Jason Barnes:

Hey there. Welcome to another episode of ENT in a nutshell, my name is Jason Barnes. And today we are joined by Dr. Garrett Choby and we will be discussing fungal rhinosinusitis. Dr. Choby, thanks for being here.

Dr. Garret Choby:

Great to be here. Thanks for the opportunity.

Jason Barnes:

I first just want to say that we'll spend a lot of our time talking about acute invasive fungal sinusitis, but there are a couple other topics that we could probably touch on really quickly here. Would you mind first, just starting with a little bit of an explanation of the different types of fungal sinusitis?

Dr. Garret Choby:

Sure. This is a fairly broad topic. Again, we'll focus mostly today on invasive fungal sinusitis, but when you think about this in a larger scale, there's both a non-invasive and invasive forms of fungal sinusitis. Most often described, there are three forms of non-invasive fungal sinusitis. The one we see most commonly is the fungal ball or the mycetoma. Allergic fungal is another version of the disease process, more common in the American South. And then lastly, there's an unusual form called a saprophytic fungal sinusitis, which is pretty unusual. And then with our invasive fungal rhinosinusitis species, there's both the acute invasive as well as the chronic invasive, which is a little bit more rare. And lastly, there's an unusual one that we don't see very often called a chronic granulomatous invasive, which again is more commonly seen in other countries like the Middle East and Africa and less so in the United States.

Jason Barnes:

And will not. We won't focus on the non-invasive today so much. Can you just briefly tell us about chronic invasive fungal sinusitis?

Dr. Garret Choby:

Sure. Chronic invasive, is a bit different from acute invasive in the sense that it usually go on for a long period of time as its name implies. Most commonly described as at least three months or more, and these patients are usually more immunocompetent than those folks that get acute invasive. Perhaps someone who has a diabetes that's fairly well-controlled or a low grade leukemia, or one of those kinds of things. And they do get an invasive fungal process, but it's a very slowly progressive thing. They may not present to them are more advanced with things like orbital findings or a cranial neuropathy. That's more unusual and it's just more of an indolent slowly, progressive kind of thing.

Jason Barnes:

So let's move on now to the bigger topic here, the acute invasive fungal sinusitis. Can you tell us how a patient typically presents with this process?

Dr. Garret Choby:

In this disease process? These patients are uniformly immunocompromised patients. Most commonly, they have either poorly controlled diabetes or a hematologic malignancy. Other scenarios exists like a long-term heavy steroid use, et cetera. But more commonly it's a poorly controlled diabetic or someone

with something like acute leukemia when they present. Usually it's when they're undergoing chemotherapy or in things like a DKA crisis. And they present with things like neurologic findings, unilateral, facial swelling, edema, or other symptoms of sinusitis.

Jason Barnes:

Do you want to talk a little bit more about presenting symptoms? Because as a Resident, this can sometimes be confusing when we get consulted for this, how would you describe the classic presenting symptoms for acute invasive fungal sinusitis? When you get this kind of call.

Dr. Garret Choby:

It can be challenging because there can be a fairly broad set of symptoms that can exist. However, things that are more commonly associated with this are, a patient who is quite immunocompromised admitted again for something like induction chemotherapy. And they all of a sudden out of the blue get progressive symptoms of sinusitis that can be congestion, nasal blockage, pain in one side of face, and then commonly a neurologic symptom or an orbital symptom can also manifest Itself.

Jason Barnes:

And what kind of symptoms would that be?

Dr. Garret Choby:

Certainly things like a blurry vision or change vision, inability to look certain directions when a certain interlock or muscles are involved or things like numbness in a portion of the face from a trigeminal involvement will be the things we look for from a neurologic standpoint.

Jason Barnes:

And oftentimes these consults are performed on the inpatient basis because of the acuity of the patient's health. When we first see these patients, how should we evaluate them? What should we be looking for?

Dr. Garret Choby:

All of these patients in general deserve a nasal endoscopy, especially if our suspicion is pretty high. This disease in most citations most often involves the middle terminal. So certainly attention being paid there for things that look like a dead tissue, necrotic tissue, black tissue crusting will be fairly classic for an invasive fungal species. It can manifest itself anywhere in the nose, but especially looking at those areas of the middle meatus, middle turbinate, inferior turbinate are good areas to look on your endoscopy.

Jason Barnes:

And when we move on to pathophysiology, what exactly is invasive fungal sinusitis?

Dr. Garret Choby:

This disease typically involves one of two species of fungus. The first is aspergillosis and the second one is a mucormycosis. As a matter of fact, this disease used to loosely be called mucormycosis just as a sort of a slang term. The unique thing about these fungal species in immunocompromised patients is that they actually will invade blood vessels called agiovesion.And This leads to ischemia, just like a heart

attack of the tissue. If you will, which quickly then leads to tissue, death, pain, necrosis, crusting, et cetera.

Jason Barnes:

And this might go without saying, but we like to talk about the natural history of disease. What happens if we just don't treat this?

Dr. Garret Choby:

Okay, this is without treatment, a universally fatal disease. So this is a rapidly progressive disease. It can progress over hours to a few days, especially again, in these very immunocompromised patients and will quickly lead to death if untreated.

Jason Barnes:

And what else should we consider on our differential diagnosis, when we're consulted for these patients?

Dr. Garret Choby:

The first thing I would mention in those inpatients, as you mentioned earlier, Jason, is that. This could be a routine sinusitis, a bacterial sinusitis, viral sinusitis, or otherwise. There are some patients whom you may see in consultation for this in clinic as well, who maybe are less immunocompromised. And if this destructive process more so involves the anterior nasal septum, other things could be entertained like GPA formerly known as Wegener's disease entries with drug use like cocaine as well can cause perforations and nasal destruction. And some of these can also have fungal elements superimposed on top of them, which can make a pathologic diagnosis, somewhat challenging. And the last thing I'll mention is, again, with more extensive midline destruction, you could entertain the possibility of a midline destructive lesion, which is an oncologic destructive process, which can also occur in the nasal cavity.

Jason Barnes:

Now, we talked a little bit about what to consider when we first see these patients in terms of physical exam, but can you describe to us the main workup these patients deserve? If you have suspicion for invasive fungal sinusitis.

Dr. Garret Choby:

The first step up in the workup is that they oftentimes will come to you with imaging studies. A CT scan is easiest and quickest to get, and that's probably the initial imaging study in most patients. This usually shows non-specific findings to be quite honest with you, especially early in the process. As this process becomes later, bone erosion is a fairly typical finding you can see, especially around the orbit and TeraGo pelting fossa. But early on this may show unilateral involvement or an early destruction, which could be a tip off for you. We'll talk about MRIs here in a few minutes, but if the patient comes to you with, or without a CT scan and you perform nasal endoscopy and have a high index of suspicion, a frozen section biopsy is the earliest and quickest way to diagnose this.

Jason Barnes:

And when you say biopsy, what are some of the things that we should consider when we're thinking about obtaining a biopsy in these patients?

Dr. Garret Choby:

The first thing to consider is that during your nasal endoscopy, a fairly pathognomonic sign is that they lack some of the sensation in these areas, because again, the nerves have likely been destroyed from the angioinvasive process. So, numbing them or energies is probably less important if it's a true invasive process. Other to think about is that, especially those leukemia patients, they may have significant thrombocytopenia, which can lead to quite a bit of challenge with bleeding during these biopsies. Now, again, if it's really Angioinvasive, the blood vessels have been destroyed and there's less bleeding associated with it. But if it's more questionable, bleeding can be a significant source of consternation for the junior Resident. Who's on consult service.

Jason Barnes:

Fair enough. Now you mentioned MRI. What we're getting around, what we're getting to here is that this is a very destructive process and I imagine needs to be dealt with very quickly. Is an MRI worthwhile in this setting?

Dr. Garret Choby:

As far as a truly diagnostic work up in someone who you have a high suspicion of, an MRI is probably not worth it initially. However, if someone who is more questionable or comes to you from other hospitals who have undergone imaging studies, it frequently is obtained ahead of time. Before you see the patient, it's also can be useful in monitoring the patient long-term. So, after they've undergone debrief and have gotten therapy and monitoring their progress it can be a useful, I adjunct. An MRI scan with contrast is a very good study to investigate for an invasive fungal species. It does have a few classic findings. The first of which is that a post contrast T1 image in routine inflamed mucosa who see a lot of that post contrast T1 signal in that mucosa. However, if there is an angioinvasion and the conscious cannot get to those tissues, they know something would be hypointense post contrast that T1 images, which is a fairly pathognomonic sign for the invasive fungal species.

Jason Barnes:

Now we've talked about imaging workup and the need for obtaining a biopsy to lead to next steps. Before we talk about treatment, are there any ways that you counsel your residents in terms of seeing this patient, these types of patients that leads you to believe this really isn't invasive fungal?

Dr. Garret Choby:

The first thing I would mention is that all of these patients who are immunocompromised deserve a very high index of suspicion again, without treatment, this is a relatively uniformly fatal disease. So, I would have a very high index of suspicion to closely monitor these patients. If you have a high index of suspicion, you scope the nose looks normal, perhaps consider scoping them again, six to 12 hours later to make sure there's not an early progression of this disease process. We actually have some data that we presented recently at, at a, at a meeting, which looks at the development of a model to help to predict this, that can be useful for both Otolaryngologists as well as primary care physicians in some, in some cases.

And Dr. Linda Yin was the one really behind this, as well as Dr. Stokken. And what we found was that with a three or four component model, I'll look at things like a fever or involvement of the

pterygopalatine fossa or Brown imaging studies. As well as things like nasal endoscopy, you can predict pretty well if a patient you're being consulted for, for consideration of acute invasive species is in fact don't have that.

And that was in, I believe a 280 person or so study that we completed here. That data should be published pretty soon, but there are models that can be predicted. However, again, to my junior resident, I would say, have a high index of suspicion and very thoroughly investigate these patients.

Jason Barnes:

Yeah, it sounds like this is not something that should be taken lightly. If there's any suspicion. Now moving onto treatment, what are the main treatment modalities? Once you have a biopsy proven acute invasive fungal sinusitis?

Dr. Garret Choby:

What I would say Jason is that the backbone and the mainstay of treatment is a very thorough surgical debridement to put it quite bluntly. This is a surgically managed disease. There are adjuncts if we'll talk about shortly things like amphotericin B and other anti-fungal treatments, which are important to consider, but really surgeries are mainstay of therapy. This can be challenging because these patients can be quite sick in many scenarios, again, with things like advanced leukemia and low blood counts, but getting into the operating room are soon improvement doing this, is something that should be done on an emergent basis.

Jason Barnes:

And do you find that it only takes one time going to the operating room to get this done?

Dr. Garret Choby:

No, quite the opposite. This usually is an initial, a large debridement followed by multiple repeat examinations in the operating room and repeat debridement when necessary. This again, can be a progressive process. So by taking the operating room and even, in some cases clearing negative margins with frozen pathology, you will still need to take them back. In some of the cases, many times in order to monitor them in, in their disease progression.

Jason Barnes:

And what are some of the medical therapies that can be used with surgical treatment?

Dr. Garret Choby:

The one that should be probably started upfront and very quickly is infiltration, be it an IV anti-fungal therapy. And again, this is usually done in conjunction with many other specialties, including infectious disease, medical oncology, and in many cases, ICU physicians as well. There is a liposomal variant, which is a little bit easier on the kidneys, which is oftentimes considered as well. And this should be ensued ASAP whenever possible, and usually continued for multiple weeks until the patient gets a good response. Other medical therapies are available. Things like voriconazole and posaconazole as well. Those may be reserved for outpatient medical therapy for long-term prophylaxis, especially after fungal cultures, have returned as well.

Jason Barnes:

And there are some nuances to surgical treatment. Can you discuss a little bit about chasing margins? And also what you do in orbital involvement, intracranial involvement, that kind of thing.

Dr. Garret Choby:

Sure. In these are challenging decisions, for many are treating physicians and patients as well. The first thing that I'll mention is that areas such as the pterygopalatine fossa are commonly involved. And if you look closer in imaging studies, this is an area that can, has a lot of highways to enter it in fungi can really jump on those highways. Things like nerves, V2, things like the SPA as well, an entering of the pterygopalatine fossa. So special attention should be paid here to clearing that fossa. And I usually routine these samples this area in most of my IFS cases. Now, when it comes to the orbit, this can be a challenging scenario. We know from many studies that once the periorbital has been breached with invasive fungal species, that is an independent risk factor for a poor prognosis. And I'll mention as well that even with our current medical and surgical therapy, mortality still reaches about 50% in many series.

So it is still a very, very high mortality. But in most studies, there has not been shown to be a survival benefit with oral exoneration when the orbit is involved. So, we do not routinely perform oral exoneration unless there's an outstanding reason why I think would be beneficial in most patients. Dural enhancement is another area that we typically will not resect dura for most cases. And when there's enhancement there we'll rely mostly on our IV amphotericin therapy to try to address those areas. If there is gross intracranial extension involvement of the prank mother brain, that's a discussion with my neurosurgical partners, whether there's any benefit in doing an open craniotomy or other procedure in. If it's at that advanced in most cases, the mortality is very high. It takes a pretty in-depth discussion with the patient and their family and the treating physicians Well.

Jason Barnes:

Yeah, and I don't want to be a Debbie downer, but can you discuss a little bit more, how you talk with patients and families about overall outcomes, complications, and prognosis.

Dr. Garret Choby:

We have a very Frank discussion upfront of the challenging nature of this disease process. There is hope, and there is hope in many scenarios. Some data's shown that reversible disease processes like poorly controlled diabetes may have a better prognosis than things like very advanced leukemia with ongoing chemotherapy, because ideally, you can reverse though the blood sugar and then hopefully they have a better immune system to fight it themselves as well. But again, with mortality, about 50% in most series, it is a very significant and challenging scenario. So, try to have that really upfront discussion. And we also quite frankly have discussed about the morbidity as well. So if this extends into soft tissue of the face or the palette, you're the only way to cure this. If, the part of the patient desires is to resect those things. So we have many patients who are undergoing disfiguring surgeries in many scenarios in order to try to best treat this disease process. That's also something that someone who perhaps is an elderly patient, whereas other advanced comorbidities may not wish to go through at the end of their life.

Jason Barnes:

Well, I think we've had a pretty good discussion here before I summarize this. Is there anything you'd like to add or anything we've left out?

Dr. Garret Choby:

The last thing I'll mention just to reinforce a few concepts is that, this takes a great multidisciplinary care. So, your very trusted colleagues in infectious disease in neurosurgery, agranuloplastic and medical oncology all play a role in this disease process. And, I wouldn't mention that if you're going to go after this thing, with a goal of curing or limiting the destruction of this disease process, you must be aggressive and you must be aggressive early and often.

Jason Barnes:

Well, thanks so much for being here, Dr Choby. I will just do a quick summary here. So acute invasive fungal sinusitis is a serious disease that most commonly affects severely immunocompromised patients. Presenting symptoms are often things like facial pain, rhinorrhea possible, facial numbness or orbital symptoms. Workup includes imaging, but biopsy is what's ultimately required for the official diagnosis and treatment requires quick and aggressive, local debridement and Ivy anti-fungal. And as you said, prognosis is generally not great with up to a 50% mortality rate though, early treatment can actually be beneficial for this patient subset. Is there anything you'd like to add? No, I appreciate the time. Well, it's about time to bring this episode to a close, but before we do, we'll end with some questions as always, I'll ask a question, wait a few seconds to give you the time to pause or simply think about the answer on your own. And then I'll give the answer. The first question is, what are the classic presenting symptoms for invasive fungal rhinosinusitis?

The most classic presenting symptoms for this disease are sinus symptoms such as rhinorrhea and congestion, but it should also include facial pain, numbness possible orbital symptoms, such as diplopia or blurry, vision and fever should also be considered in these things as well.

The question is what is the most classic MRI finding in patients with acute invasive fungal rhinosinusitis? Well, not all patients will present with an MRI and there might always be, might not always be time to obtain an MRI. The classic sign due to angio invasion is a hypo intensity with T1 with contrast. And that happens because the blood vessels have been invaded and the contrast is not taken up into the effected tissue. And for our final question, what is the treatment for this disease? And is there survival benefit to orbital exoneration?

The treatment for this disease is early and aggressive surgical debridement. If cure is the desired outcome for the patient. Additionally, IV anti-fungals are required and should be given in conjunction with your infectious disease colleagues. And finally, once the orbit has been breached, orbital exoneration has not been shown to be beneficial in terms of survival. Thanks so much. And we'll see you next time.