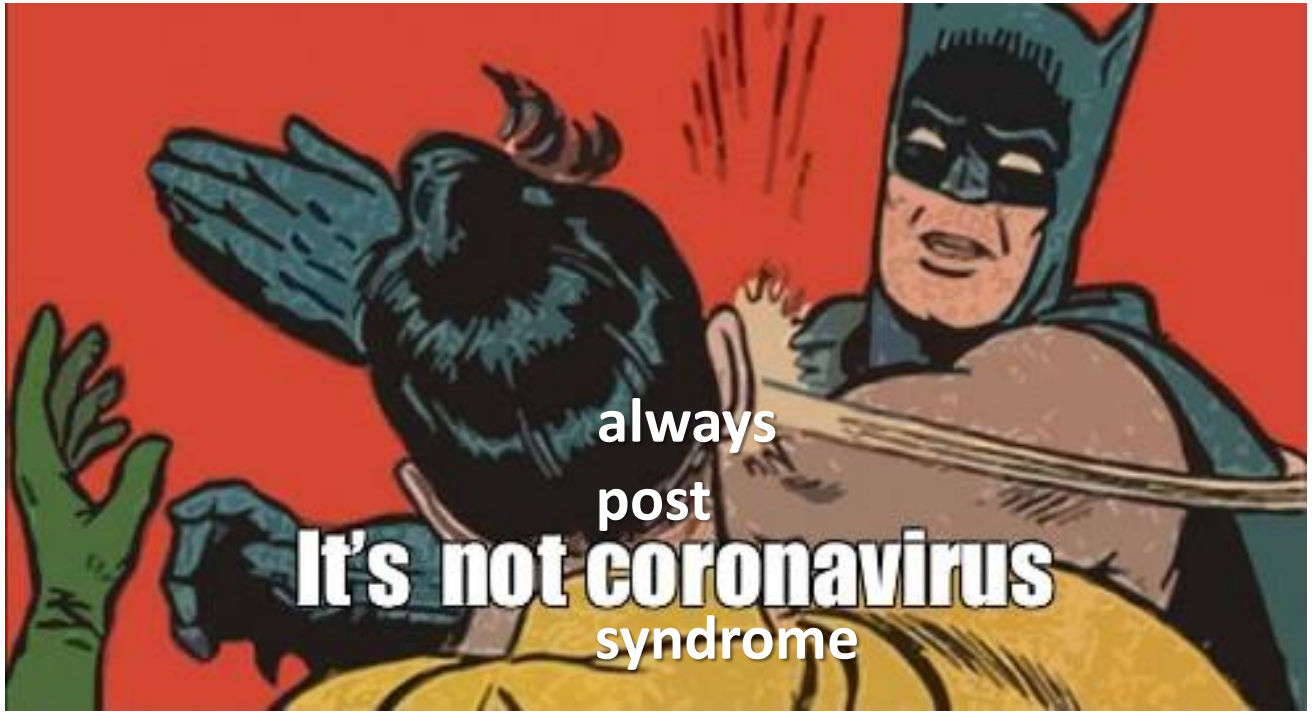
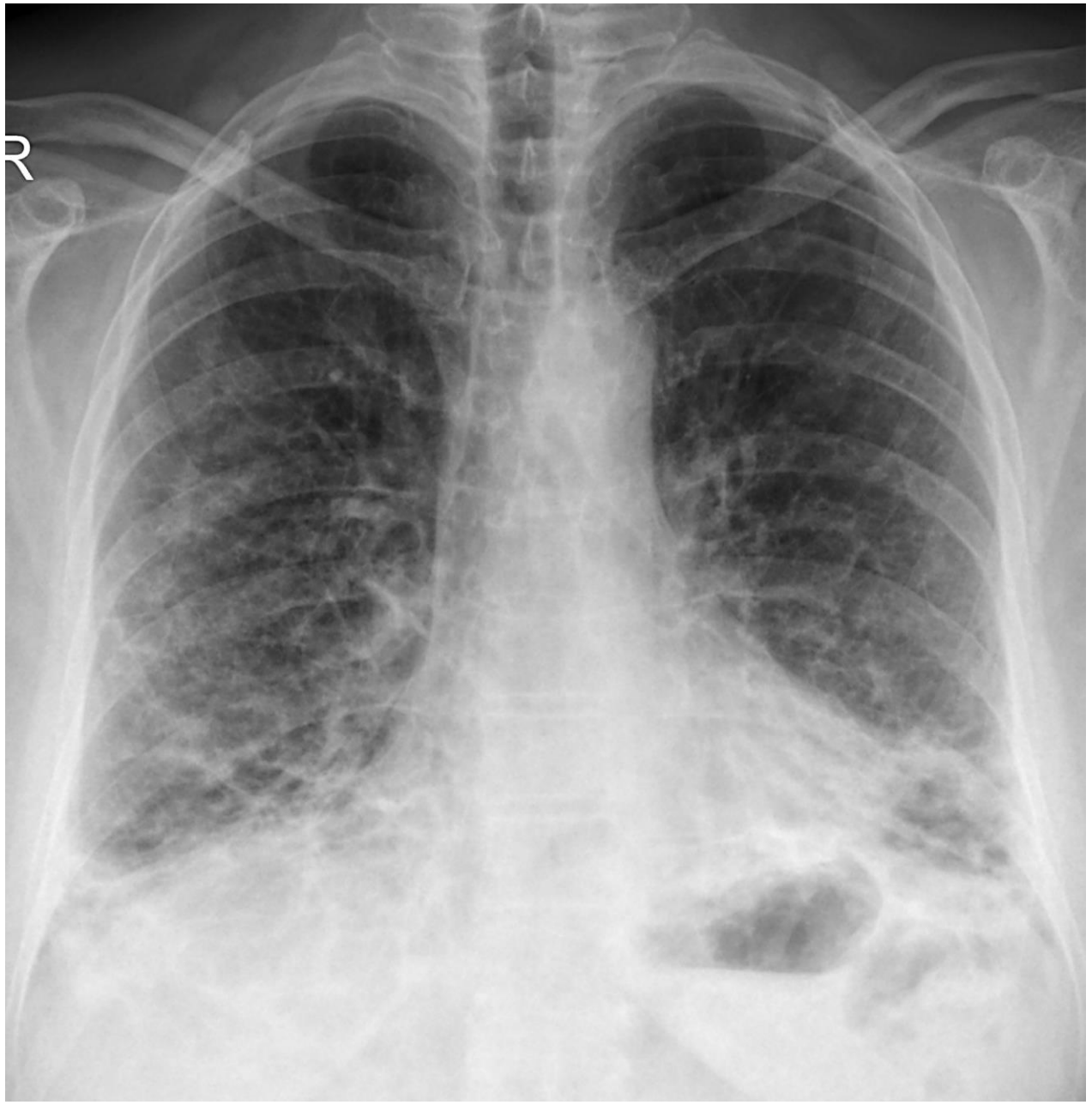
Ασθενής με προοδευτικά επιδεινούμενη δύσπνοια κοπώσεως & σκιάσεις πνευμόνων

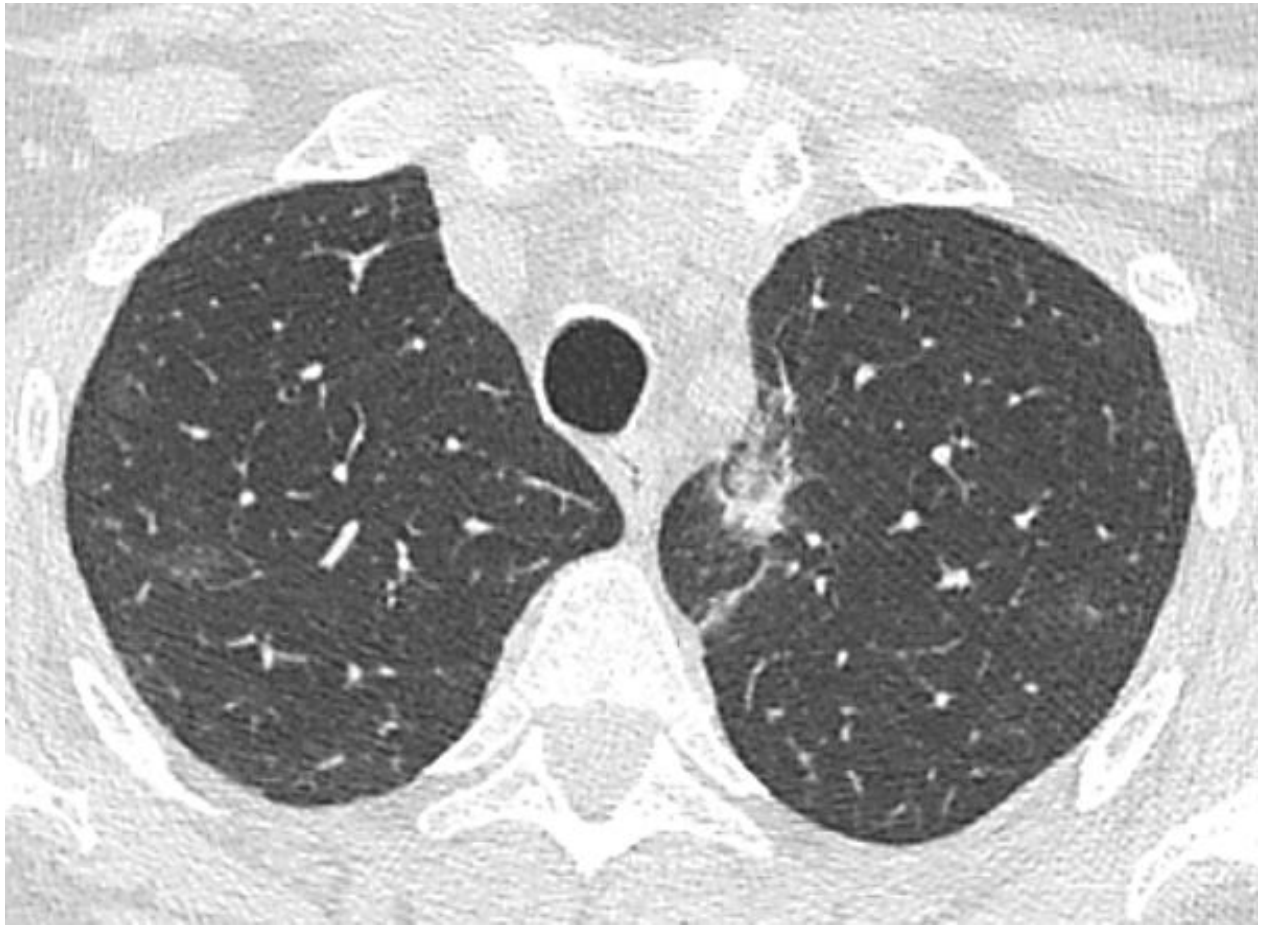


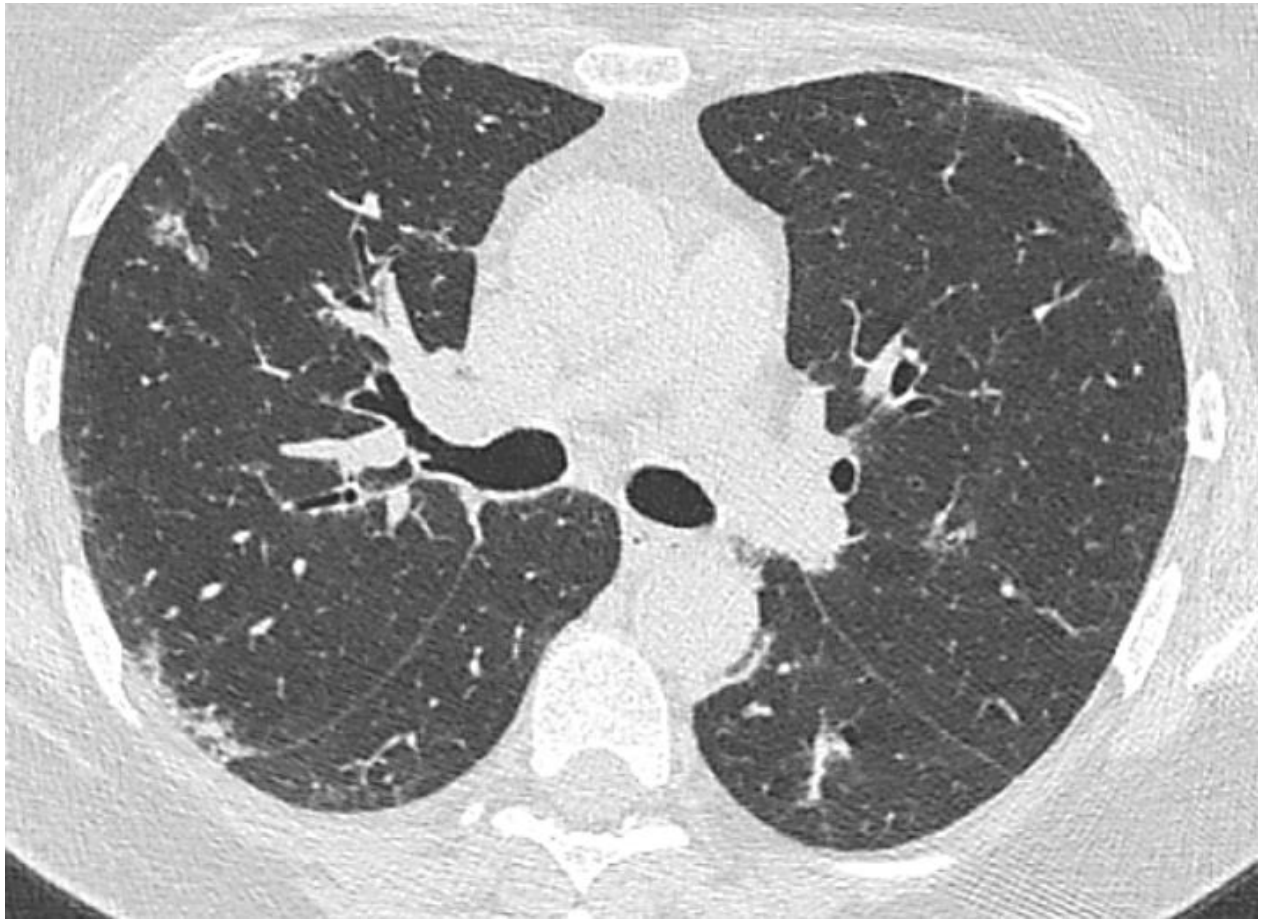
Δημέας Ηλίας
Ειδικευόμενος Πνευμονολογίας
Πνευμονολογική Κλινική ΠΘ
ΠΓΝ Λάρισας

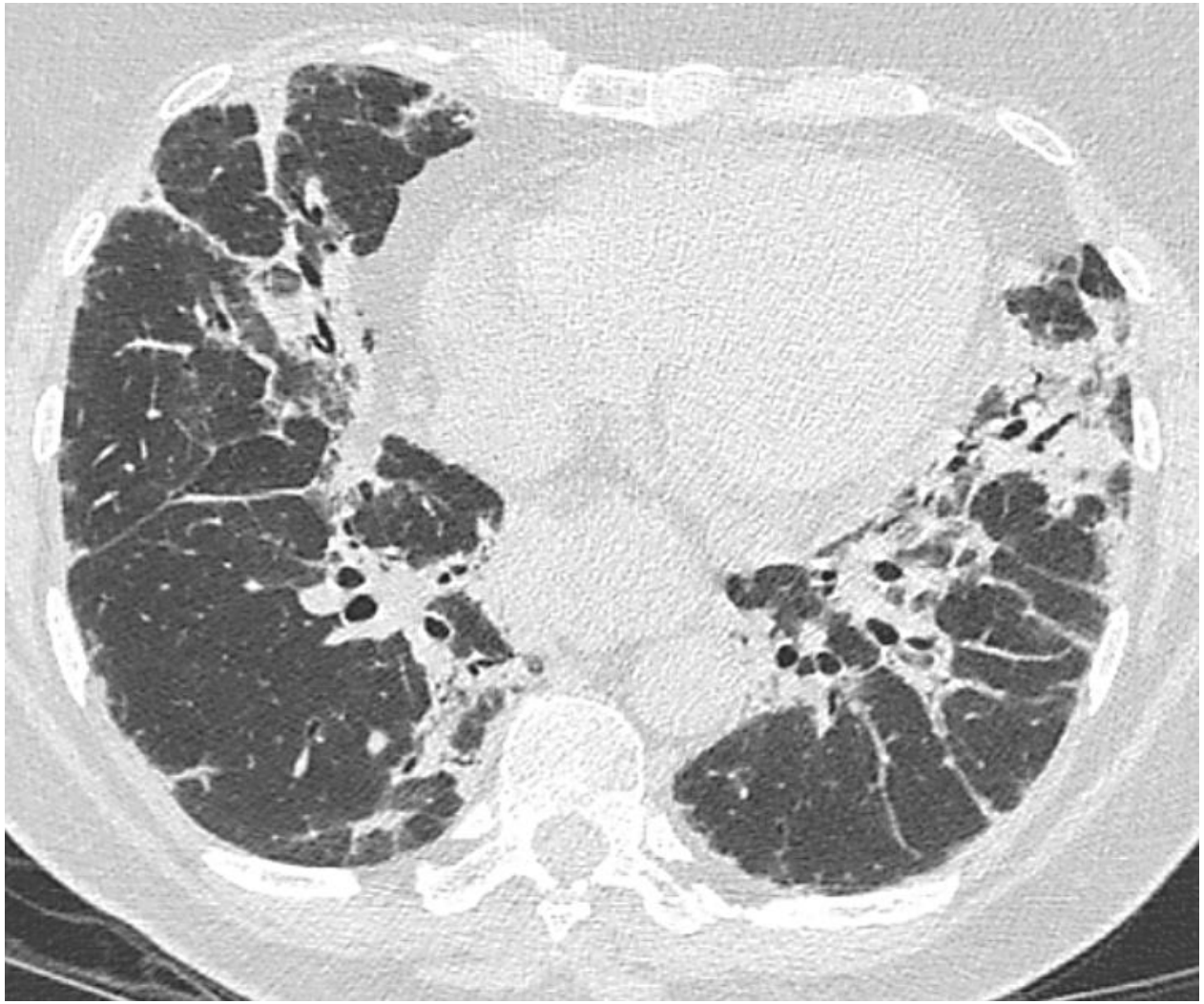
Δεν υπάρχει καμία σύγκρουση συμφερόντων

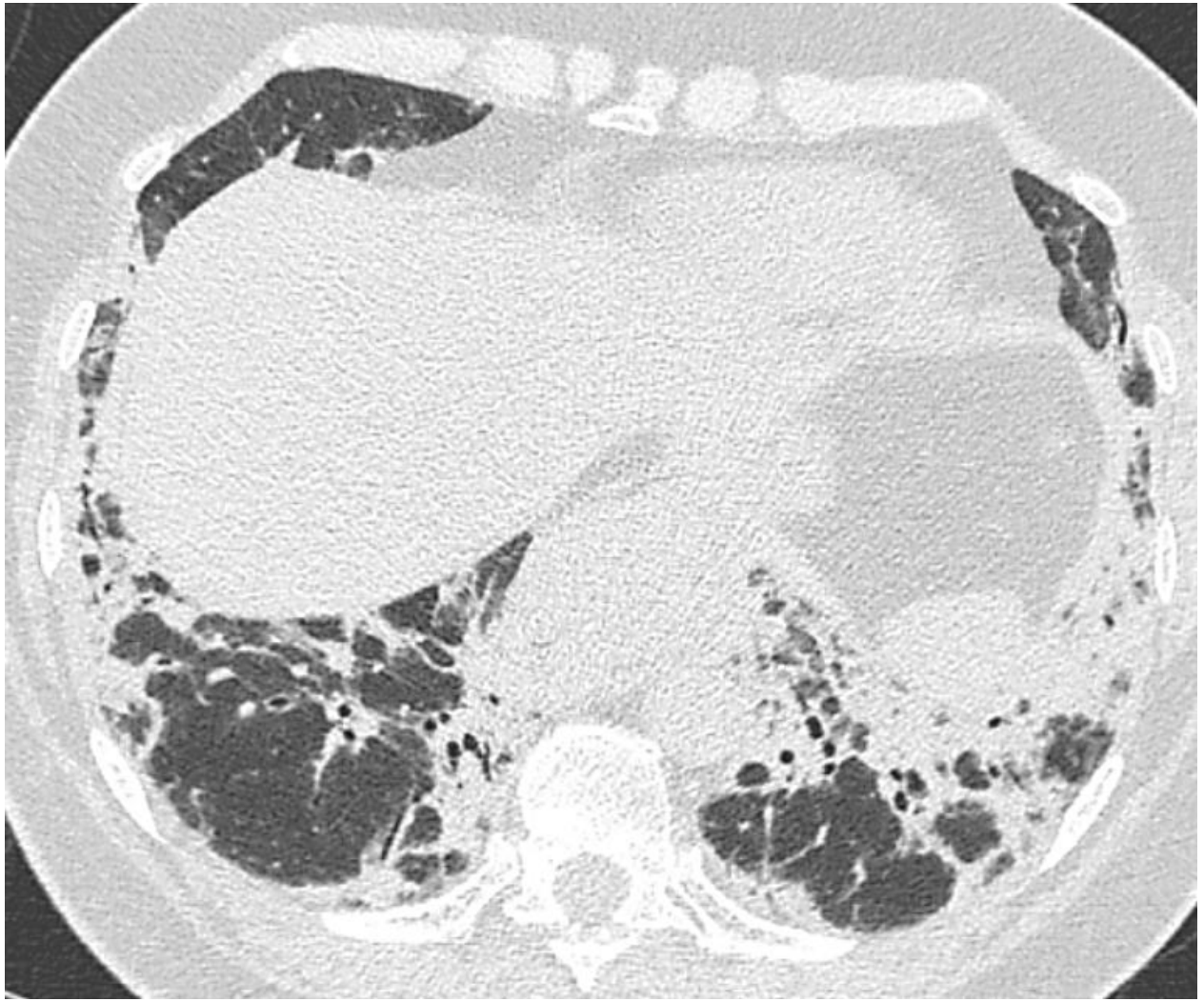


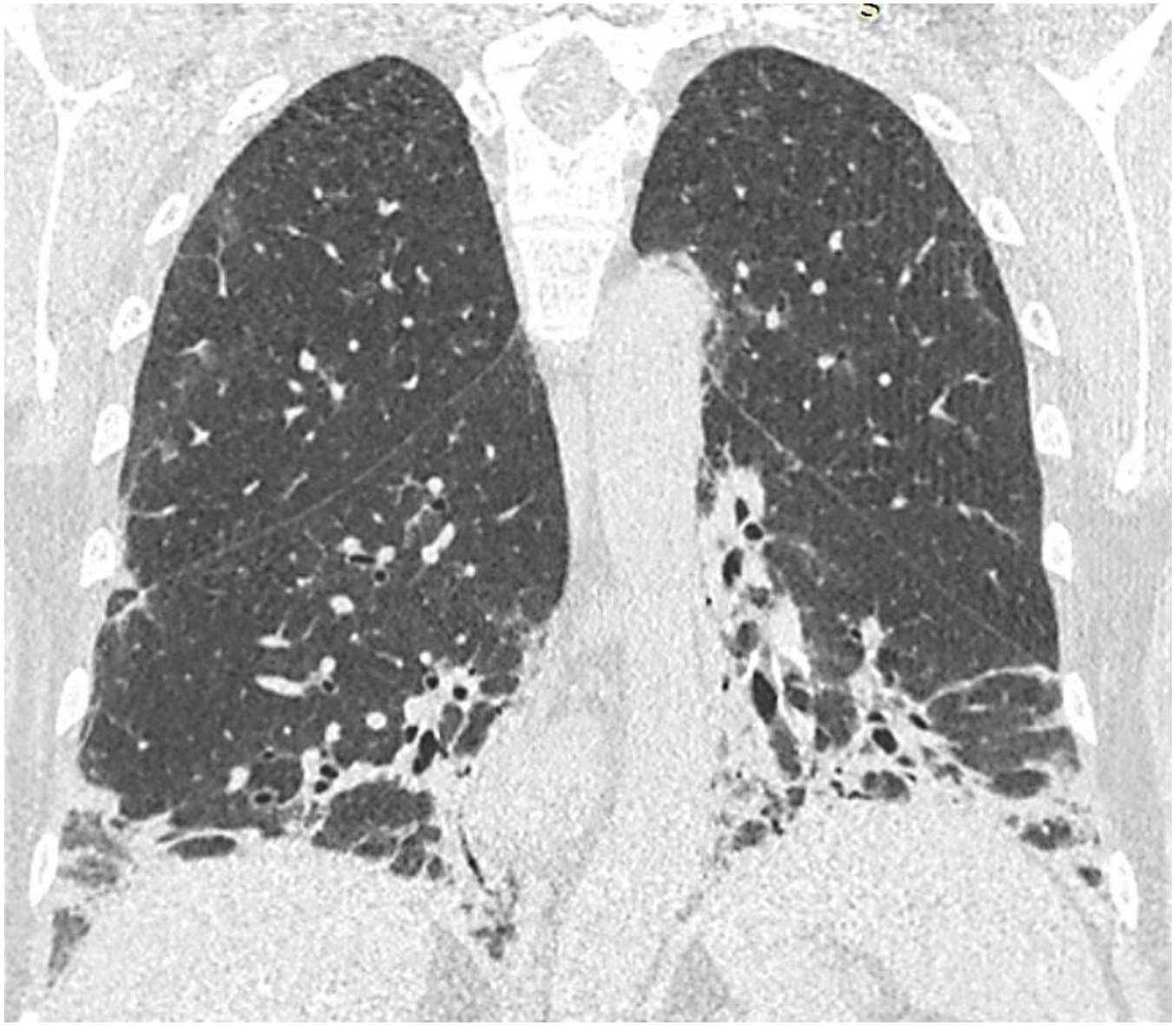
- 55χρονη καθηγήτρια, πρώην καπνίστρια 45pys, νυν ηλεκτρονικό τσιγάρο, έκθεση σε τζακούζι, θυρεοειδεκτομή, tb T4 125mg 1*1
- COVID19 προ τριμήνου, ήπια, κατ’ οίκον, χωρίς φαρμακευτική αγωγή
- Από 2μήνου, από 5χλμ τρέξιμο, 1χλμ τρέξιμο
- Ξηρός βήχας
- Ήπιες μυαλγίες σε ωμική ζώνη
- Ψωριασικές πλάκες σε αγκώνα
- Αναπνευστική ανεπάρκεια

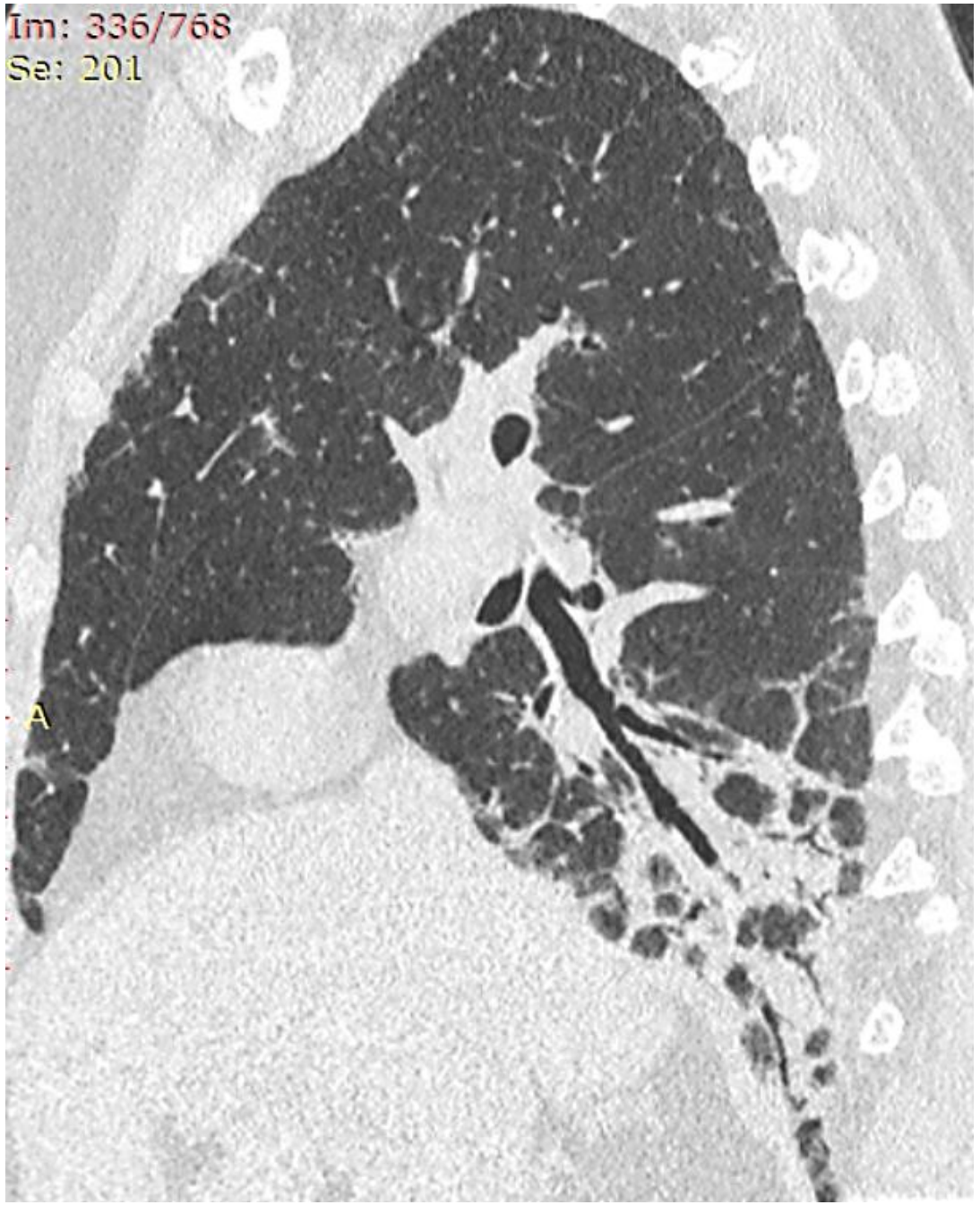








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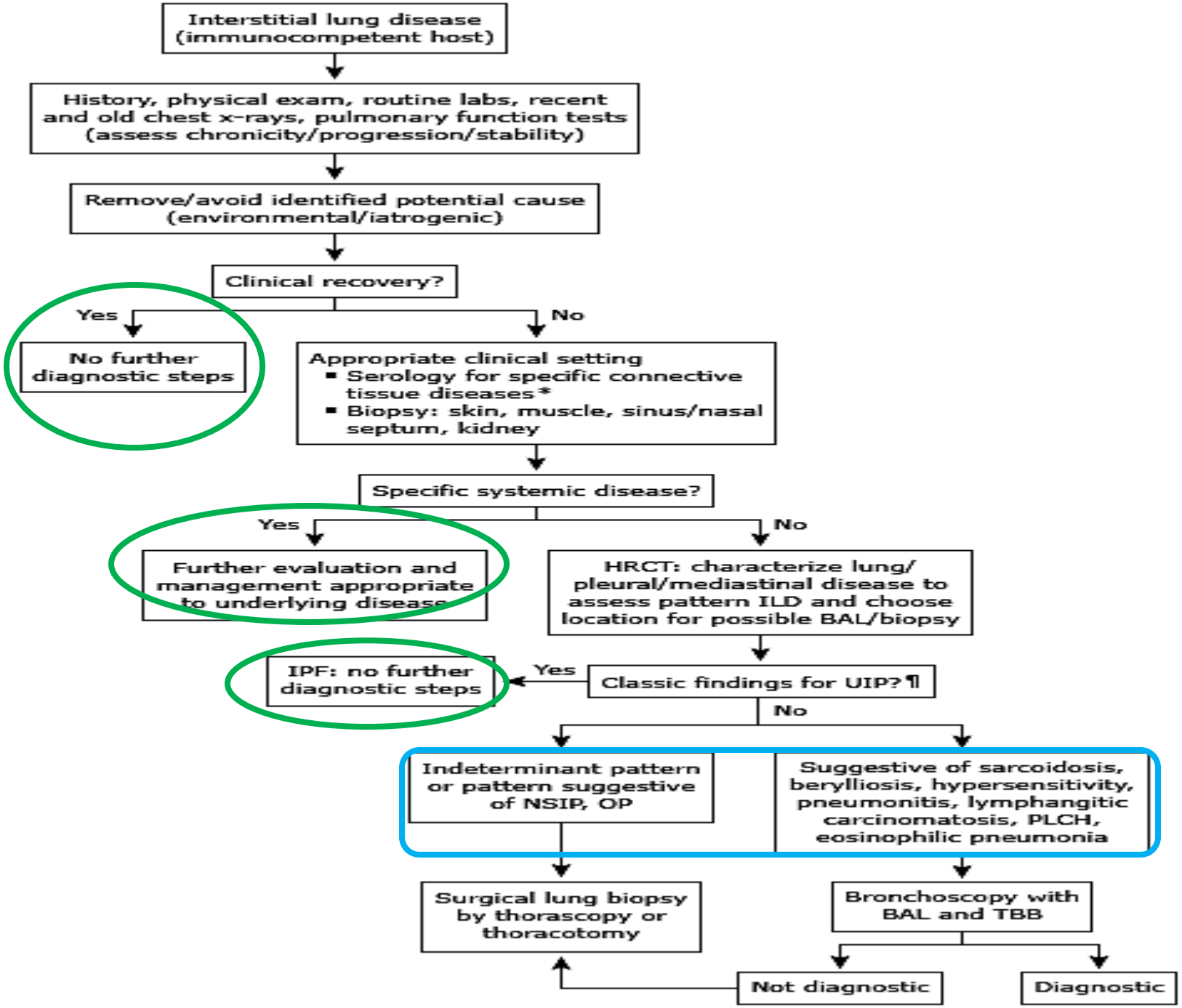
A

Duration of interstitial lung disease prior to diagnosis

Acute (days to weeks)
Acute idiopathic interstitial pneumonia (AIP, Hamman-Rich syndrome)
Eosinophilic pneumonia
Hypersensitivity pneumonitis
Cryptogenic organizing pneumonia
Subacute (weeks to months)
Sarcoidosis
Some drug-induced ILDs
Alveolar hemorrhage syndromes
Cryptogenic organizing pneumonia
Connective tissue disease (systemic lupus erythematosus or polymyositis)
Chronic (months to years)
Idiopathic pulmonary fibrosis
Sarcoidosis
Pulmonary Langerhans cell histiocytosis
Chronic hypersensitivity pneumonitis

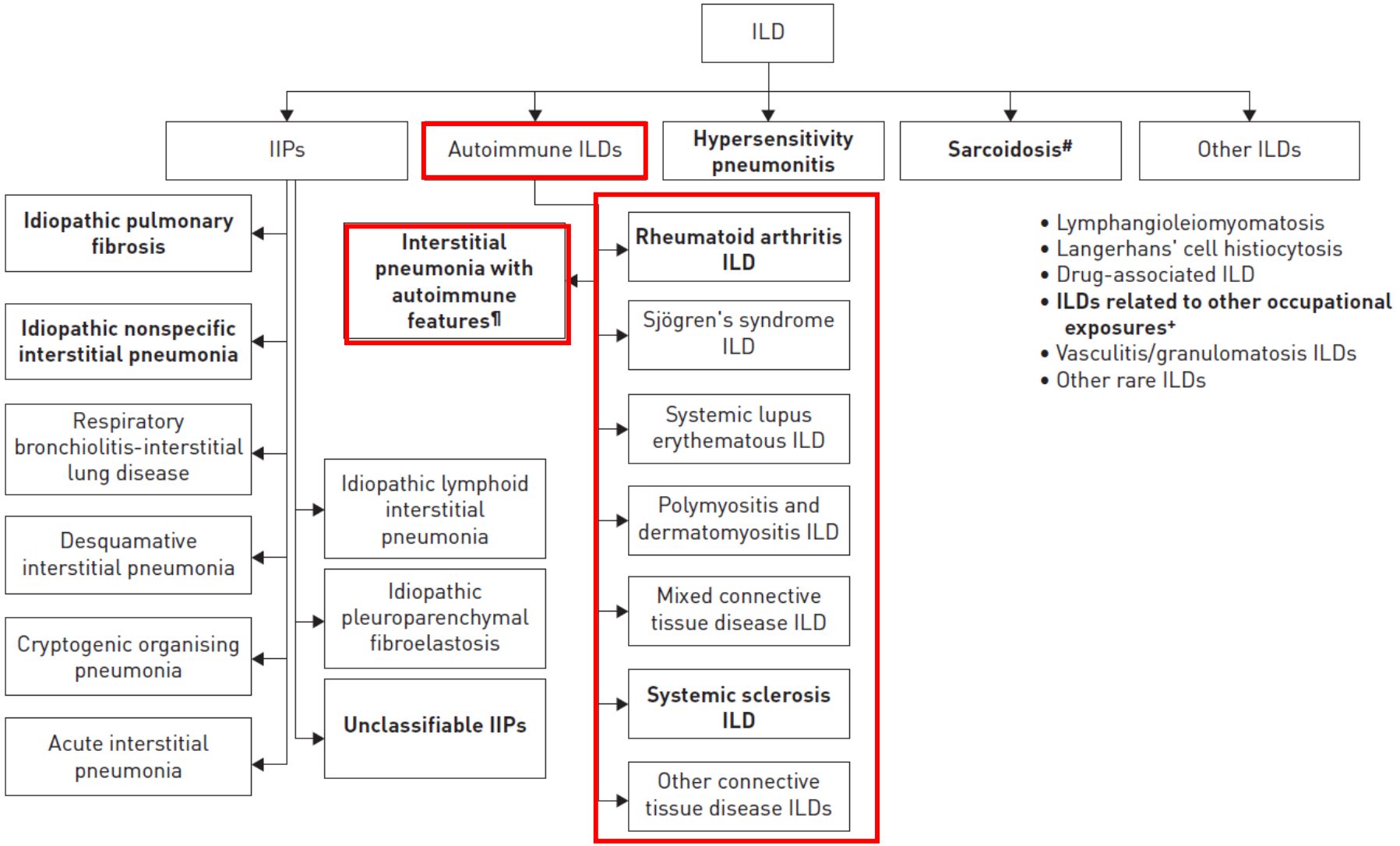


- Ιστορικό
- Κλινική εξέταση για εξωπνευμονικές αιτιολογίες

Λήψη βιοψίας

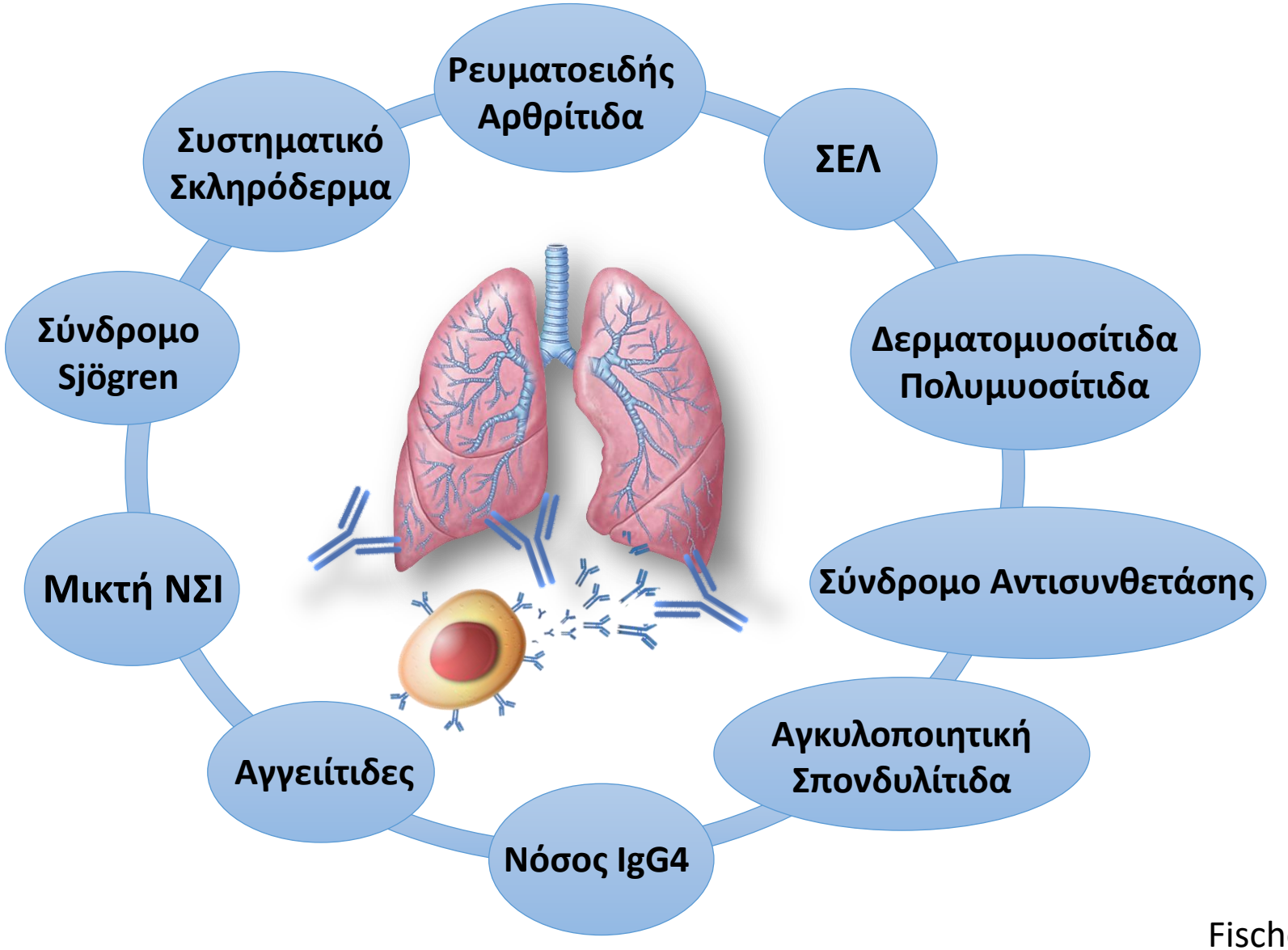
- Βρογχοσκόπηση?
- Χειρουργική βιοψία?
- Θέση για βιοψία ή BAL
- Έκθεση σε περιβαλλοντικό ή σε φάρμακο και πιθανή απομάκρυνση

Διάμεση Πνευμονοπάθεια: Ταξινόμηση



Cottin et al. Eur Respir Rev. 2018

Πνεύμονες και Αυτοάνοσα Νοσήματα



Fischer et al. Lancet. 2012

Ποικίλες μορφές πνευμονικής προσβολής

	ILD	Airways	Pleural	Vascular	DAH
Systemic sclerosis	+++	–	–	+++	–
Rheumatoid arthritis	++	++	++	+	–
Primary Sjögren's syndrome	++	++	+	+	–
Mixed CTD	++	+	+	++	–
Polymyositis/ dermatomyositis	+++	–	–	+	–
Systemic lupus erythematosus	+	+	+++	+	++

The signs show prevalence of each manifestation (–=no prevalence; +=low prevalence; ++=medium prevalence; +++=high prevalence). ILD=interstitial lung disease. DAH=diffuse alveolar haemorrhage. CTD=connective tissue disease.

Table 1: **CTDs and common pulmonary manifestations**

Fischer et al. Lancet. 2012

Πρότυπο Βλάβης
NSIP>>>UIP
UIP>NSIP>OP=DAD
NSIP>LIP>OP=UIP=DAD
NSIP>UIP
NSIP=OP>DAD>UIP
NSIP>DAD=LIP=OP=UIP

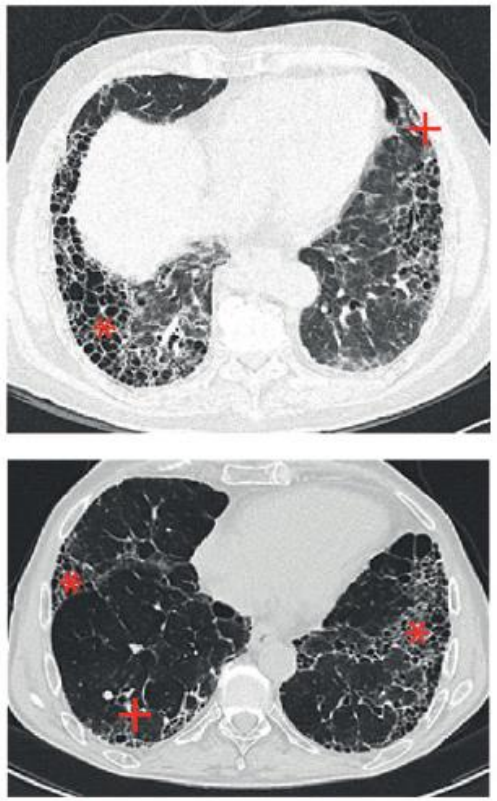
Κλινική ετερογένεια

Lauretis et al. Chron Respir Dis. 2011

Συνήθη πρότυπα βλάβης

UIP

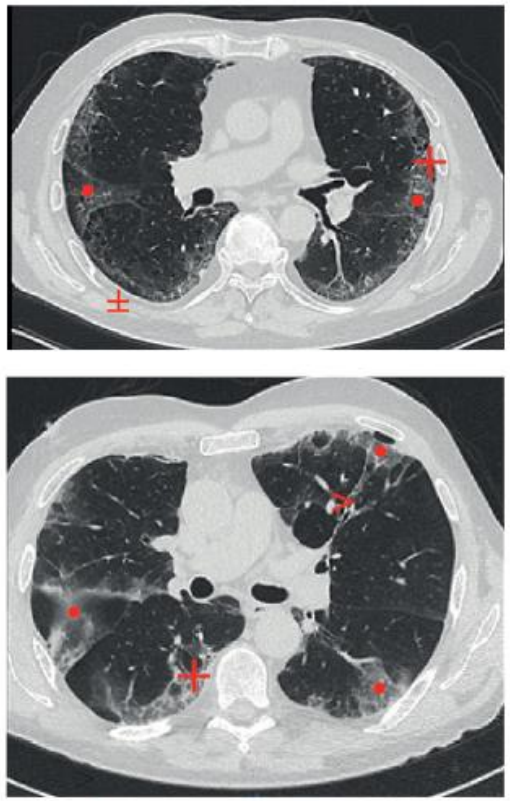
Usual interstitial pneumonia



Honeycombing (*) with or without peripheral traction bronchiectasis (+), in a subpleural and basal predominant, often heterogeneous, distribution.

NSIP

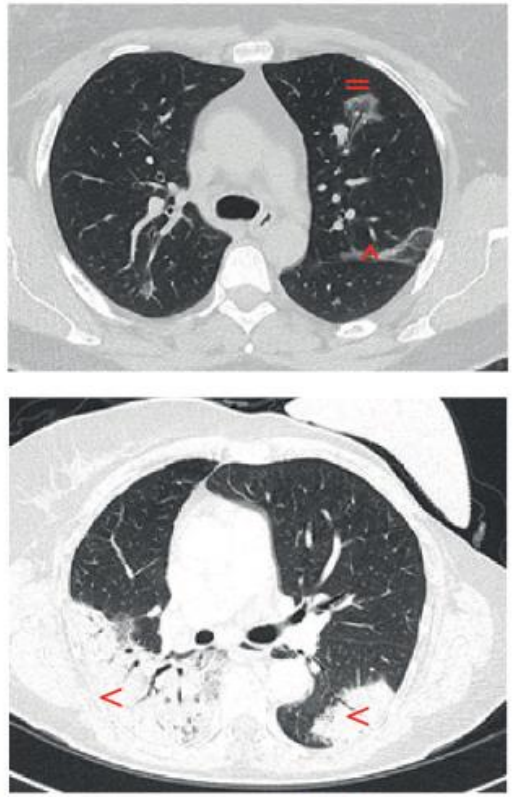
Non-specific interstitial pneumonia



Ground-glass opacities (•) with traction bronchiectasis (+), often peribronchovascular (>) predominance with subpleural sparing (±).

OP

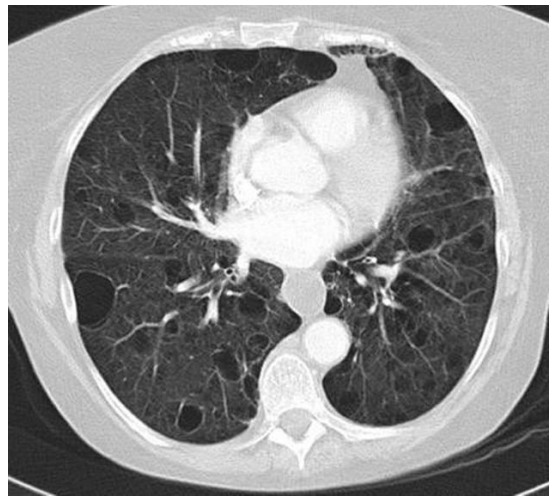
Organising pneumonia



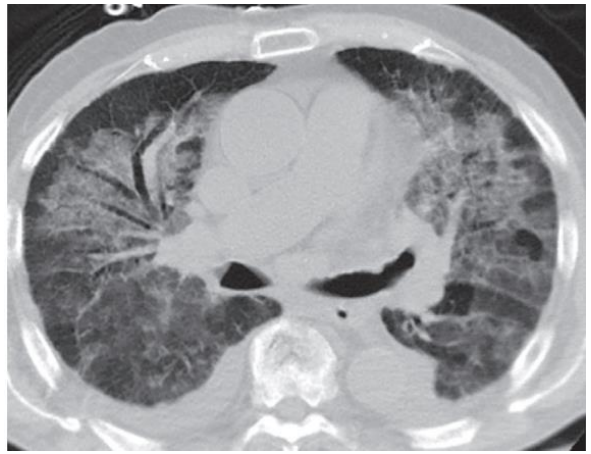
Peripheral consolidation with air bronchograms (<), bronchocentric distribution, a perilobular pattern, reversed halo sign (=), and band-like consolidations (^) can also be seen.

Σπανιότερα:

LIP



AIP



Wijsenbeek et al. Lancet 2022

- Velcro βάσεων άμφω
- ΤΚΕ = 120 mm/h, CPK =
- FEV1 1,93 81%, FVC 2,2
- Βρογχοσκόπηση: κυτταρ
- BAL: 54% L, 30% P, 3,5%
- Ανοσολογικό panel: Ro5

Lineblot (γραμμική ανοσομέθοδος) γ *νίχνευση αυτοαντισωμάτων που σχετίζονται με*

dsDNA:	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
nucleosomes :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
Histones :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
SS-A :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
Ro-52 :	**ΘΕΤΙΚΑ (+) (A**	**77; cutoff<11AU)**
SS-B :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
RNP/Sm :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
Sm :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
Mi-2a :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
Mi-2b :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
Ku :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
CENP A :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
CENP B :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
Sp100 :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
PML :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
Scl-70 :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
PM100 :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
PM75 :	ΑΡΝΗΤΙΚΑ (AU	**cutoff<11AU)**
RP11 :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
RP155 :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)
gp210 :	ΑΡΝΗΤΙΚΑ (AU	*: 8; cutoff<11AU)*
PCNA :	ΑΡΝΗΤΙΚΑ (AU	
DFS70 :	ΑΡΝΗΤΙΚΑ (AU	utoff<11AU)

Review > Open Access Rheumatol. 2020 Jan 14;12:9-14. doi: 10.2147/OARRR.S231195. eCollection 2020.

Myositis Specific Autoantibodies: A Clinical Perspective

Fahidah M Alenzi [1]

- DM-specific autoantibodies include anti-MDA5, anti-NXP2, anti-SAE, anti-Mi-2, anti-ARS, anti-TIF1-gamma
- anti-NXP2 antibodies are associated with transcriptional regulation and production of various proteins targeted by other DM antibodies

> J Rheumatol. 2022 Aug;49(8):922-928. doi: 10.3899/jrheum.211234. Epub 2022 Jun 15.

Clinical Heterogeneity of Patients With Antinuclear Matrix Protein 2 Antibody-Positive Myositis: A Retrospective Cohort Study in China

Shanshan Li [1], Chao Sun [1], Ling Zhang [2], Junfeng Han [3], Hanbo Yang [1], Suhao Gao [4], Linrong He [1], Peiyao Zhang [2], Xin Lu [1], Xiaoming Shu [5], Guochun Wang [1]

- 21/70 patients ILD
- No patients rapidly progressive ILD
- Cluster 2 had a higher frequency of ILD, lower levels of lymphocytes and higher levels of serum ferritin with worse prognosis

Case Reports > Eur Respir Rev. 2015 Jun;24(136):370-2. doi: 10.1183/16000617.00006714.

Interstitial lung disease in an adult patient with dermatomyositis and anti-NXP2 autoantibody

Morgane Gossez [1], Marianne Levesque [2], Chahéra Khouatra [3], Vincent Cottin [3], Lorna Garnier [4], Nicole Fabien [5]

> Med Clin (Barc). 2022 Jul 13;S0025-7753(22)00241-X. doi: 10.1016/j.medcli.2022.03.023. Online ahead of print.

Cancer associated autoantibodies in idiopathic inflammatory myopathies: A retrospective cohort from a single center in China

[Article in English, Spanish]

Yin Zhao [1], Haiyuan Su [1], Xiaoyang Yin [1], Hou Hou [1], Ying'ai Wang [1], Yong Xu [1], Xin Li [1], Nang Zhang [1], Wenwen Sun [1], Wei Wei [2]

Clin Exp Rheumatol. 2022 Jul 12. doi: 10.55563/clinexprheumatol/lqjx4h. Online ahead of print.

Interstitial lung disease in adult patients with anti-NXP2 antibody positivity: a multicentre 18-month follow-up study

Tingting Yan [1], Yan Du [2], Wenjia Sun [2], Xiaofeng Chen [3], Qingjie Wu [3], Qiao Ye [4], Sheng Chen [5], Jing Xue [6]

- 14/33 patients ILD
- 11/14 NSIP/OP
- ILD in older patients, no association with prognosis
- NXP2 + means dermatomyositis

Expert Rev Respir Med. 2020 Aug;14(8):845-850. doi: 10.1080/17476348.2020.1767598. Epub 2020 May 27.

Lung involvement associated with anti-NXP2 autoantibodies in inflammatory myopathies: a French monocenter series

Julien Bermudez [1] [2], Xavier Heim [2] [3], Daniel Bertin [3], Benjamin Coulon [3], Basile Puech [4], Nathalie Bardin [2] [3], Martine Reynaud-Gaubert [1] [5]

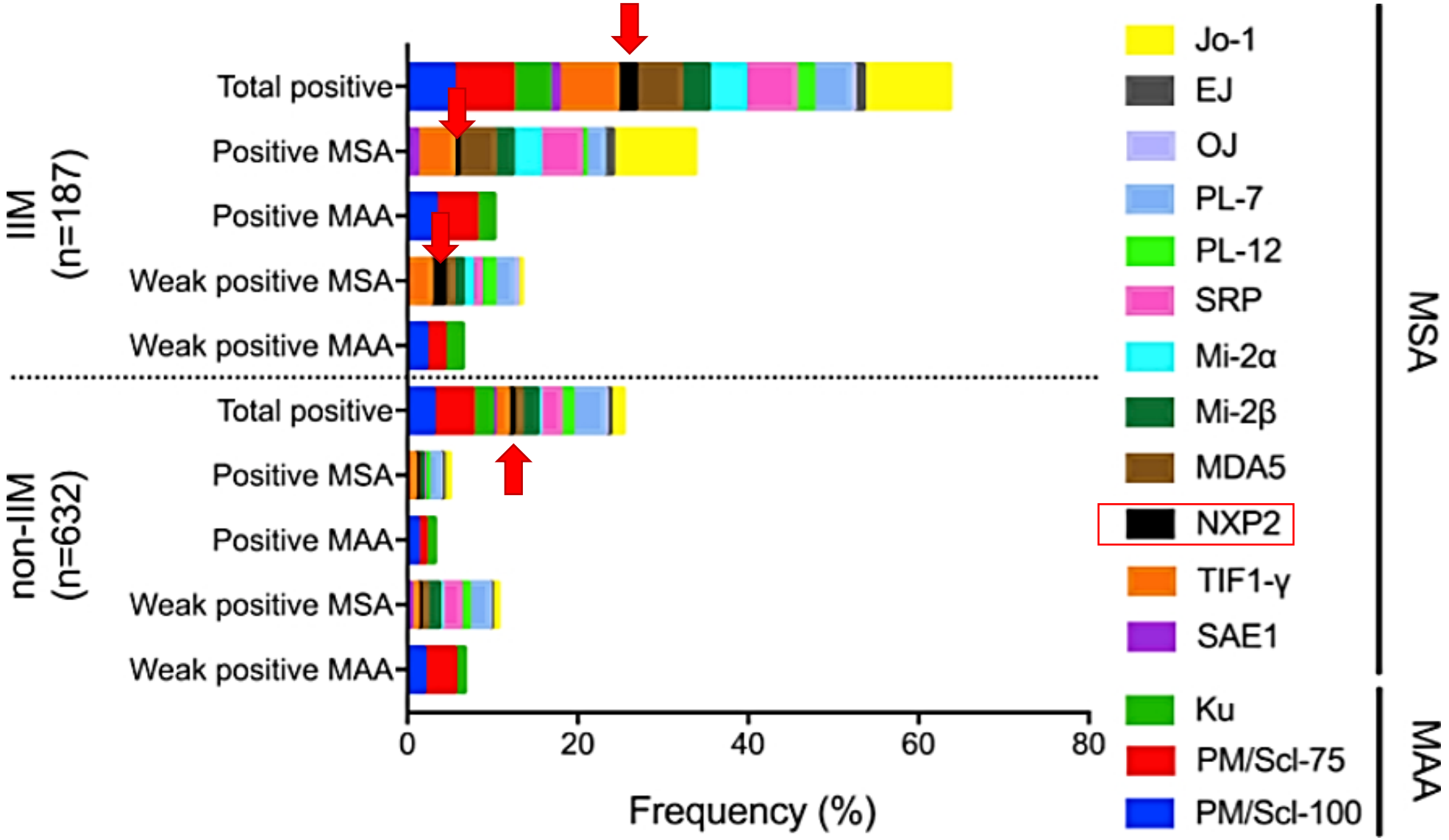
- 7 patients IM NXP2+
- Subclinical lung involvement
- Mean age 55 ± 13 years
- Female predominance
- 2/7 with respiratory symptoms
- CT-scan abnormalities in 3/7
- 4/7 with altered DLCO

Review Rheumatol Int. 2022 Dec;42(12):2267-2276. doi: 10.1007/s00296-022-05176-3. Epub 2022 Aug 8.

New-onset dermatomyositis following SARS-CoV-2 infection and vaccination: a case-based review

Marie-Therese Holzer [1] [2], Martin Krusche [3], Nikolas Ruffer [3] [4], Heinrich Haberstock [4], Marlene Stephan [4], Tobias B Huber [3], Ina Kötter [3] [4]

- Increase in new-onset dermatomyositis
- Center: One case after SARS-CoV-2 infection
- Review: 17 new-onset dermatomyositis in association with a SARS-CoV-2 infection or vaccination, 10 after infection and 7 after vaccination



Platteel ACM et al. Frequencies and clinical associations of myositis-related antibodies in The Netherlands: A one-year survey of all Dutch patients. J Transl Autoimmun. 2019 Aug 23;2:100013. doi: 10.1016/j.jtauto.2019.100013. PMID: 32743501; PMCID: PMC7388388.

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

1. Presence of an interstitial pneumonia (by HRCT or surgical lung biopsy) *and*,
2. Exclusion of alternative aetiologies *and*,
3. Does not meet criteria of a defined connective tissue disease *and*,
4. At least one feature from at least two of these domains:
   - A. Clinical domain
   - B. Serologic domain
   - C. Morphologic domain

A. Clinical domain

1. Distal digital fissuring (*i.e.* "mechanic hands")
2. Distal digital tip ulceration
3. Inflammatory arthritis *or* polyarticular morning joint stiffness ⩾60 min
4. Palmar telangiectasia
5. Raynaud's phenomenon
6. Unexplained digital oedema
7. Unexplained fixed rash on the digital extensor surfaces (Gottron's sign)

B. Serologic domain

1. ANA ⩾1:320 titre, diffuse, speckled, homogeneous patterns *or*
   a. ANA nucleolar pattern (any titre) *or*
   b. ANA centromere pattern (any titre)
2. Rheumatoid factor ⩾2× upper limit of normal
3. Anti-CCP
4. Anti-dsDNA
5. Anti-Ro (SS-A)
6. Anti-La (SS-B)
7. Anti-ribonucleoprotein
8. Anti-Smith
9. Anti-topoisomerase (Scl-70)
10. Anti-tRNA synthetase (*e.g.* Jo-1, PL-7, PL-12; others are: EJ, OJ, KS, Zo, tRS)
11. Anti-PM-Scl
12. Anti-MDA-5

C. Morphologic domain

1. Suggestive radiology patterns by HRCT (see text for descriptions):
   a. NSIP
   b. OP
   c. NSIP with OP overlap
   d. LIP
2. Histopathology patterns or features by surgical lung biopsy:
   a. NSIP
   b. OP
   c. NSIP with OP overlap
   d. LIP
   e. Interstitial lymphoid aggregates with germinal centres
   f. Diffuse lymphoplasmacytic infiltration (with or without lymphoid follicles)
3. Multi-compartment involvement (in addition to interstitial pneumonia):
   a. Unexplained pleural effusion or thickening
   b. Unexplained pericardial effusion or thickening
   c. Unexplained intrinsic airways disease[#] (by PFT, imaging or pathology)
   d. Unexplained pulmonary vasculopathy

Aryeh Fischer, Katerina M. Antoniou, et al. An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features European Respiratory Journal Oct 2015, 46 (4) 976-987; DOI: 10.1183/13993003.00150-2015

“high sensitivity index”

- Organizing Pneumonia (OP) like post Covid 19 reaction?
- Anti-Ro52 Interstitial pneumonia with autoimmune features (IPAF)?
- Covid 19 related anti-NXP2 Dermatomyositis-Polymyositis (DM-PM)?
- Anti-NXP2 Idiopathic Inflammatory Myopathy (IIM) [amyopathic DM-PM] with Interstitial Lung Disease (ILD)?
- Anti-Ro52/Anti-NXP2 Idiopathic Inflammatory Myopathy [amyopathic DM-PM] with connective tissue disease overlap & with Interstitial Lung Disease (ILD)?

“high sensitivity index”

- Organizing Pneumonia (OP) like post Covid 19 reaction?
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Δερματομυοσίτιδα/Πολυμυοσίτιδα

- Πνευμονική Προσβολή: 50% (20-78%)

PFTs: Το περιοριστικό πρότυπο ενδέχεται να οφείλεται στη **μυοπάθεια** των αναπνευστικών μυών

- **Υποκλινική νόσος** έως και **απειλητική** για τη ζωή

NSIP (82%) > DAD > UIP

Παράγοντες Κινδύνου:

1. Ηλικιωμένοι
2. Υψηλή ΤΚΕ ή CRP
3. Αντισώματα έναντι συνθετάσης (Anti-Jo1, Anti-MDA5)

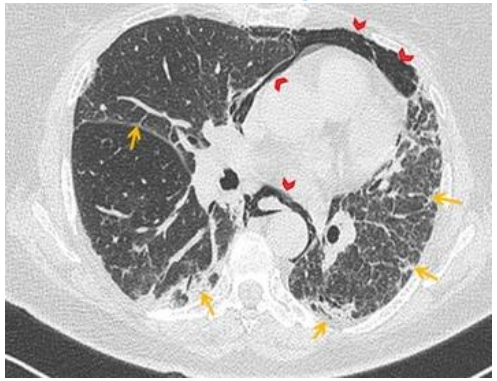
Gutsche et al. Curr Respir Care Rep 2012
Lega et al. Eur Respir Rev. 2015

«Acute»
Anti-MDA5 (+)

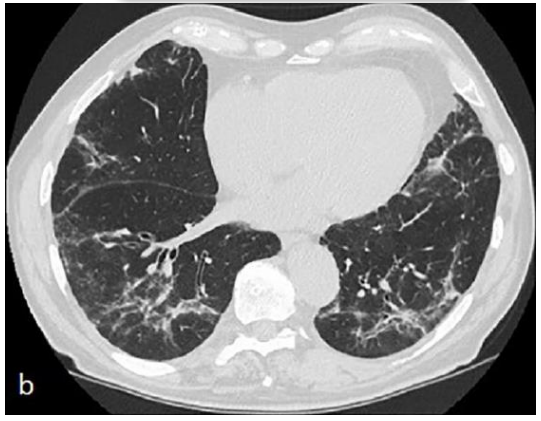
Case Reports › Rheumatol Adv Pract. 2017 Aug 31;1(1):rkx003. doi: 10.1093/rap/rkx003. eCollection 2017.

Pneumomediastinum in MDA5-associated clinically amyopathic dermatomyositis

Ourania S Kotsiou [1], Zoe Daniil [2], Konstantinos I Gourgoulianis [2]



«Insidious»
Anti-Jo1 (+)



Το αντισωματικό προφίλ ως καθοριστής του φαινοτύπου

Table 1 Myositis-specific antibodies

Myositis-associated antibodies	Target antigen	Prevalence in IIM[17–19,27,37–39,44,48,93]	Clinical features[17,27,37–39,42,54–57,59]
Anti-Ro52	Extractable nuclear antigen Ro52	13–26%	Associated with more severe ILD
Anti-MDA-5	MDA-5 RNA helicase	20–25%[a]	Skin ulceration; CADM; rapidly progressing/ acute interstitial pneumonitis
Anti-155/140	155/140-kDa polypeptides	7–16%	Highest risk of malignancy, lower risk of ILD
Anti-SRP	Cytoplasmic signal recognition particle	5–6%	Severe myopathy and weakness; risk of ILD is not increased
Anti-Mi-2	Nuclear helicase protein	14%	Milder myopathy and classic DM findings; risk of ILD is not increased

Το συχνότερο anti-ARS Ab

Table 2 Antisynthetase antibodies

Antisynthetase antibodies (ARS)	Target antigen	Prevalence in IIM[18,31,48,78,93]	% of ARS antibodies detected[14,20,23,26,31,50,79,93]	Clinical features[34,77,79]
Anti-Jo-1	Histidyl-tRNA synthetase	8–18%	36–88%	Classic DM, ILD
Anti-EJ	Glycyl-tRNA synthetase	5–10%	7–23%	Classic DM and CADM, ILD
Anti-PL-7	Threonyl-tRNA synthetase	5%	9–25%	Classic DM, ILD
Anti-OJ	Isoleucyl-tRNA synthetase	3%	5–8%	Isolated ILD
Anti-PL-12	Alanyl-tRNA synthetase	1%	2–11%	Isolated ILD, CADM
Anti-KS	Asparaginyl-tRNA synthetase	1%	4–8%	Isolated ILD
Anti-Zo	Phenylalanyl-tRNA synthetase	< 1%	< 1%	
Anti-YRS	Tyrosyl-tRNA synthetase	< 1%	< 1%	

Hallowell et al. Semin Respir Crit Care Med. 2014

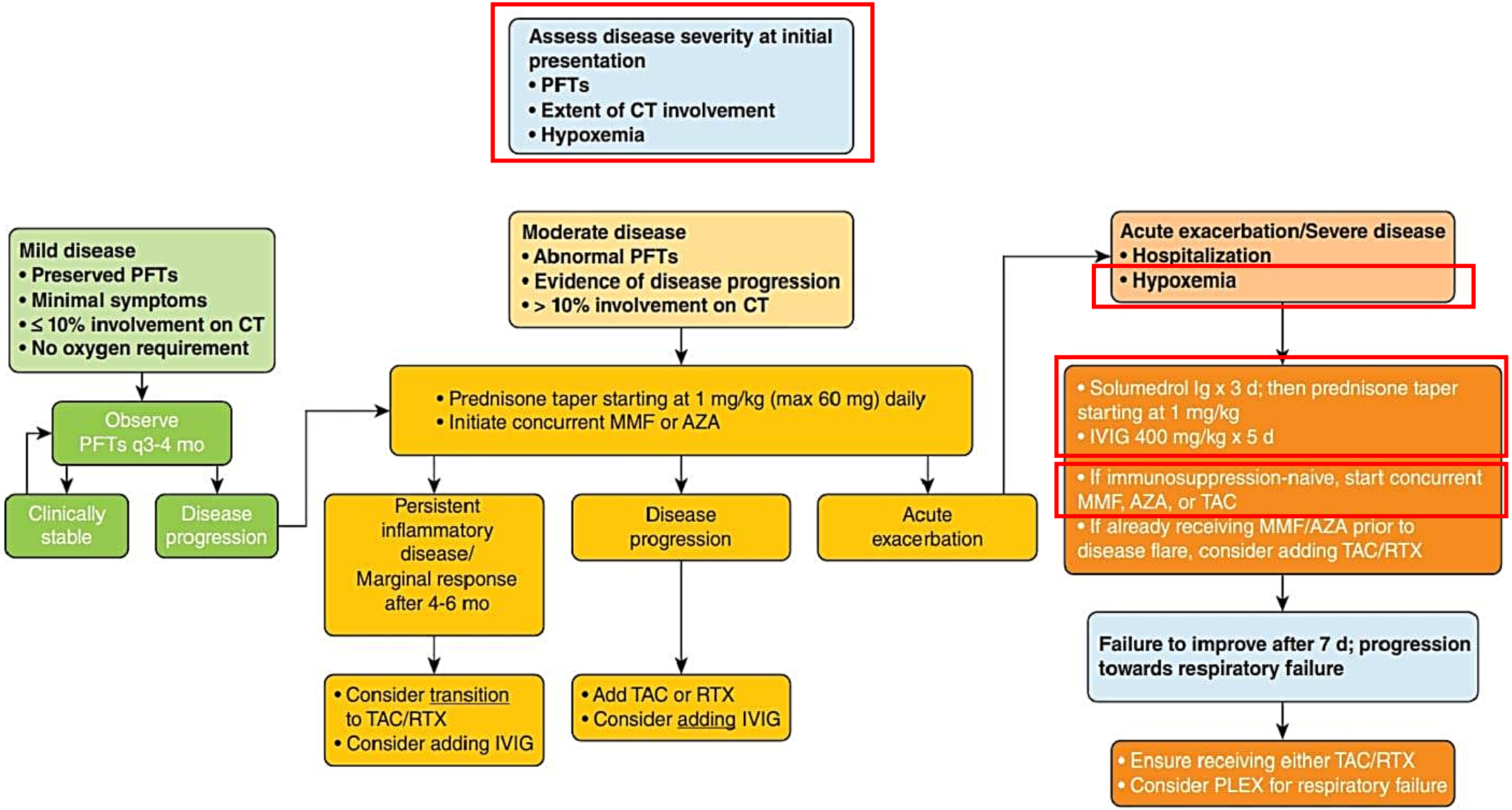
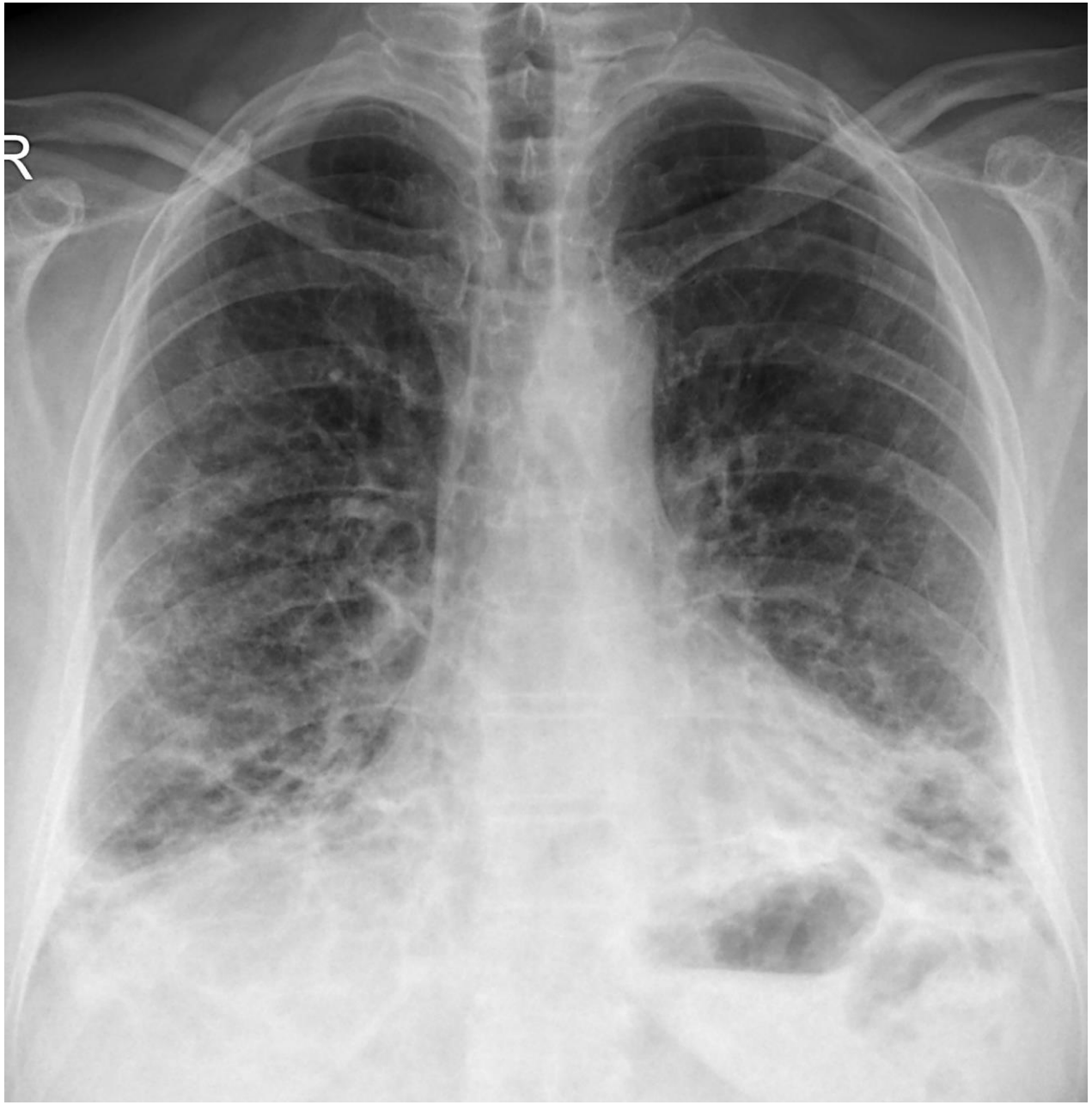
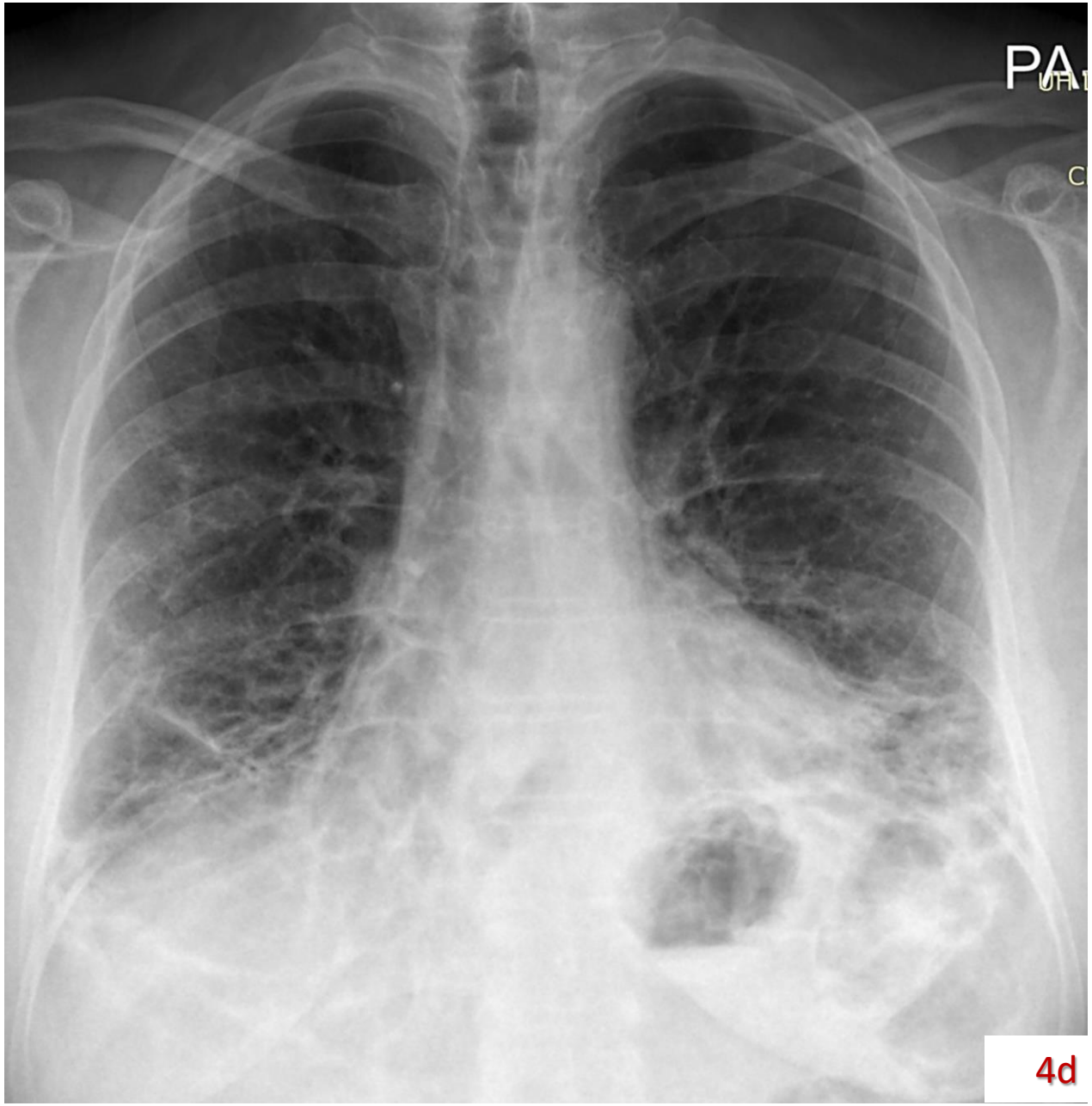


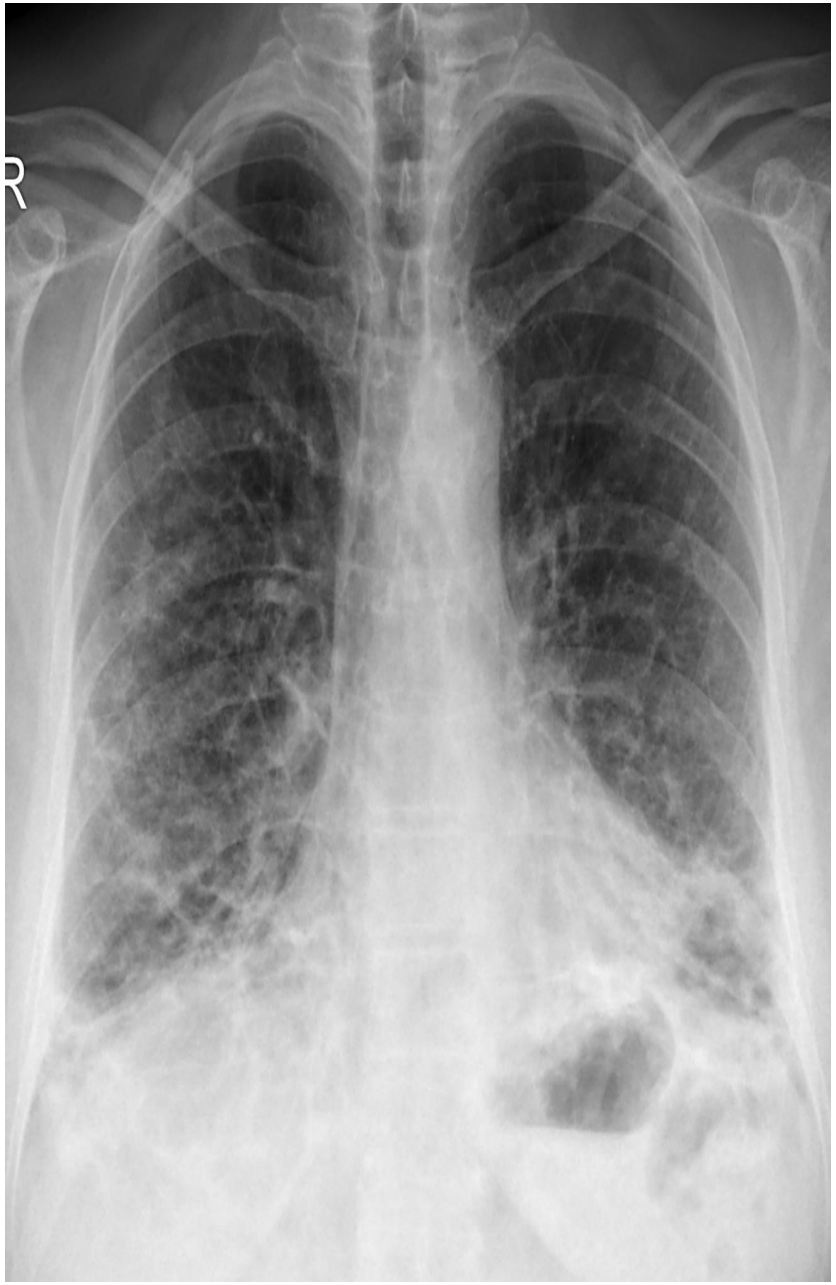
Figure 2 – *Diagram showing treatment approach to myositis-associated interstitial lung disease (ILD). The decision to use chronic immunosuppression in patients with myositis-associated ILD and the agent of choice is influenced by the severity of disease at diagnosis, disease trajectory, response to initial therapy, patient comorbidities, and provider familiarity with the treatment methods available at a given institution. AZA = azathioprine; IVIG = IV immunoglobulin; MMF = mycophenolate; PFT = pulmonary function test; PLEX = plasma exchange; RTX = rituximab; TAC = tacrolimus.*

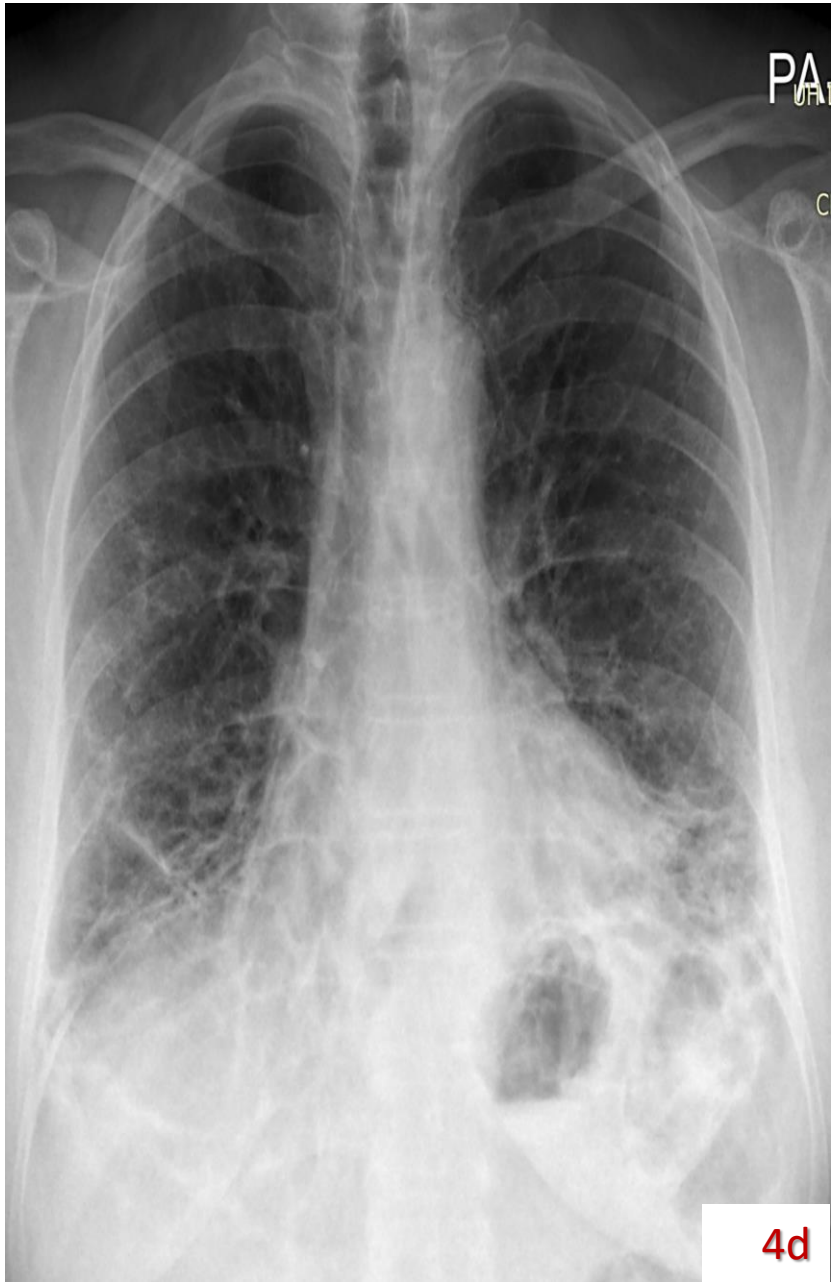
- Αποκλεισμός κακοήθειας με full-body CT
- Λεμφοκύτταρα: 3.050 cells/mL
- Φερριτίνη: 100 ng/mL (< 1500 ng/mL)
- Αρνητικός Ιολογικός
- Mantoux: 0mm
- Πρεδνιζολόνη με 1,5mg/Kg για 4 ημέρες
- Calcioral D3
- TMP-SMX προφύλαξη

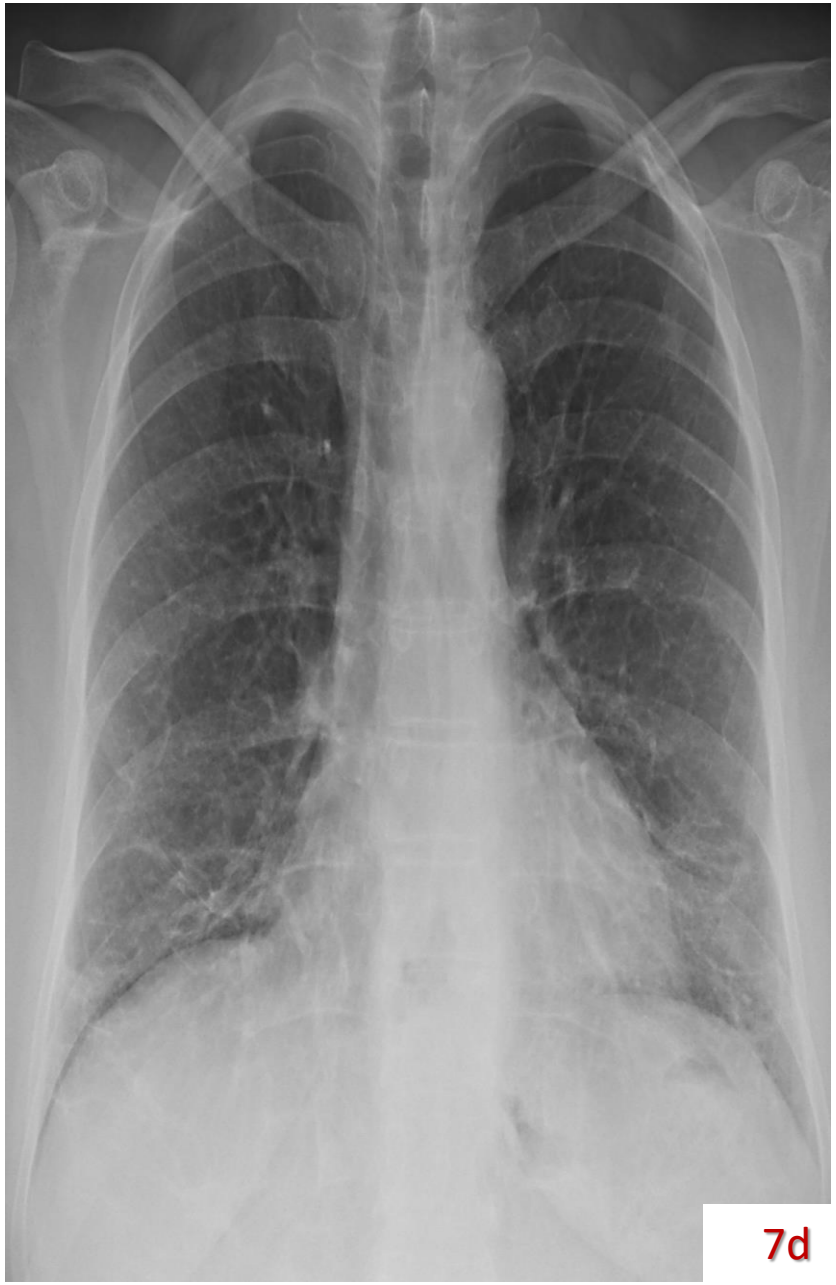




Οδηγία στη συνέχεια για πρεδνιζολόνη με 0,45mg/Kg (40mg) για 1 εβδομάδα

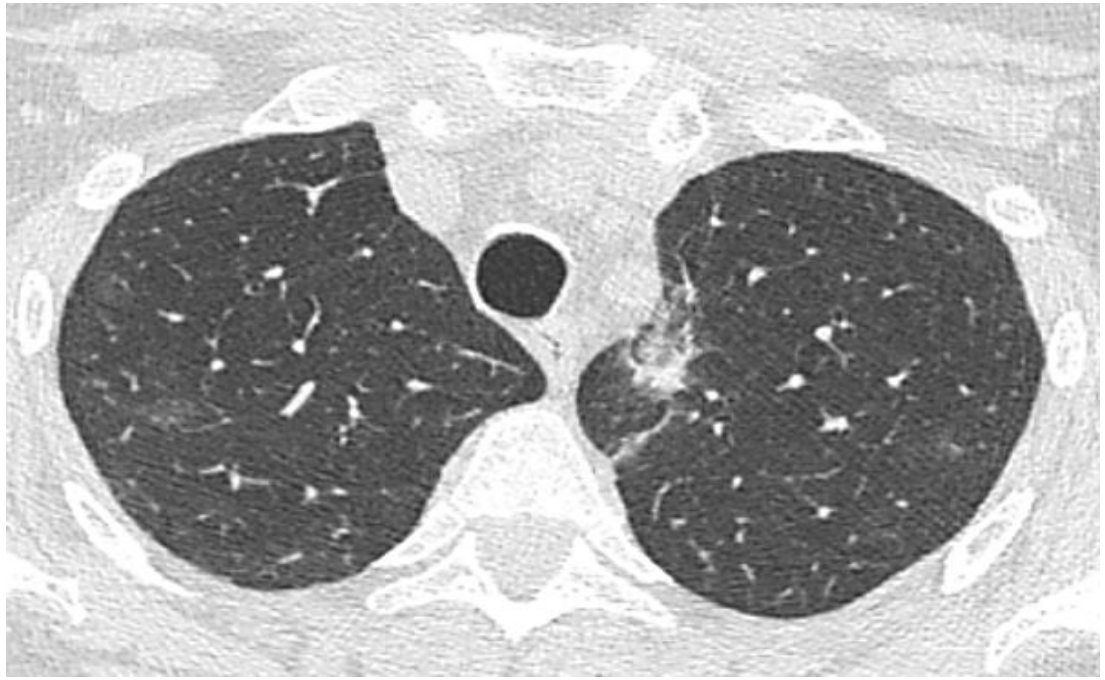


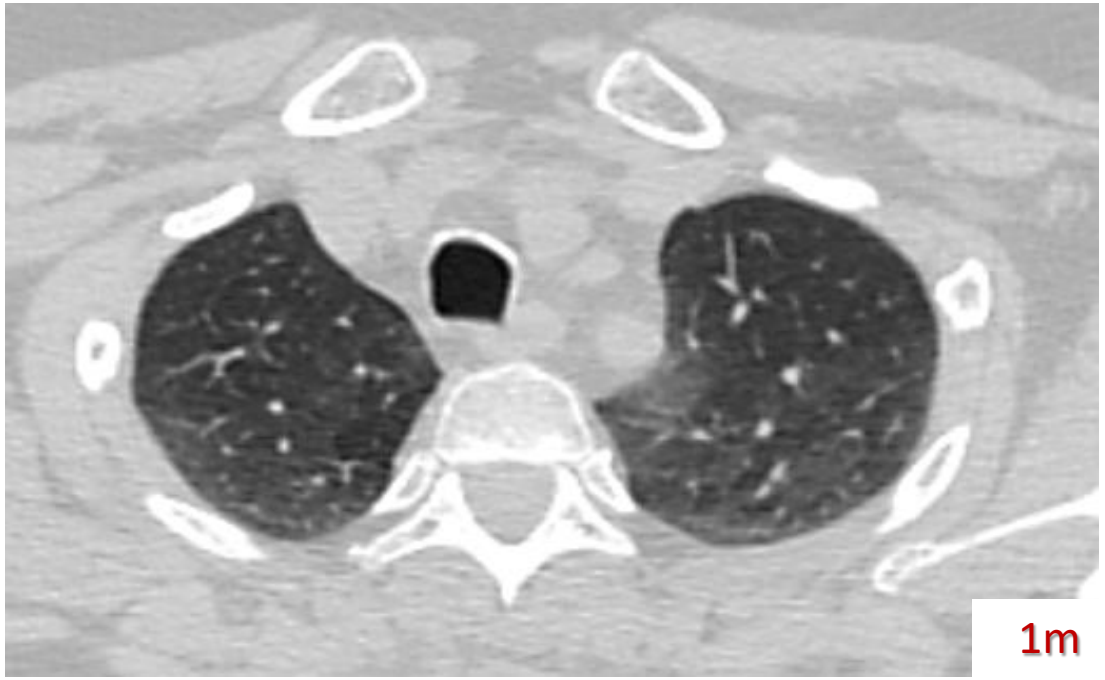




- FEV1 1,93 81%, FVC 2,26 81%, FEV1/FVC 85
- FEV1 2,28 101%, FVC 2,53 95%, FEV1/FVC 90

Οδηγία στη συνέχεια για πρεδνιζολόνη με 0,33mg/Kg (30mg) για 3 εβδομάδες

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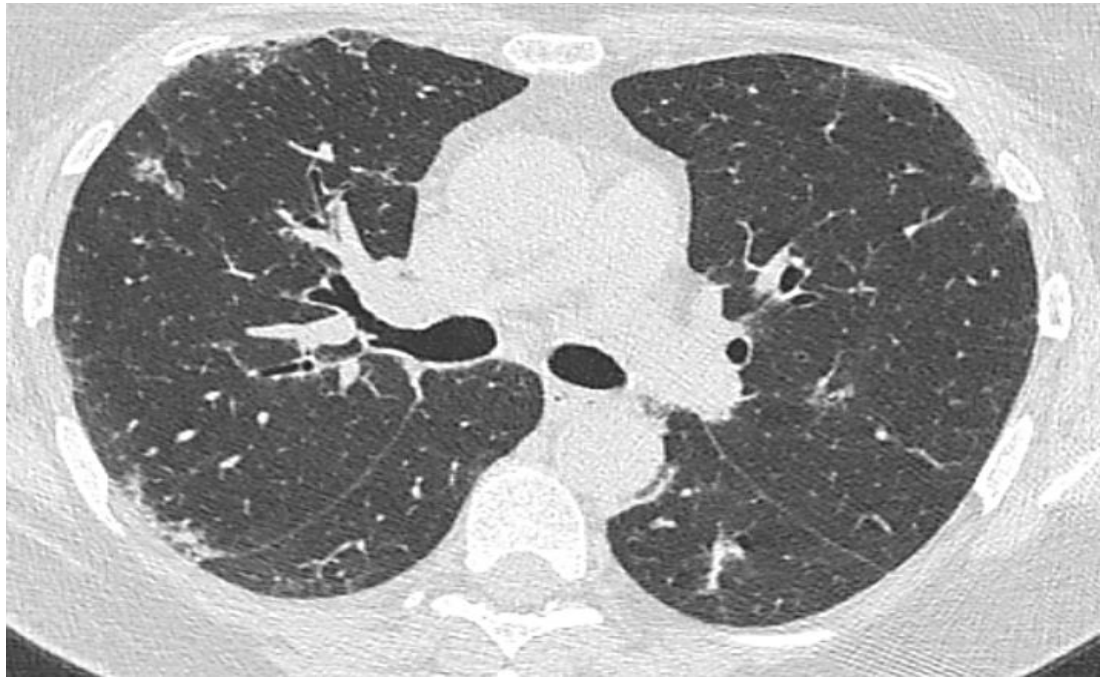

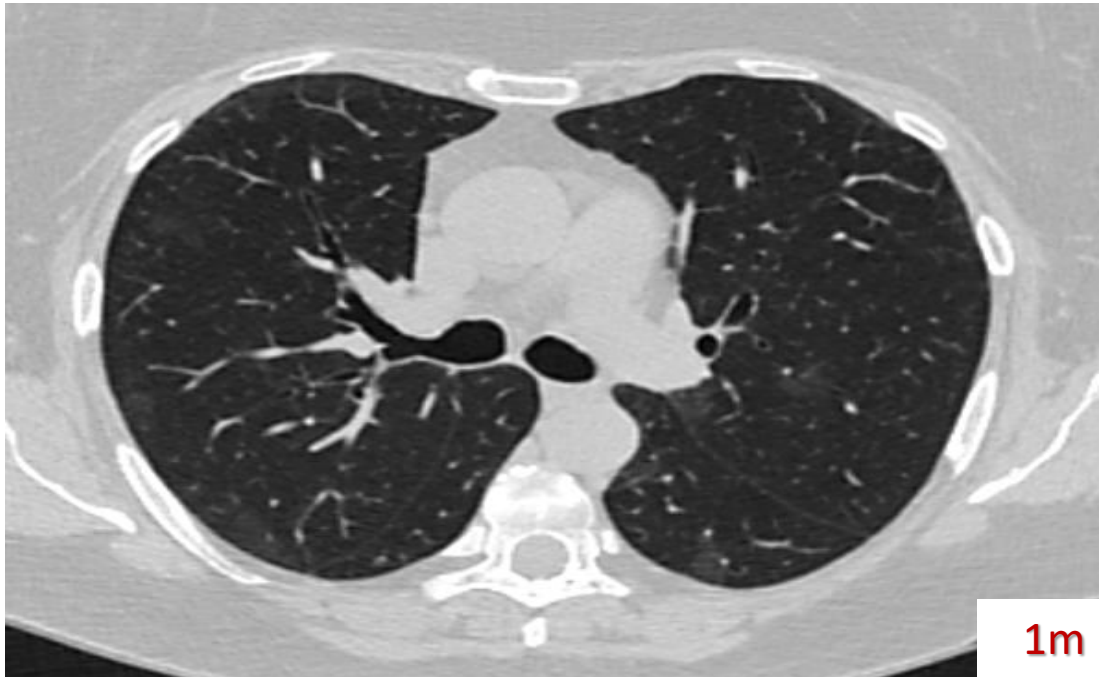
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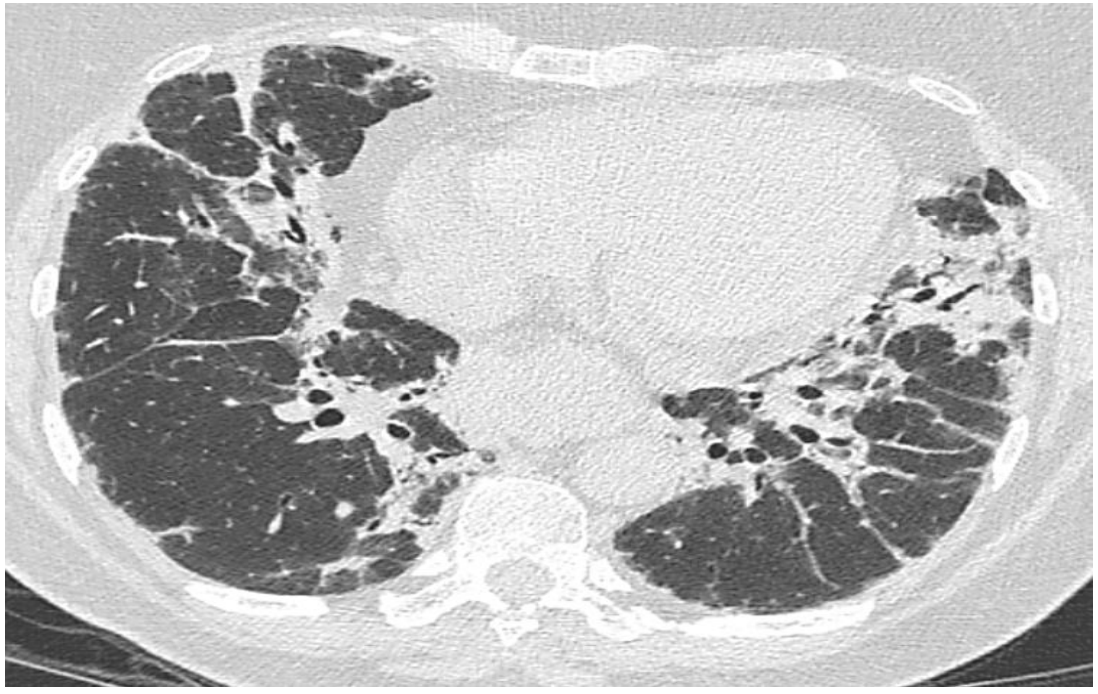

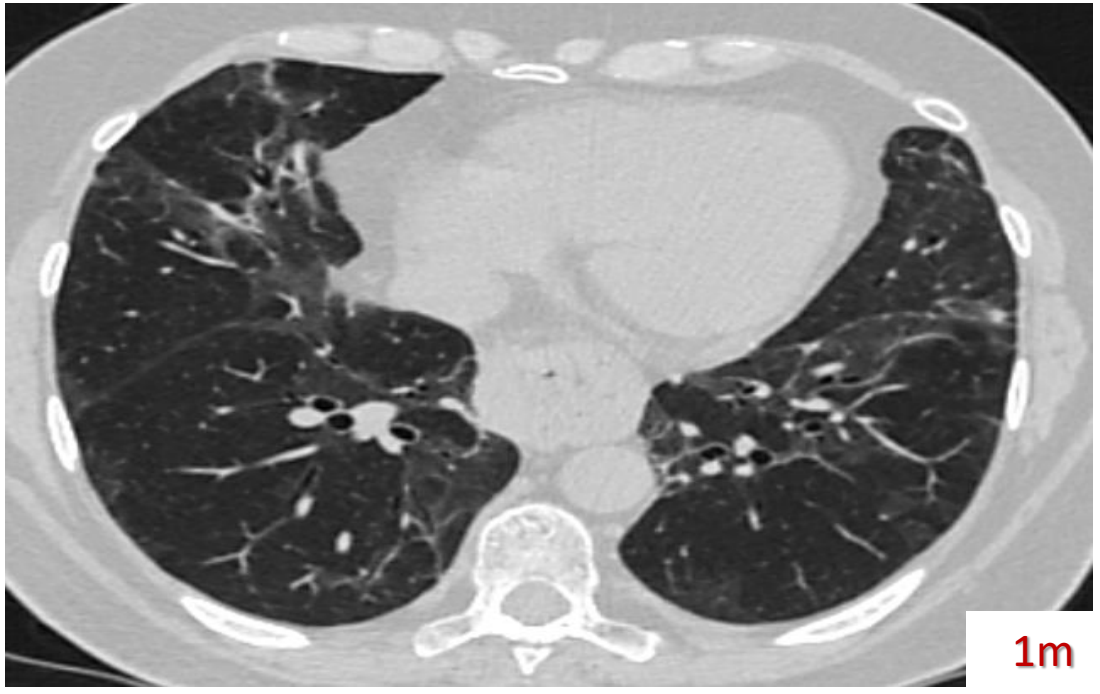
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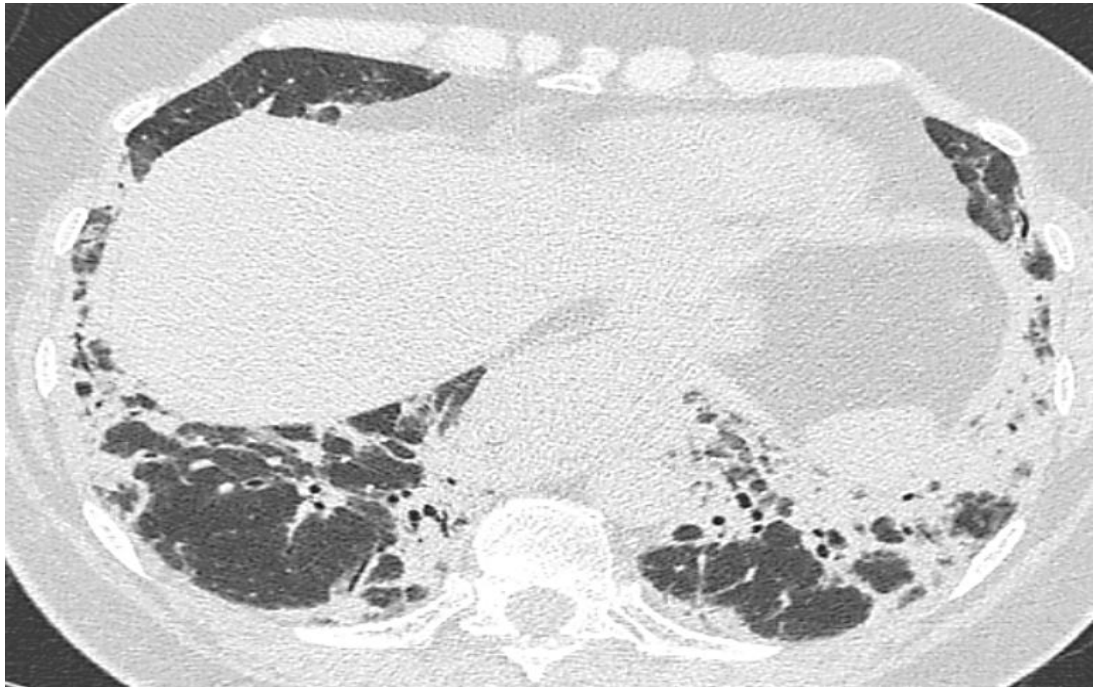

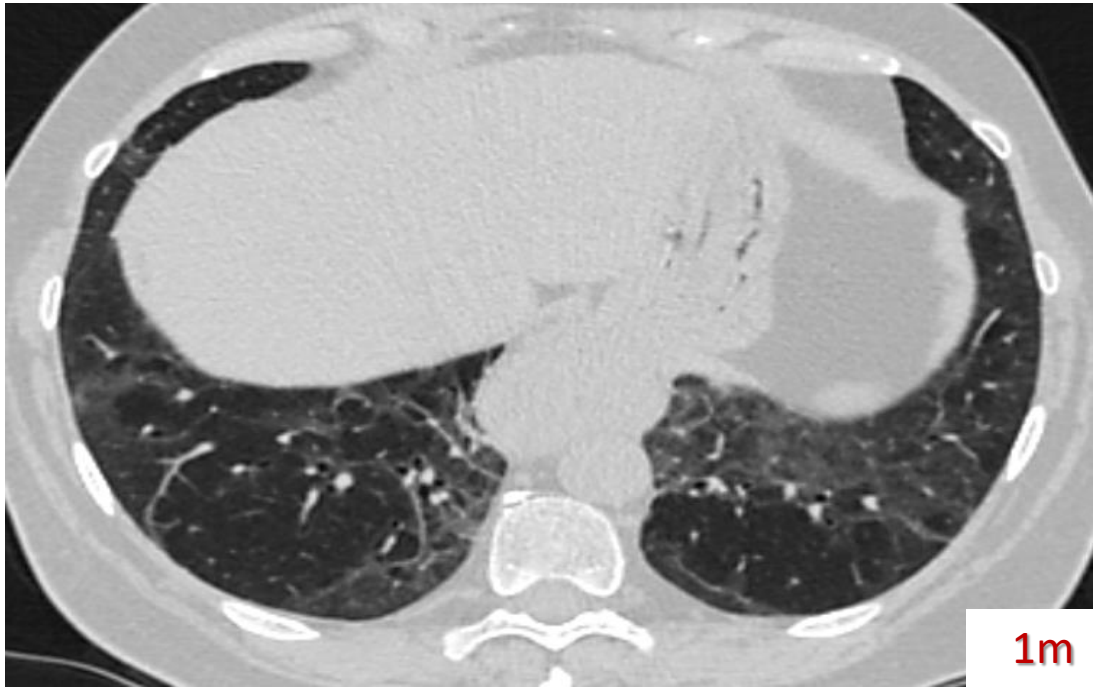
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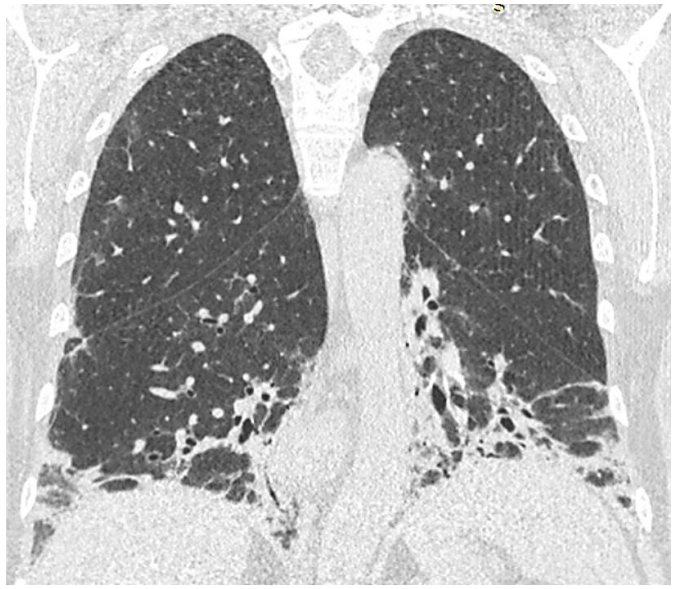
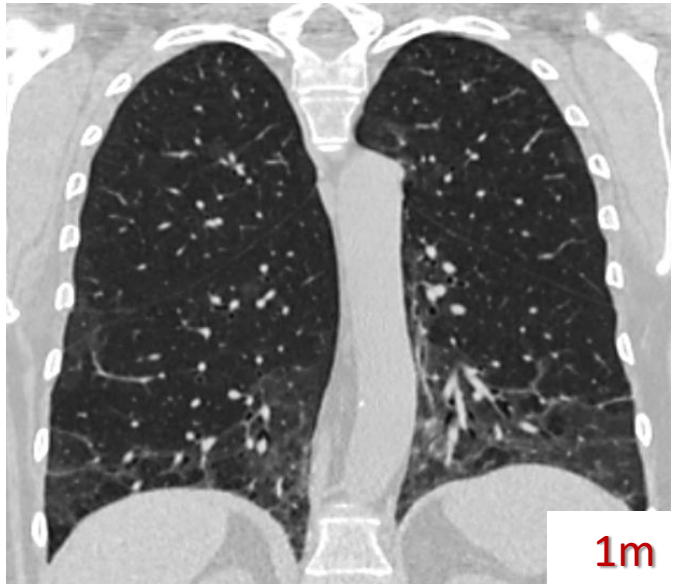
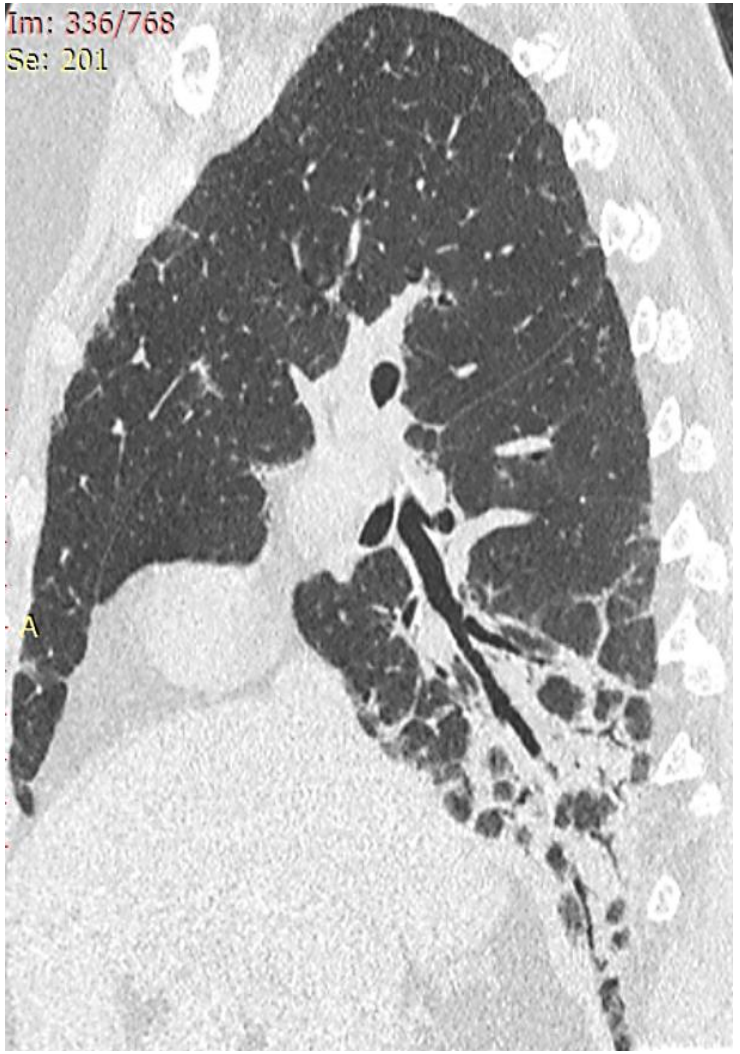
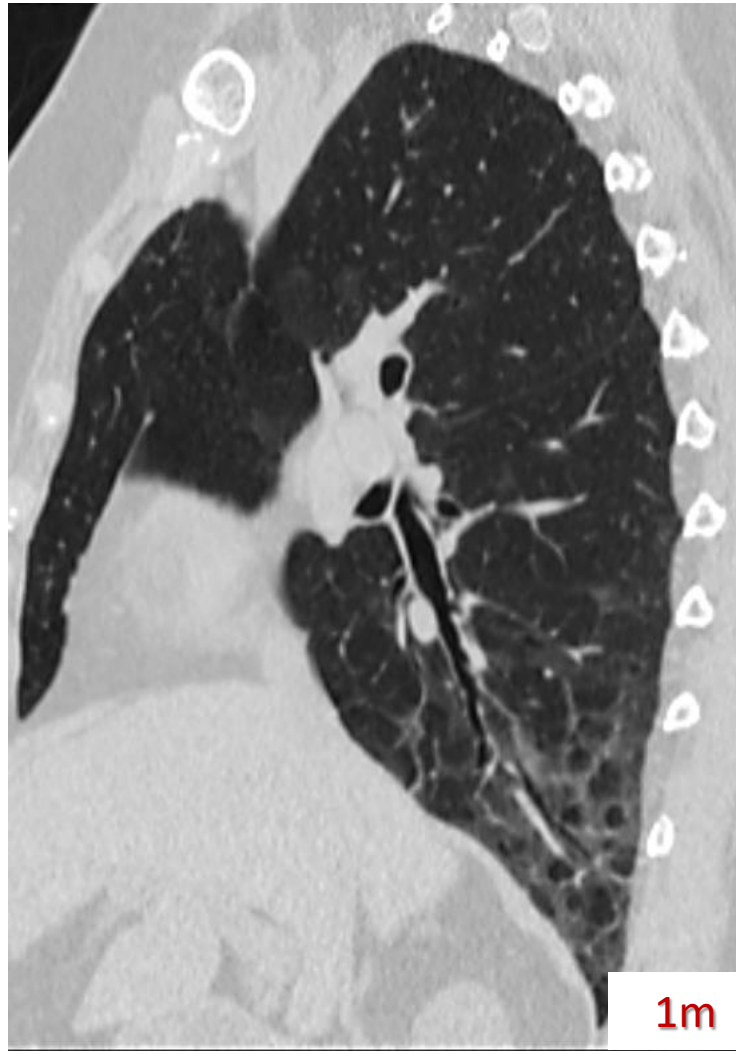






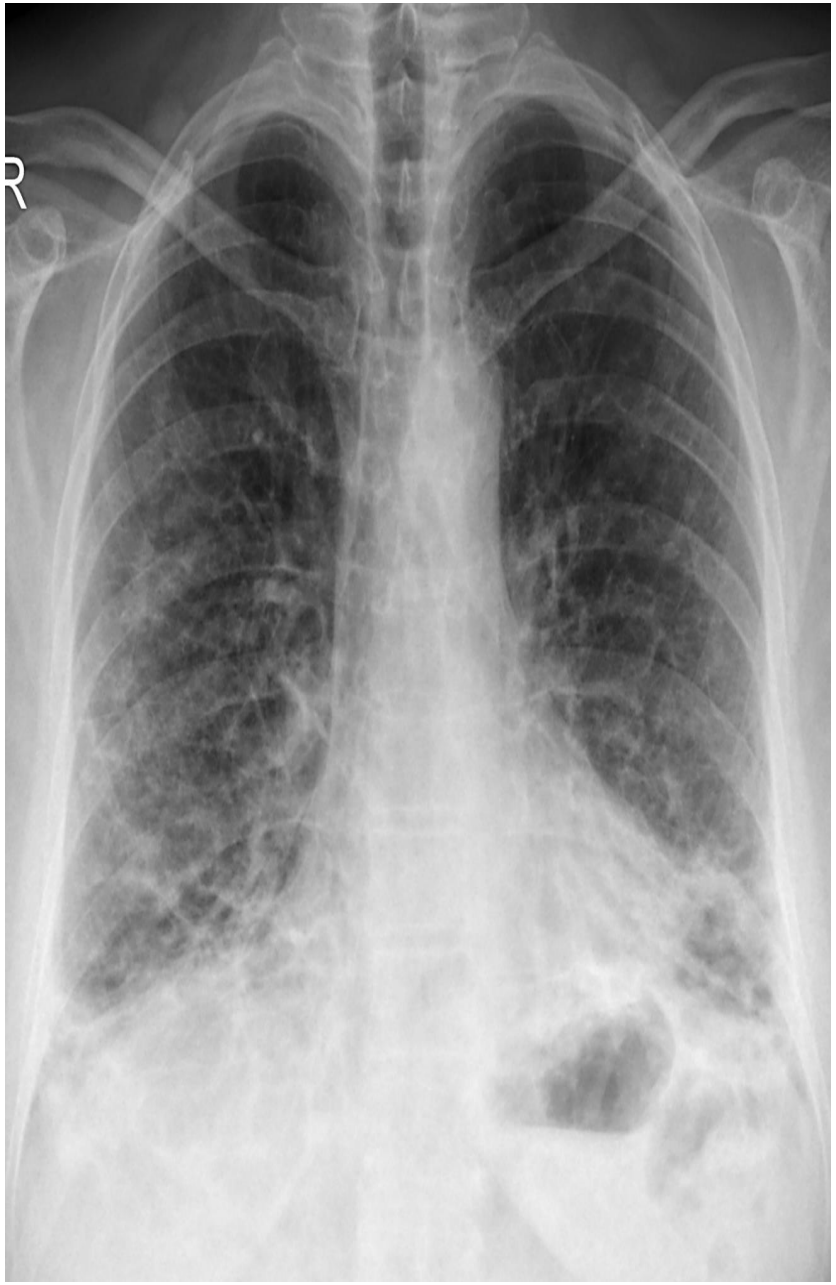


- FEV1 1,93 81%, FVC 2,26 81%, FEV1/FVC 85
- FEV1 2,28 101%, FVC 2,53 95%, FEV1/FVC 90
- FEV1 2,46 104%, FVC 2,91 104%, FEV1/FVC 85, DLCO 77%

Οδηγία στην συνέχεια για πρεδνιζολόνη
με 0,22mg/Kg (20mg) για 1 μήνα

“Βλέποντας & κάνοντας”

time	mg methylprednisolone	FEV1	FEV1%	FVC	FVC%	TIF	DLCO%
0d	0→125	1,93	81%	2,26	81%	85	-
3d	125→32 (0,5mg/kg prezolon)	-	-	-	-	-	-
7d	32→26	2,28	101%	2,53	95%	90	-
1m	26→24 (prezolon->medrol)	2,46	104%	2,91	104%	85	77%
2m	24→16	2,71	114%	3,07	110%	88	76%
3m	16→8	2,59	106%	3,20	111%	81	81,5%
4m	8→4	2,52	114%	3,00	115%	84	78,2%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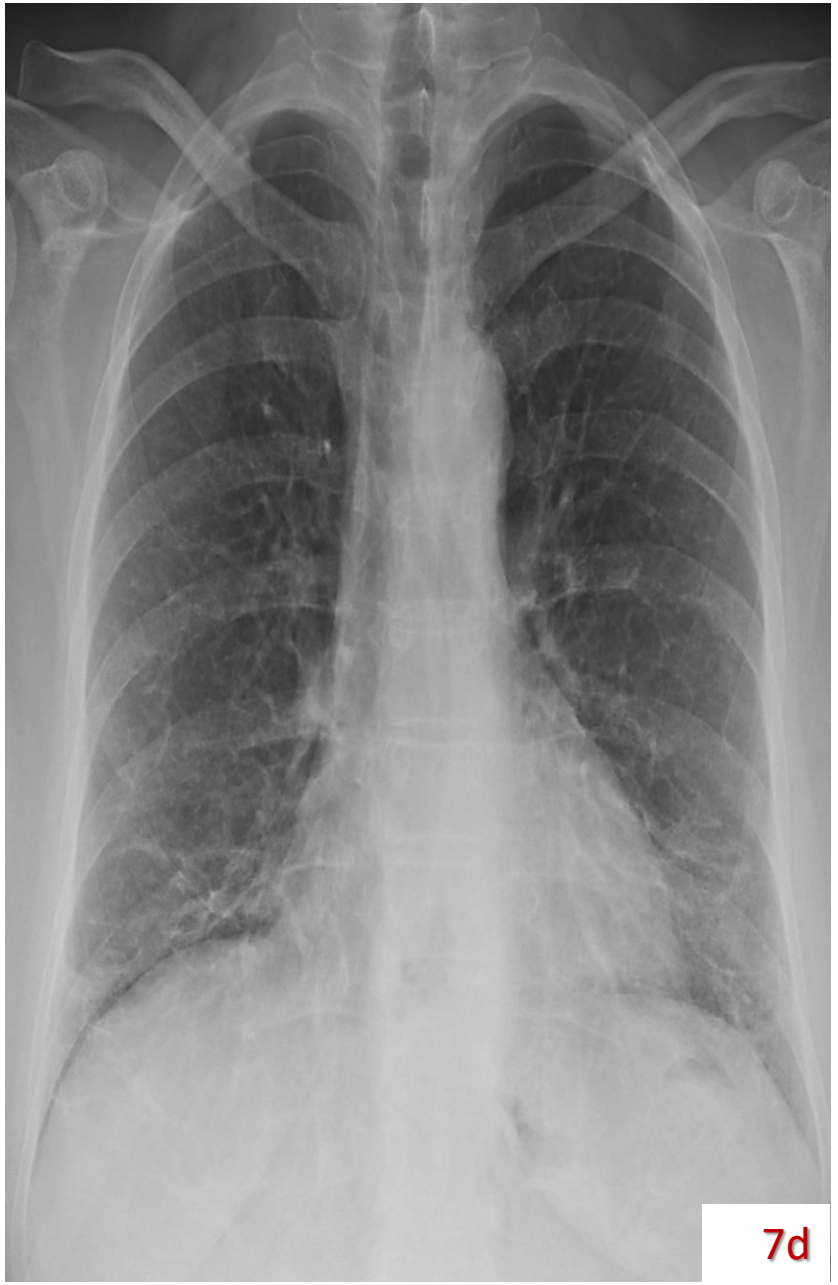
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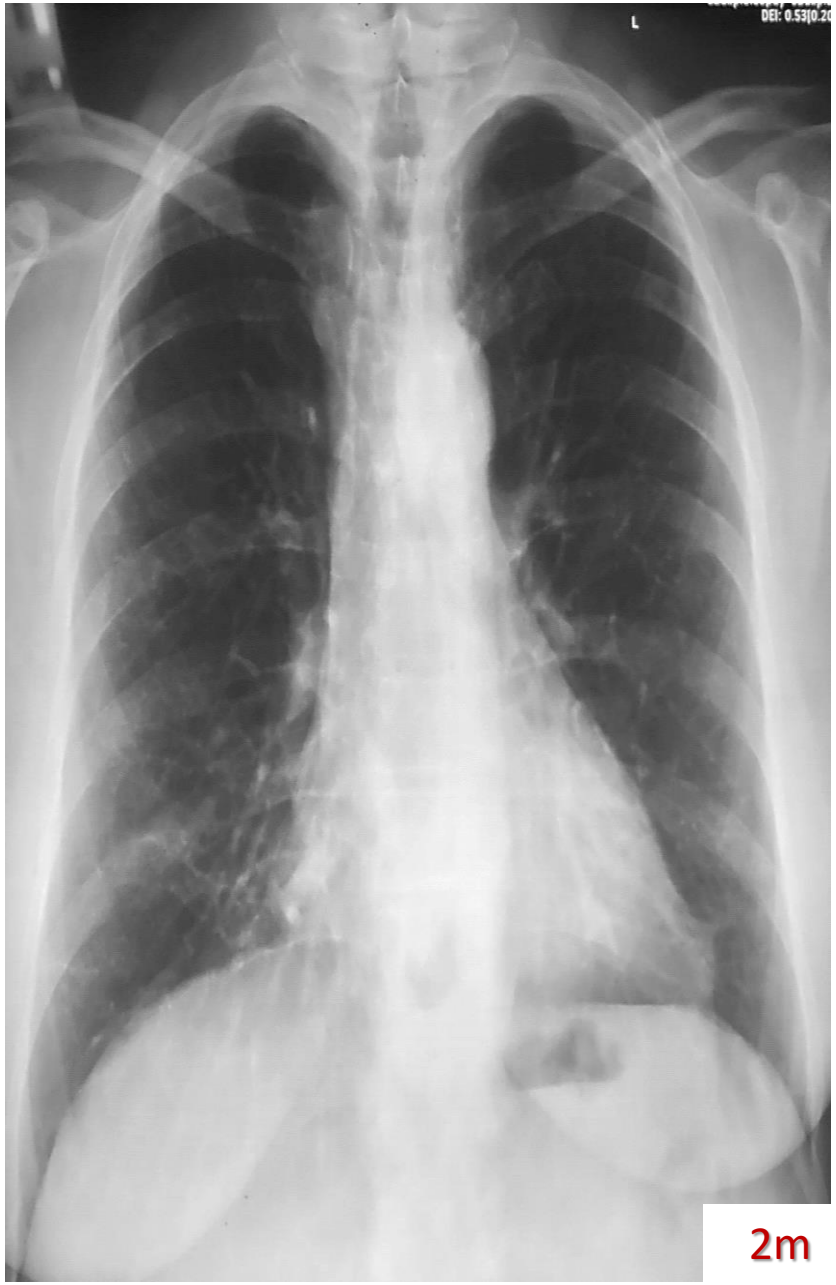
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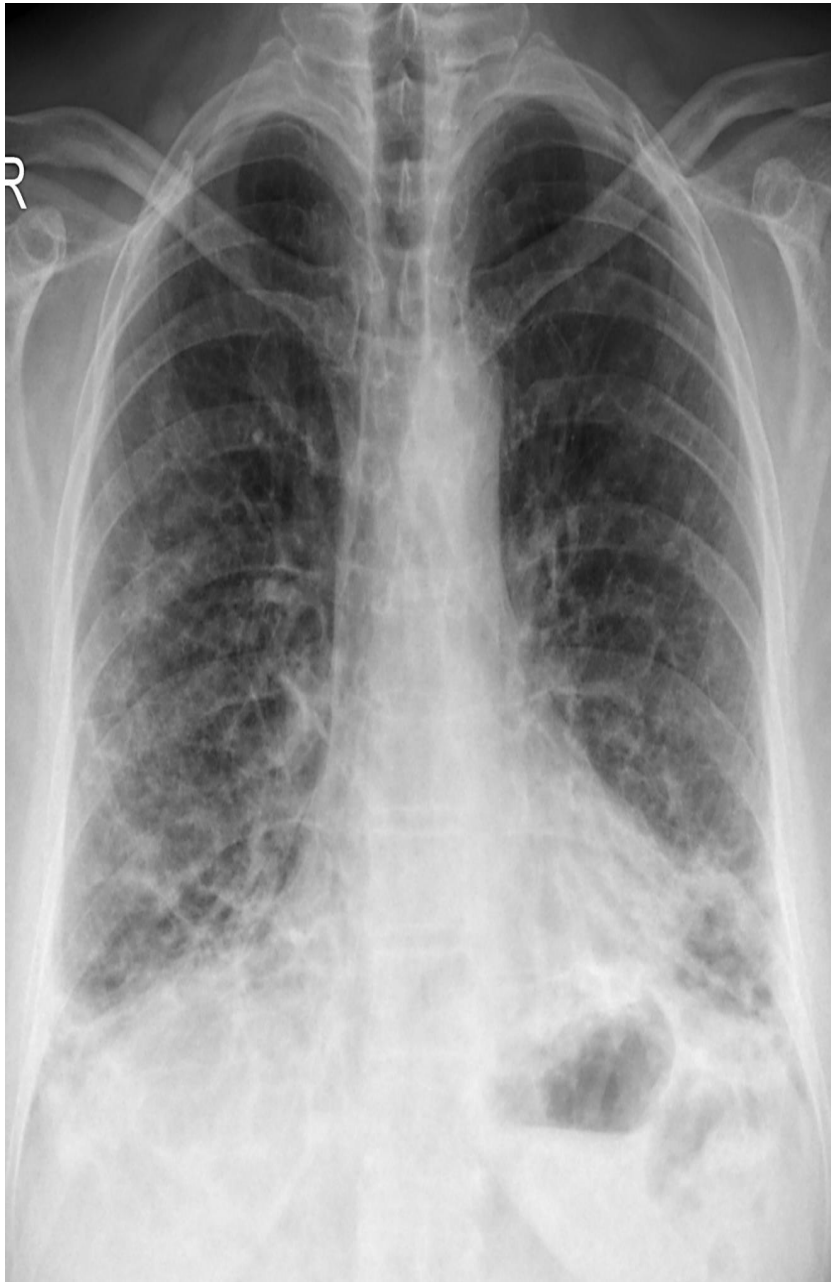
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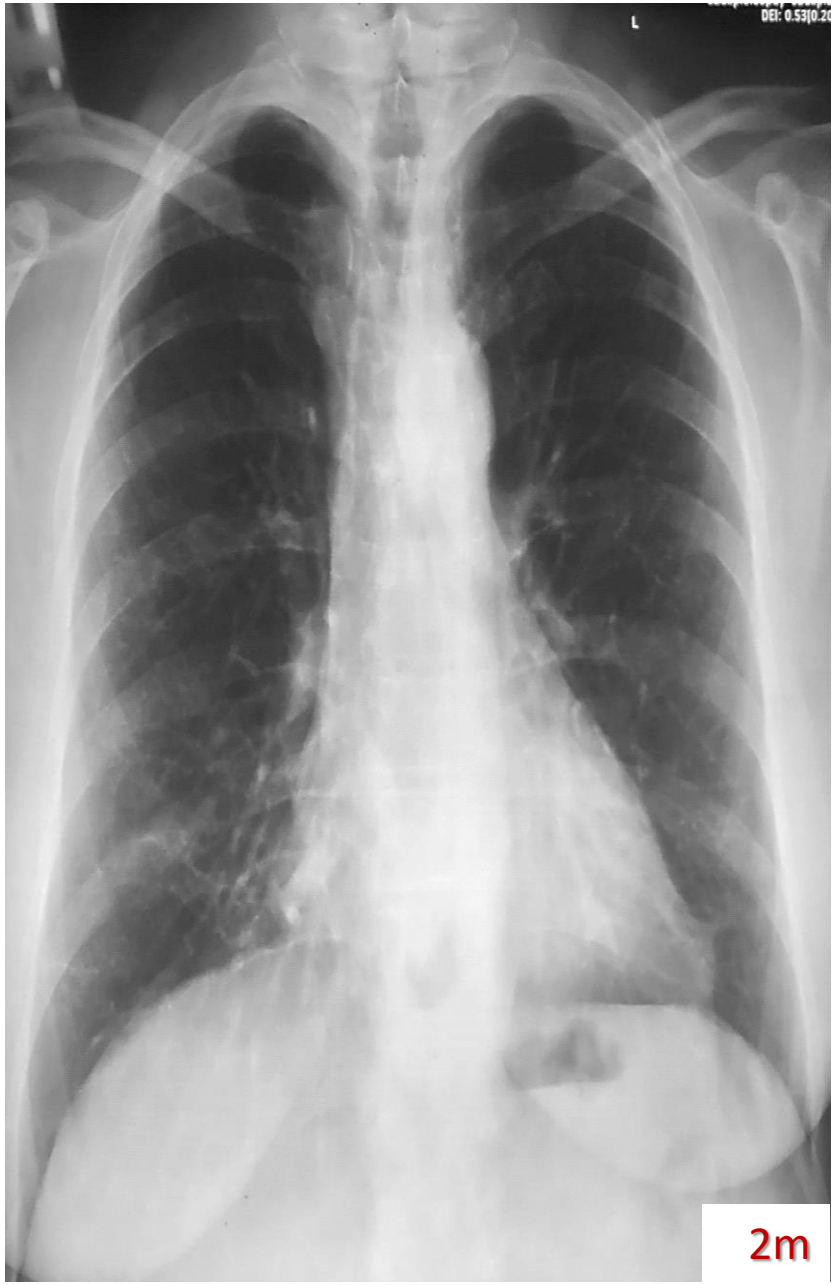
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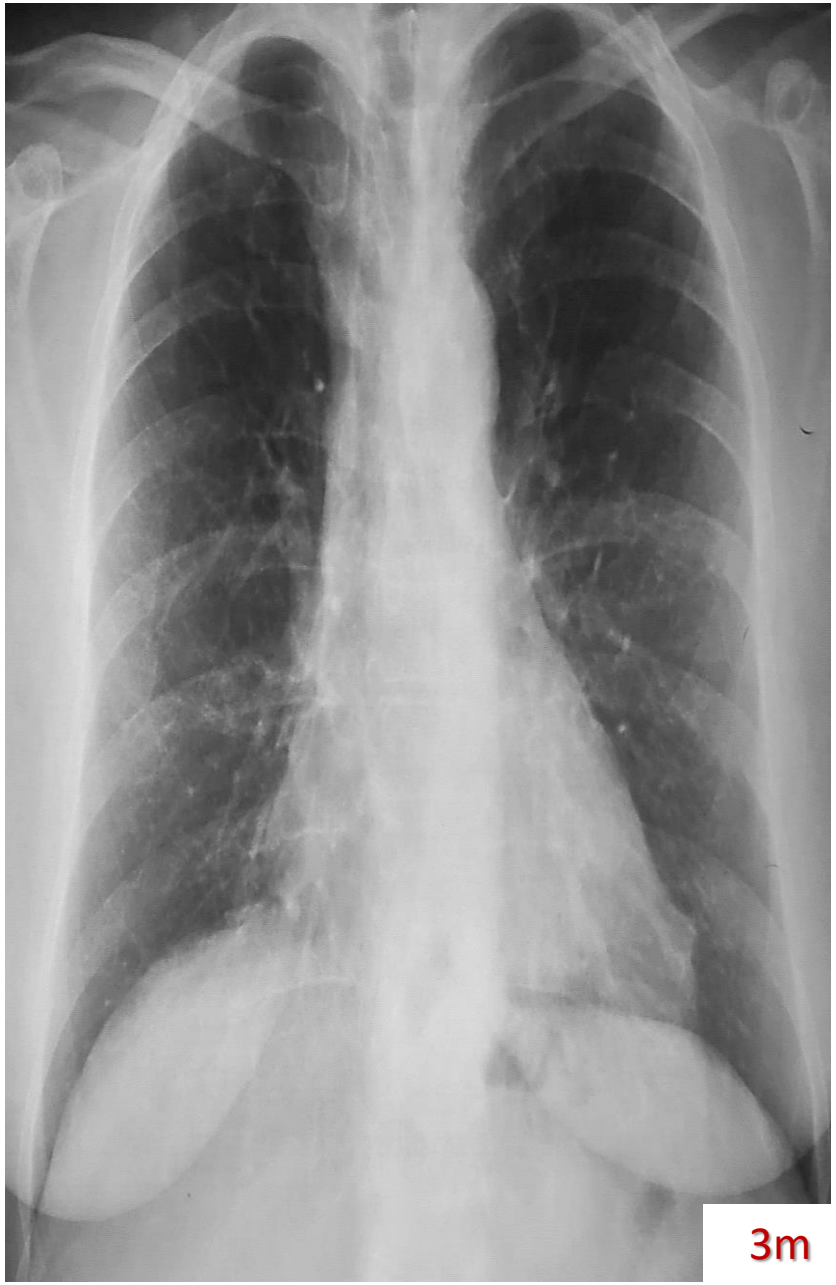
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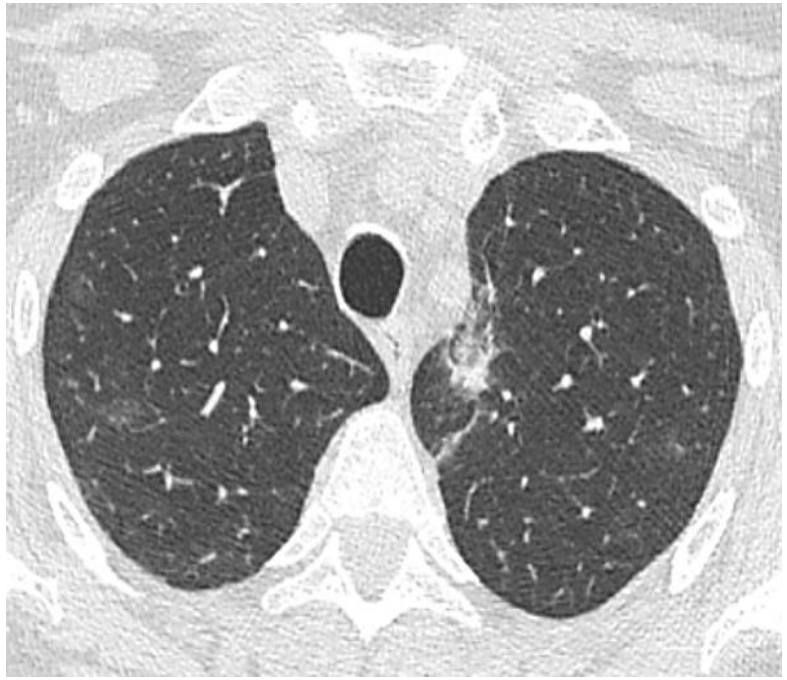

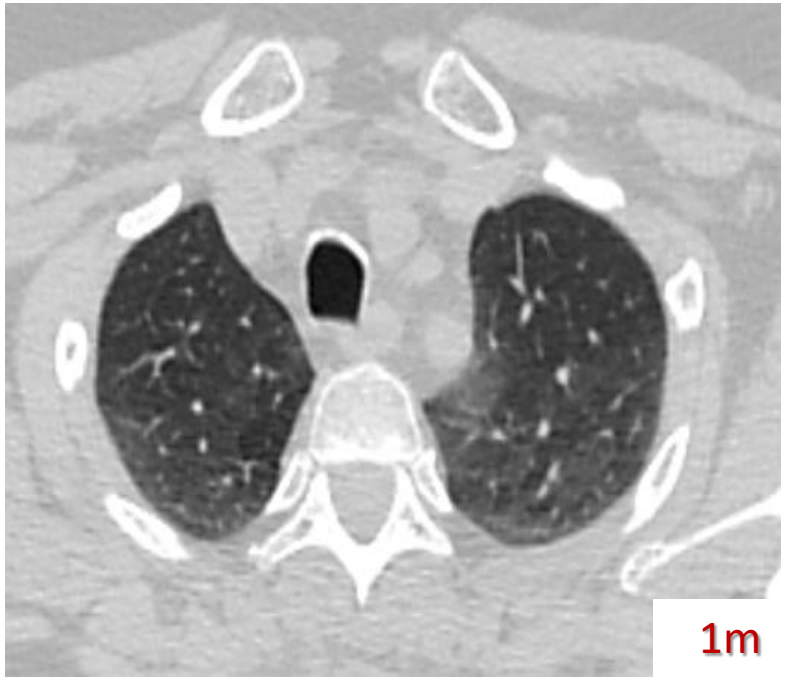
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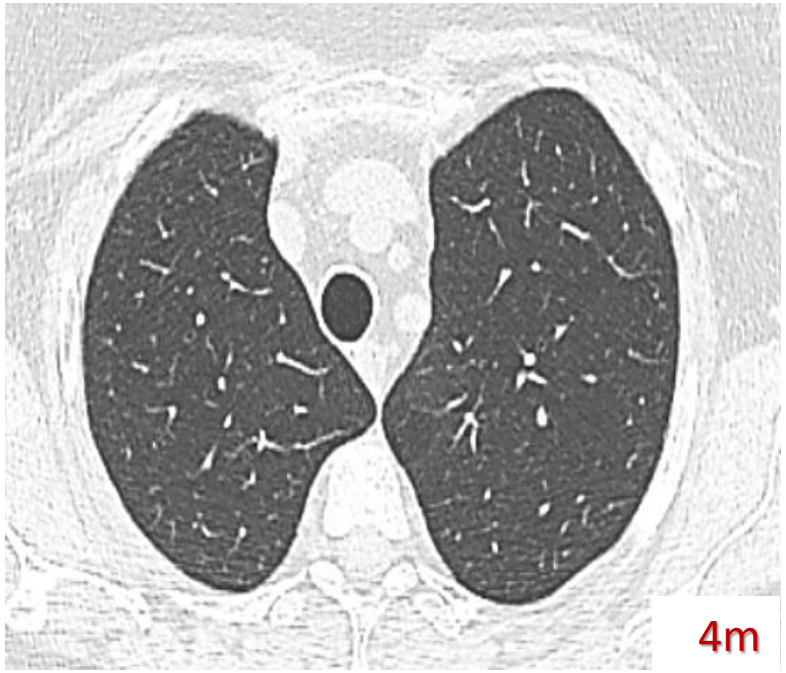
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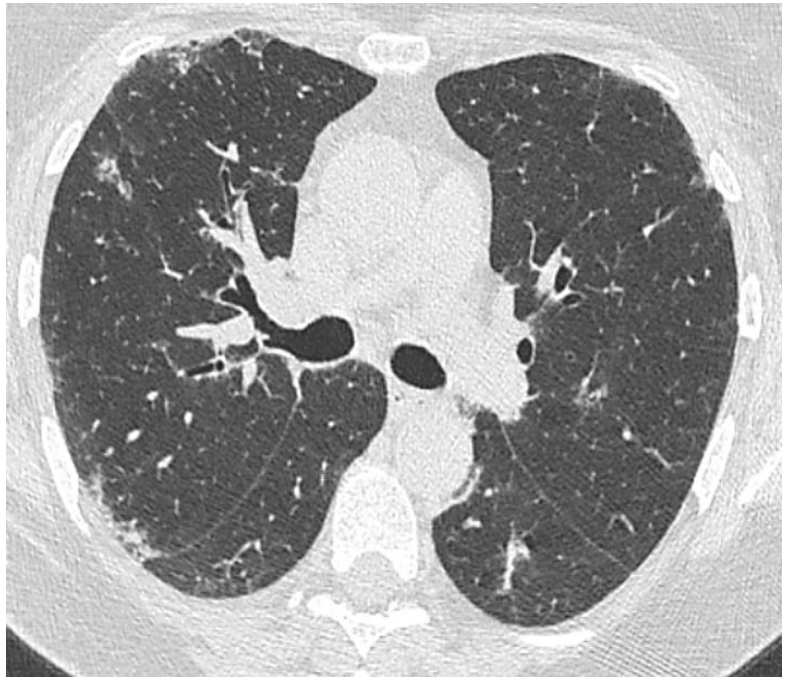

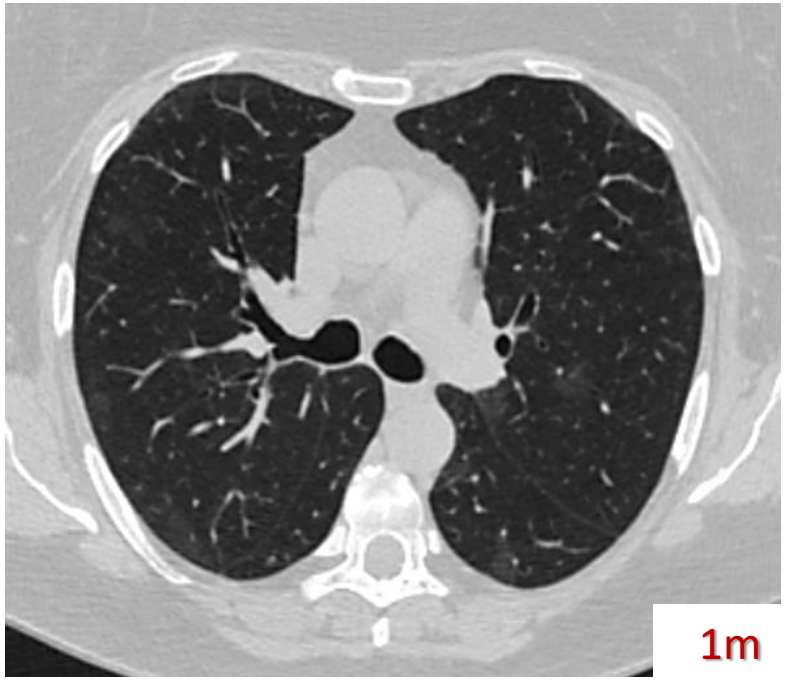
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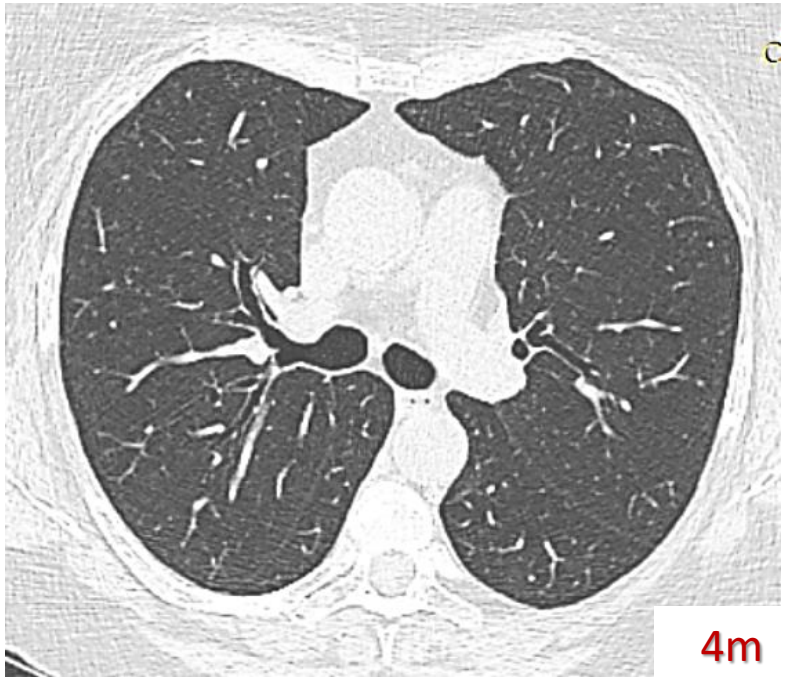
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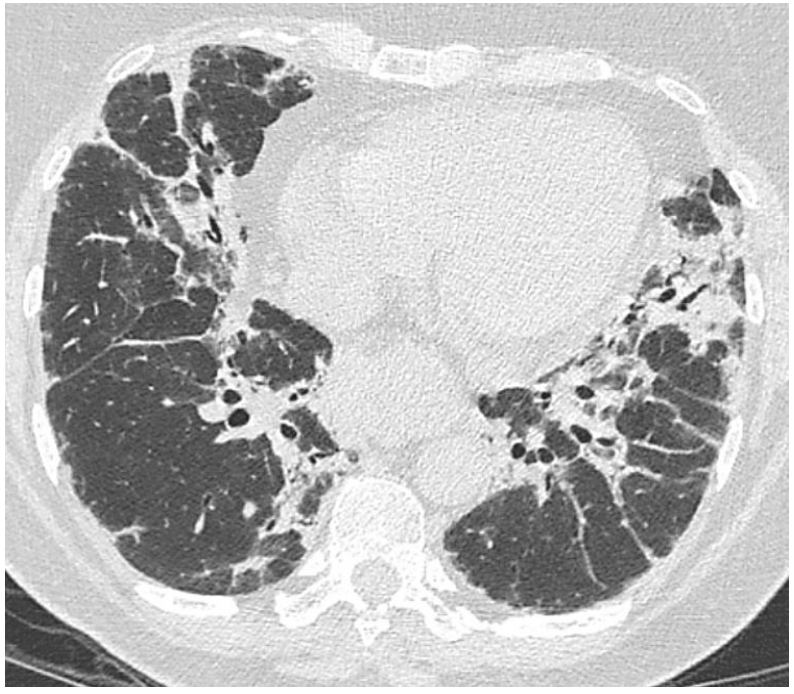

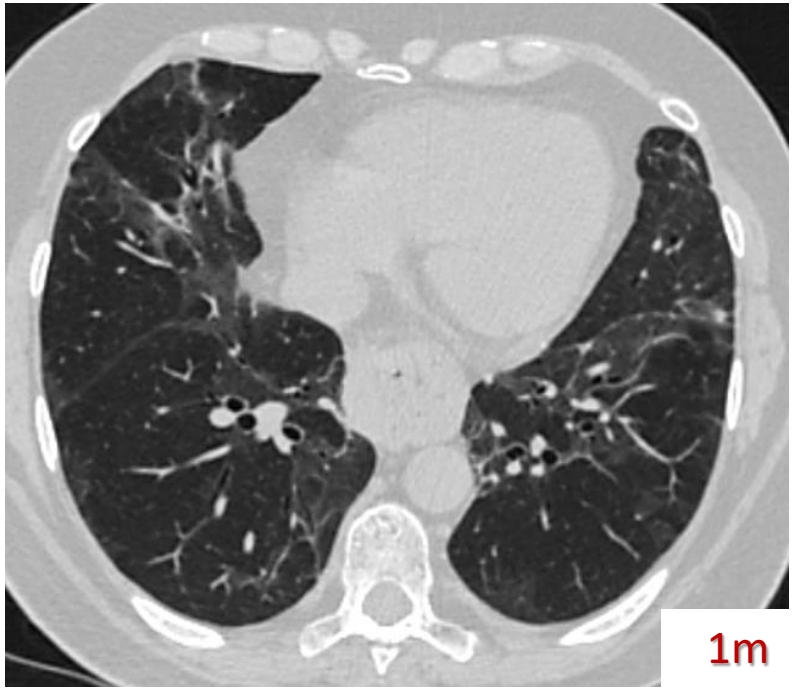
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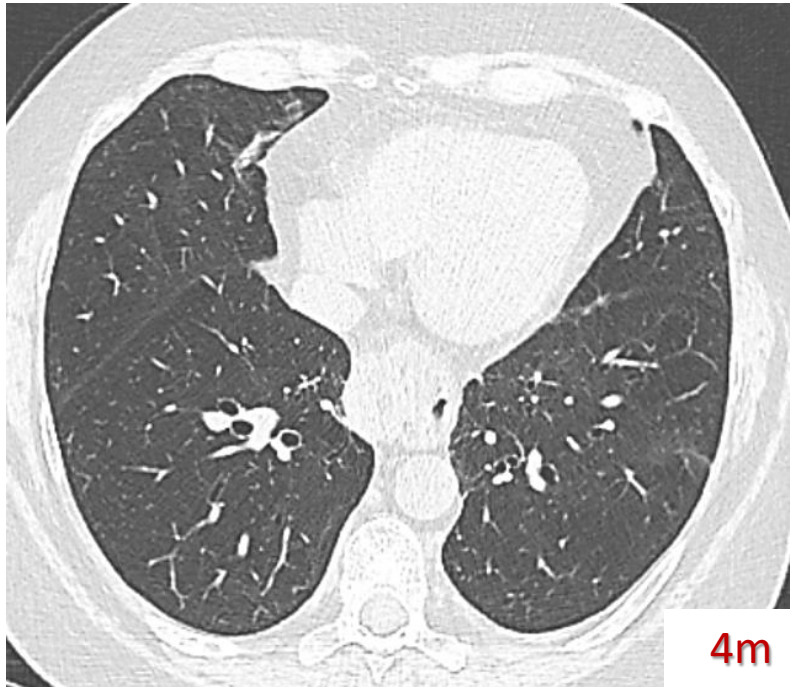
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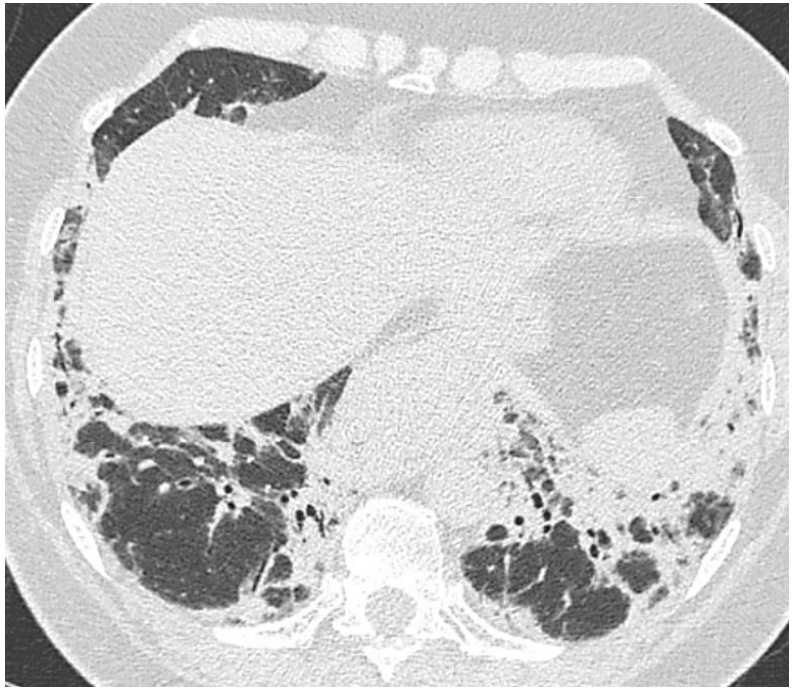

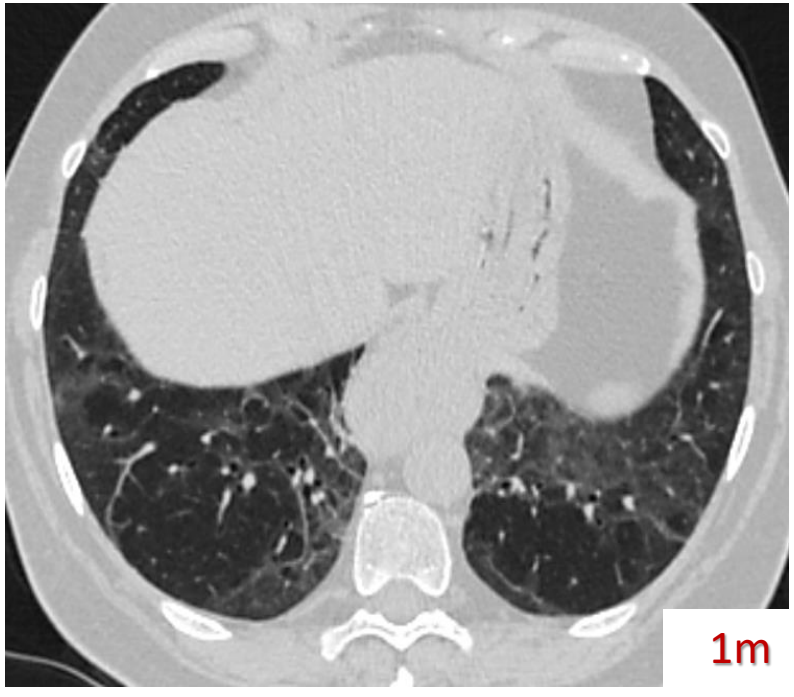
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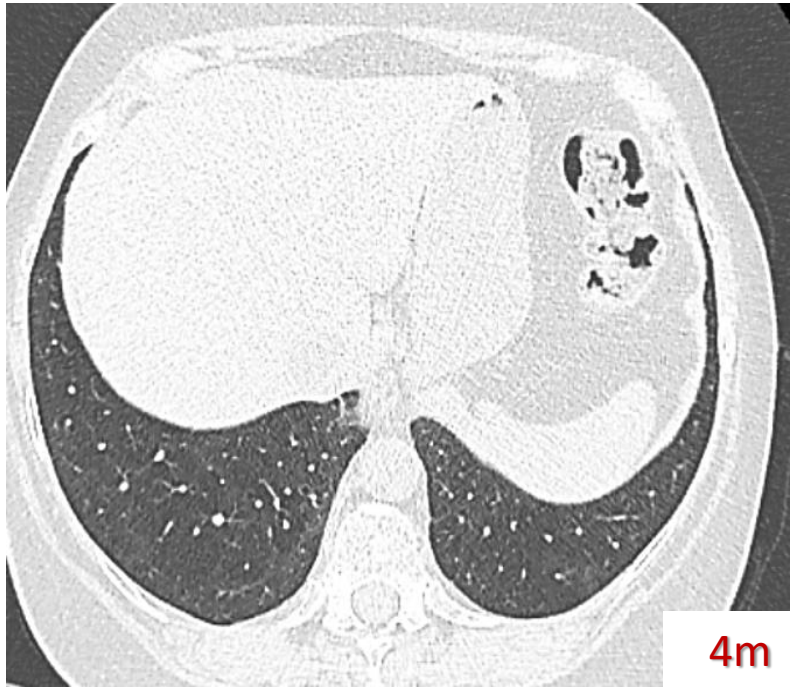
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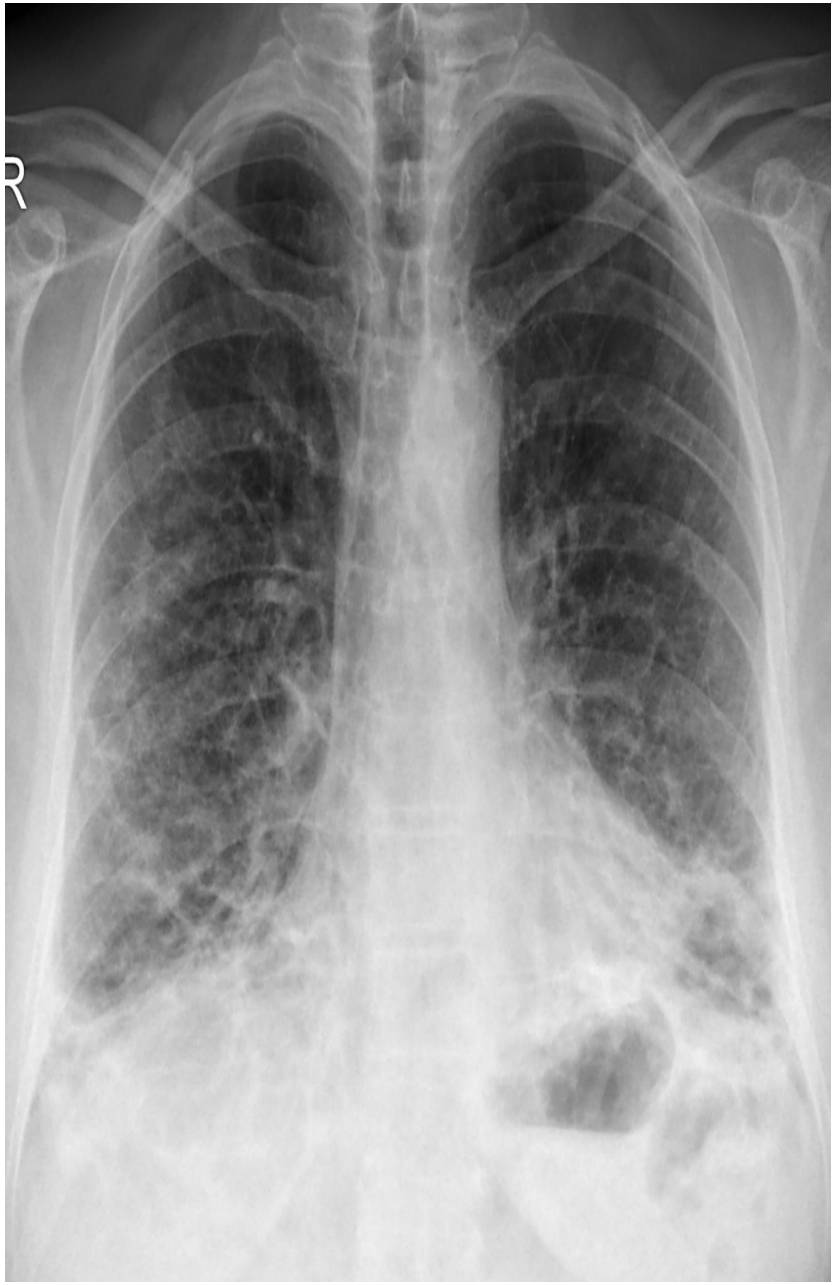
“Βλέποντας & κάνοντας”

time	mg methylprednisolone	FEV1	FEV1%	FVC	FVC%	TIF	DLCO%
0d	0→125	1,93	81%	2,26	81%	85	-
3d	125→32 (0,5mg/kg prezolon)	-	-	-	-	-	-
7d	32→26	2,28	101%	2,53	95%	90	-
1m	26→24 (prezolon->medrol)	2,46	104%	2,91	104%	85	77%
2m	24→16	2,71	114%	3,07	110%	88	76%
3m	16→8	2,59	106%	3,20	111%	81	81,5%
4m	8→4	2,52	114%	3,00	115%	84	78,2%
5m	4→2	-	-	-	-	-	-
6m	2→0	2,67	106%	3,09	104%	86	73,1%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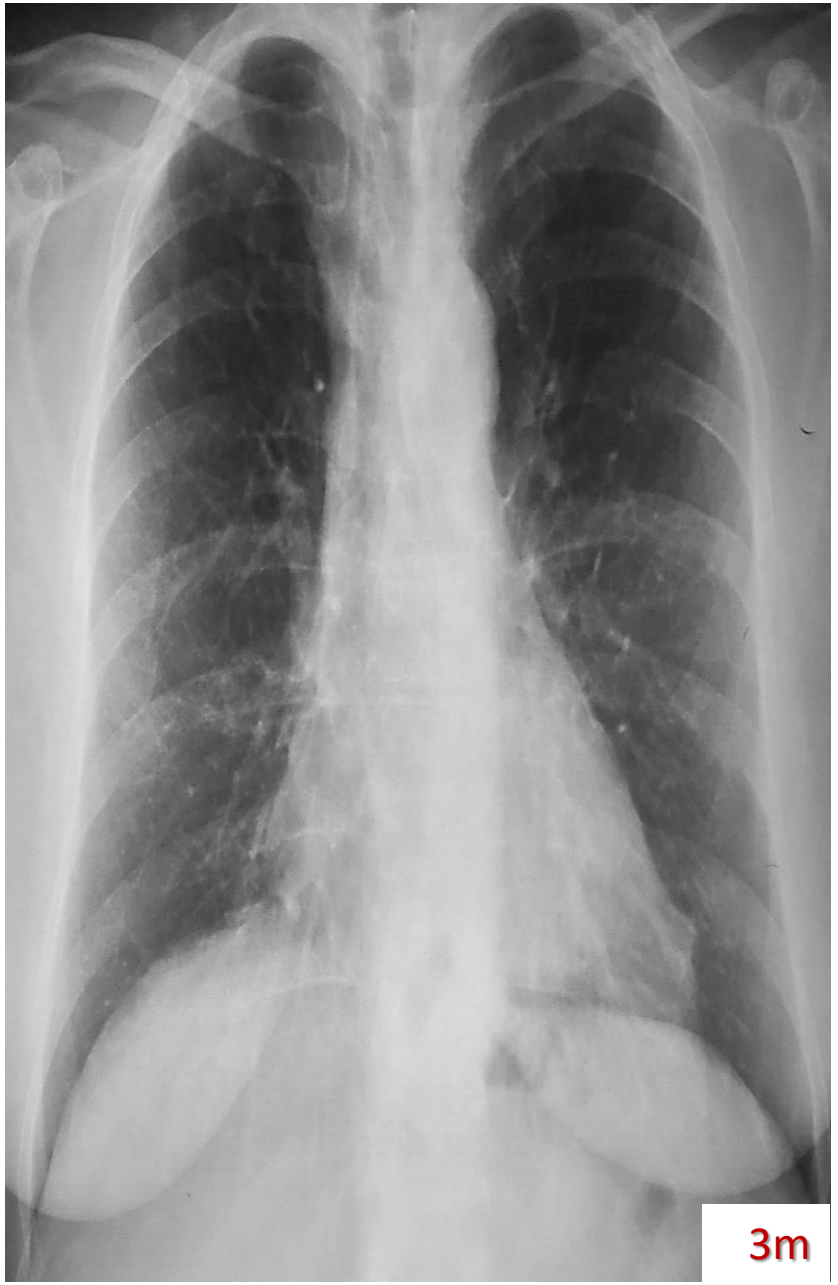
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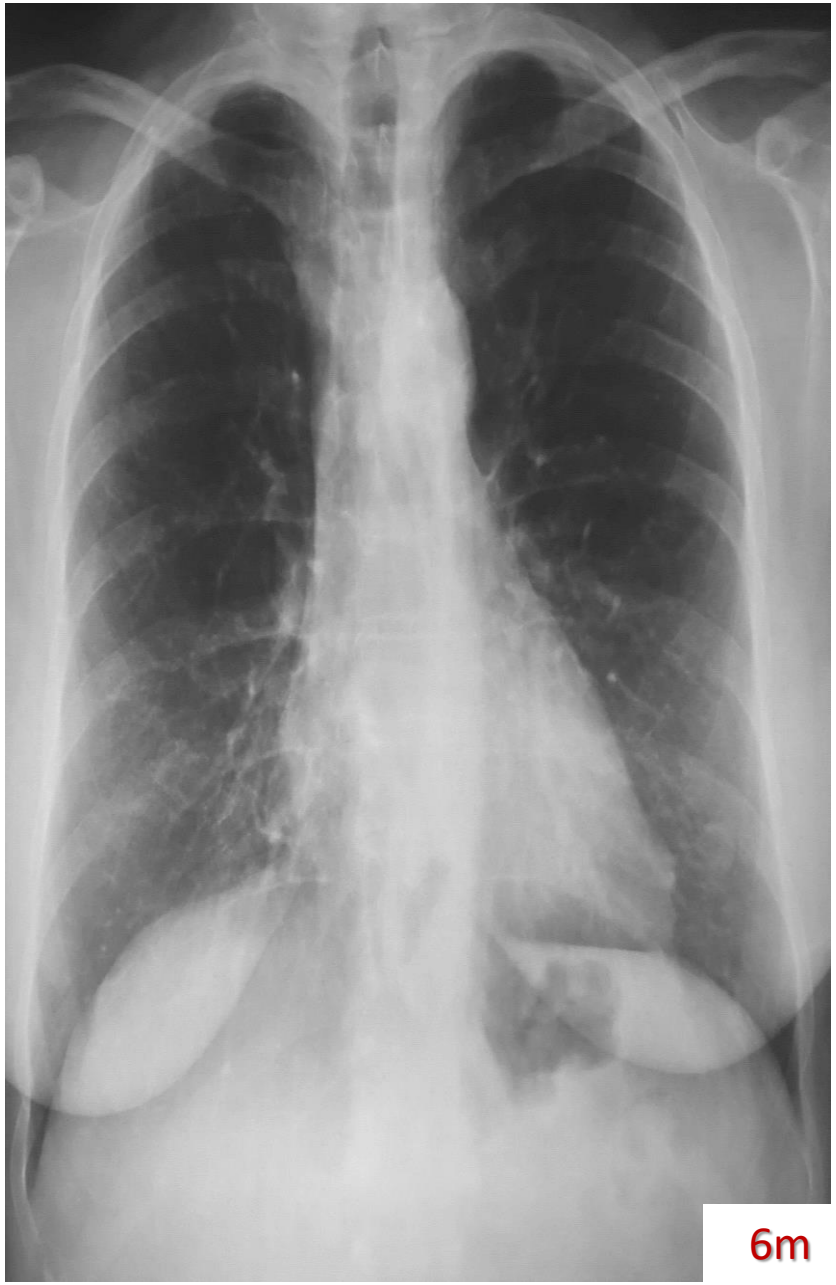
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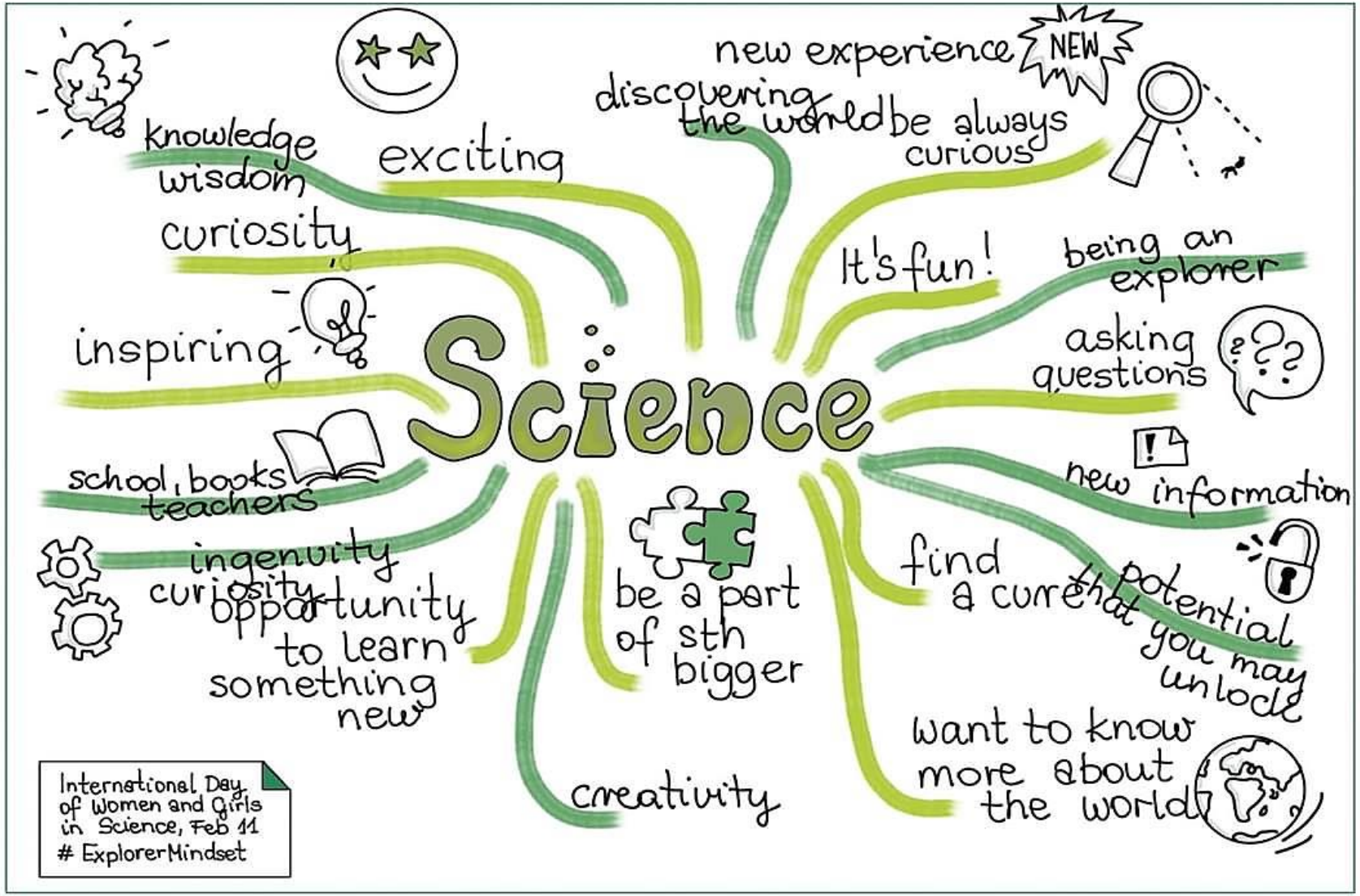
“Βλέποντας & κάνοντας” ⟶ “Βλέποντας & κάνοντας”



Σας ευχαριστώ