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Keys to Overcoming Diagnostic Delays in NTM Lung Disease

Announcer:
You're listening to Deep Breaths: Updates from CHEST on ReachMD. This series is produced in partnership with the American College of CHEST Physicians, and is sponsored by Insmed Incorporated.
Here's your host, Dr. Tim Aksamit.

Dr. Aksamit:
The prevalence of non-tuberculous mycobacterial, or NTM, lung disease in the United States has almost doubled from 6.8 to 11.7 per 100,000 persons from 2008 to 2015. Since the symptoms of NTM lung disease are nonspecific and similar to other lung disease like COPD, bronchitis and bronchiectasis, the diagnosis is often delayed. So, how can we keep NTM lung disease at the forefront of our minds when evaluating patients?

Welcome to *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Tim Aksamit, and joining me are pulmonary nurse practitioner Amy Levinger from NYU Langone Health and Dr. David Griffith, Professor of Medicine at National Jewish Health in Denver, Colorado.

Miss Levinger, Dr. Griffith, welcome to you both.

Amy Levinger:
Thank you so much for having me here today.

Dr. Griffith:
Thank you, Tim.

Dr. Aksamit:
Let's start with you, Dr. Griffith. Since MAC infections are the most common of the NTM lung infections, what are the clinical, microbiologic, and radiographic criteria needed to establish the diagnosis of MAC lung disease?

Dr. Griffith:
There are 3 criteria required for establishing a diagnosis of MAC lung disease. The first, of course, is symptoms. The patient should have compatible symptoms for MAC lung disease. The microbiologic criterion involves evaluation of respiratory specimens, usually sputum. We prefer spontaneous sputum. If that's not available, then sputum induction is the next choice. For a small percentage of patients, bronchoscopy might be necessary to obtain respiratory specimens for acid-fast bacilli or AFB smear and culture. But the diagnosis cannot be made without meeting the microbiologic criterion. I would say also that the ATS criteria require only 1 positive bronchoscopic specimen, and I think that's a weak part of the diagnostic criteria. I certainly would try very hard to get either spontaneous or induced sputum from patients. Radiographically, patients also need to meet criteria for changes compatible with MAC lung disease. That can occur with chest radiographs but frequently requires chest CT scanning. When the cultures are returned, usually they are accompanied by in vitro drug susceptibility testing results, and I want to emphasize that there are only 2 antibiotics for which those drugs susceptibility test results are meaningful, and that is for macrolide and amikacin. That's a point that gets made over and over again, but unfortunately somehow it doesn't seem to sink in. Frequently, on first or second encounter it's not clear whether someone has established disease or whether that disease is going to be progressive, so I would emphasize that longitudinal follow-up is absolutely essential for these patients. That is not the case for patients with cavitary disease where once the microbiologic criterion is met then treatment needs to be started.

Dr. Aksamit:

Thanks for those thoughts, Dr. Griffith, and can you share what has been the most difficult of these criteria to establish an NTM diagnosis?

Dr. Griffith:
Really, it's the longitudinal follow-up. We frequently meet patients who meet all the criteria but have relatively mild symptoms. They invariably have bronchiectasis. When they begin bronchiectasis therapy, they have symptomatic improvement, and we follow those patients and do not see evidence of radiographic progression. So, I would say that there is patience and persistence that are necessary frequently for establishing a diagnosis in our nodular bronchiectatic patients.

Dr. Aksamit:
And turning to you, Miss Levinger, who should be evaluated for MAC lung disease?

Amy Levinger:
We do know that there are certain underlying conditions that make people more susceptible to MAC lung disease. These include having prior lung infections as well as bronchiectasis, COPD, and genetic diseases such as cystic fibrosis, alpha-1 antitrypsin deficiency, and primary ciliary dyskinesia. In order to evaluate for the MAC lung disease, having that chest CT scan is an important diagnostic tool as it will provide a detailed look at the extent and location of diseases. It is important to differentiate if there are nodular findings on the scan versus the fibrocavitary findings on the exam, and I know that Dave touched on this, but it is important to not delay initiation of therapy for patients with fibrocavitary MAC lung disease.

Dr. Aksamit:
And, Miss Levinger, can you comment on your experience of patient responses when you are able to establish a diagnosis of MAC lung disease, sometimes after a very prolonged delay?

Amy Levinger:
Usually when it's after a very prolonged delay, our patients are relieved that they finally have answers and they are encouraged when we do tell them information about MAC and ways that we can treat them and that this is treatable, and we hope that they can live a quality of life.

Dr. Aksamit:
Excellent. And, Dr. Griffith, could you elaborate further on the evaluation of patients who are immunocompetent, that is non-HIV, versus immunocompromised patients with NTM lung disease?

Dr. Griffith:
Well, in terms of presentation and therapy, there is actually remarkably little difference in the management of patients. As Amy previously pointed out, what is important is identifying those patients who have underlying conditions, which do alter the immune system and put patients at risk for MAC lung disease. But, in terms of diagnosis and radiographic presentation and therapy, generally, there's not a lot of difference. I think it's also, again, in communicating with patients, it is very important to point out that most of our patients who have nodular bronchiectatic and even cavitary MAC lung disease, do not have significant or systemic immunocompromise. I think there is a conventional wisdom out there, which comes from the role of MAC and HIV infection, that patients must be immunocompromised if they are infected with MAC, whereas fortunately that's not the case for the vast majority of these patients.

Dr. Aksamit:
I'd like to tackle yet another confusing aspect of MAC lung disease, knowing who we should evaluate, Dr. Griffith. Can you share with us or help us understand and differentiate between MAC lung disease, refractory MAC lung disease and macrolide or amikacin drug-resistant MAC lung disease?

Dr. Griffith:
It's an extraordinarily important question. Once patients are begun on therapy, we hope that they have conversion of their sputum to AFB culture negative within 6 months. Somewhat arbitrarily, if a patient does not have sputum conversion in that time, we refer to them as refractory MAC lung disease. The most important reason that might occur would be the emergence of macrolide resistance for a patient who is receiving standard macrolide-based therapy. Most patients are not initially started on amikacin therapy, so if someone is not on amikacin but is on macrolide-based therapy, their cultures are still positive at 6 months, the initial evaluation must include repeat macrolide in vitro susceptibility testing. Certainly, if the patient has received amikacin either parenterally or by inhalation, it would be absolutely equally important to evaluate in vitro amikacin susceptibility at that point. Let me, again, say that other in vitro susceptibilities are not helpful, even at this juncture. If someone has macrolide-resistant MAC lung disease, then they go to a completely different part of the decision tree than if they are refractory but remain macrolide susceptible.

Dr. Aksamit:

For those just tuning in, you are listening to Deep Breaths: Updates from CHEST on ReachMD. I'm Dr. Tim Aksamit, and today I am speaking with Nurse Practitioner Amy Levinger and Dr. David Griffith about diagnosing patients with non-tuberculous mycobacterial lung disease.

Dr. Griffith, now that we have a better idea as to why it can be difficult to diagnose MAC lung disease and the various types of MAC lung diseases, can you walk us through what diagnostic tools are available that can help us make a timely diagnosis?

Dr. Griffith:
Well, the critical diagnostic tool is the clinician's suspicion about the diagnosis and then his or her awareness that a patient is not responding appropriately to guidelines-based therapy. As everyone knows, MAC lung disease is a frustrating process where even in the most experienced hands response to initial therapy is, at best, in the 80 to 85% range. So, we know, just starting out, that at least 15 to 20% of our patients are going to fall into that category of refractory MAC lung disease. So, I would only stress that once these patients are diagnosed, once they are put on therapy, it is as important as the decision-making process during the evaluation of initial therapy to do careful follow-up of patients with frequent monitoring of sputum, appropriate monitoring of radiographs, to determine if they are responding appropriately to therapy. Really, that close clinical follow-up is absolutely essential.

Dr. Aksamit:
Excellent, and once a patient is diagnosed then with NTM lung disease, Miss Levinger, what comorbidities should we be on the lookout for?

Amy Levinger:
It is important to recognize and address the underlying comorbidities for patients with NTM lung disease. The most common comorbidity of NTM lung disease is bronchiectasis. Bronchiectasis may go undiagnosed for many months or even years in some of these patients, and this could be often associated with repeated episodes of lung infections which then could ultimately lead to a loss of lung function over time. This is also why some patients, like we mentioned earlier, do have relief when they do get to a clinician who is able to identify bronchiectasis as well as the NTM lung disease. Going further along with that, when a patient is diagnosed with NTM lung disease, it is important to complete a full workup as there can be many multiple conditions and comorbidities making their symptoms or contributing to some of the radiologic findings on the chest CT scans. For example, patients should undergo a full GI workup to evaluate if they may have any GERD, esophageal disease, or silent aspiration. Some tests that the GI doctor may perform include an esophagram, a motility study and impedance, or BRAVO testing. In addition, patients may undergo a swallow study evaluation that could be beneficial, and then if there is anything abnormal, patients could then undergo swallow therapy. Further, patients may benefit from an ENT evaluation for possible chronic sinus disease that could be contributing and/or worsening to their symptoms and radiologic findings.

Dr. Aksamit:
These are some great thoughts on how we can provide the very best care for our patients and really make sure that we are doing what patients need and what patients are asking us for. Before we wrap up, I'd like to open up the floor to you both to see if you have any final takeaways on NTM lung disease. Dr. Griffith, let's start with you.

Dr. Griffith:
Tim, I think there are several aspects of MAC lung disease that Amy and I have discussed that deserve emphasis. The first is the importance of identifying and managing bronchiectasis. I think bronchiectasis is as mysterious for patients as MAC lung disease, and there is a lack of understanding in the medical community about bronchiectasis just in general. So, as Amy pointed out, patients are relieved when they are told about MAC lung disease. I think they are equally relieved when they learn about bronchiectasis and ways to manage it. I also think it's very important to emphasize following guidelines for therapy. Certainly, they are imperfect and treatment success rates, even in the best of hands are only 80–85%, but nevertheless following those guidelines helps avoid the emergence of macrolide resistance, which is probably the worst possible outcome for patients on therapy. As we discussed, it is important to follow patients closely so that you can identify those who meet criteria for refractory MAC lung disease. Once a patient is labeled as refractory MAC lung disease, there are other treatment options and another treatment algorithm that can be followed.

Dr. Aksamit:
Excellent. And, Miss Levinger, any other takeaways you'd like to share?

Amy Levinger:
I would just like to add that when these patients do come in for initial diagnosis and evaluation, I think we've made it clear that there are some patients that have gone undiagnosed for months to even years. So, I think Dr. Griffith noted it too, that education here is key, not only to the diagnosis and the evaluation but education on how they can better themselves, education on what treatment and the guidelines would look like once everything is diagnosed, and providing them with hope.

Dr. Aksamit:
Well, that unfortunately brings us to the end of today's program. But, for more resources on NTM lung disease as well as a checklist for evaluating patients, please go to the CHEST Foundation website. I'd like to thank Dr. David Griffith and Nurse Practitioner, Amy Levinger, for joining me to talk about non-tuberculous mycobacterial lung disease. Miss Levinger, Dr. Griffith, it was great having you both on the program.

Amy Levinger:
Thank you.

Dr. Griffith:
Thanks Tim.

Announcer:
This episode of *Deep Breaths: Updates from CHEST* was produced in partnership with the American College of Chest Physicians and sponsored by Insmed Incorporated. For more resources on this topic, visit CHESTFoundation.org/NTM. And to access other episodes of this series, visit reachmd.com/CHEST, where you can be part of the knowledge. Thanks for listening!