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Surgical and Medical Advances from the Brain Tumor Center

ReachMD:

Welcome to Medical Breakthroughs from Penn Medicine, advancing medicine through precision diagnostics and novel therapies. Your host is Dr. Lee Freedman.

Dr. Lee Freedman:

Being diagnosed with a brain tumor can seem like a death sentence to our patients. What progress has been made in the diagnosis and treatment of this feared disorder that might improve prognosis? I'm your host Dr. Lee Freedman and with me today is Dr. Steven Brem, Director of Neurosurgical Oncology, Co-Director of the Brain Tumor Center and Professor of Neurosurgery at the Hospital of the University of Pennsylvania. Dr. Brem, welcome to the program.

Dr. Steven Brem:

Thank you so much. Thank you.

Dr. Lee Freedman:

We are thrilled to have you and maybe we could start just by talking about what are some of the signs and symptoms that a patient might present with that should get a physician thinking, "It may be a brain tumor?"

Dr. Steven Brem:

The most common symptom is that of a headache that gets worse and worse often in the morning and just doesn't clear. Another important symptom is that of an adult onset seizure. That certainly would trigger concern for a brain tumor. Now because the brain is complex and there are many other nerves involved and almost any neurologically symptom that doesn't clear such as a visual loss or hearing loss or difficulty with memory, these might also trigger some concern.

Dr. Lee Freedman:

So some focal neurologic sign that does not appear to be transient or that progresses?

Dr. Steven Brem:

Correct.

Dr. Lee Freedman:

Yeah. Change in personality, do you see that often or change in cognition?

Dr. Steven Brem:

Usually it's a blunting. Someone who is "depressed" that's not usually acting out but it's usually someone who's lethargic. That could be a brain tumor.

Dr. Lee Freedman:

And I know there's a gamut of types of brain tumors but how often in general do we see brain tumors in our population?

Dr. Steven Brem:

The most common cause now of cancer death in children are brain tumors and the third most common cause of cancer death in young adults and certainly for older patients, tumors like glioblastoma. While relatively rare compared to lung cancer, there about 20 thousand deaths in the United States from primary malignant brain tumors or glioblastoma. If we consider cancer metastases or spread to the brain, this is becoming an increasing problem and probably the most common form of brain tumor in adults is metastatic cancer. Those

would be some of the major types of brain tumor.

Dr. Lee Freedman:

So this is certainly not a minor issue and it doesn't sound like there's any specific predilection in terms of certain age or gender or other characteristics. We see this across the board it sounds like.

Dr. Steven Brem:

That's correct.

Dr. Lee Freedman:

And when a primary care physician is faced with someone where brain tumor comes up on the differential, what should the approach be? What tests should be pursued?

Dr. Steven Brem:

The gold standard for diagnosis of a brain tumor is an MRI of the brain with and without contrast.

Dr. Lee Freedman:

Okay. So it is important to get that contrast and we have different options now with MRIs in terms of open and closed. Is the initial MRI better to be done one way or the other?

Dr. Steven Brem:

For a patient who's claustrophobic, an open MRI is probably good enough. The closed MRI is more sensitive but some patients just find it difficult to have a closed MRI if they're claustrophobic.

Dr. Lee Freedman:

And then once a tumor is seen on imaging, is that the point where referral should take place and should that be to a neurologist or to a neurosurgeon?

Dr. Steven Brem:

Well the major question in all the guidelines are if the tumor is resectable. So the neurosurgeon is best positioned to make that determination. So it should be referred to a neurosurgeon and it commonly is.

Dr. Lee Freedman:

And I would think certain types of brain tumors, maybe they're not really brain tumors, meningiomas, pituitary issues. Are those things that often you don't think about resection right away?

Dr. Steven Brem:

Well the guidelines for meningioma if we first detect it and we do a neurological examination of course and we want to correlate what we see with what the patient has and if it's an asymptomatic small meningioma, then we can afford to watch it with serial MRIs but if it's a larger one that's symptomatic, clearly we will remove them and if we see it in a follow up MRI or surveillance MRI if it's growing, then we can consider treatment either radiosurgery or surgical removal.

Dr. Lee Freedman:

And then something like a pituitary adenoma, does that depend on whether it's hormonally active or not?

Dr. Steven Brem:

Correct. It depends whether it's causing some endocrine dysfunction by being hormonally active or whether if it's a large chromophobe adenoma. If it's non-secretory but large enough to threaten vision or causing severe headaches, then we might want to remove that one as well.

Dr. Lee Freedman:

Got you. So start with that MRI with and without contrast and if there is a tumor discovered, the key question is resectable or not resectable and that's really in the neurosurgeon's ballpark.

Dr. Steven Brem:

Correct.

Dr. Lee Freedman:

Are there other specialists that become involved as you develop a treatment plan?

Dr. Steven Brem:

We will consult with neurology colleagues if the patient has severe epilepsy that's intractable and we can't correct it with surgery alone.

We commonly work hand in hand with medical or medical neuro-oncologists because today there are targeted therapies that work. Avastin has been the anti _____ (05:49) of therapy. Bevacizumab has been approved for recurrent glioblastoma. The standard of care today is radiation therapy with temozolomide which is effective.

There may be clinical trials available for patients with molecular genomic alterations so what we do is that we have next generation sequencing of all the tumors once they're removed of course and we will look at that at our tumor board and we work with the medical oncologists so there may be some drug that works on BRAF mutation or EGFR mutation that might be tried off label for brain tumors. So we're entering the era of precision, personalized medicine.

Dr. Lee Freedman:

That is very exciting. So there are several types of disciplines that get called into the mix when you're planning treatment for these patients.

Dr. Steven Brem:

Absolutely. We will review everything with a radiologist or radiation oncologist since radiation therapy is very important and medical oncologists. We actually work as a closely cohesive team.

Dr. Lee Freedman:

If you're just tuning in, you're listening to Medical Breakthroughs from Penn Medicine on ReachMD. I'm your host, Dr. Lee Freedman and joining me today is Dr. Steven Brem, Co-Director of the Penn Brain Tumor Center. Now Dr. Brem, is it important to distinguish benign versus malignant brain tumors or is it all just location and adjacent healthy tissue that makes the difference in how we approach this?

Dr. Steven Brem:

Well both are very important. There's the World Health Organization, recognizes 120 different types of brain tumors but we have three main categories. There are the benign brain tumors that are surgically curable and these are on the surface or under surface of the brain. These include the meningiomas we discussed and the pituitary tumors we discussed and also acoustic neuromas. So those tumors are brain tumors because they're in the skull but they're pressing on the brain but they can be removed surgically or treated with radiosurgery.

The malignant tumors or the tumors that are of the brain. Glioma is the one, the type of tumor that Ted Kennedy had or Tug McGraw. These are bad tumors but more hopeful these days than ever before. And then there are the metastases that go to the brain, but those are the three types of tumors. Of course malignant tumors are very serious because they are growing rapidly. Even a slow growing benign tumor, it can be potentially fatal so we don't take those lightly just because they're benign.

Dr. Lee Freedman:

And so the decision to take out a benign tumor might depend on what symptoms the patient has and the adjacent structures?

Dr. Steven Brem:

Correct.

Dr. Lee Freedman:

And have there been any advances in terms of the actual reception of tumors? We hear a lot about Gamma Knife and other techniques. Are these employed?

Dr. Steven Brem:

Well the advances in computer science, especially at Penn, we're accredited with the first computer, the ENIAC, many years ago, but our radiology department is very sophisticated and has developed for surgeons what's called an MRI DTI, diffusion tractography, to enable us to see the white matter fiber tracts and we can actually see how they're displaced, how they're replaced sometimes and how the tumor's invading the fibers, the highways in the brain and we can plan our surgical approaches to spare these brain pathways.

That's been a big advance and has had dramatic improvements and outcomes. The Gamma Knives are continuously upgraded. We now have a model called the Perfexion which is very advanced software. It enables us to treat more tumors precisely with less spillage of radiation to the surrounding brain. So that's been a big advance, but I think the software that guides surgery, the cyber surgery, we have a device called a CyberKnife. These have had very significant advances over the last few years, making that much safer and more effective.

Dr. Lee Freedman:

And are these mostly used pre-surgery to plan the surgery or are any of these real time as you're actually resecting and operating?

Dr. Steven Brem:

These are done in terms of an overall plan. We will see the patient and we will be able to remove whatever is safely resectable but for small deep tumors, we will consider that up front but sometimes following surgery, sometimes instead of surgery, but we usually don't do it the same setting.

Dr. Lee Freedman:

And is there a difference in approach in terms of a primary brain tumor versus metastatic lesions?

Dr. Steven Brem:

We're more likely to use stereotactic radiosurgery for metastatic lesions than for primary lesions. The primary lesions tend to be more diffuse and we want a larger field.

Dr. Lee Freedman:

And are there other standard medications that we would see used in these patients, steroids, anti-epileptics, other standard treatments that go with the surgical procedures?

Dr. Steven Brem:

Most patients will be on steroids certainly before and shortly after a surgery and most patients will be on anti-epileptic medications. Currently the favorite one is Keppra because of a relatively good safety profile and we may leave patients on that if they've had a seizure for up to six months and then reevaluate.

Dr. Lee Freedman:

Now it sounds like the Penn Brain Tumor Center has a number of specialists that help the patients. Are there some novel therapies? You mentioned the Avastin. Are there other things that Penn is doing now to treat this devastating problem?

Dr. Steven Brem:

Well there are three things we're extremely excited about. Number one, as you may know, Penn has developed immunotherapy to the point where last year the journal called Science, the major scientific breakthrough in all of science was cancer immunotherapy. And Carl June's group has tackled somewhat formerly incurable leukemias, published in the New England Journal of Medicine using chimeric antigen T cell receptors, the CART technology.

Well that is about to be rolled out in neurosurgery by Don O'Rourke and his team. I'm proud to be part of that team but also Dr. Desai, but Don O'Rourke is the principal investigator on that trial with Carl June and Dr. _____ (12:49) is the immunologist on that. So we will be launching that. We currently have open a trial that is being looked at nationally called dendritic cell vaccine or DCVax which is also the ultimate in personalized therapy since the patient uses their own white cells to fight their tumor through leukapheresis and developing a dendritic cell vaccine that is specific for their tumor antigens. We've had also peptides against EGFRvIII and other vaccine trials. So that is an area that is very fertile and exciting.

Dr. Lee Freedman:

Absolutely. That's very exciting.

Dr. Steven Brem:

Another area is electrical field therapy. The patient wears a cap of electrodes and that has been FDA approved for recurrent glioblastoma. We have a trial open for newly diagnosed glioblastoma. We are also one of a handful of institutions nationwide that is looking at a new molecular pathway driven drug that is coming from the National Cancer Institute through a consortium called the Adult Brain Tumor Consortium and Dr. Arati Desai is our principal investigator there and is working with a number of us to bring in these clinical trials that show a lot of promise.

Dr. Lee Freedman:

That certainly sounds very exciting. And some of these products, are they introduced intrathecally? Does the blood-brain barrier make them not able to be introduced into the bloodstream? How do these work?

Dr. Steven Brem:

Well each inhibitor has its own mechanism, own pathway. Since the advent of Avastin, we found the blood-brain barrier not to be the ultimate barrier they once thought of it. As it turns out, tumors will secrete angiogenic factors that breakdown the blood-brain barrier. That's the reason we can visualize them with the contrast agents we spoke about earlier. So around the tumor, the blood-brain barrier may be actually open and so systemic drugs like temozolomide may penetrate that blood-brain barrier.

Dr. Lee Freedman:

And as we look ahead, we can look down the road five, ten years, do you see other breakthroughs, other new approaches in the

treatment of brain tumors?

Dr. Steven Brem:

Yes, I do. I think we're at the stage now where HIV research was 15 years ago that we're developing drugs that are effective but the brain tumor develops an escape mechanism. Ultimately we have to find the right combination of inhibitors. So we've identified through The Cancer Genome Atlas, the TCGA project, a number of major driver genes, we understand the molecular pathways. We have dozens of drugs that are now effective inhibitors but we don't have the optimal combination to have a sustained, durable response. We do that, we will convert glioblastoma to a manageable disease the way HIV now is managed.

Dr. Lee Freedman:

Dr. Brem, thank you so much for being with us today and for outlining for us not only the approach to brain tumors and their diagnosis but even more excitingly some of the new developments in terms of the treatments that are on the horizon for brain tumors. There's a lot of exciting stuff being done at Penn Medicine and it seems that the future for treatment of brain tumors is brighter than it's been in a long time. Thank you very much.

Dr. Steven Brem:

Thank you so much, Dr. Freedman. Thank you.

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