Dr. Ashley Nassiri:

Hello. Welcome to ENT in a Nutshell. My name is Ashley Nassiri, and today we are here with Dr. James Netterville to discuss head-neck schwannomas. Dr. Netterville is a Senior Professor of Otolaryngology specializing in Head and Neck Surgical Oncology. Thank you so much for being here, Dr. Netterville.

Dr. James Netterville:

I'm very honored to be with you, Ashley.

Dr. Ashley Nassiri:

Today's talk will focus on head-neck schwannomas, and we have differentiated these from vestibular schwannomas, which were reviewed by Dr. Matt Carlson in a separate podcast episode. While head-neck schwannomas are relatively uncommon, Dr. Netterville has extensive experience treating these tumors through his specialized clinical practice. Dr. Netterville, what are the typical presenting signs and symptoms that patients with head-neck schwannomas describe?

Dr. James Netterville:

Approximately 50% of these people present with a neck mass, it's a very slowly growing neck mass, and so they eventually notice it or their family notices it. Because of the propensity to image patients now, about 50% of the patients are identified because they were imaged for some other reason, evaluating some other head and neck symptom, so they're silently identified. They can often be very large, even though they're silently identified.

If we look at specifically vagal tumors, a small minority of those patients present with voice changes, secondary to rare paresis, or very rarely a paralysis. When one does present with a paralysis, you got to rule out a vagal paraganglioma as well because their paralysis right of the paraganglioma is significantly higher-ed around 25%. If the patients present with a sympathetic trunk tumor then probably 40% of them will present with some degree of the Horner's triad, they are often surprised when we point out the mild ptosis or meiosis is they have not noticed it.

In evaluating these patients, it's often hard to pick up the ptosis in an animated patient because they're moving their head and neck and their facial expressions so much during your exam. So you've got to train yourself to ask the patient to sit very still and observe their eye exam. It is often much more noticed in pictures of the patients when you take them. You also have to realize that meiosis is a little harder to find in people with darker eyes than folks with light colored eyes, rarely these tumors present by the dentist picking them up. Lesions in the very high parapharyngeal space can be amazingly asymptomatic. And on the dental exam, the pallet being displaced over toward the midline is noticed. And they're often sent to you very quickly after that.

When we look at tumors of the cervical and brachial plexus that present in the neck, they rarely have neural deficits and they're most often present with just a slowly enlarging mass. And the same is true for facial nerve schwannomas. They rarely have symptoms they present and have to be in, or usually are identified as a parotid mass until they're looked at very closely on MRI.

Dr. Ashley Nassiri:

So how common are these tumors?

Dr. James Netterville:

No, that's very hard to decide. They are so rare that a busy Head-Neck Department may only see one to two per year. So it's really hard to find a true incidence in the literature. I suspect many of them are treated and never reported.

Dr. Ashley Nassiri:

If these tumors are so rare, how have you developed a practice that sees more than one to two tumors a year?

Dr. James Netterville:

I'll try to make this brief. In my 34 years, working in Head and Neck Surgery, I experienced these tumors as early as 30 years ago, we were taught at that point to resect the entire tumor. The first young lady that I performed enucleation on was a 19 year old college student opened her neck. There were vagal fibers displayed across the surface. And my training said, cut out the nurse. I stopped and called a very famous doctor, Dr. Jack Gluckman and said, "Jack, what do you do in these?" He said, "I've never published my series, but I have been peeling the nerve off or enucleating the tumor for a few years, and I haven't seen a recurrence yet."

So I started doing that about 27 years ago, and I would see one to two or three patients a year, like any other head and neck surgeon until Social Media developed and has had a huge impact on rare diseases. So my patients and others proliferate a Facebook site and other sites where patients go to seek healthcare advice now, and now because of this and because of our very good success with enucleation of tumors, we probably see one to two or three patients a month, basically out of social media referrals.

Dr. Ashley Nassiri:

Out of that group of patients, have you identified any specific risk factors?

Dr. James Netterville:

In review of our series so far that's over 100 patients, we cannot find any common risk factors that these patients share.

Dr. Ashley Nassiri:

Is there a specific or typical age range that patients present with these lesions?

Dr. James Netterville:

If we discount the children that present with malignant schwannomas, from other diseases, our series ranges age 14 up into the 80's. A significant number of these patients present in their twenties and thirties. However, the vast majority present the fourth and fifth decade of life.

Dr. Ashley Nassiri:

So when you first evaluate these patients in clinic, what are you looking for on exam?

Dr. James Netterville:

The vast majority of these patients come to us with scans in hand, they've already been evaluated. They mail their scans to us. So we have a pretty good idea of the tumor location and possibly the nerve of origin. So we are already starting with a good base. So the exam begins is I asked the patient to give me

a summary of their history. As they communicate for the next five minutes, I'm subtly watching their eyes discover the ptosis or meiosis. I am listening to their voice to assess weakness and nasal quality indicating a palatal weakness. I'm listening to their articulation to assess for tongue paralysis and I'm watching their swallowing as they speak to assess from mild aspiration, or if they turn their head, when they're swallowing, that would indicate an unconscious compensation for unilateral pharyngeal weakness in these patients. It always amazes me how much we can discover by carefully listening to the patient and observing them during our initial conversation before we ever touch the patient.

I then perform a methodical exam of the potentially of all cranial nerves based on the tumor location, on the scan in the superior pharyngeal lesions, the different nerves that this could arise from would be the sympathetic or the vagal commonly, or less commonly the hypoglossal glossopharyngeal spinal accessory, or the palatal branch of the 10th cranial nerve. So our exam is going to be focusing on their eyelids, their pupils, that palate, their tongue, their pharyngeal sensation, shoulder function, and vocal cord function to discover the nerve of origin. In a patient, we're obviously going to examine the oropharynx to determine if there's oropharyngeal impingement. We talk about these patients is asymptomatic, but a moderate number of these patients with severe deviation of their palate present with significant snoring and sleep apnea. This is a real factor in deciding whether to observe or enucleate otherwise "asymptomatic tumor."

If we look at the ones in the lower to mid to lower neck, the majority of those are vagal or sympathetic. There is no other nerves to arise from there. So then our exam concentrates on the eye and laryngeal exam, rarely if you palpate one of these tumor and the patient starts coughing, it is likely a vagal tumor. If the scan indicates a cervical plexus, then we certainly evaluating the sensory aspect of the head and neck to discover which nerve root it comes from. And if the scan demonstrates a brachial plexus tumor, then we're going to go completely examine the sensory and motor function of the arm and hand.

Dr. Ashley Nassiri:

That's a very thorough examinationing clinic.

Dr. James Netterville:

It's critical as most of these patients arrive to see us, they have been scared to death by someone else that they have a huge tumor in their head and neck, and they're going to get all their nerves cut out and they're not going to speak or eat the rest of their life. So a part of what we're doing is reassuring these patients that they have a very slowly progressing benign tumor that we can help them live with.

Dr. Ashley Nassiri:

Well, you perfectly led right into the next section, which is pathophysiology. Can you describe what a schwannoma is of?

Dr. James Netterville:

Schwann cells produce the insulated myelin sheath that in cases the nerve. So I explain to patients, the Swan cell is like the plastic around the copper of the cable that's going to your computer or your light in your home. So if the tumor starts growing from the Schwann cells, it expands off the surface of the nerve fortunately, instead of engulfing the axon fibers, it grows on the surface of the axon fibers. And when we look at this, we can see a fairly encapsulated tumor with all of the axons or nerve fibers draped across one of the surfaces.

Dr. Ashley Nassiri:

How has the schwannoma different when we compare it to a neuroma?

Dr. James Netterville:

Neuromas are usually smaller tumors and they actually arise from the nerve cells themselves. So the nerve is completely encased in the lesion. And as we've just noted, thank goodness the schwannoma, the nerve fibers are draped over the surface and really not a part of the tumor at all.

Dr. Ashley Nassiri:

So what do schwannomas look like on histology?

Dr. James Netterville:

On histology, these are biphasic tumors with the Antoni A and Antoni B, which is the highly ordered cellular component, the Antoni A, the palisades and otherwise known as Verocay bodies; and that's mixed in with the myxoid hypocellular component. The Antoni B. When we look fortunately these have a capsule, and if you look closely, you can see the axons of the nerve of origin located on the surface, but not involving the tumor. The pathologist, like to note that there's a very strong immuno reactivity to S100. These can be found almost anywhere in the body and they're histopathologically very similar to the more common vestibular schwannomas that my neurotology colleagues treat all the time.

Dr. Ashley Nassiri:

When we look at these tumors in the neck, which nerves do these usually involve?

Dr. James Netterville:

If I look at our series, let's go back to a paper in 2014, where we looked at 43 head and neck schwannomas. We excluded the facial nerve at that time and since then we've had about 10 patients with facial nerve schwannomas. At that time, we had 20 vagal tumors, 13 sympathetic tumor, six in the brachial plexus, two in the cervical plexus and two patients with no major neural involvement. Since that publication and partially due to Social Media, we now have a series of way over a hundred patients with head and neck schwannomas and other sites that have now shown up, we've had two that occurred in the floor of the mouth, on the lingual nerve, two on the hypoglossal nerve, one on the superior laryngeal nerve, and several on the spinal accessory nerve. So we're seeing virtually every nerve in the head neck can be involved.

Dr. Ashley Nassiri:

Is there any risk for malignant transformation in these tumors?

Dr. James Netterville:

I have not seen that in our series of patients presenting with this more enlarged form of isolated schwannoma. It can be seen in children with von Recklinghausen disease, as they present with a small schwannoma that has a very high likelihood of malignancy.

Dr. Ashley Nassiri:

So when you evaluate these patients in your clinic, what other head-neck masses that are located in these spaces, do you consider on your differential?

Dr. James Netterville:

Certainly the number one tumor to differentiate is the paragangliomas because they arise from the same nerves and certainly on imaging, we can usually tell the difference, especially CT scan, which we'll talk about in a few moments. Neuromas are much rarer, and they're usually much smaller. If we look at the more common lesions, just the parapharyngeal space lesions, which are pleomorphic adenomas, lipomas, other salivary gland diseases that present as a mass, rarely lymphomas can present in this region. The malignancies, usually by the time they get this large are fairly symptomatic and it's easy to differentiate those.

Dr. Ashley Nassiri:

When you're doing your workup for these patients, do you regularly obtain imaging?

Dr. James Netterville:

People think that the MRI is the most valuable scan for head-neck lesions, but in this situation, a CT with contrast is far more valuable. These lesions do not enhance with contrast on a CT scan so we can rapidly differentiate them from a paraganglioma. An MRI with gadolinium is useful, but the tumors actually enhance with gadolinium and contrast, and it leads to many radiologists to falsely interpret these as vascular in nature, which confuses everyone.

Dr. Ashley Nassiri:

What does a schwannoma look like on a CT scan?

Dr. James Netterville:

It's usually a well-defined, often ovoid slightly football shaped mass. They're avascular, so they don't really absorb the contrast on the CT scan, which is very valuable. Commonly schwannomas have a lot of cystic fluid and multiple little spots. So even on a CT scan, you can see these hypodense areas of cystic fluid. They displaced the vessels, and we'll talk about that to some degree, whether they're a vagal or a sympathetic lesion. If you look at the position of the vagus nerve related to the carotid artery and the jugular vein higher in the infra temporal fossa, it lives between the two. So as it grows, it displaces the internal carotid artery into the nasal pharynx or medial and anterior, if the tumor rises from the vagus nerve, it also pushes the jugular vein posterior and lateral. So the carotid and the vein are separated by the vagal tumors.

If we look at the position of the sympathetic trunk, it lives medial to the carotid sheath. So as he grows, it typically pushes the carotid artery, anterior and lateral in the vein is anterior and lateral as well, and often these are adjacent to each other. Now, as every young astute doctor knows, we can't say always. And so these are rough guidelines, but I have seen these tumors forget to read the book and do not present in their usual fashion. So even though we think that one may be a vagal or a sympathetic way, we never actually know until we're in the operating room, looking at the nerves.

Dr. Ashley Nassiri:

What are some of the characteristics that we see on MRI for these teams?

Dr. James Netterville:

Again, they're well-defined and ovoid mass, they are ISO or hypointense on T1 and T2. On T2, we can see the cystic component that reassures us, that what might be thought of as flow voids is really just the

fluid component of the tumor. They enhance on T1 with gadolinium, again, which leads to a false diagnosis of a vascular tumor or a paraganglioma at times. They're a little more homogeneous than the paragangliomas without the typical half flow voids that we see in there.

Dr. Ashley Nassiri:

So after you've evaluated the patient in clinic and you've reviewed their imaging, what is your approach in deciding whether or not to perform FNA?

Dr. James Netterville:

In general, the diagnosis of these benign lesions is made from clinical history and examination. After we reviewed the imaging, we can see that as a slow growing benign lesion. So we very rarely perform an FNA. One of the problems with an FNA of a nerve sheath tumor is often no cells are extracted and that in an indirect fashion implies that it is a schwannoma as the cells do not release for the needle aspiration.

Dr. Ashley Nassiri:

So we'll move into treatment options next as a brief overview, what are the treatment options for head-neck schwannomas?

Dr. James Netterville:

Well, we've got three basic treatments as we have in most head-neck lesions. We can observe them. We can give radiation therapy to them, or we can perform surgical excision, which most of the time now is a surgical enucleation of the tumor.

Dr. Ashley Nassiri:

How do you counsel patients about their options?

Dr. James Netterville:

As we first sit with the patient, one of the most important things you can do is to reassure them that they have a very slow-growing benign tumor, which will not urgently affect their life. Most have been alarmed by things that they have read or may be inexperienced physicians. They have discussed this with, I tell them that we need to fit the treatment, their social calendar. We need to work this into their life so that we can even observe these for years, if we need to. Most patients are very alarmed in trying to change their entire life based on this tumor. So after that initial discussion to reassure the patient, then the counseling depends on the nerve of origin. Certainly, if it is a vagal tumor, I discuss the odds of a paralysis or a paresis. We discussed their effects on speech and their effects on swallowing.

When I looked at our first 20 patients with vagal schwannomas, we had good follow-up on 16, after enucleation, 50% of those or eight had normal vocal cord function and a normal voice. In the next seven, they either had a vocal cord paresis or paralysis, but at one year they had an excellent voice. And only one of that group that I have to perform a medialization two years later. So we can explain to them, with the enucleation, they have very good odds of having excellent voice outcome and therefore swallowing outcome that goes along with that. If the patient presents with a sympathetic tumor, our counseling will be to discuss the Horner's syndrome and its outcome. We're going to discuss the ptosis, the meiosis and the anhidrosis. Although we, as physicians see a Horner's syndrome is a minor change in the overall quality of life. It can be very distressful, especially for young females.

Also discuss first bite syndrome with the patient, noting that they may have mild to moderate pain when they eat for a number of months after the procedure. Depending on the age of the patient and their comorbidities, their functional status, as well as their life's goals. We decide whether to observe or go on and perform enucleation on these patients. If you look at two extremes, I saw a 16 year old patient with a six centimeter tumor in her infratemporal fossa. She had been seen by five other major universities, four had suggested observation. One had suggested surgical resection of the nerves. But if you practically look at a 16 year old who has already grown a six centimeter tumor, this child is going to have to deal with this someday. This is not something we can really continue to observe. So in that patient, we would recommend an enucleation.

If we look at patients that are older than 60, and it's really hard to put a number on at what age we started observing tumors, then we look at the mini modifying factors. An extremely healthy 60 year old patient with a large tumor and severe sleep apnea, we're going to enucleate the tumor. If they have a very large mass, that's very cosmetically disturbing. We're probably going to enucleate the tumor. If they present with vocal cord paralysis already, and it's a large mass, we're probably going to nucleate the tumor. However, in the vast majority of people, older than 60 or folks that are relatively unhealthy, we're going to observe these. If we look at another extreme, a 44 year old patient with a 6.5 centimeter tumor, he was a poorly controlled diabetic. He had already had a coronary artery bypass grafting. It had multiple stents, then we're certainly not going to operate on this patient because his longevity is in question.

Dr. Ashley Nassiri:

So if we decide that observation is the best option at the time for the specific patient we're evaluating, what does follow-up look like?

Dr. James Netterville:

Well, there's two groups of patients that come to see us, the first is they've had one initial scan it's initially discovered, and we don't have any history of the growth of the tumor. In those patients, if we elect to observe their patients, then I repeat the first scan, six months after the initial scan, this rarely ever shows growth. So as we see no change in these two scans, then we set the next scan one year later. It's usually only by four or five years that we can really see the one to two millimeters of growth per year. In the other group of patients, they've had multiple scans and multiple opinions before they come see us. So we already have the growth rate or the history of the tumor. And in those patients, if we choose to observe those, then we get a scan once a year, probably that could be stretched out longer. But I explained to each of the patients are scanned once every year, it's not only helping them, but it's allowing us to collect very valuable data in order to inform other patients of their options.

Dr. Ashley Nassiri:

So we've talked a little bit about surgical enucleation. What exactly does that procedure involve?

Dr. James Netterville:

As we tried to decide how to approach these tumors initially, and this is based on if it is a young female versus an older male. In the younger female, where cosmesis is very important, we can perform hairline incisions to assess the tumor. It's very important to note that this is not about the cosmetic nature, but if one can perform a cosmetically sensitive incision and still do the exact right operation, then that's a consideration. In patients that have tumors in the superior temporal fossa, we were going to perform a limited skull-based approach. We're going to take down the digastric, the stylomandibular ligament in

order to really gain visibility of these tumors. Most all of these patients who are going to have neuromonitoring so that we can test the vagus and even the hypoglossal will stimulate well, even though we're not monitoring the tongue.

Once we have exposed the tumor, whether it's in the infratemporal fossa, the mid, the lower neck, our next major goal is to map out the surface of the tumor. If we're fortunate and we open the neck and the vagus nerve is obviously adjacent to the tumor and it's of sympathetic origin, then neuromonitoring does not help us to identify where the sympathetic fibers are. So with magnification, we carefully examine the surface and often we can see the neural branches. Then we're going to roll to the side of the tumor and carefully open through the capsule. I usually open with a 15 knife blade very carefully until I can see the final layer. And then I often cut through that final layer to see the meat of the tumor that shows me I'm as deep as possible. There's no evidence that opening one of these results in recurrence.

If it's a vagal or hypoglossal tumor, then we can use a map out the surface very well with the nerve monitoring, and then find a region that we can open without disturbing these nerves. The next part of the dissection can be very gratifying if it's an avascular plane and quite a nuisance, if it oozes. We're taking a blunt object, such as a freer or a number nine and carefully dissecting out the entire plane around the lesion. And lesions that we can see most of the top and the bottom of it, then you can almost always enucleate them whole taking out the entire tumor. If it's a very large tumor extending up to the skull base, then it may be wise to open inside the tumor and debulk a significant amount of the tumor before we enucleate it. This could be much more gentle on the nerves as we'd enucleate the tumor.

Dr. Ashley Nassiri:

Great, thank you for that overview. If we decide to go with our third option of radiation for a patient, what does that schedule look like?

Dr. James Netterville:

In the rare situation that a patient elects radiation therapy and there's two options for this one is stereotactic radiation therapy, where they go in for one or two sessions targeting the tumor. And the other is external beam radiation, where they receive about 5,000 units of radiation over about 25 treatments.

Dr. Ashley Nassiri:

So next we'll move into outcomes and prognosis. And we already talked a little bit about the risks of surgery, but how do you go ahead and counsel patients on prognosis and outcomes of surgery? And what's the risk of recurrence?

Dr. James Netterville:

There's really no long-term follow-up on patients in the literature that helps us to answer that question. If I look at our series, I have not seen a patient return yet with a recurrent tumor that we have initially operated on. I've seen patients go away and several years later have a scan and it is read as a recurrence. But when we really look at the scan, it's a three or four millimeter glowing area, which is probably just the residual nerve that's glowing. I've had up on patients for 10 and 15 and 20 years, and none have had significant recurrence yet. I suspect if a patient that we performed enucleation on here at Vanderbilt did have a recurrence. I suspect we would hear about it from our colleagues in the country. Also tell the patients, if this tumor does grow back slowly, and you're 30 years old now, and we

enucleated and saved your voice and we get a slow recurrence over 30 years, then that would be a tremendous success as we may have significantly different options to treat these 30 years from now.

Dr. Ashley Nassiri:

So it sounds like most of your patients have very long-term followup. How long do you follow up your patients?

Dr. James Netterville:

I will follow patients as long as they will put up with me. I begged them to continue getting post-operative scans for years to come. So we have a significant series of these patients who do not come back to see us, but mail a scan to us once a year. I have patients that I know of that are out 20 years with no recurrence. The problem is most of these patients after four, or five, or six years move on with life, they don't want to pay attention to this and we lose direct follow-up with them. But as I said earlier, I suspect that at 15 or 20 years out, if a scan was performed and they had a recurrence that we would hear about it soon.

Dr. Ashley Nassiri:

Well, I think that just about sums up our discussion of head-neck schwannomas. Thank you so much, Dr. Netterville at this point, I'll go ahead and give a summary of our discussion. Head-neck schwannomas or benign nerve sheath tumors of the Schwann cells that are responsible for making myelin sheaths for nerves. Most commonly, they involve the sympathetic chain in vagus nerve in the head and neck and can extend to the infratemporal fossa and jugular foramen. The differential diagnosis includes paraganglioma, lymphoma, pleomorphic adenoma, and other masses found in the infratemporal fossa or pharyngeal spaces. Workup includes physical exam with special attention to the sympathetic and cranial nerve functions.

A nasopharyngeal examination is completed to check true vocal fold function and imaging, including CT or MRI are completed to confirm the diagnosis. If the imaging and history are consistent with schwannoma an FNA is generally not needed. Treatment usually consists of observation or surgical and nucleation of the growing tumor. Some patients opt for radiation for vagal schwannomas. Surgical enucleation aims to preserve nerve function by leaving the capsule attached to the nerve and removing the internal tumor component. Overall, the outcomes are very favorable for these patients with rare complications that may include weakness of the nerve associated with the tumor. Long-term followup with imaging is recommended for these patients. Dr. Netterville it's been an absolute honor interviewing you about this topic. Thank you so much for your expertise. Is there anything else you'd like to add?

Dr. James Netterville:

If we look at the change in treatment options for these benign tumors over the last 30 years, we've gone from a period where schwannomas in paragangliomas were seen as evil masses. That must be resected, including all their nerves. We've learned that both in schwannomas and paragangliomas, they are a benign very slowly growing tumor that often do not affect patients for many, many years. So we have to outline a treatment plan that takes this into account. And in schwannomas, we have this wonderful option of enucleation that can preserve nerve function. So I'm thrilled that we're seeing patients now, that we are preserving nerve function, and giving them a treatment option that can allow them to have a more normal life. It is a tremendous honor to hang out with you this morning, Ashley, and hopefully this podcast will be useful to our colleagues out there.

Dr. Ashley Nassiri:

Thank you, dr. Netterville. It's now time for us to bring this episode to a close, but before we do, I'll go through some questions as always. I'll ask a question, wait a few seconds. So you can think of an answer on your own, and then I'll give the answer. First question. Describe the characteristic findings on physical exam for patients with a vagal or sympathetic schwannoma. For vagal schwannomas, we typically see well-defined from neck masses along the path of a vagus nerve and potentially vocal fold weakness. For sympathetic schwannomas, we can see a Horner syndrome and potentially extension into the parapharyngeal space on oropharyngeal examination. Next question, what vessel displacement patterns are typically seen in vagal versus sympathetic schwannomas. Vagal schwannomas generally displaced the carotid artery, medially and anteriorly and splay the carotid and internal jugular vein. Sympathetic schwannomas generally displace the carotid artery laterally and anteriorly.

Third question, what are some indications for surgical enucleation of these schwannomas? Surgical enucleation is generally recommended in cases where tumors are growing or symptomatic in younger patients. In some cases, patients desire to have the tumor removed for cosmetic reasons. Last question, describe the vagal schwannoma and enucleation technique. Importantly, even in cases where a sympathetic schwannoma suspected a vagal nerve monitor is set up as intraoperative examination sometimes reveals a vagal schwannoma. During the approach, the vagal nerve and surrounding nerves are identified and traced out to identify the source of the tumor. While in common, it is sometimes difficult to identify which nerve is associated with the tumor itself. Next, the exposed portion of the capsule is examined and the nerve monitor is used to map out the location of the associated nerve in order to prevent injury. Once an area of capsule without nerve involvement is identified a long incision on the capsule is taken down to the layer of the capsule closest to the tumor.

The tumor is then carefully shucked out of the capsule, leaving the capsule and associated nerve intact. In general, the tumor is removed in block if possible, but internal decompression is sometimes required for very large tumors. Once removed the space is examined to ensure complete tumor excision and neural integrity is confirmed using the nerve monitor. Well, folks that concludes our show. Thank you for listening to ENT in a Nutshell, and we'll see you next time.