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Cranial Base Disorders: Etiologies, Surgical Approaches, and Research Innovations

Narrator:

Welcome to *Medical Breakthroughs* from Penn Medicine: Advancing Medicine through Precision Diagnostics and Novel Therapies.

Mr. Birnholz:

You're listening to ReachMD. I am your host, Dr. Matt Birnholz. Joining me are Drs. John Y.K. Lee and Jason G. Newman. Dr. Lee is Medical Director of the Gamma Knife Center and Associate Professor of Neurosurgery and Associate Professor of Otorhinolaryngology Head and Neck Surgery at the Pennsylvania Hospital. Dr. Newman is Associate Professor of Otorhinolaryngology Head and Neck Surgery at the Center for Cranial Base Surgery at the University of Pennsylvania. Today we'll be talking about cranial base disorders.

Drs. Lee and Newman, welcome to the program.

Dr. Newman:

Thanks for having us.

Dr. Lee:

Hello.

Mr. Birnholz:

Why don't we start with defining the conditions and disorders that fall under this cranial base classification? Dr. Lee, can you lead us off?

Dr. Lee:

So, there's a diverse pathology that we treat, but in general, what we are talking about today are tumors that are difficult to access from the top of the head or superficially from the face or nose or ear. These are deep-seated tumors that traditionally have been considered very, very risky for surgery.

Dr. Newman:

I would add that the cranial base is really the space between the brain and everything below it, including the face and the ears, so it's kind of, as Dr. Lee mentioned, it's a very broad space that anteriorly is defined between the sinuses and the brain and laterally is defined between the temporal lobe and the middle or/and inner ears.

Mr. Birnholz:

Interesting.

Dr. Lee:

I guess another way, also, of thinking about it is because it's the base, it's holding up the brain, so any structure that is holding up the brain, but also, I guess the other way to think about it is a lot of other things come from the brain down into the face and the rest of the body, and all of the important nerves are going down through the cranial base in order to get to their respective parts.

Mr. Birnholz:

I see. And I think when a lot of people hear cranial base disorders, majority they think tumors, cranial base tumors, but it's not only tumors, is it? There are other disease states, disorders, that occur within the cranial base that require special expertise to be able to access. Isn't that right?

Dr. Newman:

Yes, that's right. I think probably on the neurosurgical side and on the otolaryngology side, there are a host of things outside of tumors that involve this area, things like CSF -- cerebrospinal fluid leaks is one of them -- pain syndromes, that Dr. Lee probably can talk even more to than I can that have to do with abnormal nerve function at the base of the skull, and a whole list of other relatively rare things that we see in this region.

Mr. Birnholz:

Well, when there is discussion about cranial base tumors, both from the neurosurgery and the ENT side, as well as from general practice sides, it seems like it's among the most complex groups of disorders to be able to treat. Why is cranial base disorder so especially difficult to treat?

Dr. Lee:

There are a few factors, but number one, the prototypical diseases that we tend to treat are generally benign tumors. They are slow-

growing tumors. They cause problems by mass effect and by compressing cranial nerves. Consequently, these patients live a long time, and so your surgical outcome is paramount, your surgical skill and, therefore, these are intricate surgeries; they're careful surgeries; they test our skill, our patience, and require the ultimate finesse and dexterity.

Dr. Newman:

I would also say the other part that lends itself to the difficulty is the location of the cranial base, so in several parts of the body, getting to the tumor is not the tricky part. In the cranial base, there are a lot of things that can go wrong just physically getting to the tumor and, traditionally, some of the big open surgeries that we needed to do to get out tumors that were kind of centered between the face and the brain were just getting there was some of the more complicated parts, which is part of what has lent itself so nicely to some of the minimally invasive approaches that help try to do away with the need for such dramatic approaches.

Mr. Birnholz:

And before we even get to the surgical approaches, which is the mainstay on your end and the area where the two of you have so much expertise, what about before it even gets to you? Are there significant challenges in the process of diagnosing cranial base disorders?

Dr. Lee:

I think, in general, because these tend to be benign, they grow slowly; patients have very mild symptoms at first and then gradually start noticing some type of problem. It is remarkable, for example, the classic tumor that Jason and I will treat through the nose and tackling the skull base is a pituitary adenoma, and these can grow to an immense size before a patients even complain. Surprisingly, patients won't even really confess that they have a visual problem until you do formal testing. And similarly, another tumor that I treat is acoustic neuromas, which are skull-based tumors of the lateral skull base, and those patients tolerate the hearing loss for many, many years and dizziness before they get an MRI scan. So, I think it just speaks to the chronicity and the slow growth of these tumors.

Dr. Newman:

Right, and the physical exam on these patients outside of the hands of a specialist is essentially normal, so it's not like something that a primary care doctor is going to easily see on a routine exam unless the patient has a very specific complaint; and frankly, even then, unless a scan is done or some type of testing, usually it's very hard to see what's going on.

Mr. Birnholz:

Well, for those who are just tuning in, you're listening to Medical Breakthroughs from Penn Medicine on ReachMD. I am your host, Dr. Matt Birnholz, and I'm speaking with Drs. John Lee and Jason Newman from the University of Pennsylvania, and we're discussing cranial base disorders.

So, doctors, I'd like to turn then to some of the work that's being done specifically at Penn Medicine and Penn Medicine's approach to cranial base surgery. How is it different from other institutions?

Dr. Newman:

Cranial base surgery has come a long way over the last 1 to 2 decades, and at Penn Medicine we've been on the forefront of helping to push that forward movement. The changes that have occurred have occurred in a few different parts. Probably one of the earlier changes was the movement from open surgery to endoscopic surgery, so the physicians at Penn through both the neurosurgery and the ENT department were some of the earliest teams using endoscopic equipment to do surgery through the nose. Then moving into the next domain, we were looking at using things like image guidance surgery to further help make these surgeries less complicated, reducing the risk of inadvertent damage to structures surrounding the tumors. And then, I'll leave the rest to Dr. Lee because we've been doing some pretty exciting stuff recently, and I want him to talk a little bit about some of that.

Dr. Lee:

Yes, just to reinforce what Dr. Newman just said, the endoscope actually wasn't really embraced by neurosurgeons early on. I think there was a lot of resistance, and I think part of it is that neurosurgeons became very facile with the use of a microscope. The microscope is an excellent instrument. It provides incredible illumination, incredible detail, and you're operating with your 2 eyes in 3 dimensions and you're not encumbered. The problem though is you have to make a big opening in order to see. In order to get the light in there, you have to really take big flaps on the head, big openings through the face, big retractors in order to get to the pathology. So, you can imagine a triangle. We're going all to the tip of that triangle where the tumor is located, but we're opening a big path in order to get there.

The endoscope really changed a lot of that. With the endoscope you just stick the small endoscope through the nostril or through different portals, and all of a sudden you have this brilliant illumination, and it's almost the triangle is now reversed. Your tip of the endoscope is the triangle, and now it's fanning out and you see this beautiful panoramic view of the skull base, but it requires a lot of different skills. The skill sets are a little bit different. You're operating in 2 dimensions rather than 3 dimensions, and so, consequently, Dr. Newman and I were one of the pioneers in pushing the use of the 3D endoscope to improve our visualization. Also, it's just a different way of operating, because we do actually have a little bit less dexterity when you're not making a big path towards the tumor, so that requires new instrumentation, which took time to evolve. And I was very fortunate because I got to see this field develop during my residency, and so I was able to continue that work when I came to Penn, and Dr. Newman and I became early partners in that over a decade ago. So, that's been really one major revolution in skull base surgery that Penn has been a pioneer in that field.

Now, something new that we've also continued to develop is our new Center for Precision Surgery here at Penn, and this piggybacks off of work that was pioneered by my colleague, Dr. Sunil Singhal, and basic premise of this is that we are injecting optical contrast agents, dyes, to help us visualize even better. Now, with endoscopic skull base surgery, we're always looking on a screen, and the benefit of that is that it's computer-processed image as opposed to the raw image that you would see through a microscope. The computer-processed image can be better. Sometimes it has more sensitivity to low light. In other ways it can be worse because if the camera systems are not ideal. Fortunately, one of the nice things is with the use of endoscopes and with the use of computer-aided vision, we now actually can expand the spectrum of what we're seeing. So, what I mean by that is, we're no longer confined to seeing only what is in the visible light spectrum. We can now expand our spectrum and see into the near infrared, and this has really been nice because our dyes are focused primarily in the near infrared range. There's a lot of contamination in autofluorescence when you use dyes in the visible light range, but when we move into the near infrared, which we humans can't see with our own eyes, when we move into that near infrared range, there is almost no contamination in the brain. It's a beautiful view

because the brain itself does not have any natural autofluorescence in the near infrared. And so, when we tied this to our endoscopes, we were able to see more than just the visible. We have an expanded spectrum. We can see more targets of tumor that perhaps would have been unseen in the visible range alone.

Mr. Birnholz:

Fascinating. So, in a way, turning the concept of glowing tumor on its head.

Dr. Lee:

Exactly. That's the pun. We're turning the head upside down or inside out in order to show the tumor that's in the skull base.

Dr. Newman:

Right, and it's really augmenting normal visualization, so it's adding another layer of information to the layers that we have. We have imaging that's coming from our image guidance systems. We have the natural light that's coming from the endoscope that we're using that is attached to digital processing. And now we're having augmented another layer of information coming from this glowing tumor concept.

Mr. Birnholz:

Augmented is a great catch word here, because as I'm hearing the two of you speak about these innovative new treatments, it sounds like some very unique partnerships have come up that your center, the Center for Cranial Base Surgery, for instance, has pioneered, and that there are these new team approaches perhaps required or demanded because of these new methods. Can you talk a little bit about how the two of you work alongside the broader team to help treat patients?

Dr. Lee:

As you're mentioning, this is very much a team approach, and as Dr. Lee reminded me that we've now been doing this for over a decade, a team has to be part of this. This is not a one person or even one department approach and, actually, as time goes on, I think we have even included larger and larger circles of people into this. But the least that you need is a team of surgeons who are capable of helping each other get to and expose and do the surgical approaches that are needed, but frankly, that's only the beginning. We also need a team of people who are pathologists and neuroradiologists and reconstructive surgeons, and a whole team of radiation oncologists and medical oncologists to help with this patient. And I'm sure I'm missing, frankly, a whole other list of people who are involved, but that's only on the clinical side. And then on the research side, there's a whole other set of people, like Dr. Singhal, that Dr. Lee has mentioned. Their level of interest in helping to expose tumor biology or even working with the team on the genetic side to help understand a little more of the gene basis of some of these tumors. So, there really is a very large team approach. I think it's one of the best examples within medicine of how this needs to be done by a group of people who are committed to this category of patients.

Dr. Lee:

Yes, I would agree with that. Many times we meet with different companies, and I'm always very curious, and then I go talk to our

general surgeons and say, “Oh, what are you doing with your laparoscopes? Tell me about that. Show me how many instruments. I’ve seen some of these.” And then I talk to the companies and I say, “Well, can you miniature eyes this? Can you make this a little smaller? Can you do this?” And it doesn’t always happen. The cross-fertilization of ideas and techniques doesn’t always work, but Penn has certainly been very good at this, and Dr. Newman can talk about this in the TORS program in the transoral robotic surgery, which we did collaborate, actually, in 2010 and wrote several papers where we tried to use the da Vinci robot, not just for the prostate, which everyone knows, and not just for the abdomen, which is very popular, but also the Head and Neck Program at Penn was a pioneer in using it in robot, in cancers, of the throat and neck. But Dr. Newman and I worked really hard to see if we could make it work in the skull base.

It's not ready for primetime, and we really have not been able to push that along, but it does speak to the importance of a fertile landscape here at Penn which allows for the creativity and innovation to proceed in order to provide better results and better outcomes for the patients, which even the Center for Precision Surgery, which has recently opened at Penn, the glowing tumor effort, that too is a multidisciplinary collaborative effort now with many different cancer types being targeted, so it is really very exciting.

Mr. Birnholz:

Well, before we wrap up our interview, I just want to get one parting question there for both of you, and I apologize for it's brevity, because I'm sure you could speak on this for a long time, but that's just to get your impressions on some new avenues of research on the horizon into cranial base disorders that the two of you are either working on or particularly excited about from your colleagues? Dr. Newman, maybe you can start us off.

Dr. Newman:

Dr. Lee mentioned robotics, and to me, I've worked with robotics in a lot of other programs. To me, robots are some of the future of surgical medicine but, as Dr. Lee also mentioned, they're not ready for primetime in this body part because we're still at the phase where robots are barely able to get under 8 millimeters of size, which is, as you can imagine going through the nose, that's already too big, but I've been working diligently for a long time and now with several robot companies, and I think that's really going to ultimately be one of the new, exciting areas of surgery. And I would be happy at some point in the future to relook at this with this program, because I think there's going to be a lot of information to tell you about.

Dr. Lee:

On my end, I've continued my focus on the fluorescent dye work, and we've now partnered with a company from Indiana based out of Purdue University, and we have dyes that are now targeted. So, our first-generation dyes were not targeted. They were nonspecific, kind of like a contrast agent you give during MRI or CT scan, which is very, very good but not as specific as a targeted dye. So our next generation is involving targeted dyes which target a specific ligand or a specific cell surface receptor for your particular tumor. And we're just now starting to evaluate and talk about our preliminary results, but this is also a very exciting area of work.

Mr. Birnholz:

With that I very much want to thank Drs. Lee and Newman for joining us today to provide the latest updates on cranial base disorder treatments. Doctors, this has been a fantastic conversation. It's been great to have you with me today.

Dr. Newman:

Matt, thank you so much for having us.

Dr. Lee:

Thank you very much.

Mr. Birnholz:

I am your host, Dr. Matt Birnholz, reminding our listeners to join us at ReachMD.com to be part of the knowledge. Thanks as always for listening.

Narrator:

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