesions with medical importance are

- **Erythema Nodosum**

Tender, 1-2cm bumps mostly on the shins; often accompanied by arthritis in the ankles, elbows, wrists and hands (as in Löfgren syndrome)

Erythema Nodosum →

- **LUPUS PERNIO**

Large bluish-red and dusky purple infiltrated nodules and plaque-like lesions on nose, cheeks, ears, fingers and toes

ملحوظه هاااامه :

1/3 of patients with Cutaneous Sarcoidosis come with only skin lesions without other organ affection

II. Eye Lesions in Sarcoidosis

✓ **Uveitis:** present with red eyes associated with blurring of vision {the most important & common eye lesion in sarcoidosis

لابد من تشخيصه بواسطة طبيب العيون

III. Liver affection

The sarcoidosis causes Granulomatous inflammation of the liver

Most of cases with Hepatic Sarcoidosis are asymptomatic

Some of them have

✓ Hepatomegaly
✓ Splenomegaly
✓ Elevated liver enzymes

IV. Heart affection in Sarcoidosis

Heart affection carries bad outcome

Features:

✓ Heart block
✓ Picture of Restrictive Cardiomyopathy RCM

ملحوظه هاااامه :

يعتبر ال restrictive Cardiomyopathy أحد أهم العلامات المميزه لل sarcoidosis ،،

لانه يعتبر أحد ال infiltrative disease ،،

حيث إن ال granulomas هى التى تتسبب فى عملية ال Myocardial infiltration

ولما أطباء القلب بيجيلهم مريض ويشخصوه

Restrictive Cardiomyopathy by ECHO

بييجى فى بالهم ال sarcoidosis كسبب مهم لل RCM

RCM is caused by "OSIS" Diseases

✓Sarcoidosis
✓ Amyloidosis
✓ Hemochromatosis
✓Eosinophilic endomyocardial fibrosis

Dx: Transthoracic ECHO ± biopsy {if available}