Dr. Seth Pollack - DTRF 2022 Patient Meeting Webinar #1

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Jeanne Whiting: So the first presentation is by Dr. Seth Pollack, who's Director of the Sarcoma Program at Lurie Cancer Center at Northwestern University. He's going to talk to us, a general overview of the disease entitled Desmoid Tumors 101. Dr. Pollack, thank you.

Dr. Seth Pollack: Thank you. This is such a great event.

Really so happy and honored to be here. So, so I'm Seth Pollack. I'm here at Northwestern University in Chicago. We'll be talking about Desmoid Tumor 101. I mean, this is a really educated group, I know. So, you know, some of this stuff may be basic, but hopefully you'll get my my take on things and you'll find it interesting.

And please ask lots of questions in the chat. So, or in the q and a. So we'll talk about what our desmoids, we'll talk a little bit are about are they benign? Are they cancer? Where do they occur? And we'll talk about what are the commonly used treatments. And I'll tell you about a couple of interesting cases I've had that I think you might find interesting.

So desmoid tumors, I consider them to be benign tumors, and we'll talk a little bit more about that. Now, of course, there are patients with really serious desmoid tumors, right? Disabling desmoid tumors. Desmoid tumors that require morbid procedures and even some patients who die from their desmoid tumors.

But in I think we're getting much better as you'll, as we'll talk about at knowing which desmoid tumors that we need to treat. And we have a lot better treatments than we used to. And I think it's really an area of medicine where things have really changed. When I first started treating desmoid tumor patients, There were so many patients who had multiple terrible surgeries, who were stuck on opioids, who really were not really weren't doing well, who really, the desmoid tumor was you know, one of these, one of the defining things of their life.

And you know, they were really debilitated by it. And now I find for a great majority of my desmoid tumor patients it's something that they can live with and doesn't become the major focus of their life. That they're able to either just be watched or they're on sorafenib for a while. Eventually they come off and we're doing scans regularly, and we're managing them in a way where they can live their life and do the things they wanna do.

That's not everybody, but that's most of my patients these days. And it's really, I think, a great source of hope. They're often associated with we know a lot about the biology and there was some great talks yesterday about some of the research that's going on about some of the biology that's driving these tumors and and and we can talk about that as we go forward.

So, you know, a couple of things I wanna mention about are they cancer? Are they deadly? Of course there are rare cases, not rare cases, but cases where these tumors can be deadly. That's not the typical patient though. You know, since I've been here at Northwestern over the, you know, past year and a half, we haven't had patients die of a desmoid tumor.

We do have a patient who. We have over 40 patients that we're actively following with desmoid tumors. And there is a patient who I do worry about. But most of our patients are doing really well. And you know, I think one of the biggest problems with desmoid tumors is that they're invasive.

You know, I made this little illustration to show that the desmoid tumors, they kind of have fingers that go into the surrounding tissues. So, when people get surgery or radiation or any of the different cry ablation, any of the different treatments that we use to sort of, get at these tumors, they have a very high rate of recurrence.

They get into the surrounding tissues and they're very likely to come back and keep causing problems. And that's the kind of like, feature about them that I wouldn't say that, you know, it's not cancer, but it's kind of a little bit of a malignant type behavior. What a high rate of recurrence they have.

On the other hand, what's very different from cancer is that they can sort of spontaneously regress, They can go away on its own. So this is a from the sorafenib trial that showed the efficacy of sorafenib. That was a placebo controlled trial. So the patients on that trial were randomized to either get sorafenib or to get the placebo.

And you could see that people who got the placebo, actually they actually did pretty well. I mean, there were a lot of patients on the placebo whose tumors shrank quite a bit. And there were quite a few patients who started the trial. All these patients were required to have pain from their tumors or progressive tumors.

And there were a lot of patients who, you know, not being on any real medical therapy, their tumor stopped growing. They just naturally on their own had relief from their pain and the tumors sort of either shrank or they just stopped being bothersome. So, now of course, patients on sorafenib did a lot better.

That's why sorafenib is such a important part of the medical treatment of desmoid tumors now. But this is what we're talking about when we sit when we talk about how desmoid tumors are benign is that a lot of the time you know, if you just give it time, the desmoid tumors will be okay.

So desmoid tumors can occur anywhere. They can occur in the extremities, they can occur in the abdominal wall. This this picture on your left is a picture of an abdominal wall desmoid. So, you can see on the top is, I'm not sure if you can see my cursor, but on the top is the patient's front, on the bottom is their back.

You could see their spine is that sort of white thing kind of towards their back. And you could see there they have a layer of fat. And then the next layer is what we call the abdominal wall. And you can see there's sort of a swelling on the right side of their belly, and that's an abdominal wall desmoid.

And you can just imagine that if a surgeon wanted to remove that abdominal wall desmoid they need to really protect all of this stuff inside, which is basically the patient's intestines. And you know, that's, that could be a pretty decent size surgery to try and remove something like that. So that's a really tough thing.

The mesentary is another common commonly discussed location for desmoid tumors. The mesentary is the connective tissue that basically keeps all of the intestines in place and it has a lot of very important blood vessels that flow through it. So if the tumor that, so there are patients who who this could be

really terrible for because the tumor can really choke the blood vessels that are trying to get to the intestines.

Now on the other hand, there are patients who this becomes a real problem for because you know, we try and remove the tumor with surgery and it's really hard to remove the tumor with surgery without injuring those blood vessels. And then there's some patients who have these tumors in the extremities, in the head and neck, and and those can also be really tough patients. And this is a patient of ours patient. He's a 50 something year old man. And he was just, he had a routine health scare, turned out to be nothing, but he had a CT scan as part of that workup and was found to have a 10 centimeter tumor. That this is the tumor in the middle. Again, I don't know if you could seem a cursor, but it's right in the midline.

That big thing that's kind of, right in the center of the skin. You could see his backbone is the sort of white structure in the back, in the middle. And you could see he has some blood vessels over here. And then this is this big structure in the middle that's a tumor. It's a, it was a 10 centimeter tumor, bigger than 10 centimeters size of a grapefruit.

And he didn't know it was there. And the question is, what are we gonna do about it? So we, he was asymptomatic, so we started just watching and now it's over two years later. The tumor hasn't changed at all. He still has this tumor there. And I think he'll probably be a little old man in a nursing home someday with this tumor sitting there.

I don't think it's gonna cause him any problems in his life. Because and it's probably been there for many years. The tip, you know, most people get desmoid tumors when they're young adults. And that's the most common age for people to get if people can get it at any age. But that's the most common age, and my guess is this guy's had this tumor for years. We're gonna watch this tumor and he's gonna be fine.

So how are patients treated with desmoids? We've moved to try and observe as many patients as possible. That's our feeling about the best way to do it. My, I was telling you about the battle days before when we had so many patients who had been through so much. And I, my personal feeling about it is there was a lot of patients where we really couldn't tell how much of their current predicament was caused by the multiple surgeries they had, and how much of it would, was really resulting from the desmoid tumor.

So if we can get away with just watching you and keeping our eye on the desmoid tumors that's what we're gonna try and do. Now, surgery, radiation, cryoablation, these are all things that we do in select cases, but more and more for patients who are progressing or still having pain after a period of observation, or who are having pain severe enough that we don't wanna try observation, we're putting them on sorafenib.

And here, let me so I put, so this is just, you know, we have, I just took a look at our patients here at Northwestern. Over a third of them we're able to watch with just observation - over a third. And and I think that they'll turn out to be like that patient I was telling you about before. About 15% of our patients were sending to either surgery, radiation, or cryoablation.

And then over half, these days and this is an so, over half these days, we're either putting sorafenib or these are patients who are sorafenib for a period of time and now are watching sorafenib and. This is every time I start a patient on sorafenib I have a conversation with them about coming off sorafenib because I think that's a really important part of it.

I think that we don't wanna have people who are on sorafenib for the rest of our rest of their lives. Our goal is to have people living their life like it's a normal life and have them watching their desmoid tumor. Like they watch their blood pressure, like they watch cholesterol, like they, you know, maybe they have well-controlled diabetes and they're getting scans every now and then and making sure their desmoid tumors are under control.

Now we do have a handful of patients who have very difficult to treat desmoid tumors, who have progressed, who've been on sorafenib and had problems nevertheless. But that's just a handful of patients.

How effective is observation? The this is from a study where they watch patients and they found that about 20% of the patients that they observed went on to get surgery at our center. They might have gone for, oh, sorry. They might have gone for cryoablation or radiation or surgery depending on the tumor.

About 20% of the patients got medical therapy. So to get all together a majority of the patients that they watched with observation were fine. And if they didn't, they were under close observations so they were able to get the treatment they needed.

Now I showed you before those fingers that come out of the tumor it's very important. That the surgeons are able to get a margin of tissue around the tumor

to ensure that none of those fingers are left behind. So a margin that means that they can't just take the tumor and cut it close to the edge.

They need to just, they need to get the margin the tumor, and then also get a bunch of healthy tissue around the tumor to make sure that all of those fingers are removed. So, and this makes it so that if you have a tumor that is in a really tough area, like that abdominal wall patient that I was showing you, or the mesenteric tumor that I was showing you before, it could be really tough to remove that whole thing with a margin of healthy tumor around it.

Now, if you get negative margins, most patients don't recur. Even with a positive margin, the chances are 50 50. So, you know, there's a, they, it's like a coin flip, whether the tumor's gonna come back. But if the surgeon is very confident they can get negative margins, I do think it's worth a try.

For some people. I mean, because you I just think a lot of people, they just like the idea that this tumor's gone. Right? It's just like psychologically, they don't want, nobody wants a tumor inside of them. Now, you know, I, if you're okay with having the tumor I think it's, I, my personal feeling is it's fine to just watch it.

I think it's just fine to just watch it. But this is really just, you know, some people wanted out. Now, but what if it comes back? Okay, so I showed you like 80% with the negative margin, it's gone, but there's 20% of people who it comes back and if there's a positive margin, it's really 50 50. And if you are in that situation, I really think that

It's time to stop with the surgeries. And I would, I think it's time for medical therapy because the rates of recurrence for people who have recurrent desmoid tumors are really through the roof. And this is where I think we really got it wrong in the past where we thought, well, surgery's a surgery works a lot of the time upfront.

Let's keep trying it. And I think that the, so, so this is called a Kaplan Myer Curve where the percentage of success is on the y axis and time is on the x axis. So you could see that you know, 40 months afterwards, you know, you're like 20% of patients are, have local control, right?

So, the rates are really high for if you get surgery and you have recurrent disease. How effective is radiation? It's, you know, it's it's pretty good. It's pretty good. It's kind of like surgery. You know, of course this margin issue isn't

an issue. For some patient. Of course the radiation doesn't provide you the satisfaction with getting your tumor gone.

But there are a lot of patients with durable control from radiation. And you can see here that you know, over 60% of the patients that are treated with radiation have long term control of their tumor and don't have problems, again from their desmoid tumor. So more than half of patients get radiation and they don't have another problem.

And then, Lots of patients are asking us about cryoablation. It's very exciting. We do have cryoablation at Northwestern. I do send patients for it. I think that there's a little bit of an overhyping of cryoablation right now. I think it's kind of like the in thing. Everybody is getting excited about it.

I do like it and the thing I like about it is that patients don't have to go through a surgery. You know, you don't have to be opened up. You don't have to go through the recovery. Does it provide excellent long-term control from desmoid tumors? I'm not sure that it's so much better than surgery or radiation.

I think it's probably similar in terms of its success rate, but of course it's great not to have to go through a surgery and have that kind of success rate.

This is another patient of mine. She was found to have incidentally to have a desmoid tumor on her chest x-ray. And so it was asymptomatic. This is before she came to me. They did a big surgery. They removed the tumor, they put a goretex mesh, then it started bleeding. She had to go back to the operating room and evacuate the hematoma.

She developed pain from the goretex mesh. The goretex mesh is like, a material that they put in her chest wall to basically keep everything contained to basically re replace her chest wall. Then she developed pain from the goretex mesh, and she required another surgery. So she's had three surgeries for, and then she had actually, she had to have several surgeries for the revision of this original surgery.

So she had one surgery, then she had three additional surgeries. Just to kind of clean up this first surgery, all for an asymptomatic desmoid tumor. And I think this is not uncommon, or at least it wasn't uncommon back in the day. And then two years later, the tumor reccurred anyways, despite everything. The tumor was painful at this.

So she started out having an unpainful asymptomatic tumor, but when it occurred, it was painful. So we put her on sorafenib. So, now I'm gonna show you, this is the curve comparing sorafenib to placebo. Remember I showed you the placebo is effective for some desmoid tumor patients. And I don't think it's a placebo effect.

I mean, maybe there's a little bit of that, but I think it's really just if you watch patients with desmoid tumor, sometimes they regress, Sometimes they just, you know, a tumor that's angry that's outta control just falls into line. But sorafenib is a lot better. It's a lot better. So here you could see that most patients who get treated with sorafenib, and these are all patients with progressive desmoid tumors with painful desmoid tumors.

Most patients who go on sorafenib get very good disease control over 80%. And And that's not the true and with placebo. So, so remember when I talked about observation that it's so effective? That's all comers. That's people who might who, who may have discovered their desmoid tumors incidentally, who don't have painful tumors, who have tumors that are not necessarily progressing.

But these are all patients with progressing or painful desmoid tumors. And for those patients doing placebo is not enough most of the time. But sorafenib is excellent. And this is showing you just how much, you know, there are a lot of patients who have tumors shrink with sorafenib, with placebo, but a lot more with sorafenib.

And you can see the very few patients have tumors that grow significantly while they're on sorafenib. So this is called a waterfall plot. And the here, the Y axis represents the biggest change in the tumor size for the patient on the trial. So, oh, sorry. So you could see there are a number of patients with placebo who had tumors grow.

There are some patients with, there are a lot of patients with placebo whose tumors still shrink on sorafenib. There's only three patients maybe like a little bit of four patients who had their tumors grow other on sorafenib and a lot who had their tumors shrink.

So this patient we treated with we tried to just watch her because her tumor was hurting her, but she kind of didn't wanna go on a drug. So she said, you know, can I just watch for a little while? So we said, Okay. We watched it, but her tumor was more painful. So we decided to try her sorafenib, we started her sorafenib, her pain got better.

Her she was on sorafenib for a year and then the hand foot syndrome started bothering her. More, she, that's a common side effect with sorafenib is hand foot syndrome. And we took her off and she's still doing well, years later now. So, some lessons from this case is that surgery can sometimes more cause more problems than it solves.

A limited course of sorafenib can a lot of the times be all you need. And I think for patients like this Nirogacestat is gonna be a great option in the future. That's that's this new drug from SpringWorks that everybody's really excited about. So we talked a bit about what our desmoid tumors, we talked about whether they're benign, whether they're cancer.

We talked about some of the locations they occur in. We talked about some of the commonly used treatments for desmoid tumors. And I talked about a case of mine. So that is sort of like our intro. Let's talk about some questions that you guys have.

Jeanne Whiting: Okay, Seth, I'm gonna take the questions from the q and a. One question is about recurrences. Are there any studies to track recurrences after five years? Of being tumor free. There are many doctors that are releasing their patients after five years, and yet there are patients within the Facebook group that do have recurrences after five years. So do you keep tracking, how long do you keep observing and tracking a patient doing repeat scans and are there any statistics on this?

Dr. Seth Pollack: Yeah, that's a good question. I don't think there's really good studies after five years. There are I think most of the time if you haven't had a recurrence in five years, you're probably okay. But there are these cases of late recurrences. Of course I think some guidance that,

Well, I, I think it's if you've been free for five years I still watch people for like annual follow up for a little while even after five years. But I do think you want to stop surveillance at some point. And what is the right time for that? I don't know that there's a great answer. I think five years is probably not a bad idea unless you've had a really difficult time with your desmoid tumor.

If it was in a place, a location where we're extra worried, a about it coming back those might be some situations to make an effort to watch longer. Otherwise I think either stopping after five years or just doing annual surveillance is probably okay.

Jeanne Whiting: Okay. When you say a limited course of sorafenib might be all you need, what's the average length of treatment you have used for adults and children?

Dr. Seth Pollack: Right. Well, there's not good data about how long we should be keeping people in sorafenib. That's a really important question. I can tell you that I've seen patients with just six months of sorafenib, and that's all they needed. I usually try and treat till their maximal response so their tumor isn't shrinking anymore. That's my goal. And that we've been watching them for an extra six months after they've had the maximal response. That, I think that's the best case. Now, if in patients whose tumor isn't shrinking, I watch them for, I like to watch them at least a year. But

If patients are, are tolerating it fine if like they're, you know, some patients are like, some patients have a lot of side effects and they wanna get off as quickly as possible. So for those patients I try and get them off at sooner. And then other patients, if they're not having any side effects I might keep them on for two years, but I don't I, I don't try and keep patients on beyond two years.

If I can, I'll try and get them off as long as everything is going well with their tumor. Now I have had a couple patients whose tumor started to grow when they came off sorafenib. So it's really important to watch closely when you pull somebody off sorafenib. But the patients who that's happened to, we got them back under control really quickly.

Like, you know, as soon as their tumor started to grow, we put 'em right back on sorafenib and their tumor was under very good control.

Jeanne Whiting: Okay. So another question related to sorafenib, a patient with FAP, a mutation of the APC gene has had bad experience with sorafenib, is just wondering if it only applies to desmoid tumors, how does it impact an FAP patient differently?

Dr. Seth Pollack: Yeah. So I think FAP is a different thing. For sure some FAP patients. So, so the general, my general principles that I treat FAP patient who has desmoid tumors is gonna be the same. In terms of trying, you know, I, I have a less, is more kind of approach to treating desmoid tumors. I but I think FAP patients are more difficult to treat. Their tumors do tend to be more resistant to sorafenib. I, these are patients that I, you know, patients with who've had really aggressive tumors. I've used Doxil in the past and had some success with getting those tumors under control. Sutent I've, I've tried, which is a

medicine that's very similar to sorafenib, but I think my work just a little bit better for FAP patients.

That's something that's that I've seen work. It's tough. You know, I, again, my, the general principles are the same, but sometimes these are more difficult patients to treat.

Jeanne Whiting: Okay. And I would also say that our third webinar today is all about FAP and desmoid. So, hopefully this person will be able to attend that as well for another chance to ask another question. We have to stop our time here's at an end. Dr. Pollack, if you'd like to go in and answer any of the remaining questions in writing. That's up to you that are on the chat. Thank you so much. Very enlightening presentation. Appreciate it.

Dr. Seth Pollack: Pleasure. Thank you.