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Cases in Severe Asthma Care: The Importance of Early Detection

### Announcer Introduction

This is *Deep Breaths: Updates from CHEST* on ReachMD. This is a non-promotional, non-CME disease state education podcast series brought to you by American College of CHEST Physicians, in collaboration with and paid for by GSK. Your host is Dr. Tom Corbridge, a pulmonologist at Northwestern University and a senior medical lead at GSK.

#### Dr. Corbridge:

This is *Deep Breaths: Updates from CHEST* on ReachMD. I am Dr. Tom Corbridge, and today, we will be talking about severe asthma and the asthma patient journey. But first, I'd like to welcome and introduce our guests: Dr. De De Gardner, Dr. Diego Maselli, and Dr. Praveen Akuthota. Dr. Gardner is the Chief Research Officer at the Allergy and Asthma Network in Fairfax, Virginia and Adjunct Faculty in the Department of Respiratory Care at Boise State University. De De, welcome to the program.

#### Dr. Gardner:

Thank you for having me.

#### Dr. Corbridge:

Dr. Maselli is a Professor of Medicine and Chief of the Division of Pulmonary Diseases and Critical Care at UT Health San Antonio. Diego, it's a great pleasure to have you with us.

#### Dr. Maselli:

Thank you. Thank you, Tom, for having me. It's a pleasure to be here.

#### Dr. Corbridge:

And last but not least, Dr. Akuthota is a pulmonary and critical care physician and a Professor in the Department of Medicine at UC San Diego Health. Praveen, a warm welcome to you as well.

#### Dr. Akuthota:

Thanks, Tom. Great to be here.

#### Dr. Corbridge:

So, we would like to ground today's discussion in a patient case, and so to start us off, Diego, please tell us about one of your patients.

#### Dr. Maselli:

This is a patient that I have been seeing for some time. She's a 46-year-old lady with a history of asthma and allergic rhinitis. She actually never smoked, and she was diagnosed with asthma around the late 20s. And she initially presented with various visits to the ER with acute shortness of breath, and that's how the diagnosis was kind of suspected. She would come very frequently with wheezing. A chest x-ray was normal, and the workup was normal, and she responded quite well to corticosteroids.

The problem with her is that she traveled a lot. She works as a contractor, so she travels a lot in different parts of Texas and around the country, and it was hard for her to really establish kind of a continuity of care with her PCP. She would really come to the ER to often get

prescriptions for inhalers, and then also prescriptions with corticosteroids, and that's kind of how she managed. But unfortunately, after several days of corticosteroids and a couple of weeks afterwards, she would still feel bad and have shortness of breath and wheezing and would come back to the ER. So it looked kind of like a revolving door for her.

**Dr. Corbridge:**

Wow, well, she clearly is not meeting goals and no doubt her need for frequent travel is certainly not helping. De De, let's turn to you. What are some of the consequences in a patient like this of having those frequent exacerbations and uncontrolled asthma?

**Dr. Gardner:**

Sure. So what we know is that about 60 percent of patients with asthma are actually uncontrolled. The ATS and ERS have defined uncontrolled asthma with one of the following: we look at poor symptom control, we look at frequent exacerbations, we look at serious exacerbations, and then, airflow limitations. If we think about our patient that Diego is speaking to today, these exacerbations are not benign to someone who has asthma. However, the more exacerbations a person has, the greater loss of lung function that they'll experience, and additionally, severe exacerbations actually result in inflammation and airway remodeling, which then translates to more impaired lung function. So typically, we'll treat exacerbations with a course of oral corticosteroids, and in fact, a recent study by Price demonstrated that about 44 percent of the adults who had severe asthma reported OCS use in the last 12 months. All of us are familiar with long-term sequelae or long-term side effects of oral steroids, such as osteoporosis, hypertension, cataracts, and type 2 diabetes. But what's becoming more appreciative here is that short-term use of oral steroids are even more associated with complications. And even low-dose, cumulative oral steroid use or exposure is associated with significant adverse events. We see that the most adverse events become significant above the dose of 1 gram of oral steroid, and this is equivalent to 4 lifetime bursts of oral steroids.

**Dr. Corbridge:**

De De, thank you. That's great information. Diego, I want to go back to your patient. Tell us what happened next.

**Dr. Maselli:**

Fortunately, she was able to come to our clinic. We did some phenotyping as we do with all of our asthmatics, particularly those that are uncontrolled. So we performed pulmonary function testing, and her FEV1 – forced expiratory volume in the first section – actually was quite reduced at 58 percent, and she had some reversibility with albuterol to around 15 to 17 percent. A chest x-ray was normal, and then we did perform some bloodwork. We did a CBC with a differential that revealed a blood eosinophil count of 380 cells per microliter. We measured her IGE level, which was 230 international units per milliliter, and we did an exhaled nitric oxide measurement, and that was 28 parts per billion. I also looked back at her records, which is something that I am now doing more and more, to see what her previous CBCs with differentials looked like because she had been to the ER many times before I had that luxury of looking kind of back at her records. And she had some eosinophils that were elevated in the past, ranging between 300 to up to 500 in the previous years.

**Dr. Corbridge:**

Thank you, Diego. Praveen, let's bring you in now. How can we detect severe uncontrolled asthma earlier in the patient journey?

**Dr. Akuthota:**

Yeah, it's a difficult one, Tom, with a patient like this who's been traveling from place to place. But I think there probably were some missed opportunities with this patient that may be a good lesson for us. In particular, the frequency of exacerbations; so getting a good history about the frequency of exacerbation, I think, is one of those key factors that tells us that somebody is, in particular, uncontrolled: frequent symptoms and frequent exacerbations. And then, doing all the things that Diego did when this patient got to him for evaluation: establishing the correct diagnosis and getting lung function with bronchodilator reversibility.

This patient had a dramatic FEV1 response in her spirometry, so that really helps us know that this is, indeed, asthma and not some asthma mimic or something else that's causing episodic frequent episodes of dyspnea. And then, again, as Diego did, asking the right questions: asking about response to therapy, doing things like making sure you're reviewing inhaler technique and adherence to determine that this isn't a technique issue rather than a true severity issue, identifying the exposures in either occupational or environmental settings that might be driving a particular patient's asthma, and then considering comorbidities that might point you toward a diagnosis of asthma, as well. There are things that co-travel often with asthma, like allergic rhinosinusitis and other atopic diseases, and then finally, considering biomarkers, again as Diego did.

**Dr. Corbridge:**

Praveen, thank you. That's great information. For those of you just tuning in, this is *Deep Breaths: Updates from CHEST* on ReachMD. I

am your host Dr. Tom Corbridge, and I am speaking with Drs. De De Gardner, Diego Maselli, and Praveen Akuthota on severe asthma. So Dr. Gardner, let's turn back to you. Tell us about the importance of early intervention in your patients with asthma.

**Dr. Gardner:**

Sure. So we talked earlier that with these severe exacerbations, they are definitely linked to type 2 inflammation and airway remodeling. And that link between exacerbations and accelerated lung function is defined in asthma, but there is also data that demonstrates year-on-year lung function loss with increasing exacerbation burden – that this is also associated with the speed of lung function decline. And it appears that this occurs more frequently in younger patients – between the ages of 18 and 39 – and this patient seems to fall within that. So this underscores the need for early intervention, before the age of 40, in the management of asthma, especially with these patients that have frequent exacerbations who are at risk of accelerated lung function decline.

**Dr. Corbridge:**

Great, thank you. Diego, let's go back to you and back to your patient. So how did she do after you changed her treatment regimen?

**Dr. Maselli:**

After we maximized her inhaler therapy and we looked at her inhaler technique and reviewed all her testing, we decided to proceed to start a biologic on her. And that was approximately 6 months ago or so, and on her repeat visits, she came back and reported a significant improvement of her symptoms, but importantly, she has not had an exacerbation over the past 6 months. She feels much better; she reports that her asthma is definitely better controlled. No ER visits, and fortunately, no need for corticosteroids. She's back in her work, and again, traveling a little bit, but feeling much better. On her last visit, we did perform spirometry and looked at her FEV1, and she improved from 58 percent to actually 70 percent, and again, she continues to feel better.

**Dr. Corbridge:**

Excellent. So there has been a lot of discussion lately about how we can do better about achieving aspirational composite outcomes in patients like Diego's. And this has been framed around the evolving concept of clinical remission on treatment in patients with asthma. Praveen, tell us what your thoughts are on where we stand with clinical remission.

**Dr. Akuthota:**

I think these are still early days for defining remission. There was a recent consensus statement by the ACCI, the ACAAI, the AAAAI, the ATS, and the European Work Group to try to come to at least a starting point, a straw man for proposing a definition for remission, which I think is a reasonable starting point that will be refined going forward. But their definition starts with looking at the last 12 months, and over those 12 months having no exacerbations, no missed work or school, stable pulmonary function tests, and the use of their ongoing controller therapies, but not high-dose inhaled corticosteroids. So if somebody needs high-dose inhaled corticosteroids, maybe that's not a person who has remission. But again, that's something we can debate going forward. How their symptoms are doing, particularly with the symptom score, and then again, their use of reliever therapy is baked into this remission definition as well.

**Dr. Corbridge:**

Praveen, thank you so much. So De De, let's go back to you. This is your chance to share any last messages you might have with our audience today.

**Dr. Gardner:**

Well, I think it's a novel time for asthma and the thought of having a patient who is thought to be "in remission." I find that this is going to be an iterative process as time moves on. Also, as this body of work continues to grow, we as practitioners are always being challenged to be more intentional, but especially with the thought of remission, we need to be very intentional in how we collect the data, how we record that, and then also being more aspirational to try to achieve these endpoints with our patients.

**Dr. Corbridge:**

Thank you. And before we end, Diego and Praveen, let's get your final take-home messages as well. Diego, let's start with you.

**Dr. Maselli:**

Yes, I think this is a very exciting time for asthma as we understand a little bit better now what are the inflammatory pathways that are happening behind the scene. And now we have the tools to try to achieve that control in our patients as much as we can. It's ambitious, I agree, but I think it's a good goal to try to control as much as we can, our patients, and try to reduce the exposure to corticosteroids. As De De mentioned, these can have devastating effects on our patients that are long-lasting, even after just a couple of bursts of steroids.

I think now we have the tools to prevent some of these exposures, and again, it's an exciting time for asthma because we now have more tools than ever to help our patients.

**Dr. Corbridge:**

And Praveen?

**Dr. Akuthota:**

Yeah, I feel a lot of what De De and Diego said – two things in particular. Excitement about where we are and the fact that we have a lot of tools now that have emerged over the last several years to get better outcomes in asthma. And now, our task going forward is not just to create even more tools, but also to get frameworks to use the tools that we have to achieve even more aspirational goals.

**Dr. Corbridge:**

Well with those final comments in mind, I would like to thank my guests today, Drs. Gardner, Maselli and Akuthota, for sharing their knowledge and insights on severe asthma. De De, Diego, and Praveen, such a pleasure to have you on the program. Thank you so much.

**Dr. Akuthota:**

Thanks. This was fun.

**Dr. Gardner:**

Yes, thank you for having me. I appreciate the time today.

**Dr. Maselli:**

Thank you very much for having me today.

**Announcer Close**

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