Anti-Synthetase Syndrome with an Unsuspecting Chest Radiograph

Jimmie Mar, Dimple Varughese

Department of Medicine, Arnot-Ogden Medical Center, Elmira, NY

Background

Anti-synthetase syndrome is a rare rheumatologic disease that is characterized inflammatory myositis with interstitial lung disease (ILD). Most common ILD include nonspecific interstitial pneumonia (56.3%), followed by usual interstitial pneumonia (17.5%) and cryptogenic organizing pneumonia (14.6%). (1) Patients often present with dyspnea, non-productive cough, fever, and arthritis which are non-specific and may be confused for infectious etiology. (2) Estimated prevalence is thought to be 1/25,000 - 1/33,000 worldwide and most commonly effects people around the age of 50. (3) This case presents a young female with an fairly unremarkable initial workup and an unremarkable chest radiograph who's physical exam raised concern for further work up. If there had been no suspicion for ILD, the patient may have not received the appropriate treatment of systemic steroids.

Case Presentation

Patient was a 24 year old Hispanic female who presented to the emergency department for shortness of breath. About 3 weeks prior, she returned from a trip from Mexico not feeling well. She had dyspnea with a non-productive cough. Unfortunately, her symptoms progressively worsened. About 2 weeks prior to coming to the emergency room, she started to develop fatigue and arthritis in the hands, feet, and jaw. She was given 3 days of azithromycin, and afterwards symptoms did not improve. Just prior to admission, she woke up in the night with dyspnea, chest pain, and nausea and went to the emergency room. Cardiac work-up was negative including a normal POC echocardiogram, but she was in respiratory distress and required 1.5L of oxygen. Chest x-ray demonstrated small pleural effusions with associated bibasilar atelectasis. She was admitted for sepsis secondary to pneumonia. Primary team considered rheumatoid arthritis with interstitial lung disease as a possible cause of symptoms, given her history with Raynaud's phenomenon. Otherwise, she had no other significant past medical history, past surgical history, family history, or social history. Rheumatoid factor returned positive and inflammatory markers were elevated. Since the patient did not exhibit muscular symptoms, the disconnect between the urinalysis and urine microscopy was not pursued. X-ray of hand did not demonstrate arthritic changes. Rheumatology was then consulted.

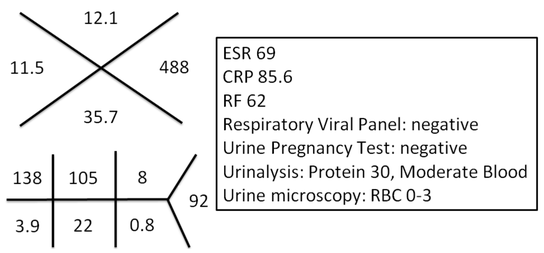

Figure 1. Initial Workup
Rheumatoid factor and inflammatory markers are elevated. Urine microscope demonstrated no RBC despite moderate blood on dipstick. AST was also moderately elevated at 63.

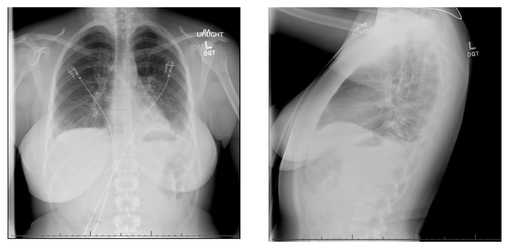

Figure 2. Chest radiography on admission
Initial chest radiography read by radiologist as small pleural effusions with associated bibasilar atelectasis

Rheumatology's examination of the hands were unimpressive. Joint spaces were palpated indicating no synovitis, a cardinal feature of rheumatoid arthritis. The lung exam was impressive with bibasilar dry crackles. At that time, the most likely diagnosis was viral respiratory infection with viral arthritis. Rheumatoid arthritis with ILD was still being entertained. Evaluation for ILD involved high-resolution CT demonstrated (HRCT) which is demonstrated below. Results suggested an organizing pneumonia and possible anti-synthetase syndrome given history. Reviewing the previous work-up, the urinalysis demonstrated moderate blood with no RBC's and mild elevation of AST. Creatine kinase was ordered that evening. While waiting for the creatine kinase that evening, the patient rapidly decompensated. She developed a fever and started to require 8L of oxygen. By that time, the creatine kinase returned at 17,121. She was given antibiotics and systemic steroids and her condition had improved. She was diagnosed with anti-synthetase syndrome with inflammatory myositis and the antibiotics was discontinued early. While on the systemic steroids, her creatine kinase improved and her oxygen requirements decreased. She was eventually discharged with a long course of steroids, 4L of oxygen, and follow up with Rheumatology. When the myositis panel returned. She was positive for anti-Jo1 and SSA which solidified her diagnosis of anti-synthetase syndrome.

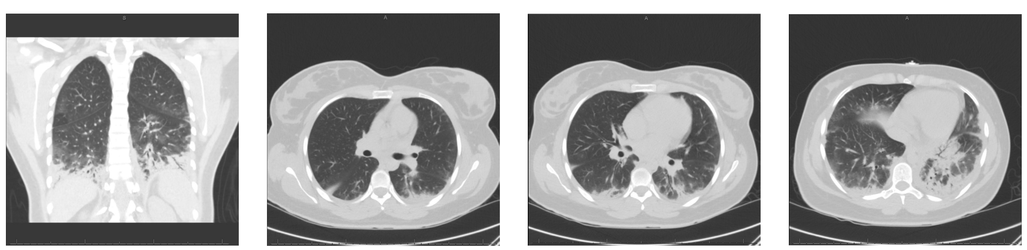

Figure 3. High Resolution Computed Tomography
HRCT read by radiologist as peripheral and basilar predominant ground glass opacities and consolidation. Favored diagnosis of organizing PNA. No definite fibrosis, but NSIP is also a possibility. Consider anti-synthetase syndrome

Discussion

Anti-synthetase syndrome is a rare disease where autoantibodies react to tRNA synthetase. There are 8 known anti-synthetase antibodies, the most common being Jo-1 which is anti-histidyl-tRNA synthetase. (1) Diagnosis of anti-synthetase syndrome requires the presence of an anti-amino acyl tRNA. Supporting evidence for anti-synthetase syndrome involves ILD and/or inflammatory myositis with arthritis, mechanic's hands, or Raynaud's phenomenon as seen in Figure 4. (4) Figure 5 outlines the anti-synthetase antibodies. (4)

Required Criteria
- Positive serology for anti-amino acyl-tRNA synthetase

Major Criteria
- Unexplained interstitial lung disease
- Polymyositis or dermatomyositis

Minor Criteria
- Arthritis
- Raynaud's phenomenon
- Mechanic's hands

Figure 4. Proposed Diagnostic Criteria for Anti-Synthetase Syndrome
In addition to the required criteria, two major or one major and two minor criteria are required for diagnosis of anti-synthetase syndrome

Name	Antigen
Jo-1	Histidyl - tRNA synthetase
PL-7	Threonyl - tRNA synthetase
PL-12	Alanyl - tRNA synthetase
EJ	Glycyl - tRNA synthetase
OJ	Isoleucyl - tRNA synthetase
KS	Asparaginyl - tRNA synthetase
Zo	Phenylalanyl - tRNA synthetase
SC	Lysyl - tRNA synthetase
JS	Glutaminyl - tRNA synthetase
YRS	Tyrosyl - tRNA synthetase

Figure 5. Known Anti-Synthetase Antibodies
Most common anti-synthetase antibody is Jo-1.

Our patient presented with fatigue, dyspnea, and arthritis are nonspecific symptoms with wide range differentials, most of which are more common and relatively benign when compared to anti-synthetase syndrome such as viral pneumonia with viral arthritis which also presents with swelling. With unsuspecting labs, normal white blood cell count, and a fairly unremarkable chest radiograph, the HRCT may have not been ordered, and her symptoms may have persisted and worsened without systemic steroids. Due to the physical exam and suspicion for rheumatoid arthritis and ILD, the HRCT scan rather than a conventional CT was obtained.

Chest radiography is an invaluable tool for evaluating patients with dyspnea, yet it is not without limitations. About 10% to 15% of patients with known ILD will present with normal chest radiography as opposed to HRCT that has a sensitivity of 95% and specificity of 100%. (5) HRCT has become an invaluable tool in evaluation and diagnosis of ILD. (6) Organizing pneumonia is treated with a lengthy course of steroids which demonstrate resolution in 70 to 80% of patients. (7)

Although anti-synthetase syndrome often includes inflammatory myositis, the presenting symptom does not always include muscle weakness as in our patient. Symptoms of ILD may precede, follow, or occur at the same time as the symptoms of inflammatory myositis. (1) In one report, about 18% of patients did not have muscle symptoms at time of ILD diagnosing. (8) As in our patient, she did not develop proximal muscle weakness often seen in inflammatory myositis, but the presence of fatigue may have masked the presence of weakness.

Conclusion

In conclusion, we presented a case of a young Hispanic woman who presented with an indolent course of fatigue, dyspnea, and arthritis. Initial work up was benign with a unremarkable chest radiograph. Abnormal physical exam with suspicion for ILD associated with rheumatoid arthritis lead to the pursuit of HRCT which changed the clinical course to investigate anti-synthetase syndrome. Rheumatologic diseases can often affect multiple organ systems and without suspicion for specific diseases. The underlying cause may be missed as in this case where the HRCT changed the course of work up.

References

1. Connors, G. R., Christopher-Stine, L., Oddis, C. V., & Danoff, S. K. (2010). Interstitial Lung Disease Associated With the Idiopathic Inflammatory Myopathies. *Chest*, *138*(6), 1464–1474. doi: 10.1378/chest.10-0180
2. Antisynthetase Syndrome. (n.d.). Retrieved from https://www.myositis.org/about-myositis/complications/antisynthetase-syndrome/
3. Inserm. (n.d.). Orphanet: Antisynthetase syndrome. Retrieved from https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=81
4. Witt, L. J., Curran, J. J., & Strek, M. E. (2016). The Diagnosis and Treatment of Antisynthetase Syndrome. *Clinical Pulmonary Medicine*, *23*(5), 218–226. doi: 10.1097/cpm.0000000000000171
5. Stark, P. (2019, August 23). High Resolution Computed Tomography of the Lungs. Retrieved March 15, 2020, from https://www.uptodate.com/contents/high-resolution-computed-tomography-of-the-lungs
6. Ryu, J. H., Daniels, C. E., Hartman, T. E., & Yi, E. S. (2007). Diagnosis of Interstitial Lung Diseases. *Mayo Clinic Proceedings*, *82*(8), 976–986. doi: 10.4065/82.8.976
7. Schlesinger, C., & Koss, M. N. (2005). The organizing pneumonias: an update and review. *Current Opinion in Pulmonary Medicine*, *11*(5), 422–430. doi: 10.1097/01.mcp.0000175521.41729.07
8. Fathi M, Dastmalchi M, Rasmussen E, Lundberg IE, Tornling G. Interstitial lung disease, a common manifestation of newly diagnosed polymyositis and dermatomyositis.*Ann Rheum Dis*. 2004;63(3):297-301

For additional information please contact:
Jimmie Mar at jmar@arnothealth.org
Dimple Varughese at dvarughese@arnothealth.org