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Early Recognition and Diagnostic Confidence in NTM Lung Disease

Announcer:
You're listening to *Clinician's Roundtable* on ReachMD, and this episode is supported by an independent grant from Insmed. Insmed had no editorial control over this program, and all views expressed belong to the speakers. And now, here's your host, Dr. Brian McDonough.

Dr. McDonough:
This is *Clinician's Roundtable* on ReachMD, and I'm Dr. Brian McDonough. Here with me to explore how we can improve the early recognition and diagnosis of nontuberculous mycobacterial, or NTM, lung disease is Dr. Doreen Addrizzo-Harris. She's the Fiona and Stanley Druckenmiller Professor of Pulmonary, Critical Care, and Sleep Medicine at NYU Grossman School of Medicine, as well as the Director of the Bronchiectasis and NTM Program at NYU Langone Health. Dr. Addrizzo-Harris, thanks so much for being here.

Dr. Addrizzo-Harris:
Thank you, Brian, for inviting me.

Dr. McDonough:
To start us off, Dr. Addrizzo-Harris, NTM lung disease is often described as a condition that hides in plain sight. From your perspective, what continues to drive delayed or misdiagnoses in clinical practice?

Dr. Addrizzo-Harris:
Many patients who have NTM lung disease have it for many years before it is diagnosed. It can hide as some of the more common diseases that patients with pulmonary disease get diagnosed with, like asthma and chronic bronchitis, and often patients will be treated with antibiotics that may actually initially improve their symptoms but not get rid of the NTM lung disease. So without doing sputum samples to specifically look for NTM lung disease, it unfortunately will go undiagnosed, and many patients who do get sick nowadays with an episode of acute bronchitis will just call their physician, a prescription will be sent to the pharmacy, and no sputum samples or even imaging, whether it's chest X-rays or CAT scans, will be done. So I tell our patients if they're having recurrent episodes of pulmonary infections, they should definitely ask their physicians to please send sputum before starting antibiotics.

Dr. McDonough:
Given that symptoms can overlap with other pulmonary conditions, are there any specific patient populations or clinical scenarios that immediately raise suspicion for possible NTM lung disease?

Dr. Addrizzo-Harris:
We know that patients who have underlying bronchiectasis or other structural abnormalities of the lung, such as COPD, can get super infected with nontuberculous mycobacterial organisms, and then that can go on to producing active lung disease. There are other etiologies that cause bronchiectasis and increased risk for NTM lung disease, and those would include immunoglobulin deficiencies, alpha-1 antitrypsin deficiencies, ciliary dyskinesia syndromes—primary ciliary dyskinesia has an increased incidence. We also know that patients who have recurrent aspiration also can be at increased risk.

There is a subgroup of patients that you would want to pay attention to, and these would be postmenopausal females who have thoracic abnormalities—often scoliosis, kyphosis, or pectus—and they also have mitral valve prolapse, often with asymptomatic reflux. In these patients, there's an increased incidence of NTM lung disease. When you look at their chest CAT scans, you'll often find predominant bronchiectasis in the right middle lobe and lingula.

Dr. McDonough:
And when it comes to imaging, can you tell us about the radiographic patterns that stand out as diagnostic clues?

Dr. Addrizzo-Harris:
The most common thing we're looking for is a chest CT scan that shows areas of bronchiectasis and dilated airways. This can be throughout the lungs. It can be in one lobe. So there are certain classes of patients that we'll see. We'll see the post-infectious bronchiectatic patient who may have NTM lung disease, and this may be a patient who had bad TB at one point in their life or a bad pneumonia that left them with bronchiectasis, and then NTM likes to colonize that area and can sometimes become active in that area. So that would be a localized form of NTM lung disease that we would see on a CT.

A more diffuse form would be bronchiectasis in multiple lobes or what we call bronchiolitis. Bronchiolitis is where we just have thickened airways. They may not yet be dilated, and within those airways, there's a lot of inflammation seen on chest X-ray, often described as tree-in-bud, meaning that the branches of the airways are the trees, and you see little buds, which are mucus cut on sagittal sections that look like little buds on the airway. And so that is an early form, probably, of pre-bronchiectasis.

So if a patient has bronchiolitis, nodular disease, that would be one class of NTM lung disease radiographically. The other would be cavitary disease. Usually with cavitary disease, we will also see a combination of nodular disease, but when we think about treatments, once we make a diagnosis of NTM cavitary disease, the treatments will be different. So that's why it's important to make that distinction.

And the last class I would say we would see is a COPD patient who may have multiple bullae and areas of hyperinflation. Those areas can get colonized, and then active NTM infection can occur in those areas, and that may be a COPD patient where you're wondering, why all of a sudden are they having a more rapid decline of their COPD? Their PFTs might be more rapidly declining. Again, think about co-infections with nontuberculous mycobacterial disease in that group of patients.

Dr. McDonough:
For those just tuning in, this is *Clinician's Roundtable* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Doreen Addrizzo-Harris about recognizing and diagnosing NTM lung disease.

So, Dr. Addrizzo-Harris, when it comes to confirming our diagnosis, we know that one key challenge is distinguishing true disease from colonization. Currently, the ATS and IDSA guidelines recommend integrating compatible symptoms, characteristic imaging findings, and microbiologic confirmation. How can those recommendations help clinicians more confidently diagnose patients with NTM lung disease?

Dr. Addrizzo-Harris:
First, you'll have to be thinking about NTM lung disease. Once you start to send cultures for someone who you think may have it, we know that regular bacterial cultures will not pick up NTM lung disease. You must be sending AFB cultures for these patients. You may see smears that are positive. You may see negative smears. That will help you tell what the bacterial load is of your mycobacterium, and then you'll wait for the culture to be identified.

There are more than 200 species of NTM lung disease. The most common one in the United States is *Mycobacterium avium* complex, and the second most common is *Mycobacterium abscessus*, both treated slightly differently based on the antibiotic profile. But whatever mycobacterial disease you see on culture, you need to then correlate it both with the CAT scan, as we discussed—there must be findings of either nodular disease or cavitary disease, right? It's very rare that a patient will have mycobacterial lung disease when they have a normal chest CT scan.

So you need to have abnormalities on the CT, abnormalities in the culture, and then you have to have clinical abnormalities. So a patient is most commonly going to be complaining of cough, sputum, recurrent infections, and pulmonary infections. Sometimes they may have night sweats or low-grade fevers, weight loss, and fatigue.

There are a number of constitutional symptoms. But in order to make a true diagnosis, you need to have all three, and you need to have more than one culture that is positive. Based on the IDSA and ATS guidelines, you must have at least two cultures positive with the same organism or a bronchoscopy culture that is positive. Because we know these mycobacteria live in water, and so there can easily be contamination from the lab. Patients can inhale a large burden if they're gardening. They may have it there temporarily in their sputum, but then by the time a few days go by, they'll be negative again on their next sputum. So we like to get sequential cultures to be sure that we have reproducible culture positivity.

Dr. McDonough:
Obtaining reliable samples isn't always straightforward. What practical barriers do you face during sputum collection? And when do you start thinking about introducing bronchoscopy?

Dr. Addrizzo-Harris:
So in most cases, bronchoscopy is not needed. Of course, not all of the patients are going to be symptomatic with cough and sputum. I'd say in my clinical practice, probably about two-thirds of the patients do have symptoms and do have sputum that they can spontaneously produce. So you'll ask them to give you a sputum and send it to the lab.

But there are patients where induced sputum is needed. So we give patients a little bit of hypertonic saline, and then we'll have them cough, or we'll do some chest physical therapy on them to assist them in bringing up sputum. Sometimes they can do this maneuver at home. Most patients who have underlying bronchiectasis are on an airway clearance daily regimen with hypertonic saline. So in the morning, they're often most productive. They can capture a sputum at home. They can keep it at home for a day or two until they come in. Sending it for acid-fast bacilli will still be effective even two days later. And so in most of the patients, if we try induction, we are successful.

There still will be a percentage of patients who, even with induction, cannot bring up sputum. You'll have a CAT scan that's significant, meaning there's a lot of bronchiolitis. As I said, the post-menopausal female will see classic bronchiectasis and bronchiolitis in the right middle lobe and lingula. You'll be pretty convinced that that's what the patient has, but you still need that sputum to be able to get the culture, make the diagnosis, and then treat them appropriately. So in that case, bronchoscopy would be the next step.

Dr. McDonough:
As we bring all of this together, Dr. Addrizzo-Harris, what practical steps can clinicians take to reduce missed or delayed diagnoses, particularly in high-risk patients?

Dr. Addrizzo-Harris:
So Brian, I say this for any disease that we want to capture early, and that is having a good communication strategy with your patient. We're all busy clinicians, but patients get sick every day, and we want to capture them early in the illness before they decide to go to urgent care or reach out to their primary care physician. If you're a pulmonologist treating one of these patients, you want to hear about their exacerbation or their persistent cough early so that you can actually get sputum cultures performed before you start antibiotics. It's very important not to use macrolide monotherapy in patients who you think have underlying NTM lung disease, because doing that on repeated occasions can cause macrolide resistance in the NTM, and then it becomes extremely hard to treat. So patients will often get azithromycin treatment at urgent care centers, and that is not something we want to be using in this cohort of patients. So I really like to have them drop off a sputum and see them early.

Often, they will need antibiotic therapy. Sometimes these patients have bacterial superinfections. They may need to be treated for that. Many of them have multiple organisms in their sputum. It's hard to determine which one to treat first. We try and tell our physicians, "Treat what's easiest to treat first." So if there's a staph or a *Pseudomonas*, treat that first. If the patient is still symptomatic, still coughing after that, and CT is still progressing, then you are pretty confident that it's from the underlying NTM lung disease, and you'll want to start treatment for that.

The hardest question in patients who have underlying NTM lung disease and have the clinical, radiographic, and sputum abnormalities —you know they have it—is when to treat and when not to treat. So you really want to make sure that the symptoms that they're having are related to the underlying NTM that's in their sputum. And when you do determine that that is the cause, early treatment is recommended by the guidelines. And then there are multiple different treatment regimens that are recommended based on the findings of your specific patient.

Dr. McDonough:
With those considerations in mind, I want to thank my guest, Dr. Doreen Addrizzo-Harris, for joining me to discuss our approach to recognizing and confirming nontuberculous mycobacterial lung disease in clinical practice. Dr. Addrizzo-Harris, it was great having you on the program.

Dr. Addrizzo-Harris:
Thank you so much for inviting me.

Announcer:
This episode of *Clinician's Roundtable* was supported by an independent grant from Insmed. Insmed had no editorial control over this program, and all views expressed belong to the speakers. To access this and other episodes in our series, visit *Clinician's Roundtable* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!