

Melanie Cole, MS (Host): Welcome to the podcast series from the specialists at Penn Medicine. I'm Melanie Cole, and we have a chordoma panel for you today. Our guests in this physician round table are Dr. Neil Malhotra, he's the Vice Chairman for Clinical Affairs for the Department of Neurosurgery, a Professor of Neurosurgery and the Chief of Neurosurgery for the Hospital of the University of Pennsylvania; Dr. Najjia Mahmoud, she's the Chief of the Division of Colon and Rectal Surgery at Penn Medicine; Dr. Kristy Weber is the Vice Chair of Faculty Affairs in the Department of Orthopaedic Surgery and the Director of the Sarcoma Program at the Abramson Cancer Center; and Dr. James Schuster, Director of Neurotrauma and Professor of Neurosurgery at the Hospital of the University of Pennsylvania.

Melanie Cole, MS: Welcome, Dr. Malhotra, Dr. Mahmoud, Dr. Weber and Dr. Schuster. I thank you all for being with us today. Dr. Malhotra, I'd like to start with you. Please provide an overview of what you and the other doctors are going to be speaking about today. Tell us a little bit about chordomas.

Neil Malhotra, MD: Well, Melanie, thank you so much for having us today. We're going to be talking about chordoma. Chordoma, as you know, is a rare type of cancer that originates from the notochord, which is an embryonic structure. Although chordomas can occur anywhere in the neuroaxis, they most commonly occur at either the top or the bottom of the spine. Chordoma has a prevalence about one in a million, making it a true medical rarity. Because of this, research is pretty limited and expertise in treating chordoma can typically only be found at top medical centers.

Advances in molecular biology have shed light on chordoma's genetic underpinnings. The discovery of the Brachyuri gene mutation has been a breakthrough. This gene, normally active during embryonic development, goes awry in the notochord-derived chordoma cells. The notochord plays a crucial role in the formation of spine during fetal development. It serves as sort of an initial scaffold for the spine. Small groups of notochord cells remain in the body after birth. And over time, these residual cells can give rise to chordoma, which is a slow-growing, yet very aggressive tumor.

Under the microscope, these chordomas are characterized as clusters of unique cells resembling notochord. These are large vacuolated cells. This distinct pattern is very useful to pathologists as they confirm the diagnosis and diagnostic biopsy performed at a center of excellence is critical to determine the diagnosis and guide the treatment plan.

Melanie Cole, MS: Thank you for that. And Dr. Schuster, I'd like you to expand a bit for us. Tell us about chordomas and how they behave.

James Schuster, MD: Well, chordomas are malignancies. Biologically, they're malignant. They have an unrelenting growth pattern. They compress vital structures, including the brain, the spinal cord, the critical nerves that are in the sacrum. And if you don't remove them completely, they grow back. And like other malignancies, they can metastasize. And with chordoma specifically, they will go to the lungs and people lose function and people die from these tumors.

While, there are therapies and research going on for better treatments, now the best chance for cure for these tumors is surgery. And in this case, removing these tumors without violating the capsule or removing them en bloc. Because of that, and Dr. Malhotra mentioned, that this requires an expertise and a team, you know, these things are near vital structures and really takes a team to successfully manage these tumors.

Neil Malhotra, MD: If I could just jump in, Jim, that's a great description of what happens with these chordomas as they grow and sort of indicates why it's so important to resect these. What we didn't touch on is their local growth and recurrence. These chordomas at the top of the spine can certainly metastasize down throughout the spinal cord if not properly addressed. So, addressing these at the outset is what allows us to protect the patients from further consequences of this disease.

Melanie Cole, MS: Dr. Malhotra, sticking with you for just a minute here, what makes Penn Medicine so unique in its ability to care for chordoma patients? Tell us a little bit about the multidisciplinary nature, how that benefits these patients. You represent, especially in this podcast, many specialties. Tell us about this combined clinic. What are you finding are the largest benefits and why is this multidisciplinary team so important for these patients?

Neil Malhotra, MD: Well, Penn Medicine has been an excellent center for many, many years, and we on this call as well as our other partners who couldn't fit into the space today have been investing the last decade or more building a more ideal model of care for these patients. While we started with a focus on chordoma, our work now benefits really all patients with spinal cancer or oncologic issues.

First, we built pathways of care so that physicians who don't have expertise in this space know exactly what to do with these patients when they discover them. They know what those patients will need and when they will need it.

Then, we established our Spinal Oncology Conference, where experts from every specialty offer input for every single patient on how to achieve the ideal outcome for that individual patient. As we've grown, we've learned from patients that the path through our enormous health system can be daunting. In response to that, we built a multidisciplinary clinic so that all the critical specialists evaluate the spinal oncology patients in a singular location. We bring the specialists from these different diverse groups to the patient, rather than having the patient go to every separate building on our large campus. Recognizing that these patients require special imaging, we worked with musculoskeletal radiology and neuroradiology to build our RAPID pathway. This is a pathway that speeds up the imaging process, reduces the use of the emergency department and expedites our diagnoses. We worked with our radiation oncologists to make simulation planning and treatments easier when radiation is an adjunctive treatment or the primary treatment.

So, our efforts have not only resulted in high satisfaction for patients, but have quantifiably reduced the time to diagnosis, the time to treatment, and the duration of treatment as we've accelerated the patient's return to normal life whenever possible.

Melanie Cole, MS: As we're talking about the importance of the multidisciplinary approach and the team, let's talk about each of your roles for these patients. Dr. Schuster, describe the role of spine surgery. Why specialists like you and Dr. Malhotra play such a crucial role in the care of these patients?

James Schuster, MD: Well, the location of the tumor dictates the team that you need to assemble. So when these are in the base of the skull, that really is the neurosurgeons and the ENT surgeons that have expertise. But if this involves the thoracic spine, we involve the thoracic surgeons. If it's in the lumbar spine and near the abdomen, again, it's a team of spine surgeons, whether that's neurosurgeons or orthopaedic surgeons, orthopaedic oncologists, gastrointestinal surgeons, vascular surgeons. The most challenging tumors that we deal with are the ones that involve the sacrum and the pelvis. And again, that incorporates all of the team members that I've mentioned but, in addition, plastic surgeons. Those are really the tumors of the sacrum and the pelvis that really demand expertise from multiple subspecialties.

Melanie Cole, MS: Dr. Weber, you're next up. Can you describe the role of orthopaedic oncology in the surgical care of these patients?

Kristy Weber, MD: Well, orthopaedic oncology is another key player. When chordomas impact the adjacent bones, as Jim Schuster was just mentioning in

the pelvis, the orthopaedic surgeons that are specialized in cancer participate as part of the surgical team to address structural concerns, ensure stability. Sometimes the chordomas can be so large, they extend into the pelvis and they rest near the acetabulum or the ischial spine. And so it really is just part of a team approach and everybody brings their own particular expertise. You know, I think the spine surgeons are the key surgical team, because these occur in the spine and in the vertebral column. But orthopaedic oncology gets involved when we're involving the pelvic bones as well.

Melanie Cole, MS: Dr. Mahmoud, to you now, you're a leading expert in colon and rectal surgeries. Can you please provide insight into how you joined this team and your role as it relates to chordoma cases?

Najjia Mahmoud, MD: Sure, of course. Thank you. I joined the team, as Dr. Schuster said and Dr. Weber implied, because chordomas do exist in proximity to key pelvic structures like the rectum. So, I'm a colon and rectal surgeon. When chordomas are in proximity to the rectum and the anus, or when chordomas affect the nerves that affect the function of these key structures, then I'm called to participate in the team. What that looks like really depends on the level of nerve involvement, because that affects the function of these structures and also the degree of local invasion or involvement of the chordoma with the rectum or the anus.

We have all seen cases or been involved with cases where patients have required temporary or permanent colostomies as a result of curative surgery for chordomas, and understanding that in the preoperative setting and understanding what the functional limitations and effects of surgery are on key functions like urination and defecation is crucial. So being able to liaison with my teammates, Dr. Weber, Dr. Schuster, Dr. Malhotra, in a preoperative way in a planning session with appropriate imaging and then counseling the patient appropriately preoperatively and setting those expectations is one of the things that I think that we do exceedingly well, and it's really important when it comes to bowel and bladder work. I would add that because the pelvis is such a small space, other organs that may be affected and other specialists that may be needed include urologic oncologists as well as GYN oncologists occasionally.

Melanie Cole, MS: Well, thank you for telling me about all of your roles for these patients. Dr. Weber, you built and now lead the Penn Sarcoma Program. Can you describe how you use your expertise with that center of excellence in order to support the Spinal Chordoma Program and Spinal Oncology?

Kristy Weber, MD: Well, I think the key to the Penn Sarcoma Program is exactly what we're talking about. It's a multidisciplinary team. So, sarcomas are malignancies of connective tissue, so that includes bone and muscle and fat and nerves. Chordoma is not exactly a sarcoma, but we utilize the same techniques. We utilize primarily surgical resection in addition to radiation therapy, which is increasingly used before surgery and potentially after surgery. These are very similar to how we treat sarcoma.

The key to the program is really communication between the different physicians and ancillary staff that work with our teams. I think what Najjia was saying is the critical need to be able to set expectations and to talk to patients ahead of time about what the outcomes will be. And we kind of do a trial run on that when we have our multidisciplinary conferences and we discuss what the major issues are going to be and how we're going to address the patient and their various concerns.

And so, I think it's really about the communication in the multidisciplinary team. I would also say that as part of the sarcoma program, and there's also separate science related to chordoma, but what we pride ourselves here at Penn Medicine is having scientists that are pushing the envelope of what we know about these particular malignancies. And so, when we identify particular targets that we're going to be able to use to help patients with chordoma, that's going to make our job as surgeons much easier, and that work is ongoing.

Neil Malhotra, MD: If I could just add, Kristy came here really to build and grow the sarcoma program, which as she said, chordoma doesn't truly entirely fit into that, but it's this model approach that she's taken to getting all of the appropriate team members to the table to discuss the case. You heard Najjia talk about getting that input, how crucial that is so that we can have the right plan. These are not cases that we should go into without a very consistent, solid plan with which all of the experts have offered their input. And truly, Kristy was at the vanguard of this more than a decade ago at Penn Medicine, bringing the right teammates to the table. And we've followed that model with this group, is get the right team together, prepare everyone for this case and this patient and get them through it as safely as we can.

Kristy Weber, MD: And I think what we're saying here is that there's not one approach to a particular chordoma. I mean, every patient is different, how much it affects the rectum, which nerve roots it affects. Each patient is going to require a slightly different approach. So, it requires physicians and surgeons that understand that flexibility and nuance and we can both talk to the patient and

also execute in the operating room in a way that is going to give the patient the best chance of local control in which the patient does not have recurrent tumor.

Neil Malhotra, MD: And I would just add, it's not even really just about our chordoma experience. It's about our experience and our expertise with other diseases. So, this patient with this chordoma in front of us, you know, with Jim, for example, they benefit from his spinal oncology experience, protecting a nerve, approaching, taking a corridor that gets him to other types of tumors while protecting the nerve. With Kristy, you have this unique knowledge of the pelvis. With every member of the team, they bring this expertise from their entire extra practice to how to treat this individual patient in the best and most efficient manner.

James Schuster, MD: And I would just like to say, you know, with the emphasis on team, I mean, these, as far as I'm concerned, are the most challenging cases that we undertake. But at the same time, for me, professionally, it's the most gratifying cases that I'm involved with. And it really has to do with everybody bringing their expertise to the table, literally.

Neil Malhotra, MD: Yeah, that is so true. When we got together for this conversation today, Melanie, before you started to get ready for your prep for the interview for us, we were all talking about a chordoma patient, Jim and Kristy, you know, when I joined in, we're talking about a patient and the difference we make in those patients' lives and how important that is in our own lives to make that difference.

Melanie Cole, MS (Host): Those are the stories that really make a mark. You're absolutely right, Dr. Malhotra. And Dr. Schuster, I'd like to ask you this next question. We're so pleased that all of you could gather, and we have four of you thought leaders together on this panel to discuss chordoma care at Penn Medicine. As Dr. Malhotra said earlier, unfortunately, we couldn't fit everyone from your large team of experts on this call. Dr. Mahmoud mentioned a few earlier, your urology colleagues and more. Can you tell us a little bit about some of the other specialties that may not have been mentioned, but that are crucial? And this would include ancillary providers.

James Schuster, MD: Absolutely. And we're very reliant and dependent on our radiology colleagues, not only for accurate diagnosis, but they very often do the biopsies. Biopsy is a key component to making surgical decisions. And again, we've talked about some of the other subspecialties, the non-surgical subspecialties, including radiation oncology, whereas these are generally not treated primarily with radiation is a very useful adjunct. Not so much with

chordoma, but some of the other primary tumors that we see, medical oncology, very important. As you said, all the ancillary services, all the expertise provided by our nurse practitioners, so the team extends well beyond the surgical subspecialties. The key is it's all patient-focused.

Melanie Cole, MS: I think that's the most important message about what you are all doing at Penn Medicine, and I'd like to give you each a chance for a final thought for other providers. So Dr. Weber, I'd like to start with you. What would you like the key takeaway to be? You have such an expertise in this particular topic. What would you like other providers to know about that expertise and what you're doing at Penn Medicine?

Kristy Weber, MD: Well, I think what I'd like folks listening to know is these are incredibly complex situations. Now, there may be some simple chordomas out there that don't require a lot of multidisciplinary care. But I think the ones that we see here at Penn Medicine are the ones that require so much expertise, so much understanding of the disease, and not only the disease and the surgery itself, but the postoperative care to allow the patient to get back to their lives.

And so frankly, I think care for these particular patients with these tumors should be concentrated at centers that are regularly working with these patients. And I think that the Penn Medicine team is fully equipped to manage any chordoma anywhere in the spine or pelvis.

Melanie Cole, MS: Dr. Mahmoud, next word to you. What would you like from your specialty and your role for these patients?

Najjia Mahmoud, MD: Well, I think what I would like others to know, and what I think is exceedingly important is that it's really a hands-on approach. Physical examination, speaking with the patients personally, taking a really patient-centered approach that involves sitting down with the patient and getting to know them and their tumor via physical examination, as well as a thorough evaluation of the radiologic imaging, and then a multidisciplinary discussion is really, I think, what both sets us apart, but it's also really necessary. It's necessary to set patients expectations very, very clearly. And the only way that you can do that is if you sit down with the patient themselves. You do your own physical examination, and sometimes we do these in a multidisciplinary way. I want people to know sometimes I'm there in the office examining a patient along with urologic oncology, so we try to do whatever we can to consolidate some of the many visits these patients may be facing, and to try to make it as comfortable for them as possible because it really can be uncomfortable and we do our best to try to ease the path forward.

Melanie Cole, MS: I can hear the passion in your voice as you speak about this, Dr. Mahmoud. Thank you for that. And Dr. Schuster, next up to you, what would you like the key takeaway to be?

James Schuster, MD: I think, again, the point is that these are rare tumors, they require an expertise. And when practitioners run across cases that don't seem quite right or, you know, it doesn't seem like the sort of the run-of-the-mill, let's say, metastasis from a more common tumor, we rely very heavily on biopsy. And all of us are always available for consultation by phone or anything like that because, you know, as we've sort of emphasized the first time, treating these tumors is the best time, so that's really the key point.

Melanie Cole, MS: Dr. Malhotra, last word to you. This is an exciting time in your field, and you've all four come together to let other providers know about these complex chordomas. What would you like them to know about referral to the experts at Penn Medicine and the importance of this multidisciplinary approach?

Neil Malhotra, MD: You know, I would just echo what Najjia and Kristy and Jim have said about our experience and the years of building up this program to care for patients with these complex problems. If you're a patient that's facing something like this, a multidisciplinary team that each brings their own expertise to the table is critical. These problems demand a united front. When we work together, we create personalized strategies to offer a best shot at beating these rare and challenging cancers. In this case, specifically, we're talking about chordoma.

So, I'd say that when you are seeing a patient with a problem like this, you want to direct that patient to a center of excellence with a team that is dedicated to getting that patient the quickest, most efficient, and most critically, the best outcome possible. I feel very fortunate when I think about my time at Penn Medicine. What brings me the most joy and fulfillment is the people that I work with, like the people on this call, and the patients we treat. I feel lucky to get to do the work that I get to do.

Melanie Cole, MS: Well, your patients certainly benefit from this multidisciplinary, comprehensive approach. I want to thank you all for joining us today. To refer your patient to Drs. Malhotra, Weber, Mahmoud and Schuster at Penn Medicine, please call our 24/7 provider-only line at 877-937-PENN or you can submit your referral via our secure online referral form by visiting our website at pennmedicine.org/referyourpatient.

That concludes this episode from the specialists at Penn Medicine. I'm Melanie Cole. Thanks so much for joining us today.