January 2018 Pulmonary Case of the Month

Lewis J. Wesselius, MD

Department of Pulmonary Medicine
Mayo Clinic Arizona
Scottsdale, AZ USA

History of Present Illness

A 67-year-old man from Idaho was seen in November 2017 for a second opinion. He has a history of slowly progressive dyspnea on exertion for 7 to 8 years. He has a significant smoking history of 50 pack-years, but is still smoking “a few cigarettes”.

He saw an outside pulmonologist in September 2017 and was noted to have abnormal pulmonary function testing with the primary abnormality being a low DLco. A thoracic CT Scan was reported to be abnormal with evidence of interstitial lung disease. He underwent video-assisted thorascopic surgery and the biopsies were reported to show usual interstitial pneumonitis (UIP). His pulmonologist questioned whether this was interstitial pulmonary fibrosis or UIP associated with rheumatoid arthritis.

PMH, SH and FH

He has a history of rheumatoid arthritis and had been treated with methotrexate for approximately 8 years. His methotrexate had been discontinued in September with no change in symptoms. FH is noncontributory.

Medications

Prednisone 5 mg/daily and tiotropium (these also did not change his dyspnea).

Physical Examination

- Chest: bibasilar crackles.
- Cardiovascular: regular rhythm without murmur.
- Ext: no clubbing, no edema, no joint deformity noted

Which of the following are **indicated at this time**?

1. Obtain a complete blood count and rheumatoid factor
2. Begin pirfenidone or nintedanib
3. Review his pulmonary function testing and radiographic studies
4. 1 and 3
5. All of the above

Correct!
4. 1 and 3

His referring pulmonologist was not sure of the diagnosis and so the diagnosis is not firmly established. Therefore, beginning pirfenidone or nintedanib is premature. His CBC showed a hemoglobin of 17.8 g/dL and his white blood cell count was WBC 10×10^9 cell/liter with a normal differential. Rheumatoid factor was elevated at 506 IU/mL (normal <15 IU/mL). Serum cyclic citrullinated peptide (CCP) antibodies were normal at < 15.6 U.

Pulmonary function testing is shown in Figure 1.

	PREDICTED		CONTROL		POST-DILATOR**	
	<u>Pred</u>	<u>LLN</u>	<u>Actual</u>	<u>% Pred</u>	<u>Actual</u>	<u>% Chng</u>
-- LUNG VOLUMES --						
TLC (Pleth) (L)	6.15	4.92	5.81	94		
SVC (L)	3.94	3.29	3.68	93		
RV (Pleth) (L)	2.26	1.81	2.13	94		
RV/TLC (Pleth) (%)	35	28	37	104		
-- SPIROMETRY --						
FVC (L)	3.94	3.29	3.70	93	3.92	+5
FEV1 (L)	2.91	2.43	2.55	87	2.77	+8
FEV1/FVC (%)	74	62	69	92	71	+2
FEF 25-75% (L/sec)	2.28	1.25	1.48	64	2.14	+44
FEF Max (L/sec)	7.82	5.87	6.74	86	6.44	-4
MVV (L/min)	122	102	*100	*81		
-- DIFFUSION --						
DLCOunc (ml/min/mmHg)	19.85	15.88	*10.93	*55		
DLCOcor (ml/min/mmHg)	19.85	15.88				

Figure 1. Pulmonary function testing.

Thoracic CT scan is show in figure 2.

Figure 2. Representative axial images from thoracic CT scan in lung windows.

Which of the following are **true**?

1. The history and physical and laboratory testing is compatible with advanced rheumatoid arthritis
2. The pulmonary function testing is compatible with advanced usual interstitial pneumonia (UIP)
3. The thoracic CT scan is **not** typical of usual interstitial pneumonitis (UIP)
4. 1 and 3
5. All of the above

Correct!

3. The thoracic CT scan is not typical of usual interstitial pneumonitis (UIP)

Although the course of rheumatoid arthritis is variable, the patient does not have changes associated with rheumatoid arthritis on physical examination. He does have a positive rheumatoid factor. Although 50% to 90% of patients with rheumatoid arthritis are rheumatoid factor-positive, the specificity of the test is known to be relatively poor (1). Rheumatoid factor is found in many patients with other autoimmune diseases, infectious diseases and some healthy individuals. Cyclic citrullinated peptide (CCP) antibodies have about a 78% sensitivity for rheumatoid arthritis and positive results have reported in approximately 40% of seronegative RA patients (1).

The pulmonary function testing shows mild obstruction, normal lung volumes but a moderate reduction in diffusing capacity. Advanced UIP would be expected to show restriction on spirometry, reduced lung volumes and reduced diffusing capacity.

The thoracic CT scan was interpreted to show moderate centrilobular and paraseptal emphysema with subpleural reticulation and fibrosis with some associated ground glass opacity. Honeycombing is the hallmark of UIP and refers to clustered cystic air spaces (usually between 3-10 mm in diameter) resembling a beehive honeycomb. UIP is often associated basal reticular changes (2).

What should be done next?

1. Begin pirfenidone or nintedanib
2. Restart his methotrexate
3. Review his lung biopsy
4. 1 and 3
5. All of the above

Correct!
3. Review his lung biopsy

His diagnosis is clinically unclear, and therefore, starting therapy is not indicated. Representative images from his lung biopsy are shown in Figure 3.

Figure 3. Representative images from lung biopsy. A: Low power, H & E staining showing accumulation of cells and fibrosis. B: higher power view showing fibrosis. C: higher power showing accumulation of cells. D: high power view showing accumulation of cells containing intracellular granules with a brownish pigment (smoker's macrophages).

The biopsy was interpreted as showing “predominately smoking-related changes in the form of desquamative interstitial pneumonia. There is a significant amount of fibrosis associated with it. Superimposed, are areas of organizing pneumonia”.

Which of the following are **true** regarding desquamative interstitial pneumonia (DIP)?

1. Smoking cessation often leads to improvement
2. May progress to form a non-specific interstitial pneumonitis (NSIP) pattern
3. Usually responds to corticosteroids
4. 1 and 3
5. All of the above

Correct!
5. All of the above

Desquamative interstitial pneumonia or pneumonitis (DIP) was first described by Liebow in 1965 (2). It is the rarest of the idiopathic interstitial lung diseases. A characteristic feature is pigment in intraalveolar macrophages. There is a strong association with cigarette smoking with initial reports of up to 90% of patients being current or former smokers. Recent studies suggest a somewhat smaller percentage are smokers of 60 to 87%.

In addition to cigarette smoking there are a number of other associations with DIP (Table 1) (2).

Table 1. Diseases association with DIP

- Cigarette smoking
- Connective tissue disease, rheumatoid arthritis
- Infection: CMV, aspergillus, hepatitis C
- Surfactant mutations (DIP in children)
- Myeloid neoplasia
- Occupational dusts: beryllium, copper
- Diesel fumes
- Heavy marijuana smoking

Some patients with diagnosis of DIP have subsequent CT changes that progress to fibrotic NSIP pattern (2). One report of a surgical lung biopsy showing DIP, but subsequent explanted lung showed NSIP. Prognosis seems better in DIP than NSIP, suggesting some differences.

Smoking cessation is critical and may lead to significant clinical improvement (2). Corticosteroid therapy is usually effective, but not all patients respond, particularly if there is continued smoking.

After discussing his diagnosis of DIP, our patient wanted to try smoking cessation but continue with his current low dose of prednisone. The plan will be for close follow up.

References

1. Mayo Clinic Laboratories. Cyclic Citrullinated Peptide Antibodies, IgG, Serum. Available at: <https://www.mayomedicallaboratories.com/testcatalog/Clinical+and+Interpretive/84182> (accessed 1/1/18).
2. Tazelaar HD, Wright JL, Churg A. Desquamative interstitial pneumonia. Histopathology. 2011 Mar;58(4):509-16. [\[CrossRef\]](#) [\[PubMed\]](#)