

Dr. Sommavilla - DTRF 2022 Patient Meeting Webinar #3

Jeanne Whiting: We'll turn the time over to Dr. Sommavilla, your colleague, who's going to present be presenting on surgical considerations. Dr. Sommavilla.

Dr. Joshua Sommavilla: Hi. Thank you and thanks for the opportunity to come here. Thanks to all the patients for participating, and thanks to Dr. Shepard and Dr. Hurley for their very interesting talks.

Can everybody see my screen and hear me okay?

Jeanne Whiting: Yes, it's good to go.

Dr. Joshua Sommavilla: So I'm gonna be talking, my name's Josh Sommavilla and I'm a colorectal surgeon also working at the Cleveland Clinic as part of our Weiss Center, which specializes in treating patients with hereditary GI cancer syndromes, one of which is FAP.

So we do see a lot of patients with familial polyposis as part of our program, and we see a lot of patients with desmoid disease. And I'll be talking about surgical considerations for desmoid disease and FAP patients. So just to kind of overview what I'm gonna talk about, I'm gonna first take a step back and highlight the importance of how we think about desmoid disease when we operate on any patients with FAP, even if they don't have desmoid at that time. And then I'll talk a little bit about how a patient's risk of desmoid disease impacts our thinking about surgery and FAP patients. And often this is our thinking about colon surgery because colon surgery is often the first operation that a patient with familial polyposis will have in their life. And then I'm gonna talk a little bit about special considerations that we take into mind when we are operating on patients who have established desmoid disease and some of the surgical options that we have for these, for patients with desmoids.

So just take a step back and talk about familial adenomatous polyposis. I just want to cover some of the basics. I know that many of you probably all already know these things, but I think this kind of helps establish the rationale for how we think about desmoids in these patients. So, the APC gene is on the fifth chromosome and a mutation, everybody has two APC two fifth chromosomes and a mutation in the APC gene on one of those two chromosomes will result

in, in FAP. This carries nearly a 100% risk of colon cancer during a patient's life if they don't undergo prophylactic surgery. Now, this risk varies because depending on where that mutation on the APC gene is some patients will form thousands of polyps very early in life.

And I saw somebody ask earlier what attenuated FAP is. That's a term that we use for people who tend to form fewer polyps. So these are people who have, you know, dozens of polyps often in childhood, but they're often manageable without surgery for a long time. Sometimes patients with attenuated FAP will be able to live without developing cancer, you know, even into their forties and fifties.

But nevertheless, most people who have a APC gene mutation will at some point develop colon cancer if they don't have a prophylactic operation. In addition to risk of colon cancer, FAP carries other significant cancer risks. This is the in the duodenum, the first part, which is the first part of the small intestine, the thyroid gland, and as we're seeing a little bit more even in the stomach and some other organs as well.

And then there's a significant risk of desmoid tumors, which depending on what type of study you look at is a about a 15 to 30% risk throughout a patient's life. And as, as Dr. She mentioned, you know, this is much higher than the risk of a desmoid tumor forming in a person without FAP, but because FAP is relatively rare, if we took all the desmoid tumors that are seen in our entire population, most of those would be in patients who don't have FAP. And similarly, like Dr. Shepard mentioned we don't really consider these to be true cancers, but they are tumors that can cause significant problems. And actually our, depending on the study that you look at, either the second or the third leading cause of death in patients with FAP. But in addition to, you know, they don't just cause death, but they cause a lot of symptoms and problems.

And this is touching on things that have already been mentioned. They can be locally aggressive even if they don't grow into things. This is just a CT scan, which I understand many people here are probably not used to looking at, but I'll hover with my mouse. This kind of lighter area here is a desmoid tumor and it's not particularly big, but you could see these hollow black structures, that's the intestine.

And this looks a lot dilated, which means that the desmoids are causing a blockage in the bowels. So that's one thing that desmoids can cause and also like mentioned before when the desmoid stick to the bowels, there can be an

inflammatory reaction between those two things. That can cause the bowel wall to kind of break down and form what's called a fistula.

And that's basically where the bowel will open and develop an abscess in the abdomen causing somebody to get really sick or even septic. Septic. Or it can erode through the skin so stool will drain through the skin as a result of the relationship of the desmoid tumor and the bowel. Because of where they sit, desmoid tumors can also block these structures called the ureters. These are tubes that carry urine from your kidneys to your bladder. So if these get blocked up the urine can't travel as it should from the kidneys to the bladder, and the kidneys get swollen because they can't empty their urine.

And this can cause kidney failure. This can cause infections that can even become life threatening. So these are all really significant problems that can result from desmoid tumors, even if they're not spreading to other parts of the body. As a traditional cancer would. And they also can cause bleeding.

They can grow alongside major blood vessels and cause bleeding as a result of that. So it's really important where we can to prevent desmoid disease when we can. And part of the rationale in preventing desmoid is to know the risks of patients and families. Some people with FAP are at higher risk than others of forming desmoids.

We also know that just having surgery is a big risk for desmoid formation. So most FAP patients will develop desmoid after having another surgery, usually a colon operation. And so, I'll talk a little bit more later about whether the different operations that we do cause greater or less risk for desmoid formations.

And so how else could we prevent desmoid tumors? And the first step, as I mentioned, is knowing the risks. So we've looked at this a lot in our FAP patients at our institution. And we found looking at risk factors that have nothing to do with the way we're treating a patient, things that are just kind of inherent to a patient and their family.

There are certain things that place patients at higher risk for forming desmoid throughout their life. One of those is gender. So, female patients are more likely than male patients to develop desmoid tumors. Patients with certain FAP manifestations in other parts of their body, outside of their colon are more likely to form desmoid disease.

So people will sometimes form these lumpy bump bumpy lesions below their skin, or benign bro growths in their bone, or patients will have extra teeth. We know those patients are more likely to develop desmoid tumors. One of the biggest risk factors is just knowing that there's desmoids in the family.

And then finally, when we look at the APC gene depending on where the location is on the gene, we know we can identify patients at higher risk of forming desmoid tumors. None of these things are perfect, but they help give us an idea. And so then as I mentioned, most desmoid disease occurs after another surgery.

And we think that something about surgical trauma sets off changes that allow genes to further mutate and cause allow desmoid to form and grow. And also, like I mentioned, the most common first surgery that we do is colon surgery. So I'm gonna talk a little bit about the colon surgery that we do.

Even though it's not directly related to desmoids, we think it might have some impact on the formation of Desmoid. So this photo, this cartoon on the left, shows kind of normal colon anatomy or colon. This is all of your small intestine, which you have several feet of, and all the blood vessels to both your small intestine and your colon traveling these sheets of fat that are called the mesentery. And this is where desmoid tumors typically form in the mesentery of the small bowel or of the colon. And then, you know, this is your colon starts here on the lower right side of your body, near where your appendix is, and it travels up your abdomen over to the left side, down the left side.

And then the last part of your large intestine is called the rectum, which is about a foot long. And that's goes down to where you empty out your poop. So when we're thinking about surgeries that we do, when patients have an uncontrolled number of polyps in FAP, there's one operation called a total proto colectomy.

That's where we remove the entire colon and the rectum. There's what's called a subtotal colectomy, which we really don't do much of where we leave a little bit of colon and the rectum in place. And then we have what's called a total abdominal colectomy. Remove the entire colon, but leave this last foot of the large intestine, which is called the rectum in place.

And our decisions about which of these operations to do has to do a lot with a patient's colon cancer risk, in particular, their rectal cancer risk. So the number of rectal polyps that they have before surgery, but as I'll mention in a little bit, also has a lot to do with what we think about their desmoid risk.

So when we re, when we leave the rectum in place, we often reconstruct things with what's called an ilio rectal anastomosis. So that's when we bring the end of the small intestine down and reattach that to the rectum. So this is, we remove the entire colon. That's a total abdominal colectomy with an ilio rectal anastomosis.

And anastomosis is, we use in surgery for a connection of two things in patients who need to have the rectum removed. So we remove their entire colon and the rectum. We often create what's called a J pouch, which is making a pouch like formation out of the small intestine and correct the connect that directly to the anus.

Cause of the complexity of this surgery, we'll often give patients a temporary ileostomy bag with this operation. So these are the two most common surgeries that you'll see us do now in patients with familial polyposis. When we're deciding on these operations that surgeons are always thinking is, you know, does the operation that I do, we're always thinking about desmoid risk in patients with FAP.

So one thing that we wonder is, does my choice of the operation that I'm gonna do impact a patient's desmoid risk and does the way that I approach it? So, you know, traditional open surgery with a big incision or what we commonly do now is laparoscopic surgery with small incisions and cameras and long instruments that we can use inside the belly.

Does that approach affect desmoid risk? And our group has long hypothesized that something about when we create this J pouch that we connect down to the anus, that will cause extra stretch from the mesentery, which is where desmoid form and to something about that stretch make desmoid formation a little bit more likely to happen.

And when we looked at this in our own patients, we did find, now this is a study that we did where we just looked at we looked retrospectively, so we didn't, you know, collect this data as we went, but we looked back on all the operations that we did for FAP and we did find that patients who had a pouch surgery, this is the blue line here, typically more commonly formed desmoid tumors and formed them earlier time point after surgery compared to patients who had their rectum remaining in place.

Similarly we found that patients who had open surgery formed desmoid tumors a little bit more commonly than patients who had laparoscopic surgery. And we found this to be pretty significant factor. So these are what's called odd ratios.

So the higher number means the more strongly that factor played a part in desmoid formation.

And we found that the surgical procedure was even a stronger factor than slightly stronger factor than things like family history when causing or being associated with desmoid formation. So this is just to kind of tie up. Thinking about surgery and how we think about surgery to reduce risk of desmoids when we identify patients who we think are high risk for forming desmoids after surgery, number one thing that we do is try to manage them without surgery for as long as possible. So keeping up on their polyps with colonoscopy and really delaying surgery by removing polyps with colonoscopy for as long as feasibly safe to prevent colon cancer. Because even if we do a less risky surgery for desmoid formation, it's still better, it's still a higher risk than no surgery.

But in these people, when surgery's ultimately needed, if it's possible to keep the rectum in place without creating a, you know, too high of a risk for rectal cancer to do a total colectomy with a ilio rectal anastomosis rather than a proctor colectomy with a J pouch. And we think, you know, the evidence isn't as strong about this, but we think that laparoscopy might be beneficial compared to open surgery.

So I'm gonna transition a little bit and talk about patients who have established desmoid disease and how we think about surgery for desmoid and compared to surgery for other cancers or preventative surgery on the colon to prevent colon cancer. Surgery for desmoid disease is usually geared towards a specific quality of life issue or a symptom not to curing the disease.

Part of this is because desmoid often form in this part of the mesentery, which I shown before, where removing the desmoid tumor would compromise all of the blood flow to the entire small intestine, which is not something that you can remove and leave a person with a good quality of life from. So we really try to address where possible with surgery the symptoms that desmoid are causing.

I mentioned some of the symptoms earlier. Part of this we look at is we stage desmoid by both, not just how big they are. But by how fast they're growing and what kinds of symptoms they form. And as you can see here you know, severe symptoms would be considered a bowel blockage or a bowel fistula, or a urinary blockage or bleeding.

Those are the most severe symptoms that we consider when we're thinking about having to operate for desmoid tumors. This is always a balance, right? So, some patients will form desmoids on their extremities or their abdominal wall,

and those are easier to do surgery on without causing major comp consequences or side effects.

So we have lower threshold to do surgery in those situations because the risk is lower. When desmoids form at the root of the small bowel mesentery, the risk of surgery is very high. So we try to maximize the medical treatments and other things as much as possible before we do surgery. I just wanted to point out one other thing.

So we talk often of desmoid as tumors, but we often also see something called desmoid sheets where I know you're not used to looking at pictures like this, but this is the small intestine and this is that fatty tissue where the blood vessels flow called the mesentery. And these white plaques here are desmoid, but they're not tumors.

They're not masses, they're just sheets of tissue, which are very thin and they can cause a lot of problems. They can cause the bowel to stick to them and they can even cause blockages even without growing to the point where you can even see them on a CT scan sometimes we identified the these things just at the time of surgery when we didn't know a patient had desmoid disease.

So when patients have severe symptoms related to desmoids, as I mentioned before we can often remove abdominal wall, chest, or extremity desmoids because removing them may not have a major impact on quality of life or a lot of major downsides to it. When people have a bowel blockage from a desmoid tumor that's not removable there are options that we can relieve some of those symptoms while leaving the desmoid tumor in place.

So sometimes that would include creating a stoma, which is bringing up a loop of the intestine to the skin to empty into a bag, and that will allow relief of a lot of those symptoms without the high risk of removing the desmoid tumor and a large amount of small bowel. Sometimes depending on where a desmoid tumor is located, we can bypass the desmoid.

So that would allow a person to live without a bag, without the risk of removing the desmoid and just basically bypass one segment of the intestine to another without and relieving the obstructive symptoms when the urine tubes, the ureters become obstructive. There's a lot of options for that.

Some are placing stents in those structures to allow the urine to pass. Sometimes we have to place drainage tubes into the kidney to allow the urine to drain externally into a bag. And sometimes urologists can do an auto transplant, so it's

similar to a kidney transplant, but instead of transplanting a kidney from a another person, you just transplant a kidney from the same person to themselves just in a different place where that urine tube isn't blocked.

And then when people have mesenteric desmoid that don't involve the entire blood flow of the small intestine, we can sometimes remove those with the segment of the intestine and reattach things without having to compromise too much of the intestinal length. So small desmoid like this can often be removed, but like I was mentioning before, this CT scan shows a very large desmoid, and this white dot here is the artery that brings all the blood flow to the majority of the small intestines.

So as you can imagine, removing this desmoid tumor would require removal of almost all of the small intestine, which would leave a person in a position where they're not able to support their nutrition and would rely on a lot of supplemental nutrition to be able to continue to live.

And so, one of those supplements that we give patients that they have to have a large amount of their small intestine move is IV nutrition called TPN. And this is really, you know, it's not a cure all. Somebody who has to live on TPN will It's pretty high risk. You need to have IV access permanently and that can lead to infections.

TPN long term can cause liver failure and cirrhosis. And having these IVs in place, long dwelling can form life threatening blood clots. So leaving a patient in a position where they have to live like this is not really a great option, which is why we try to avoid operating on some of these desmoid tumors.

If we can manage the symptoms in other ways and just before wrapping up, you know, in some patients, and I just wanna make sure I'm clear about this. This is just a very small select number of patients. Small bowel transplant may be an option for managing severe desmoid disease. I'd say, you know, before the last few years we've had a pretty bad experience at our institution with small bowel transplant outcomes, and they're starting to look a little bit better.

And these are options for different intestinal transplants when the majority of the small intestine has to be removed. So, our transplant surgeons can do intestine only transplants, and patients who maybe have developed liver failure related to longstanding TPN, they could do transplants of both intestine and the liver and then even other organs together with that if needed.

As I mentioned, the initial outcomes with this are very poor. And to this point, we've only transplanted I think nine or 10 patients with desmoid tumors. It requires medications that suppress the immune system for the rest of your life, which can lead to infections and other problems. Small intestine transplants are not offered at more than a small handful of transplant programs in the country, so it's a, there's a significant issue of access for a lot of people, and as I mentioned, it has a very high rate of complications compared and a higher rate of death compared to other big surgeries that we do.

But for some people who don't have a lot of options due to really severe desmoid disease, it may still be the best option. So just to summarize desmoid disease is a really significant challenge, especially for surgeons who take care of FAP patients and obviously more than anyone for the patients with FAP. We have to do more work to figure out ways to prevent Desmoid disease formation.

In addition to some of the factors I spoke about earlier and some of the things Dr. Shepard talked about earlier. We don't know if any of those medications that we use to treat desmoids might be beneficial on high risk patients to prevent them from getting desmoids after they're having surgery. So one thing that we're looking to do at the Cleveland Clinic and with some other institutions is potentially doing a trial to see if either sulindac or other medications when given around the time of surgery, might lower the risk of desmoid is forming in the first place.

Surgeons, we have to consider desmoid risk when we're planning out our other surgeries, even people who don't have desmoids and that surgery for desmoids is challenging and should be directed towards specific symptoms. And I mentioned about intestinal transplant. It's promising, but it's a high risk option and only a reasonable option for a very small number of select patients.

So I really enjoyed having the opportunity to speak with you and I'm happy you looking forward to talking about any questions here?

Jeanne Whiting: Thank you so much. I'll just go into a couple questions that are remaining. Dr. Shepard's been answering a lot of them. Outside of the correlation between FAP and desmoids, I thought desmoids were not hereditary. Seems that Dr. Sommovilla just mentioned they are or can be. I guess we just need clarification on that for this patient.

Dr. Joshua Sommovilla: So all of the studies that I was showing and talking about were specific to our FAP patients, so that was all within the context of FAP.

So patients with the family history of desmoids, when I was talking about them, those were patients who had FAP and a family history of desmoid. We have a lot of FAP families where nobody in the family has gotten desmoid. And as I mentioned, some of that's related to the location of the mutation on the APC gene.

But there are other things that we probably don't understand as well as we could about what predisposes some FAP patients and families to desmoids more than others. I'm not aware of other hereditary conditions that are associated with desmoid disease, but again, you know, my area of expertise is in FAP. There may be something else that I don't know about, but yeah.

Jeanne Whiting: Okay. So if it's an inherited disease but no one in your family has ever had it that you know of, can you be the first one to be creating, having that disease and passing it down to your descendants?

Dr. Joshua Sommavilla: Definitely. So about one in five patients with FAP will be what we call de novo mutations.

So that mutation in the APC gene, it can develop early in development of an embryo, which means that person did not receive that mutation from their parents, but it developed spontaneously. Now usually those people will be at risk of passing it to their children, but they wouldn't have necessarily known from a family history that they had it because they're the first person.

So, you know, every family with a, at some point in their history had a person who probably developed that mutation spontaneously in a way that allowed them to pass it on to the rest of their family.

Jeanne Whiting: Okay. And as a matter of course, Dr. Shepard mentioned that I always wanna know if a desmoid has the APC patient has the APC mutation. As a matter of course, do you always do that genetic testing before surgery or treatment?

Dr. Joshua Sommavilla: Yeah, I would and Dr. Shepard probably knows this better than me because almost all the patients that I see with desmoids already come with an established diagnosis of FAP. But certainly if I were to see a patient with desmoid disease, especially desmoid disease in the abdominal cavity, I would want them to have FAP ruled out before I made any final decisions.

And I see this question about desmoid sheets occurring in patients without FAP or is it only FAP related? I would say not just desmoid sheets, but really, you know, desmoid tumors in the small bowel mesentery is highly indicative of FAP. So my understanding is like most patients who don't have FAP who form desmoid, it's usually in the abdominal wall, extremities, sometimes in the abdomen, but usually not in the mesentery or retroperitoneum.

And those types of desmoid are much more likely to be in FAP patients. And I haven't seen desmoid sheets in patients without FAP.

Jeanne Whiting: Okay. One last question. I'm excited to hear that desmoid risk is starting to be studied and calculated into the risk of colon or abdominal surgery for FAP patients. You guys rock.

Dr. Joshua Sommavilla: Thank you.

Jeanne Whiting: I would agree with that final comment. All of our presenters rock what incredible information we've been able to get today. Thank you so much for being here and answering all these questions and imparting all of your great knowledge and experience. We appreciate you all. Dr. Hurley included. Dr. Shepard, Dr. Sommavilla. I'm gonna turn the time back to Lynne Hernandez for some final comments as we close our day.