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Perspectives on the NTM Guidelines for MAC Lung Disease

Announcer:
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Your host is Dr Doreen Addrizzo-Harris, Professor of Medicine at the NYU Grossman School of Medicine. Here's Dr. Addrizzo-Harris now.

Dr. Addrizzo-Harris:
Welcome to *Deep Breaths: Updates from CHEST* on ReachMD. I'm Dr. Doreen Addrizzo-Harris, and joining me to discuss practical use of the NTM guidelines is Dr. Ashwin Basavaraj, Assistant Professor of Medicine at NYU Grossman School of Medicine. Dr. Basavaraj, welcome to the program.

Dr. Basavaraj:
Thank you, Dr. Addrizzo-Harris. It's great to be here today.

Dr. Addrizzo-Harris:
So Dr. Basavaraj, let's start off with what I think is one of the most difficult areas when treating patients with MAC lung disease. How do you decide which patients to treat and which patients to monitor clinically?

Dr. Basavaraj:
Yeah, this is a very important question that you bring up. And there's been some research investigating this particular topic. There was a few studies looking at a large cohort of patients with NTM that met ATS diagnostic criteria and about 500 patients in which a majority of those patients progressed, about two-thirds of those patients progressed without any sort of treatment. But there is a subset of patients, about a quarter of patients, that remain stable with MAC. And out of those quarter patients half of those patients spontaneously converted their cultures to negative.

And we also looked at another 500 patients who were treated and who did not receive treatment. And about 60 percent of patients received treatment and 40 percent did not. And about half of those patients that did not receive treatment, converted their cultures to negative. So we definitely want to understand which patients progress and which patients remain stable and can be treated conservatively.

Dr. Addrizzo-Harris:
So what are some of the risk factors that you look for in your patients that would tell you they might be likely to progress?

Dr. Basavaraj:
Yeah, this is a great question. And there's a number of risk factors that we look at. For one, we look at demographic factors such as male gender, older age, presence of comorbidities, or low body mass index. We know that these factors if they're present, patients are likely to progress in terms of their NTM lung disease. There's also some laboratory factors, some elevated inflammatory markers like ESR, CRP, anemia, hypoalbuminemia. Some radiographic factors. For example, if patients have a larger extent of disease, that they have cavities in their lungs, they're likely to progress. And also, the type of bacterial load and species if for example, they have a more aggressive NTM, such as a rapidly growing mycobacterium abscessus, or if they have a high burden of infection, if they're smear positive. Those are patients we want to be a little bit more aggressive with treatment, because they're likely to progress with their NTM.

Dr. Addrizzo-Harris:
Absolutely. Very good points. So there is going to be a cohort of patients that we're going to decide don't require pharmacological therapy upfront. And I think the most important thing in that group is to make sure you continue to follow those patients regularly. Would you agree with that?

Dr. Basavaraj:
Yes, absolutely. And we monitor patients, you know, clinically. We monitor their symptoms, we monitor their weight at every clinic visit. We can monitor them radiographically and see what's happening in terms of their chest x-rays and CAT scans. And we will want to monitor their sputum to see if they're clearing their cultures, if they have other organisms, such as other bacteria, or funguses, that are present along with their NTM. Those are all important points in terms of monitoring the patient for progression.

Dr. Addrizzo-Harris:
And I don't want to leave this topic without saying a little bit about nonpharmacologic therapy. In patients that we're not going to treat pharmacologically and in those that we do treat pharmacologically, but I guess both groups, what can you tell us about the importance of nonpharmacologic therapy?

Dr. Basavaraj:
Yeah, I can tell you, it's a very important management strategy. We know that airway clearance and nonpharmacologic therapy is important because it helps to break the vicious cycle in bronchiectasis, it helps to bring up mucus, to reduce infection, and to reduce inflammation. And there's a number of strategies that we can incorporate. There can be positive expiratory pressure devices, there can be high-frequency chest wall isolation devices, and mucolytic agents such as hypertonic saline that can be utilized in conjunction with exercise and other techniques from chest physiotherapy, such as active cycle breathing techniques, that all can be utilized in terms of bringing up mucus and help to break the vicious cycle, and try to prevent the progression of bronchiectasis and NTM.

Dr. Addrizzo-Harris:
Well, thank you very much, Dr. Basavaraj, for that great overview. I know there's a lot more we could say on that topic. But I do want to move on to another area. The NTM guidelines point out that antimicrobial sensitivity testing, or as we call it AST, is important in patients with MAC lung disease when they are first diagnosed. So can you tell us a little bit about the utility of AST testing, and explain its use in MAC lung disease?

Dr. Basavaraj:
Yeah, so this is a very important point that we're trying to increase awareness on. With susceptibility testing we can send sputums to various labs and check which antibiotics work for that particular strain. We may not always be able to send this on patients, but we particularly send this on patients who are progressing on antibiotic therapy, or who may be at risk for resistance, for example, if they're getting treated for their NTM.

And when we have this susceptibility testing panel that comes back, it's very important to remember that there's two classes of antibiotics that correlate with what's being reported, and what actually happens in the patient. And that's macrolides and amikacin. We want to know if those two classes of antibiotics are sensitive or resistant in patients, because that's important to see if we can include those antibiotics as part of the patient's treatment regimen.

Dr. Addrizzo-Harris:
Yes, that's extremely important. And often I think it's important to tell the listeners out there that there will be sometimes reports back on many other antibiotics outside of amikacin and macrolides. And we know that those don't correlate with you know in vitro susceptibility. So, the guidelines point out the two antibiotics that we need to look at are amikacin and macrolides. Dr. Basavaraj, what are the recommended standard regimens for patients with MAC lung disease? Both those with nodular MAC lung disease and what are the difference with those who have cavitary lung disease?

Dr. Basavaraj:
Yeah, this is an important question to understand, Dr. Addrizzo-Harris. I think the main thing is to identify if a patient has mild to moderate bronchiectasis. We normally call them nodular bronchiectatic disease. Or if they have the presence of cavities on imaging, then we call that cavitary MAC lung disease.

For those with nodular bronchiectatic lung disease, the guidelines do recommend that we initiate three antibiotics, a macrolide, rifampin, and ethambutol. And we have the option of starting these antibiotics three times a week. Which there is research that suggests that three-times-a-week therapy may be just as good with similar outcomes comparing to patients that receive that regimen every day with less side effects.

Now if a patient has cavitary MAC lung disease, we want to be a little bit more aggressive with therapy. And we want to use the same

three antibiotics, a macrolide, ethambutol, and rifampin. We normally give these antibiotics every day. And depending on the severity of the disease, we can add on I.V. amikacin up front with that regimen. Or we can see how patients respond to the three antibiotics first and give it a month or two. And if there's no improvement, we can add on I.V. amikacin at that time.

Dr. Addrizzo-Harris:
Great and we know that sometimes patients do not tolerate one or two of the three standard medications. So what are some of the second-line therapies that can be used for treatment of MAC lung disease?

Dr. Basavaraj:
Sure, and a number of these medications can still be considered under investigation. But for example, clofazimine is an option that's utilized; oxazolidinones; bedaquiline.

Dr. Addrizzo-Harris:
Great and it's certainly not an antibiotic, but I do want to point out that surgical treatment in patients with localized disease or significant hemoptysis is also kind of an add-on therapy that we would want to consider in the right patient.

And then many of these medications will have different side effects that it's important to go over with your patients. I'm sure you sit down with your patients and review the side effects. The most common ones that we see certainly are GI issues. Sometimes rash can be a problem. We start our medications intermittently, meaning they we add them on. For patients that are on azithromycin and clofazimine, we'll be monitoring their EKGs, looking for their QT interval. For patients on amino glycosides, we will be looking at their audiograms and their renal function. And then for those on ethambutol, we will be getting a routine eye exam. So important to keep up with monitoring for side effects when patients are on these regimens for many months.

So Dr. Basavaraj what is the definition of refractory disease? I'm sure there are lots of people out there that aren't sure what that means.

Dr. Basavaraj:
Sure, Dr. Addrizzo-Harris. I think the way we like to define refractory disease is in patients who with NTM and who are started on guideline-based treatment if they still have culture, AFB cultures that are positive at six months or longer while taking guideline-based treatment, that would be considered refractory. And that can be predictive of their culture positivity status a year later from that time point, which is why it's considered refractory. So that's the definition that we normally use for refractory disease.

Dr. Addrizzo-Harris:
And why is it important to clinically monitor patients that are on guideline-based therapy, particularly with frequent sputums?

Dr. Basavaraj:
It's important because one, it helps us to see how the patient is responding to therapy. Are they improving? You know, to go along with the clinical symptoms and the radiographic findings, but it also is important because it helps us to dictate how long to continue antibiotic therapy for. As we know on the guidelines, it's suggested that patients should continue antibiotics from a year from their first negative sputum culture. So it's important to identify that first negative sputum culture because then it then dictates how long to continue the antibiotics for.

Dr. Addrizzo-Harris:
We're coming to the end of our discussion. Let's spend our last couple of minutes discussing what types of communication strategies you use to enhance medication adherence in your patients who are on MAC lung disease treatment. I know this can be one of the most important areas to get compliance. So Dr. Basavaraj, what strategies do you use?

Dr. Basavaraj:
Thanks Dr. Addrizzo-Harris. There's a number of strategies that we can utilize here. And I think the first strategy that I like to utilize is just teaching the patient what bronchiectasis and NTM are. This is oftentimes on the first clinic visit. Patients come to us not knowing what bronchiectasis is, not knowing what NTM is. So it's important to review what it is how it looks like on their CAT scan and review the pictures with them. Review some risk factors and environmental risk factors. Those are all important to highlight in terms of educating the patient on the bronchiectasis and NTM.

There's a number of patient resources we can direct patients to. So for example the NTMIR Patient Support Network is a great support network, where patients can learn more information and learn from other patients with NTM. The COPD Foundation also has some great resources on their websites that patients can refer to learn more about NTM.

And there's also a multidisciplinary approach to these patients that's also included in terms of education for the patients. You know, we work with nurse practitioners, chest physiotherapists and other disciplines. And they all are part of the adherence to therapy and in educating the patients in terms of their bronchiectasis and NTM.

Dr. Addrizzo-Harris:
Yeah, those are all very important. I want to add on to that different cities have very active local groups patient groups too. So you know, be aware of that. We are lucky to have a local group here in New York City that meets monthly. And I also do know that the CHEST Foundation website has lots of educational material for patients and for clinicians to use with their patients.

With all of those considerations in mind, I want to thank my guest, Dr. Ashwin Basavaraj for joining me in today's discussion. Ashwin, it was great speaking with you today.

Dr. Basavaraj:
Thank you so much, Doreen. It was great to be here with you.

Dr. Addrizzo-Harris:
And I'm Doreen Addrizzo-Harris. Thank you for listening.

Announcer:
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