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Advancing Multidisciplinary Care in TGCT: Integrating Systemic Therapies and Surgical Approaches

Chapter 1

Announcer:
Welcome to CME on ReachMD. This activity, titled Advancing Multidisciplinary Care in TGCT: Integrating Systemic Therapies and Surgical Approaches is provided by Prova Education. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Tap:
Welcome to our educational series on advancing multidisciplinary care in tenosynovial giant cell tumors.

This is CME on ReachMD, and I'm Dr. William Tap. And I'm here with my colleague Dr. John Healey.

Dr. Healey:
Great to be with you.

Dr. Tap:
Thanks for being here, Dr. Healey. I was wondering if you can give us a brief overview of tenosynovial giant cell tumors, or TGCT as we refer to them, and how we can differentiate them by presentation.

Dr. Healey:
Yes. Well, it's a difficult question and the diagnosis is often unsuspected. It's a rare disease, maybe 7,000 a year in the United States. There are two principal forms; one is nodular or localized, that could be inside or outside the joint, and the other is diffuse. And both of these can occur really at any age. The most common, perhaps, at age 30, but you can have young teenagers and people in their 80s. And the longer the duration of the disease, there can be superimposed degenerative arthritic changes as well that can be confounding. But the nodular disease is localized, palpable, identifiable. The diffuse is more ubiquitous across the whole synovial surface in the joint, and really any joint in the body can be subject to it. Because of these diagnostic difficulties, it has an average of probably 3 years of symptoms before people recognize the diagnosis and get appropriately treated. So awareness and education here is our number one goal.

Dr. Tap:
Yeah, I agree, John. It's often a very difficult disease to diagnose. As you mentioned, it can affect a younger patient population and it may take a long time before the diagnosis is often made. And as you said, it can affect any joint within the body but tends to affect just one joint and that's very important when we think about the presentation.

Dr. Healey:
Well, I'd like to add a word about diagnostic imaging modalities, and MRI is the principal and gold standard for that.However, it's best to do specialized sequences, gradient echo sequences, that you have to ask for specifically. And standard MRI sequences don't identify the hemorrhage, the hemosiderin, that's within these lesional tissues, the so-called pigment of pigmented villonodular synovitis.And

that's highlighted on the gradient echo images and can be really definitive in helping make your diagnosis.So that can be a challenge, if people have already had an MRI, to get approval and clarification with the specific sequences, but it's worth the effort.

Dr. Tap:
Before we wrap up, can you provide us with one key takeaway from this chapter?

Dr. Healey:
I think to increase awareness and differentiating the localized nodular disease, which is a surgical condition, and the diffuse, which can be a combination of surgery and medical management, as we'll discuss.

Dr. Tap:
Yeah. Thank you very much. And so, in the next chapter, Chapter 2, we'll be discussing surgical and nonsurgical options for TGCT, so please stay tuned.

Chapter 2

Dr. Healey:
Welcome back for Chapter 2 in our presentation today. In this chapter we'll be discussing the surgical and nonsurgical management.

Dr. Tap:
Dr. Healey, I'm very interested in your approach to determining surgical candidates and treating TGCT patients surgically. And what's your process?

Dr. Healey:

Well, number one is speaking in depth with the patient and finding out what her/his goals happen to be. And the nature and severity of their symptoms, what their limitations are, and to then carve a proper strategy for how to achieve those goals.

Now, nodular disease, be it inside or outside the joint, is amenable to surgery and that's the gold standard and, I think, should be tackled first. If it's diffuse disease in the anterior part of the knee, the most common location, for example, that may well be amenable to surgical approach with arthroscopy, allowing for a rapid recovery. But when the disease extends in multiple compartments, particularly behind the knee, it's not amenable to safe arthroscopic surgery and open surgery would need to be effective to do that.

Now, that's a big challenge both from the procedural standpoint and recovery of the patient, and so there's a great incentive to consider medical management of this as a definitive treatment or as a complement to, the prelude, really, for surgery consideration afterwards.

And again, when it's localized, surgery is the way to go and the gold standard, and that can be whether it's in the joint or near the joint. But the diffuse disease is much more problematic. And so that's a situation where medical management and controlling the disease, shrinking it, making it more amenable to surgery is a good idea.

So that's my general approach to it, again, tailored to the needs of the individual patient.

Dr. Tap:
Yeah. I think oftentimes we spend a lot of time talking to our orthopedic oncology colleagues to understand if surgery is an option for patients. And if not, we often would consider the use of medical management. And a lot of that will be discussing with the patient what their goals of treatment are. And the patients are really partners when we start to think about using drugs to help their disease. One of the things we often think about is do we need to start drugs, and if so, what are the symptoms that we're trying to alleviate, or are we trying to protect the joint down the line?

But we do have several drugs that we can use for patients. We have some of the older CSF-1R inhibitors like nilotinib and imatinib, which can actually be very good drugs to help patients with TGCT. They're not as strong as some of the newer variations, so we don't always see tremendous shrinkage in the disease, but what we can often see is improvement in symptoms.

We are fortunate in that we have some of the newer and stronger CSF-1R inhibitors as well, such as pexidartinib, which was approved in the United States. And often, with drugs such as pexidartinib, you can see dramatic responses and fairly quickly, not only in seeing the tumor shrink in size, but also improvement in symptoms, range of motion, and quality of life measures. Interestingly, we still struggle with what's the right dose for patients, and we often don't need very rapid responses, so we can start with lower doses. And we don't know how long a patient should be treated. And if we treat to maximal responses, once we stop the drug, would we see a recurrence or growth in the disease? So, there's still a lot of questions. But we very much have to partner with the patient to understand the goals of therapy, and that helps us to decide if we want to start a drug and then which may be the right drugs to start. And then, of course, it requires close follow-up to understand how we're helping them.

And with medical management, all of our therapies can also have side effects. So for pexidartinib, there's a risk evaluation mitigation strategy based on a very rare cholestatic hepatotoxicity that can develop with the drug.

And I think we can now move on to Chapter 3 which will review the patient case example, so please stay tuned.

Dr. Healey:
Great. Thank you.

Chapter 3

Dr. Tap:
So for those just tuning in, you're listening to CME on ReachMD. I'm Dr. William Tap, and I'm here with my colleague, Dr. John Healey, and we're discussing recent advances in the management of TGCT.

Dr. Healey:
Welcome back for Chapter 3.We talked about, in general, the surgical approach and the medical approach, but now in Chapter 3 we'd like to discuss individual clinical examples and how we implement these overall strategies.

Dr. Tap:
So I'd like to present a 43-year-old male who presents with 1 year of worsening knee pain, swelling, and stiffness. And an MRI shows tricompartmental tenosynovial giant cell tumor with a large joint effusion and synovitis and actually bony erosion of the proximal tibia. And there are multiple low T2-weighted nodules. For example, a 7-cm nodule in the lateral patellofemoral recess, a 3-cm nodule along the popliteal tendon, a 3-cm suprapatellar recess nodule, and a 3-cm nodule at the origin of the gastrocnemius.

And so, Dr. Healey, when you see a patient with such symptoms and extensive disease, what are your thoughts about surgery?

Dr. Healey:
Well, it's clearly a patient who's quite symptomatic and needs intervention. But I can say that with major surgery, and that's anterior and posterior vascular dissection, and what's usually a 5-hour procedure, I can get most of the disease but not all of it. And there's an extremely high recurrence rate, which is over 50%.And so I'm a little cautious about that and would very much want to get your opinion about the suitability of medical management to quiet things down, get a better control of the symptoms in advance, and then revisit the question of surgery.

Dr. Tap:
Yeah. So we would spend a lot of time talking with the patient to understand really how the disease is affecting their quality of life, how it's affecting their ability to do the things that they want to do in life, and then discuss some of the different treatment options. And as we spoke about before, we have some of the weaker CSF-1R inhibitors such as imatinib and nilotinib, which can have nice clinical effects. And then some of the stronger CSF-1R inhibitors, such as pexidartinib which also has the potential of some rare side effects so that we need pretty extensive monitoring, especially early on.

We also have clinical trials of some of the newer drugs that are coming out that we also can talk to the patient about. But we really have to align them with whether or not starting medical management is the right thing for them.We expect we would see a response and improvement in symptoms, and we would have to weigh that against the time spent in our clinics, the need for blood draws, the close monitoring that we would have to have with an individual.

So if a patient such as this was on drug and had a very nice response, would you consider surgery down the line?

Dr. Healey:
I would. But again, driven by the symptoms, the degree of bone and cartilage erosion, and what the probability is of getting a near-total excision. To just debulk some disease I don't think is helpful or worth the potential surgical complications and difficulty in rehabilitation. But if we're able to control the overall disease, shrink it by a third is what a general rule of thumb that I try to observe, then I think surgery has a role. But it's, again, on an individual basis.

So that covers a lot of ground here, but it's all the time that we have for this part of the topic. And in Chapter 4, we'll conclude by discussing the overall integrated multidisciplinary approach to managing patients with TGCT.

Chapter 4

Dr. Healey:
Well, welcome back for Chapter 4 where we'll be focusing on the multidisciplinary approach to managing TGCT and carry on some of the earlier conversation about the nuances in that management.

Dr. Tap:
Yeah. Thank you, Dr. Healey. I mean, as you know, this is a disease that really needs to be approached in a multidisciplinary fashion, and it's a disease for, up until just the last few years, that really resided with our orthopedic oncology colleagues. And when we embarked on some drug development strategies, we really had to spend a lot of time with orthopedic oncologists, like yourself, and even patients to understand how the disease affected them.

And I think that carried into the management because we definitely need shared decision-making for this disease, and it's not only with the physicians that may be involved – orthopedic oncologists, medical oncologists – but also other multidisciplinary team members, such as physical therapists, occupational therapists. We talk about physiatrists, sometimes we bring in pain and palliative care doctors, integrative medicine doctors. All really important to make sure we're treating the patient holistically.

Now, most importantly in shared decision-making is the patient, right?Because, as you mentioned in the past, it's such a variable disease in how it affects people and what their goals in coming to us may be. So we really have to be able to come together and open the dialogue. And it's amazing how much I've learned in just spending time with you on almost every patient, understanding what the surgical implications are when they have the disease, what the joint implications of the disease itself may be if we treat it or didn't treat over time, because that guides me in my discussions with the patient and ultimately, I think, helps the patient make decisions that are right for them.

Dr. Healey:
And I think that's the issue, asking. And so asking the patient. Again, and some of the most profound examples I've had are from young women of childbearing age, and they're terrified of climbing the stairs or potentially falling. And that's, again, an individual, very important issue that for another patient may not be relevant at all.

Number two is getting the other specialists involved, and physical therapy or rehabilitation medicine and pain management is often important.There can be mechanical things. And so there are a variety of regular orthopedic and rehabilitation components of this that only come to bear understanding what the patient's needs are and through the multidisciplinary approach to the problem.

And so I hope the audience has been able to learn something from this presentation. Thank you for your attention.

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