Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/mac-lung-disease-considerations-in-initiating-treatment/18031/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

MAC Lung Disease: Considerations in Initiating Treatment

ReachMD Announcer:
This medical industry feature, titled "MAC Lung Disease: Considerations in Initiating Treatment", is sponsored by Insmed Incorporated. Introducing your guests, Drs Nicole Lapinel and Wael ElMaraachli.

Dr. Lapinel:
Welcome. My name is Dr. Nicole Lapinel, and I'm Codirector of the Adult Cystic Fibrosis Program and Clinical Assistant Professor of Medicine with Northwell Health in New York.

Dr. ElMaraachli:
And I'm Dr. Wael ElMaraachli, Associate Clinical Professor and Director of the NTM Bronchiectasis Program at the University of California, San Diego.

Dr. Lapinel:
And together we'll be discussing the progressive nature of untreated *Mycobacterium avium* complex, or MAC lung disease, as well as treatment options and management strategies.

Now for a little bit of background on *Mycobacterium avium* complex or MAC lung disease. So we know that NTM, MAC specifically, is an environmental pathogen. Any one of us can be exposed to it at any point in time as it's ubiquitous within the environment. Within the soil, within our water resources, certainly within our drinking water.

But there's really specific people that end up developing this infection. We know through the literature that there's risk factors that can set somebody up for developing this infection. And it could be immunosuppression.

Also though, COPD patients who have a significant smoking history are certainly at increased risk of developing MAC lung disease. Certainly patients that have underlying bronchiectasis from a variety of other factors, particularly infection in the past, or maybe they have underlying cystic fibrosis. But there are underlying comorbidities that will increase the likelihood of developing this lung infection.

When these patients present, they'll often come with a variety of symptoms, but we know, in particular, that there are certain symptoms that we see above others. So nonproductive cough, or even productive cough, is one of the more common symptoms. I've had patients that present with overwhelming fatigue and, in a subset of patients, that might actually be their only symptom that they experience. Certainly weight loss can also be associated with it as well. So those are some of the more common symptoms that we can see.

There are factors that we look at for determining whether or not a patient is a candidate for starting therapy. What therapy is can be defined in separate ways. So I know many of us start our patients on Airway Clearance Therapies or ACT's as we can call them for short. And I certainly believe that that is a very important aspect of treatment for patients. And I will often start my patients on airway clearance before we even get to the point of deciding whether or not antibiotics might be in order.

Up until the most recent 2020 guidelines, the belief was that perhaps this is a disease that we can just sit and we can watch.

The thought was that perhaps the treatment with antibiotics per se is worse than the underlying diseases. But I think over time as the evidence has accumulated we know that this is a disease that's not completely benign, and there certainly can be significant progression of disease both in radiographic forms but also in terms of symptoms that patients are experiencing.

Wael, what do the data on progression show if MAC is not treated with guideline-based multidrug therapy?

Dr. ElMaraachli:
There has accumulated quite a bit of data that shows that there's worsening of the disease if untreated or treated suboptimally with time. And there's even specifics. For example, Gochi et al publication 2015 showed over a median follow up of 5 years that there was radiographic deterioration in 41% of 536 patients who were untreated or treated with only 1 antibiotic, which, as we'll see when we talk about the treatment, is insufficient.

And in another trial, this is a prospective cohort study, Park et al in 2016 observed a decline in FEV1 and FVC of more than 40 milliliters per year in patients who have MAC lung infection who failed to achieve sputum culture conversion, meaning they were persistently culture positive. And importantly, lung damage can continue to happen without a concomitant significant increase in symptoms. That's why when we're watching these patients, especially in someone who showed up really mild and you didn't start treatment immediately, it's very important to follow these patients closely. Both clinically, radiologically in addition to microbiologically.

Dr. Lapinel:
These are very important points. We can't impress enough upon people that it's important really to follow these patients closely. And more often than not in the appropriate patients that we should be starting them on treatment with antibiotics.

Apart from those realms that we've already spoken about, we know that there's also an effect on morbidity and mortality. There was a systematic review by Diel et al, that found that the 5-year all-cause of mortality ranged from 10 to 48% for patients with MAC lung disease. From a hospitalization standpoint in the realm of healthcare utilization, rates were significantly higher with this disease and certainly can put a burden on the healthcare system at large. There was a study also by Prevots back in 2021 that demonstrated that patients with NTM lung disease, the all-cause hospitalization was nearly 2 times higher compared to individuals without NTM lung disease.

Wael, I'm curious, what has been your experience with patients that have been untreated for their MAC lung disease?

Dr. ElMaraachli:
I have a patient that I recently saw in clinic. This patient was diagnosed with MAC lung infection a few years before she presented to my clinic for the first time, and her symptoms were mild and her radiographic disease was mild. And so the clinician that saw her at the time told her that she didn't need treatment. She didn't follow up for a few years, and then a CT scan taken a few years later showed that she had developed a right upper lobe cavity. Not only was the lung damage more extensive, but the treatment now becomes much more challenging for her.

Which brings me to the latest guidelines that were published in 2020 and recommend the consideration of antibiotic treatment for all patients with MAC lung infection. The treatment recommendation is a macrolide. Azithromycin is the one that's most commonly used because it's once-daily dosing, so azithromycin, rifampin, and ethambutol, and you continue this treatment for 12 months past the point of culture conversion. Importantly, you can consider using thrice weekly rather than daily therapy in patients with nonsevere noncavitary disease, in which case there's a much higher tolerability and it's much easier for the patients to take.

And after we start these patients on treatment, it's very important to follow these patients closely, especially to check if they're having any adverse drug reactions. So, I'm interested to know, Nicole, how you approach this after you initiate treatment on your patients.

Dr. Lapinel:
You want your patients obviously to know that you are in their corner, they have your support, they have your staff support for any issues that may come up. So, for those patients that I do decide to start an antibiotic therapy typically I will have them come back at least 1 month for follow up. We like to repeat labs at that point in time just to make sure that everything has remained stable.

That said, it's also an important point at which we can go over clinically any side effects they might be experiencing. However, I always encourage the patients to contact us and let us know if there are any ill effects that they might be experiencing so that we can kind of counsel them through different management, different manners in which they can take the antibiotics that might make tolerance a little bit better for them.

However, if it is something serious that's going on, we also want to be apprised of that as soon as possible so we can intervene appropriately. Typically after that first month visit, then depending on what's going on, if everything is stable, I should say first, then I will typically have the patients come in every 2 to 3 months. I think sometimes, again, it needs to be individualized. Some patients really do want to be followed a little bit more closely. They might be a little bit more nervous about embarking on this, what can seem like a complicated regimen for them. But typically I would say it's every 2 to 3 months. But what's important during that time, as well, is to make sure that we are not only monitoring for symptoms at each of those clinic visits, but in between, we are trying to also surveil their sputum as well. We want to know when these patients are going to be converting their sputum cultures.

And the other reason that it's incredibly important to follow them so closely on their sputum is that we really need to be ready to pivot and make a change, step up our treatment if after 6 months these patients are not converting their sputum.

While speaking about that point, it's also important to mention that we, as per the guidelines, we also should be performing susceptibility testing for these MAC isolates, and that is going to help guide our therapy as well.

Wael, what do you do? Would you say that, in your experience, is your practice pattern the same in terms of your management of your patients?

Dr. ElMaraachli:
I think it's quite similar, our practice, and I like to stress reinforce the open lines of communication that you mentioned. It's important for the patients to know that they can contact us for in between clinic visits, as well. Because as you know, a lot of these side effects, they'll start to experience them in between clinic visits and we need to know right away in order to evaluate whether there are serious side effects and whether any changes need to be made. But a month after treatment, and then every 2 to 3 months thereafter, along with the testing schedule that you said, super important and super important to talk about all these things with the patients so that they know what to expect and manage their expectations.

Dr. Lapinel:
Now, we've certainly covered a lot today. So just to bring this all together, I think a key takeaway is that MAC lung disease can be progressive and result in permanent damage, especially if managed suboptimally.

Dr. ElMaraachli:
Right. Also, we touched on data that showed radiographic deterioration and lung function decline in patients who received suboptimal treatment and who did not achieve sputum culture conversion. That data also showed an increase in all-cause mortality and an increase in hospitalization rates in patients with MAC lung disease.

We also talked about the importance of timely initiation of guideline-recommended multi-drug treatment and what that treatment entails.

Dr. Lapinel:
Finally, we shared our perspective on patient education and follow-ups to ensure management is individualized. It's important to remember that we must continue to monitor for culture conversion and consider treatment response at 6 months if culture conversion has not been achieved. And once culture conversion is achieved, remember that the guidelines recommend treating for an additional 12 months.

And, as that brings us to the end of today's program, I want to thank you, Wael, for joining me to talk about MAC lung disease.

Dr. ElMaraachli:
I'd like to thank you too, Nicole. It was great speaking with you, and I'd also like to thank everyone for tuning in. So take care, and thank you.

Dr. Lapinel:
Thank you.

ReachMD Announcer
This program was brought to you by Insmed Incorporated. If you missed any part of this discussion, visit ReachMD.com/IndustryFeature. This is ReachMD.

References:

1. Ali J. A multidisciplinary approach to the management of nontuberculous mycobacterial lung disease: a clinical perspective. *Expert Rev Respir Med*. 2021;15(5):663-673. doi:10.1080/17476348.2021.1887734
2. Gochi M, Takayanagi N, Kanauchi T, Ishiguro T, Yanagisawa T, Sugita Y. Retrospective study of the predictors of mortality and radiographic deterioration in 782 patients with nodular/bronchiectatic *Mycobacterium avium* complex lung disease. *BMJ Open*. 2015;5(8):e008058. doi:10.1136/bmjopen-2015-008058
3. Park HY, Jeong BH, Chon HR, Jeon K, Daley CL, Koh WJ. Lung function decline according to clinical course in nontuberculous mycobacterial lung disease. *Chest*. 2016;150(6):1222-1232. doi:10.1016/j.chest.2016.06.005
4. Diel R, Lipman M, Hoefsloot W. High mortality in patients with *Mycobacterium avium* complex lung disease: a systematic review. *BMC Infect Dis*. 2018;18(1):206. doi:10.1186/s12879-018-3113-x
5. Prevots DR, Marras TK, Wang P, Mange KC, Flume PA. Hospitalization risk for Medicare beneficiaries with nontuberculous

mycobacterial pulmonary disease. *Chest*. 2021;160(6):2042-2050. doi:10.1016/j.chest.2021.07.034
6. Daley CL, Iaccarino JM, Lange C, et al. Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline. *Clin Infect Dis*. 2020;71(4):e1-e36. doi:10.1093/cid/ciaa241

This program is brought to you by Insmed Incorporated.
The consultants are paid speakers for Insmed.