Transcript Details
This is a transcript of an educational program accessible on the ReachMD network. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/cme/sniffing-out-problem-dive-management-chronic-rhinosinusitis-nasal-polyps/11071/

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

Sniffing Out the Problem: A Dive into Management for Chronic Rhinosinusitis with Nasal Polyps

Hello, and welcome to Sniffing Out the Problem: A Dive into the Management of Chronic Rhinosinusitis with Nasal Polyp, a CME Self-Assessment Program.

My name is Joseph Han. I am a Professor and the Chief for the Division of Rhinology and Endoscopic Sinus and Skull Base Surgery, as well as the Chief for the Division of Allergy at Eastern Virginia Medical School.

In this activity I will guide you through the diagnosis and the pathophysiology of Type 2 inflammation driven chronic sinusitis, also known as chronic rhinosinusitis with nasal polyps. I will also offer expert insight into effectively and safely incorporating biologic therapy into your practice to improve patient outcomes.

We know that chronic sinusitis is very common in the United States, affects one in seven adults, is a very common reason for being prescribed antibiotics as well as for office visits. There's a huge burden on our national healthcare, costing $23 billion in the year 2014. Personally, as an individual with sinusitis, we know that it really affects one's quality of life and when the patient's quality of life is affected, it affects not only just their personal life, but also affects their work and social activities as well.

So when we look at chronic sinusitis we break it into two categories. One is chronic sinusitis with polyp. This is a little less common. Chronic sinusitis without polyp is a little bit more common. Now within that group you can also have different subtypes, such as allergic fungal sinusitis, which is common in the Southeast part of the U.S. There's also a disease process called NSAID-exacerbated respiratory disease, is also known as aspirin-exacerbated respiratory disease or Samter's triad. These are other subtypes of chronic sinusitis.

Another way to kind of look at sinusitis is to look at two important comorbid disease. One is asthma. So whether or not you have asthma and when you have asthma, it's important, also as well as the presence of allergic rhinitis, and to which specific inhalant allergens you're allergic to.

Age of onset younger than 30 years. And the reason why I say this is because in most of patients with nasal polyposis, usually occur in the adult age. They tend to occur along the age of 50 to 60 years. If they have nasal polyposis earlier on, it's uncommon to have it below the age of 30.

Now when we're trying to diagnose patients with chronic sinusitis, what we often look for are symptoms. And what we have initially described on the diagnosis of sinusitis is to look at several symptoms, cardinal symptoms, that are associated with chronic sinusitis. These are nasal obstruction or congestion, facial pressure or fullness, discolored nasal discharge, whether it's entry or posterior, or change in smell.

Now the more likely you have these symptoms the more of these symptoms that you have, the more likely you're going to have the diagnosis of sinusitis. And the older you get the more likely you're going to have it.

Now if you really want to confirm the diagnosis of nasal polyposis, you should have an objective finding. And the objective findings can be either done with an anterior rhinoscopy. I think the best way to diagnose nasal polyps objectively is nasal endoscopy. Often if you can't see them with anterior rhinoscopy, some people use CT scan to confirm the presence of nasal polyps.

Polyposis associated with nasal polyposis usually develop within the osteomeatal complex underneath the middle turbinate.

If you have a unilateral mass in one nasal cavity we have to be concerned that it could be a tumor.

Here is an endoscopic view of a nasal polyp. This is an endoscopic view of the left nasal cavity. Here you can see the septum, you can see the inferior turbinate, and then you can see the polyp originating from the osteomeatal complex.

So if you're seeing patients with a possible diagnosis of a sinusitis, you also have to have a list of differential diagnosis. And these differential diagnosis could include patients such as allergic rhinitis or non-allergic rhinitis. You can also have patients with deviated septum causing some of these symptoms. And there could be other reasons for causing facial pain and pressure.

We talked about the typical cardinal symptoms we see with sinusitis, but sometimes you can see other symptoms that are a little less common, such as fatigue, dental pain and headaches. Headache in general is not a direct cause for sinusitis, but certainly sinusitis can indirectly cause headache.

In the U.S. most patients with nasal polyposis is driven by Type 2 inflammation. We can talk a little bit more about this later on.

In the past when we were trying to figure out what was causing chronic sinusitis, it was initially thought as an infectious process. Now we understand it's more of a inflammatory process, a chronic inflammatory process. When you look at what's driving these inflammation in the U.S. and Europe you see that what is driving the formation of nasal polyp is usually a Type 2 inflammation. Some of the recent studies comparing the polyp formation in U.S. and Asia shows that in the Asian population it could be more of a neutrophilic or a Type 1 inflammation.

Chronic sinusitis without nasal polyps in general, whether you're in Belgium, China or Korea, is usually driven by a Type 1 inflammation.

Now how we decide if it's Type 1 or Type 2 is, is through endotyping. Not everybody can do this. You usually need a lab to be able to do this, so we have to find another way to better differentiate on how to better understand what's causing these polyps in sinusitis.

Here is the mechanism of Type 2 inflammation. Now in the past it used to be called Th2 inflammation. These are some of the cells and cytokines that we see, such as IL-4, IL-5 and IL-13, which are very classically described as a typical cytokine for Type 2 inflammation. These are some of the cells that we see, such as eosinophils, mast cells and basophils, are also seen there as well.

Patients with nasal polyposis and asthma are more likely to have severe disease, not less likely.

We know that patients with chronic sinusitis with nasal polyposis have allergic rhinitis associated with it. It's not uncommon for patients with nasal polyposis to have asthma or allergic rhinitis. Now atopic dermatitis is a little less common. Even though we don't necessarily think of aspirin-exacerbated respiratory disease (AERD) as an atopic disease process, it certainly has the Type 2 inflammation associated with that. So that's why it's here on this list. Because what's driving a lot of these nasal polyposis is Type 2 inflammation. And that's where a biologic can be helpful.

In fact, dupilumab is the only biologic approved for the use in chronic sinusitis with nasal polyps.

What exactly is dupilumab? Well, dupilumab is a IgG or a monoclonal antibody that specifically targets IL-4 receptor alpha. And it's important to understand that it's binding to IL-4 alpha receptor and by doing so it blocks the signaling of IL-4 as well as IL-13. Because blocking just IL-4 and IL-13 by itself is not shown to be effective.

Dupilumab reduced the polyp size, sinus opacification and severity of symptoms, specifically nasal congestion.

Here is a complex diagram, looking at the study protocol for SINUS-24 and SINUS-52. The bottom line is SINUS-24, these were patients who were given dupilumab for six months and then we followed them for six months to see what happened. For SINUS-52 we had two groups that were given dupilumab, one group that as a control group. Both of the treatment group in SINUS-52 were given dupilumab for 52 weeks. One of them, halfway through the study, was given dupilumab every four weeks instead of every two weeks.

What do the results show from this clinical study of SINUS-24 and 52? What is shown was that there was a significant decrease in the nasal polyp score, with a reduction of 2, which is twice that of what we have considered historically significant. In the past we used to think that a polyp score change of 1 was considered clinically significant. Now we see twice that level.

When we look at nasal congestion and CT score, there was a significant reduction in both the symptom as well as objective findings with a CT score between the placebo group and the treatment group.

In the SINUS-24 and 52 we did look at other secondary endpoints. One that was very interesting for me was the use of systemic steroids or whether or not patients needed surgery. Now this was actually the first study and one of the largest studies looking at patients with nasal polyposis. And what they did during the study for a one year period was to determine, do they need surgery or not? So this is the only study that actually did that.

We also did look at other secondary endpoints such as SNOT-22, which is very commonly used. We also did a subgroup analysis of

patients in the study to see if their asthma got better and whether or not the presence of NSAID-exacerbated respiratory disease had any influence in the outcome of the use of dupilumab in these patients.

We know from the previous slides that dupilumab is effective in patients with nasal polyposis. How safe is it? And when you look at some of the commonly described adverse effects in the study, we see that the most common adverse effect was injection site erythema, not surprising. Some of the other ones that we see here is worsening of nasal polyps or nasopharyngitis. And this may be more consistent with the disease process than the drug itself.

Are there other biologics targeting the treatment of chronic sinusitis with nasal polyposis? The answer is yes. We have omalizumab, which just finished their study. There's also mepolizumab as well as benralizumab. Even though they're both targeting IL-5, the mechanism of how they work is different because benralizumab targets the IL-5 receptor, instead of the circulating IL-5 as it does in the mepolizumab.

POLYP 1 and POLYP 2 are basically the two Phase 3 studies looking at omalizumab for nasal polyposis. The study design was the same. They were both given omalizumab based on their serum IgE and their weight for six months and then they were followed again for another six months.

The initial report for POLYP 1 and POLYP 2 shows that omalizumab appears to be effective in patients with nasal polyposis and it reached its primary endpoint as well as some key secondary endpoints such as SNOT-22.

Omalizumab also appears to be safe as well and that there does not appear to be any safety concern during this clinical study.

There were two Phase 2 studies looking at mepolizumab for nasal polyposis. First study here is the larger of the two. This was a prospective, randomized, placebo-controlled study, looking at 105 patients. Based on this result it appears that mepolizumab will also be effective in patients with nasal polyposis.

So when we treat patients with chronic sinusitis, we know that this is a chronic disease process. Patients will need chronic medical therapy throughout their disease process, that will include medical treatment such as topical steroids or oral steroids, and may even require sinus surgery in some of these patients.

If we were to try to break down treatment and patient selection, this is how I would kind of look at it. If patient has an acute exacerbation, most of the time in these patients with nasal polyposis they will require a burst of short steroids, maybe even antibiotics. But what you do is try to prevent the polyps from coming back by giving the long-term topical steroids or saline irrigation.

Now if you're not able to treat them with the typical pharmacotherapy, sometimes these patients will need surgery. Not all patients want surgery and not all patients with nasal polyposis can have surgery. So in these patients biologic may be an option.

Now if patients have had sinus surgery and you have difficult time preventing the polyps from coming back, certainly biologic will be a consideration for these patients.

Here is the EUFOREA consensus guideline I had discussed earlier. There was a group of 23 physicians, otolaryngologists, pulmonologists and allergists that got together, and we had to come up with a consensus on when do we use biologics. And the bottom line is that biologics should be reserved for patients with severe nasal polyposis, as seen in the clinical studies that we have seen.

If a patient is given biologic, the next question is is the biologic working. And so these are a list of criterias that you're going to look at to see if patients are responding well. Now some people may respond poorly, some may have excellent response. This is how we have initially described how a patient responds to a biologic. Certainly the EUFOREA consensus guideline will change. It is going to be a living document. In a few years it may be adapted as we know more about how biologic plays a role in nasal polyposis.

So currently I would like to say that we know everything about the use of biologics in nasal polyposis, but we don't. These are some of the questions that we should be asking. Or these are questions that I'm asking myself. Is one biologic better than another for specific patients with nasal polyposis? Will endotype help us predict if one biologic will be better than another?

So another question is should comorbid disease be considered in considering a biologic for patients with nasal polyposis? So if someone has atopic dermatitis or EGPA, will that shift us to using one biologic versus another?

Other interesting questions that we should be asking is how long do they need to be on these biologics? Do they need to be on them for four to six months? Do we need to keep it on forever?

The last interesting question that I think I want to ask the audience is should biologic be used preoperatively or postoperatively?

These are all very interesting questions. Unfortunately, at this time we don't have an answer, but hopefully as our experience with

biologic improves and the research for a biologic in nasal polyposis continues, we should hopefully find an answer to these questions.

Thank you for participating in this self-assessment program. Please remember to complete the program evaluation to receive CME credit.