Dr. Jason Barnes:

Hey there, welcome to another episode of ENT in a Nutshell. My name is Jason Barnes. Today, we're joined by rhinologist, Dr. Garrett Choby and skull base neurosurgeon, Dr. Jamie Van Gompel, and we will be discussing clival chordoma. Thank you all so much for being here.

Dr. Garret Choby:

It's a pleasure. Thank you.

Dr. Jamie Van Gompel:

Thanks for having us.

Dr. Jason Barnes:

I will say upfront that chordoma, it's hard to talk about without at least mentioning chondrosarcoma sometimes, so we will be contrasting that. A few points throughout this conversation, but the majority of our talk will be on clival chordoma. Can you tell us, what does a patient present with when they have a clival chordoma?

Dr. Garret Choby:

The presentation is usually quite vague, to be honest with you. That's one of the reasons why they tend to present with large advanced tumors because many of their symptoms may be vague or nonspecific. A number of vital neurologic structures pass close by this area. It's one of the more common findings on initial presentation, is actually diplopia. That's usually from stretching or injury to the abducens nerve, the sixth cranial nerve. Usually, as it passes through dorello's canal, it has quite a long intracranial course. It can be stretched there. Other things are things like headache. There can be facial numbness from trigeminal involvement, but usually it's pretty vague overall.

Dr. Jason Barnes:

Is there a typical patient who's affected by this? What's the epidemiology like?

Dr. Garret Choby:

It's a very rare tumor. Depending what numbers you look at, the incidence is about one in a million patients. It's quite unusual. Usually, it occurs in folks of middle to older adult age, so sort of 50s, 60s, 70s. Although, we've seen the younger patients as well, but more class case in the late and middle age.

Dr. Jason Barnes:

What about any risk factors?

Dr. Garret Choby:

None specifically I'm aware of.

Dr. Jason Barnes:

We're talking about clival chordoma. Before I keep saying clival and clivus through this whole interview, can you tell us what the clivus is? Because I know I had a hard time with this, and still do.

Dr. Jamie Van Gompel:

The clivus is a fusion bone at the base of the skull that's part of the ex occiput and part of the basisphenoid, and then effectively, is the back of the nasopharynx and the back of the oropharynx.

Dr. Jason Barnes:

What's its relationship to sphenoid sinus, pituitary gland, brainstem, that kind of thing?

Dr. Garret Choby:

It is a difficult area to understand anatomically. It's classically broken down into three segments. In the upper one third of the clivus is roughly from the clinoids down to the floor of the sella, and the middle one third is the spheroid parts. That's from the floor of the sella down to roughly the floor of the sphenoid sinus. Then lastly, the lower third is the nasopharyngeal part, and that extends from the floor of the sphenoid, the whole way down behind the nasopharynx.

Dr. Jason Barnes:

With anatomy behind us, what is on your differential diagnosis when you consider clival chordoma, understanding that you might not have an idea that's what it is when a patient initially presents?

Dr. Jamie Van Gompel:

Clival masses can be a lot of different things. The most common things that are not chordomas are chondrosarcomas, but also we see lymphomas in the clivus adenocarcinomas. I'd say the more common finding, when patients present asymptomatically, I get a lot of dysplasias. Bone dysplasias that get sent to me as chordomas, and they can be easily diagnosed with a CT, because they're not typically disruptive, but that's most commonly what I have to differentiate from a chordoma.

Dr. Garret Choby:

The one thing I'll mention as well is that we've seen a few of these where there are actually intranasal tumors with extension, but it's subtle in the nasopharynx, nasal cavity in larger portion of the clivus. We've seen a few nasopharyngeal carcinomas that have extended there, and we thought an issue was going to be a chordoma, when in fact was a mucosal tumor with extension into the clivus.

Dr. Jason Barnes:

Can you tell us a little bit about the pathophysiology? What is a Chordoma?

Dr. Jamie Van Gompel:

Chordoma is derived from notochordal remnant. What we think of the notochord is ultimately when the spine develops, it becomes the discs in between the vertebral bodies, and there's some... It's hard to describe a picture, I suppose in this format, but that can go all the way down from the coccyx sacrum, all the way through the subaxial spine, and then in the clivus, it does some very interesting things. It takes us like bend into the inferior clivus and then, as it comes back up, it swings back more towards the posterior aspect of the clivus. Anywhere along that pathway, if those cells don't deteriorate or aren't told to become disc material somewhere, they can become a chordoma. There's discussion as to whether or not benign notochord remnants lead to these tumors. We don't know if that's true, although there are reports of having benign notochordal remnants within chordomas and there are different

pathologic diagnosis. There is a cell type that I can't frankly say. I know Dr. Choby has been practicing, that's responsible for this.

Dr. Garret Choby:

Practicing because it's a board exam question and it is the classic soap bubble-like appearances on histopathology, and we're going to give it a go. Physaliferous cells. Dr. Barnes, how did I do? How did I do?

Dr. Jason Barnes:

Sounds great to me. When we talk about chordomas, they're not all located at the skull base, like you said. What's the breakdown here?

Dr. Jamie Van Gompel:

The majority are between either the clivus or the sacrum, and we typically say they're the third up in the clivus. They're a little bit over a third down on the sacrum, and a third anywhere else in the spine.

Dr. Jason Barnes:

Just to back up a bit, Dr. Van Gompel, there is a certain aspect of this tumor that's become quite relevant. Can you tell us more about that?

Dr. Jamie Van Gompel:

Yeah. Absent of trying to identify the cells under the microscope. Right now, it's more important to actually stain them from brachyury. When we really had a hard time distinguishing between chondrosarcoma, benign notochordal cell tumors, some other types of tumors, and this tumor really gets down to them being brachyury positive. I think we'll cover it a little bit later too yet, but now a lot of this experimental therapies are actually potentially using brachyury as a targeted therap. Thankfully, there's not as much discussion as to what types of tumors they are based on. What the pathology shows, it is actually stain that can definitively diagnose this tumor.

Dr. Jason Barnes:

The reading that I've done about this topic. I can't say that it's entirely clear to me, is this a malignancy?

Dr. Jamie Van Gompel:

It's absolutely a malignancy. People die from this. They have metastatic disease from this. In a patient that has a chordoma, yes, we can cure them with a very good resection, but unfortunately, a lot of these patients will die from that disease and they're locally progressive and also can metastasize elsewhere.

Dr. Jason Barnes:

When a patient presents to your clinic, like I said, you don't necessarily suspect this diagnosis, and maybe they'll present with some imaging that's leaning you towards that diagnosis. Can you tell us about the imaging findings, what you would hope to obtain in terms of imaging studies and what you would see?

Dr. Garret Choby:

I'll start here. As opposed to many other sinonasal tumors, this is usually not accessible for a biopsy, unless it has extensive involvement of the nasal cavity and is quite locally progressive.

Dr. Jamie Van Gompel:

You should not biopsy this lesion in clinic because it can seed and you have to hopefully keep this contained. It's a very important aspect of this.

Dr. Garret Choby:

Yeah. Agreed. There are reports on the out there even from surgery, a seeding tumor elsewhere. But this is a diagnosis largely initially made on imaging studies. There's some pretty characteristic imaging studies that you can see. Most folks come with at least a CT scan, and the CT scan usually will show a very locally aggressive and destructive lesion in the clivus. Typically, it's a midline lesion. Again, arising the notochord remnants. That helps us to differentiate for other things like chondrosarcoma, which look very similar, but are typically off-midline. MRI scan is also very important. One of the telltale signs on MRI scan of chordoma is hyper intensity on T2 signal, and that's not the same as many other tumor types.

Dr. Jason Barnes:

You also want to comment on there?

Dr. Jamie Van Gompel:

Yeah. Just again, getting back to this concept of them being lumped previously with chondrosarcoma and chordomas. The reason why that is, is both were lesions in the clivus, maybe not midline lesions in the clivus, but lesions on the west that were T2 hyperintense. The CT is important because in a lot of condrosarcomas, they'll get deposition of calcium within them, and they'll have this specific bony appearance. Now, that can happen in chordomas, so that it can fool you sometimes because chordomas, although commonly are locally destructive, they can be destructive enough to have bone fragments within them, and they can look a little bit like chondrosarcomas. Then, notably both are also contrast enhanced. Now, most of the other lesions that we mentioned before in the differential diagnosis are different than that. They're not T2 hyperintense mainly. That's the primary thing you're looking for.

Dr. Jason Barnes:

Something maybe we should have talked about during pathology, but can also be fit here in terms of planning and what you expect, what are the different types or subgroups of chordoma?

Dr. Jamie Van Gompel:

Most tumors are going to be classic, or otherwise known as conventional chordomas. There is a separate subcategory that is less and less being diagnosed, and that's chondroid chordomas. They still exist, but because again, of that bruchyury being able to differentiate these from chondrosarcomas, people are not using that term as frequently and most of those are falling into the conventional category. Then, there's a de-differentiated or sometimes called atypical chordoma, which demonstrates a higher mitotic count within them. It is thought that they're probably going to be more aggressive tumors, although they're so uncommon that it's hard to know for sure if that's the case.

Dr. Jason Barnes:

When you suspect this tumor, mainly I guess you suspected on imaging, what is your approach to management?

Dr. Jamie Van Gompel:

Getting back again to what we're talking about earlier. Again, biopsy is not a good idea. You should have an extensive surgical plan to manage the lesion in a way... First off, if you can get completely around it with a margin, then you should. Sometimes we see these asymptomatic lesions in the clivus, and we're able to drill around them, reduce contamination, and in fact, that's what happens in the sacrum, is that when these are suspected, they do a needle biopsy to confirm it, but the pathway of the needle biopsy's resected with the lesion and they do a one centimeter margin around this. These can still recur despite that. There's a mystery with these particular tumors in that despite that aggressive resection in the sacrum, those tumors can be more aggressive than even intralesional, which is what we commonly do in the clivus removal.

The thought is that those tumors present so much larger than they do in the nose, because they become symptomatic quicker in the nose. In the nose, however, the goal primarily, it's uncommon that we can get around the lesion and take it all out, is to get an intralesional resection, and remove all tissue that it's been touching. But obviously, when it's touching the carotid arteries or the nerves, we don't do that. Our goal is to have an MRI negative resection and that's important because oftentimes we will do either intraoperative MRI, or immediate post-operative MRIs, and if there is positive areas that we can remove, we will go back and take those out.

In fact, when these patients are sent for proton beam later on, very commonly there'll be a residual area that we're asked to take out, and that's one of the bigger indicators for long-term survival, is having a negative MRI prior to radiation therapy. In some circumstances, we simply can't take all the disease and our goal then is to decompress the brainstem to preserve the brainstem from receiving a lot of high dose radiation with the definitive therapy for this.

Dr. Jason Barnes:

Briefly, can you describe the surgical approach, especially for our ENT listeners, of that transnasal approach?

Dr. Garret Choby:

Yeah. Again, the individual goal for a tumor is dictated by what involves in an imaging characteristics, but presuming we're going to do this through an endoscopic endonasal expanded approach, it's a pretty extensive initial approach, this tumor. What we typically do is we'll raise a unilateral large extended nasoseptal flap, and open up all the sinus on one side and tuck that flap into the maxillary sinus.

Dr. Jamie Van Gompel:

Do you mind explaining what you mean by an extended flap?

Dr. Garret Choby:

Yeah.

Dr. Jamie Van Gompel:

We don't mean more forward. We mean the floor, right?

Dr. Garret Choby:

Yeah. Good clarification. When I raise these flaps, I will bring an incision from the [inaudible 00:13:36] along the high nasal septum about a centimeter below the skull base. Once I reach the head of the middle turbinate I'll turn north and bring this entire nasal vault internally to do the mucocutaneous junction, then on the floor and include the entire mucosa, the floor of the nose, into the inferior meatus. This is a huge distal paddle, excuse me. Now, as opposed to most of our transsphenoidal case, where we tuck that in the nasopharynx, that's going to be our side of tumor resection. Again, we'll do a large extended septonasal flap and tuck that into the maxillary sinus for safekeeping during surgery. Then I'll usually also raise a contralateral, a smaller flap as well, and do a similar sinus surgery on the contralateral side to put it into the maxillary sinus.

We'll do a large sphenoid anatomy, open up to the planum, as well as a posterior septectomy. Then, we'll begin to drill down the floor of the sphenoid sinus, in most cases, to get a flush to the clivus. Dr. Van Gompel, I like to use the vidian nerve as well as a marker to lead us back towards the carotid artery. We usually trace that back as well as we drill, and get exposure in entirety. Again, depending where the tumor is involved from the sella to the lower third of the clivus with exposure. One of the challenging parts is dividing the nasopharyngeal soft tissue. This is extremely tenacious, firm tissue. We usually make a midline incision with a needle Bovie and then carefully resect that, and dissect that laterally, but it's very tenacious and stuck to the underlying clival bone as well.

Dr. Jason Barnes:

Following surgical resection, Dr. Van Gompel, you started to talk about this. What's the role of radiation?

Dr. Jamie Van Gompel:

Yeah. There's some recent literature about de-escalating therapy for this, but most people with a diagnosis of a chordoma will be sent to a proton beam therapy center. Now, not everybody believes in that, okay? Some people do still deliver classic IMRT proton-based therapy, some centers still use Gamma Knife to treat the cavity depending on how small the cavity itself is where surgery occurred, but most people are using proton beam and the reason for that is because the dose fall-off curves allow us to achieve a much higher radiation than we would otherwise would be able to achieve with photons. The goal typically is in the mid-70s for treating these, and why proton beam is so important is because they achieve that dose so close to the brainstem, we need a steep fall off curve. Having a high dose is simply because the cells don't seem to be very responsive to the radiation themselves, so delivering a high dose has been shown at least in series, especially from MGH to improve survival and reduce risk of recurrence.

Dr. Jason Barnes:

You have spoken about brachyury earlier today. Can you talk more about that and its relationship with treatment?

Dr. Jamie Van Gompel:

There are a number of experimental therapies, one for increasing sensitivity to radiation and another targeted therapy that are using brachyury because it's a unique thing that's only found in these tumors. It's found when the body's developing, but should not be present in any other cells currently. It's a unique target and I think eventually there'll probably be a therapy based on brachyury. Not that we have the answers now, but that's probably going to be the key to these things.

Dr. Jason Barnes:

How do you counsel patients on outcomes, expectations, prognosis, that kind of thing?

Dr. Jamie Van Gompel:

A lot of it has to do with what we start with and if we know we have a small mid-clival tumor and we get around it, my expectation is that they will potentially go on to 10 years old disease, but you have a nine-centimeter tumor that is about in there going around the carotids and you're debulking, that tumor will recur and I tell them that we have to watch it closely. There's usually a honeymoon period after surgery. For a couple of years, things look great after they get proton beam, and then we are then treating, and the management of recurrent chordoma is even more controversial, right? It has to do with what the comorbidities of each surgery are, but these patients can have a lot of surgery later on, if they have recurrences.

Dr. Garret Choby:

Yeah. With ongoing revision in repeat surgeries as we do somewhat frequently here, the challenges with reconstruction is also challenging in many scenarios with radiated tissue and preoperative tissue. It's a real challenge with these high flow post your faucet leaks to get them stop after multiple revision surgeries in a radiated field.

Dr. Jason Barnes:

What's your follow-up for these patients?

Dr. Garret Choby:

Initially, we see them every few weeks for the debridements postoperatively, make sure that they are healing well, and there's no CSF leak. Then long-term, we typically follow them with an MRI scan. Dr. Van Gompel can comment a little more about that, but usually roughly three-ish months after surgery, then again, six months later on, and six months later on. If it look good or doing well, maybe even then annually or every six months thereafter.

Dr. Jamie Van Gompel:

For the first several years, we do a six-month MRI, and a lot of patients will show some brainstem reaction to the radiation, depending on the size of the tumor. What is also interesting too is that those T2 signal changes that we think are synonymous with tumor, we see that very commonly in residual bone. It is helpful to be very aggressive with bony resection, so that you're not confused by that later on. These are tumors not to be timid on bony removal, to be quite honest with you, but over time, you'll see that the marrow of the clivus will change quite a bit, and it becomes confusing with these.

Dr. Jason Barnes:

Is their morbidity related to extensive bony removal?

Dr. Jamie Van Gompel:

It all depends on where these things are in the clivus. We've been talking this whole time about how these tumors are all the same in the clivus, which they're not. Upper clival chordomas have a different prognosis than lower clival chordomas, and lower clival chordomas themselves, and it's been thought there's many pathways for them to leave the area of origin, but they also can have instabilities. If we do

take down that lower third of the clivus, like Dr. Choby was talking about, there is some risk of having some spinal instability long-term, especially if the apical ligament or the attachment from the bottom of the skull down to the odontoid is disrupted. The real risk starts to be when we have to take out the condyle on one side of that, which is part of the clivus. Then, there's a lot of discussion about whether or not one needs a fusion then.

Dr. Garret Choby:

Also, just briefly mention, the morbidity with the tumor itself or surgery, especially with cranial nerve, so the sixth nerve, the fifth nerve, and then of course the ultimate, the carotid artery, which needs to be worked around very judicially in this area. These tumors almost always have abutment, if not encasement of the carotid arteries.

Dr. Jason Barnes:

I'd like to end with a summary, but before I do, anything you'd like to add that we didn't talk about that would be worth mentioning?

Dr. Jamie Van Gompel:

Having seen a lot of these tumors, I'll say you watch a case as a resident and you see the nice suckable soft jelly material that oftentimes we use. I will say one out of every 10 is a very bloody tumor or firm tumor or a very... Some of these have ceramic type of bone that occurs around. They can be very challenging cases. Again, I know Dr. Choby has mentioned this earlier, but these are cases really not to take lightly and be treated in multidisciplinary teams that have experience, to be quite honest.

Dr. Garret Choby:

Agree, 100%.

Dr. Jason Barnes:

In summary, a clival chordoma classically presents with vague symptoms like headache and possible diplopia, this is a tumor that affects adults in their 50s and 60s, and the pathophysiology includes the kind of path mnemonic cell, the physaliphorous cell, which is a soap bubble-like cytoplasm cell. Chordomas can be divided into classic or conventional chondroid and de-differentiated, though chondroid is kind of falling out of favor. Imaging can include CT to identify any bony erosion. An MRI, most classically, is described with a high intensity T2 signal. Treatment involves surgery, which needs to be extensive, especially in the bony aspect. Then oftentimes, a postoperative radiation is required. Prognosis is dependent on where the tumor is, how large the tumor was and the extent of resection and can be variable. Anything else you'd like to add?

Dr. Garret Choby:

Thanks so much for the time.

Dr. Jamie Van Gompel:

Thank you.

Dr. Jason Barnes:

Thanks. It's now time to bring this episode to a close, but before we do, I'll end with a few questions. As always, I'll ask a question, wait for a few seconds to allow you to pause or think about the answer and then give the answer. The first question is, describe the clivus. The clivus is a sloping midline bone that sits just anterior to the foramen magnum and posterior to the dorsum sellae. It's classically divided into three parts, the upper one-third is posterior to the dorsum, the middle third is posterior to the sphenoid and the lower third is the posterior nasopharynx.

Next question, what is the most commonly affected cranial nerve in this pathology? The most commonly affected cranial nerve here is going to be cranial nerve six, which leads to a lateral gaze palsy. Next question, what are the three classically described types of chordoma? These three are classic or conventional, chondroid, and de-differentiated. Next, what's the classic histological feature of a chordoma? The classically described cell is the physaliferous cell, which is a soap bubble type cell, which is basically a large cell containing vacuolated cytoplasm. For our final question, what is the almost path mnemonic MRI finding of chordoma? Chordomas have high signal intensity on T2, and this is particularly seen in the central aspect of the tumor. That's pretty specific for chordoma. Thanks so much for listening, and we'll see you next time.