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Nontuberculous Mycobacteria (NTM) in Patients with Cystic Fibrosis

Narrator:

Welcome to CME on ReachMD. This segment: Nontuberculous Mycobacteria, NTM in
Patients with Cystic Fibrosis, is sponsored by Prova Education. Your host is Dr. John Russell, who welcomes Dr. Patrick Flume, Professor of Medicine and Pediatrics at the Medical University of South Carolina in Charleston, South Carolina. Prior to beginning the activity, please be sure to review the goals of this educational activity, or if you are listening to this as a podcast, go to this activity on ReachMD.com/Prova on your computer, Smartphone or tablet device.

Dr. Russell:
Mycobacterium infection of the lung, also known as NTM lung disease, is becoming increasingly common. Today we are going to discuss how patients are evaluated and treated, including some complications we need to be aware of in the management of NTM lung disease. Dr. Flume, welcome to ReachMD.

Dr. Flume:
Thank you very much.

Dr. Russell:
So, doctor, to start, can you define NTM lung disease for us?

Dr. Flume:
So, NTM, standing for nontuberculous mycobacteria, is essentially an infection of the lung, typically a chronic infection, meaning it's been there for some time and not necessarily acute or sudden like you might see in a typical pneumonia. So these are patients who have symptoms and signs of chronic infection such as cough, sputum production, maybe even coughing up blood, but also other constitutional symptoms like fevers, night sweats, fatigue, almost like having the flu. Radiographically, you can see changes on the x-ray that would be typical of a chronic infection. This can range from little nodules that you can see on the x-ray to bronchiectasis or dilated airways, even cavitary disease. And then these patients have the presence of mycobacteria that you get from cultures, either from sputum cultures or from bronchoscopic methods of getting samples, but another key caveat is that you are trying to link that presence of the bug with these signs and symptoms, so you are looking to make sure there isn't some other explanation for their signs and symptoms such as patients having cystic fibrosis.

Dr. Russell:
In medicine, how has our understandings of NTM lung disease changed over time?

Dr. Flume:
One of the key issues with NTM lung disease, is that the prevalence is increasing. The numbers of patients that we have identified with NTM lung disease have gone up pretty considerably in the last couple of decades, and this is, perhaps, because of one or two different issues. One is, is it possible that there actually are more cases than we saw previously, such as more patients with the risk factors for infection or changes in the environment that put more patients at risk? But more likely, is that we have greater recognition of disease. It really wasn't on the radar for folks, but now as people have begun to understand that NTM lung disease is out there, as there is greater utility of high resolution CT scanning, and so the radiologists are identifying changes that could be due to NTM lung disease. So the doctors are starting to consider it and start looking for it, and so, there are a number of patients that get referred to me because they finally have sputum cultures growing mycobacteria, or that they just have an x-ray of the chest that was suggestive of it.

Dr. Russell:

So doctor, what would be the risk factors for developing an NTM lung disease?

Dr. Flume:
This is a tricky part, because we have some patients who clearly have underlying lung disease that puts them at risk for developing a chronic infection like this. So, for example, patients who have bronchiectasis due to some other cause. So, again, bronchiectasis is chronic dilation of the airways, so the airway is anatomically abnormal. We are introducing bugs into our lower airways and, in some settings, those bugs are now successful and can establish residence and chronic infection. So, there are a lot of other conditions that are associated with bronchiectasis, one of which is cystic fibrosis which is a genetic disease. We are also seeing it in patients who have other types of lung disease, most notably, COPD or chronic obstructive pulmonary disease, and another common risk factor is aspiration. This could be with or without gastroesophageal reflux disease. But people who are chronically aspirating, even just small amounts into their airways over time. But we also have patients that come to us and they have no obvious reasons for this. They don't have anything clear that would make them seemingly at risk for developing a mycobacterial infection, and a classic scenario is in a postmenopausal woman and this woman just has cough, eventually someone gets an x-ray, leads to a CT scan and you see evidence of disease, typically in the right middle lobe or lingula. But there is no other features or diagnoses that would suggest that they would be at greater risk for that.

Dr. Russell:
So, for these patients with NTM lung disease, what would be the natural history for them?

Dr. Flume:
This is the great unknown for us, because intuitively, these bugs shouldn't be there, and so, it would make perfect sense that we should treat everybody who has mycobacteria present in their airways, but the reality is, that there are some patients who have mycobacterium, it's not the cause of their symptoms, and they will show no signs of progression over years. So, you could follow these patients over time, get repeated cultures and such and they continue to grow the bug, but no obvious progression or deterioration, but then there are some patients where it clearly progresses. If you see a patient who has cavitary lung disease, that clearly didn't start with a big cavity, it started with something smaller and progressed. And so some of those patients will develop increasing abnormalities on x-rays, again, developing cavities or expansion of nodular disease in parts of the lung. Symptom-wise they can have progression of symptoms, again, the cough and sputum production, quite scary can be hemoptysis or coughing up blood. And the challenge for us is that there is no way for us to know at the beginning who is likely to progress, and so, one of the key messages is even if you decide not to begin treatment early on, it is very important to continue to monitor those patients to look for evidence of any progression.

Dr. Russell:
So, for the patients you elect to treat, how do you go about treating them?

Dr. Flume:
There are several choices, most it depends upon which mycobacterium that you are treating. So, most commonly, we have mycobacterium avium, probably accounts for about 70% of the patients that we see, and the standard treatment for that would be multiple medications over a protracted course of time. So in patients who have nodular bronchiectasis, the guidelines that come from the ATS and the European Respiratory Society and the IDSA, would suggest at least a three-drug regimen which would include a macrolide, such as azithromycin or clarithromycin along with a rifampin-based product and ethambutol. Many of those patients will be able to tolerate that regimen, others will have some trouble, and so there are other choices that you may use to replace those, to replace the medication. In patients who have more advanced disease, where they have cavitary disease, we are often adding a fourth agent and oftentimes that's a medicine like amikacin, initially with intravenous systemic therapy, and then in many cases removing to an aerosolized approach.

In patients who have mycobacterium abscessus, which is probably about another 20, 25% of our patients, these bugs have a different susceptibility profile and we worry about these bugs because the treatment options are fewer and, in many cases, available only through an intravenous route. And so, in those cases, we might institute a very aggressive approach to treatment with intravenous, imipenem, as an example, along with amikacin, and a macrolide, and oftentimes a fourth agent that will be driven by the susceptibilities, and then treat for an aggressive period of time, say 6 to 8 weeks, and then convert that intravenous therapy to an inhaled regimen. We recommend monitoring these patients because what we are looking for is culture conversion to take them from positive cultures to negative cultures, and the current recommendation is to treat those patients for a year after they have had culture conversion.

Dr. Russell:
So, with these very complicated treatment regimens, there probably will be some complications. What are some things we should keep an eye out for?

Dr. Flume:

So, all medications come with baggage, the potential for side effects. In some cases those might be more annoying side effects, such as nausea or diarrhea. In other cases those side effects might be very serious. So, for example, with amikacin you can worry about autotoxicity, with ethambutol there is neural toxicity and, particularly, effects on vision. And so what you need to have is a very careful understanding of the specific complications that can occur with each of these types of therapies. Our clinic has the luxury of having a pharmacist present in the clinic so that we can look for potential drug interactions and we do therapeutic drug monitoring, in many cases, measuring drug levels to assure that we are getting some sufficient systemic delivery and then monitoring for those potential complications.

Dr. Russell:
So, how effective are the outcomes of treatment of NTM lung disease?

Dr. Flume:
Oh, this is real challenge because when you review the studies to look at what the outcomes are, you find that they are not quite so easy to compare. So, clearly, in some patients we are going to cure them of disease. We are going to eradicate the infection and there will be no residual infection afterwards. In some other cases, we actually can control the disease in which there is marked improvement in their signs and symptoms and yet the bug persists despite the use of these antibiotics. And then, in fewer cases, we seem to struggle trying to find a regimen that we could try to get this under control. As might be expected, those patients who have nodular bronchiectasis have a much greater likelihood of eradication and cure than do those patients who have cavitary disease. Patients who have mycobacterium avium, we have a greater success rate than we do with patients who have mycobacterium abscessus. We don't typically have the luxury of knowing how long a patient has had the infection, and it may be that our eventual knowledge will be that we could take a very aggressive approach to try and eradicate these bugs early in the onset. But most of these patients come to us with symptoms for years and we don't know when the mycobacterium became present. There are some patients, like our cystic fibrosis patients, in which we could theoretically find the bug because we are doing surveillance cultures on them over time and what could institute an earlier eradication strategy in those patients.

Dr. Russell:
Well, Dr. Flume, many thanks for joining us today to discuss clinical updates in the evaluation and treatment of nontuberculous mycobacterium.

Dr. Flume:
It was my pleasure.

Dr. Russell:
I am your host, Dr. John Russell, for ReachMD. Visit us at ReachMD.com where you can be part of the knowledge. Thanks for listening.

Narrator:
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