[MUSIC PLAYING]

KATIE BERLACHER: My name is Katie Berlacher. I'm an assistant professor here at the University of Pittsburgh Medical Center, part of the Heart Vascular Institute. I'm the director of the Women's Heart Center here at Magee Womens Hospital, part of the Heart Vascular Institute. And I'm joined today by Dr. Agnes Koczo, one of the Fellows here in the fellowship program.

We are here to talk to you today about spontaneous coronary artery dissection. By the end of this lesson, we hope to have you be able to list risk factors and clinical features associated with spontaneous coronary artery dissection, or SCAD. We'd like you to be able to diagnose SCAD, describe the current understanding of the pathophysiology of SCAD, and manage a patient with SCAD in acute and long term setting. Both Dr. Koczo and I have extensive experience managing patients with SCAD, and so we are excited to share a case with you and some of the things that we've learned over the past couple of years. Agnes?

AGNES KOCZO: Thanks, Dr. Berlacher for that great introduction. As you mentioned, we're going to go through this lecture in a case based format. So our case begins with a 41-year-old female who presents to the emergency department with four hours of acute left arm pain she knows radiates to her right arm, and she describes as a "globus sensation in her chest."

Her troponin on presentation was 10, so elevated. Hemodynamically, she was noted to be stable. You can see her vitals at the bottom of the screen here. She's afebrile. Her blood pressure is 118 over 83, a pulse of 83. She's breathing 18 times per minute, and her sats were 99% en route here. She was noted to be warm and well perfused on physical exam on presentation.

As far as her past histories are concerned, she had no significant past medical history. As far as her OB history, she's had four prior pregnancies and four healthy children. And her pregnancies were not complicated by hypertensive disorders or pregnancy or otherwise. Her past surgical history is just notable for orthopedic procedures following a motor vehicle accident.

Notably, she has no family history of either early coronary disease or sudden cardiac death, as well as spontaneous coronary artery dissection or SCAD, or any sort of arteriopathy including FMD or fibromuscular dysplasia, or any of connective tissue disease. Her social history is pertinent for living with her husband and children in the Pittsburgh area, and she denies any alcohol, smoking, or illicit drug use.

Upon presentation to the emergency department, given her chest pain an EKG was obtained. And as you can see, the EKG was most notable for ST elevation noted in her inferior leads II, III, and aVF. She also had some ST elevations laterally here in leads V4 through V6. So given her chest pain, her troponin elevation, her ST elevation, she was taken emergently to the Cath lab.

The right coronary artery was first to be engaged, and I'll just show you two projections here. But essentially, her right coronary artery was noted to be free of disease. Then, attention was turned to her left circulation, and there are a couple of things to note here on the angiography. First that was striking is that she has some tortuosity actually to all of her vasculature, which is something that is actually commonly seen in SCAD patients, including and up to all of the vasculature, not just the coronary artery that's impacted by SCAD.

And then if you look at this sort of mid to large size obtuse marginal one branch coming off her left circumflex. You can see sort of that hazy area here in the middle vessel wall, and you can also see that the rest of the coronaries are sort of beating vigorously with the myocardium. But this area of the myocardium seems to be a little bit stunned. And this is just another projection showing that obtuse marginal region here as well.

So the invasive cardiologist again noted this left circumflex gave off a moderate sized vessel with its hazy appearance in the first obtuse marginal 1 branch. That diagnosed this patient with type III spontaneous coronary artery dissection or SCAD.

So let's back up a little bit and talk about the pathophysiology of SCAD. So SCAD is the spontaneous hematoma formation within the tunica media or this middle layer of the vessel wall. And it's thought that there's a couple hypotheses as to how this hematoma gets there. The first is this inside outer dissection flap hypothesis, which posits that there's actually a tear in the vessel that communicates most with the true lumen of the coronary. And then, blood from the true lumen can actually then pool out into this middle layer of the vessel, which is how we see it on coronary angiogram.

The other is this inside out or de novo hypothesis, which is that some of the perforating vasculature that supplies blood to the coronary artery spontaneously pooled and formed a hematoma do novo, in this middle layer of the vessel. And then this hematoma can expand, propagate, and then as this diagram shows cause occlusion and all the symptoms and signs of ACF.

And so we've come to understand the disease. There's been increasing evidence for this outside in, or de novo, hypothesis as patients are getting earlier to coronary angiography. We see a number of patients never have this intimal tear. They actually just have this sort of false lumen. And then for patients that are serially imaged, sometimes we'll initially see them with this de novo hematoma in the middle layer of the vessel. And then later on, this hematoma can become overwhelmed and essentially decompress, causing a secondary intimal tear, which we think is actually more of a sequelae than an inciting event for this. So depending on how the hematoma looks and how many places in the vessel wall it ends up dissecting, you can get different angiographic appearances, or if you use intracoronary imaging, imaging appearances of SCAD.

There's many different types of SCAD. Right now, these are sort of the three main types that have been identified. From left to right, you have type 1 SCAD, which is essentially that looks like dye hangup or arterial staining with several lumens of the wall. Type 2 is most commonly and sort of most classically associated with SCAD. It's this sort of long, thin, diffuse segment of narrowing or occlusion.

And then Type 3 is some of the most difficult types of SCAD diagnose, like the subtleties that we noted in our patient during the case. It's thought to be like a coronary artery disease mimicker because it's often this just focal segment of occlusion and sometimes can involve further investigation to diagnose definitively.

So what causes SCAD? In short, we don't know. It's something we are still investigating. We think it's this two-hit hypothesis. So we think, number one, patients often will have some sort of vulnerable vasculature or underlying arteriopathy. A lot of times in our patients in clinics, we end up diagnosing this after the SCAD event. So if your patient does not have a family history or personal history of this, SCAD should still be on your differential. And as you'll see from some of the predispositions on the right, fibromuscular dysplasia is one we will come back to that has the highest overlap with SCAD.

So we start with this vascular vulnerability. And then there's some sort of acute second hit or acute trigger, whether it's some sort of hormonal, endogenous or exogenous, whether it's pregnancy or hormonal use that will acutely trigger it, as well as something like emotional or physical stress that we think will actually incite the acute event.

So who ends up getting SCAD? So the overwhelming majority of patients that present with SCAD are women. And oftentimes, this is not the demographic that presents even with chest pain that we consider acute coronary syndrome for. So diagnosis and clinical suspicion is so key to this diagnosis. We actually have proposed sort of acute illness script that we want you to remember for patients where SCAD should come to mind in your differential.

And it's really along the lifetime of a woman in these two periods of major hormonal transition. So for women who choose to get pregnant, in the postpartum period, we often will see patients with pregnancy-associated SCAD present, then in this perimenopausal period, or in the fourth or fifth decade of a woman's life, is, again, the most common age for women to present with SCAD. Again, as we discussed, this is not an atherosclerotic process. And so oftentimes, women will present without any traditional risk factors for SCAD. However, in SCAD registries, we have noted that about a third of women will have coexisting hypertension. And a quarter of women will also have hyperlipidemia.

So how do we go about diagnosing SCAD? So again, to review, clinical suspicion is paramount because the gold standard is early coronary angiography. But getting your patients to cath involves high clinical suspicion for this. So we talked about a lot of different clinical features of your patient that should make you think of SCAD in your differential and pursue that EKG and pursue that troponin.

Once in the coronary angiography, we discussed Type 2 and Type 2 SCAD are sort of classic appearances of SCAD and will somewhat more easily allow interventionalists to make this diagnosis. However, this Type 3 SCAD appearance again mimicking atherosclerosis is going to often require the interventionalists or the cardiologists to come back to the clinical history. And often, the context is within the coronary angiogram. So no other parts of the coronaries are suspicious or you see this typical tortuosity of the vessels that should make you think that this could be a Type 3 SCAD.

Some interventions will pursue intracoronary imaging, including optical coherence tomography or intravascular ultrasound to better characterize this lesion and prove this lesion is SCAD. Of course, this is taken with extreme caution. There's always risk for iatrogenic dissection or hydraulic dissection in propagating and worsening the SCAD lesion with intracoronary imaging catheters. So of course, there's sort of a heavy risk benefit that should be weighed in pursuing intracoronary imaging in these patients for diagnosis. Anything to add, Dr. Berlacher, at this juncture?

KATIE BERLACHER: Thanks, Agnes. This has been wonderful thus far. I think the most important thing to highlight right now is just the evolution of the diagnosis of SCAD and our understanding of the pathophysiology. This is where we stand right now. I think this has changed even from when I was in medical school and I learned that really Type 1 only. That was all that was really being taught, and that was not that long ago.

So just this is going to continue to evolve. And I think understanding how cath plays a really important part in diagnosis right now is vital. This will probably continue to change, though, so just a heads-up to our learners out there that this is not final say.

AGNES KOZCO: Absolutely. Great. Thank you. We also wanted to highlight the emerging role of coronary CTA for diagnosis and also really for healing and resolution of SCAD. And this is a really nice, or some nice images from a case report of a patient who actually presented with a STEMI two weeks following her post-partum course. Of course, on coronary angio here, you can actually see a quite dramatic sort of dissection in the distal left main into her proximal LAD territory.

She later received CTA imaging that actually looks like the extent of this has slightly worsened within these two white arrows. But you can almost better see this sort of false lumen and thrombus formation of SCAD on CTA. And so we think really CTA may have some role up front perhaps in really low-risk ACS patients. But also if you're starting to make medical management decisions for how you want to de-escalate your antiplatelet therapy and you want to see if this SCAD lesion is healed, there certainly can be a role for CTA in the weeks following the inciting event.

CTA is really best used for sort of the proximal large vasculature. They're still not the best spatial resolution for some of the distal smaller vasculature. So in the right setting, I think CTA is starting to evolve to have a role in SCAD.

KATIE BERLACHER: Yeah, and just to comment there, Agnes. I think it's really important. I've learned a lot from our cardiac imagers because they see things a little bit more frequently than we do, obviously, and understand the scenarios in which it would be best to identify these women with a CTA. Obviously, as somebody who's under distress or unstable, that is not going to be a time that you're going to choose a CTA first.

And know that it's the same for other imaging with regards to CTAs, that you have to have your heart rate low, which can sometimes be really challenging, especially in our postpartum women. Their heart rates tend to be a little bit higher depending on the clinical scenario. So you can get lucky. But if you don't find SCAD on a coronary CTA, I would say it's not necessarily ruled out if the story is really good for it.

AGNES KOZCO: Absolutely. Yeah. Thanks for that addition. And I think we also rely heavily on our cardiology and radiology colleagues to present a clinical situation and say, hey, is this a good place to use coronary CTA for this?

So getting back to our case and continuing along, following the coronary angiogram no invasive intervention was taken. And we'll talk about the guidelines for this. A transthoracic echo was ordered for the next day. And the patient was admitted for observation, and quote, "standard therapy for SCAD" was recommended that we'll speak about it as well.

The next morning, the patient had a transthoracic echo obtained. It was notable for a reduced ejection fraction to 40% to 45% and a severely hypokinetic lateral posterior and mid to distal inferior wall. Lipids were obtained, as well as an A1C for the patient. Both are displayed here. So the lipid panel as follows is a total cholesterol of 156, an LDL of 88, an HDL is 52, a VLDL is 16, and triglycerides of 78. And the patient's A1C was 5.4%

So turning back, to Dr. Berlacher, what therapies would you start acutely for this patient? And would your management change had her EF been normal on transthoracic echo? And I'll just bring you back to the data here.

KATIE BERLACHER: Yeah, such great questions. I mean, the first thing that I think of after somebody had a heart attack, right, we're dealing with a STEMI. So we would classify that in a different area. And classically, we're taught to start aspirin and Plavix or another antiplatelet, right, so dual antiplatelet therapy. I think you and I will continue to talk about the need and the data behind dual antiplatelet therapy for patients who have SCAD specifically.

But I would definitely start her on both for right now, given she did have a STEMI at this point in time. And then with that low EF, 40% to 45% with wall motion abnormalities, I do think that it's appropriate to start medications to improve the wall motion and the recovery of the EF. So either your [INAUDIBLE], such as an Entresto medication with a beta blocker. Or if you're not ready and depending on what her blood pressure is, to do just an ACE or ARB plus a beta blocker at this point in time.

There are people who will start people on a statin if they have a SCAD at this point. And I would say that based on her cholesterol and what I understand from the pathophysiology of SCAD, I would probably not choose to start her on a statin at this point in time.

AGNES KOZCO: Excellent. Perfect. And we will go through the medical therapy shortly, which Dr. Berlacher beautifully and very comprehensively reviewed. As far as acute management for SCAD, just a note on the sort of invasive approach, and a lot of these diagrams, just to give credit to this really wonderful state-of-the-art *JACC* paper, which was recently published on SCAD, really outlines that there's two main factors to the invasive management. And it's really the clinical stability of the patient and then whether or not there's high-risk anatomy involved.

And so looking at this algorithm sort of proceeding down from left to right, if you have a patient like we had in the cath lab who is clinically stable and did not have high-risk anatomy, and by that I mean the left main and severe proximal two vessels were not involved, it is really recommended, given the concern for iatrogenic dissection, the overall lower success rate for stenting of these patients, to pursue conservative therapies, so medical management like Dr. Berlacher reviewed and then really monitoring these patients inpatient. We know that you can have hematoma propagation in the following three to five days. And so it's important to keep these patients for perhaps a little bit longer and just make sure their chest pain is under control and they're not developing clinical instability.

For patients who are clinically stable but do have high-risk anatomy, again this left main or severe proximal two-vessel dissection, it's very reasonable to have a heart team or a discussion with your CT surgeons and talk about whether or not bypass is the appropriate thing for the patient. Conservative therapy can also be pursued. It's not as extensively studied. Bypass is pursued in this high-risk anatomy for a patient.

And then, of course, if you have a patient that has active and ongoing ischemia or hemodynamic instability, then certainly based on what your local expertise and sort of technical considerations for the lesion are, either pursuing revascularization by PCI or bypass should be undertaken.

And then coming back to medical therapy for those patients conservatively approached and really in long term for all of these patients, the two things that we focused on are initiation of beta blocker and control of hypertension. So in studies, these are the two things that have been shown to be associated with increased risk of recurrence. So we sort of heavily focus on these two things.

Just like Dr. Berlacher pointed out, this is not an atherosclerotic process. So you should be treating what's done based on primary prevention. These patients are not in the secondary prevention just by nature of their SCAD.

And then there's a lot of evolving data and really a lack of consensus for use of dual antiplatelet therapy, of course referring to patients who have not been revascularized. In studies that have looked to justify dual antiplatelet with perhaps an intraluminal thrombus, that has not been shown to be the case in a majority of cases with intracoronary imaging and prior studies. There was also a recent trial noting there was actually an increase in major adverse cardiac events in patients who were just medically managed and started on dual antiplatelet therapy.

Regardless, the recommendations if you do choose dual antiplatelet therapy is to continue that two to four weeks post ACS. Again, there can be a role here in CTA coronary imaging to assess for healing if you really want to have something objective to stop your dual antiplatelet therapy. And then if you continue aspirin, the recommendation is for three to 12 months.

Coming back to our case here, the patient in our case was discharged on dual antiplatelet therapy, aspirin and Brillinta. Given the reduced ejection fraction and some coexisting hypertension during the hospitalization, the patient was started on Coreg 6.25 twice daily, as well as lisinopril 5 milligrams daily. And the primary team had also chosen to start the patient on atorvastatin 10 milligrams daily. And we discussed the decision making behind that.

Now Dr. Berlacher, I know there's a lot of anticipatory guidance to give to these patients even between discharge and that short-term outpatient cardiology visit. So how do you approach post discharge anticipatory guidance?

KATIE BERLACHER: Yeah, with a lot of care-- honestly, these women are really anxious about what happened to them. Many of them are otherwise healthy, such as our patient. And what did I do wrong, right? I am not smoking. I exercise regularly. And so there's a lot of fear that goes in the patients' minds after this happens, and so a lot of reassurance, many phone numbers. Sometimes I give my personal phone number out to these patients.

And then we talk what I think we're going to talk about now, which is the lifestyle modifications and the things for them to avoid. Some of them will be things that they may have been doing that could have been a second hit, as you were talking about, with regards to the pathophysiology. Some of them are things that we have learned as we have studied and looked at larger patient populations who have had SCAD and why people have had a recurrence of SCAD here. So we would be talking about exercise, diet, and some of the things that they can do to decrease the recurrence.

AGNES KOZCO: Absolutely. Perfect. Just to address what we mean by recurrent SCAD, so as we address before, about one in six patients will have an acute worsening in their symptoms or their clinical status within that first week of the inciting event. This is not considered recurrence SCAD. This is often attributed to the primary event.

When we talk about recurrent SCAD, it's often a de novo coronary dissection, meaning it's actually in a different coronary and vascular territory than the initial inciting SCAD event. And oftentimes, temporally we'll also denote it as occurring after a month of that initial event. Anything before that is sort of most concerning for a continuation of that primary event. And then depending, on the literature, we put patients somewhere in between 10% and 30% risk of recurrence SCAD in the [INAUDIBLE] population.

So we talked a little bit about what we're going to discuss on long-term followup. One of the things that we focus on is screening for associated medical conditions. So again, this first hit to the two-hit hypothesis, this underlying vascular vulnerability. And depending on the study, there's been between 40% and 80% of patients who are diagnosed with SCAD that were found to have underlying fibromuscular dysplasia. So the recommendations are to screen every single person that is diagnosed with SCAD from head to pelvis with either CTA or MRA imaging to ensure that there are no other vascular events that are going to be afflicted or associated with arteriopathy. And then we have some great vascular surgeons as part of our institution who we've referred our patients to for further co-management.

KATIE BERLACHER: And I think, Agnes, just a point there with regards to the imaging and FMD, there's been a handful of patients-- I think you remember a couple of them with me-- that we've actually had to get the imaging studies that have been done and read as negative. And then when we review them with our expert radiologists who see FMD with us a little bit more frequently, they reread them as actually consistent with fibromuscular dysplasia. So I think it's a really important thing to be with radiologists that see these things a little bit more frequently.

AGNES KOZCO: Absolutely. And we're more than happy, of course, to take referrals and outside imaging, and again, re-review that with our specialists. Absolutely.

And then as Dr. Berlacher highlighted, in addition to starting medications for SCAD, we talk a lot about things to avoid in which we think are potential triggers and that sort of acute event. Of course, we tell patients to avoid stimulants of any kind. Migraines are a very common comorbid condition that we find in women. And we have seen in data that triptans have been associated sort of the acute trigger and that women were taking triptan either initially or in increased frequency around their SCAD event. So we really caution against triptan use and will often send patients back to their neurologists for different abortive or prophylactic therapy for migraine.

And then we talked a little bit about the hormonal theory, Of course, in our illness script. And then, of course, there's also data on patients taking exogenous hormones and that being an acute trigger. So we make sure we review this with patients.

We touched a little bit on pregnancy-associated SCAD. But I will tell you that it's associated with more severe presentations of SCAD. And so oftentimes, we'll talk to patients about contraception up front and sort of throughout our outpatient visits to make sure that we get patients out of the acute post-acute period. And we can have safe discussions about family planning with our OB colleagues and weigh the risk-benefits if the patient is considering future pregnancy.

We do advocate for Long-acting Reversible Contraceptive devices or LARCs, which we find to be highly-effective which include intrauterine devices that can both include non-hormonal intrauterine devices as well as progesterone-releasing only devices, as well as subcutaneous implants, things like the Nexplanon.

KATIE BERLACHER: So Agnes, a quick question there-- if your patients say, can I, do you recommend-- if I have a baby, can I get pregnant again? What do you wish for your patients or hope that they say in that Moment?

AGNES KOZCO: Yeah, it's kind of always a difficult conversation, right? But I often tell my patients, or I educate them, that again, this is something that we, as of right now, cannot completely prevent. It's a sort of spontaneous-- there's no warning sign that SCAD is coming. And then we've seen many patients who can present really traumatically with severe disease in the pericardium or the postpartum state.

And so I caution patients that I would not recommend because of the risk-benefit oftentimes going forward with the pregnancy. But certainly, that's always sort of a patient-physician discussion that I have and often involve my OB colleagues.

KATIE BERLACHER: Yeah, I agree. It's not an absolute contraindication. But man, do we get nervous when we have a patient who's had prior SCAD. We do keep them on a beta blocker during those pregnancies. And we're really careful we actually bring them down to lower blood pressures during those pregnancies when that happens. And then we also think really closely with our maternal fetal medicine colleagues about the delivery plan. We won't get in the weeds on this one. But if there is somebody that you know has SCAD that wants to become pregnant again, that is certainly a discussion to have before that decision is made.

AGNES KOZCO: And as Dr. Berlacher highlighted, it's a conversation we have often. And so if you also have a patient who you just don't feel comfortable talking about future pregnancy, we're really happy to go through the risk-benefit with them as well.

And then lifestyle is also something that Dr. Berlacher-- we touched on. You know, a lot of these women will commonly have chest pain after their SCAD event for days, weeks, and months. And cardiac rehab is a really important part of their success in getting back to even their baseline activity, knowing that under supervised condition, if they do have symptoms, whether or not those are or are not related to their heart is a really important step for them.

As Dr. Berlacher again highlighted, a lot of these women are extremely active. Some of them are running marathons and doing strenuous exercise. And unfortunately, we know that that's a trigger. And so we do advocate for them to keep active, keep going with the low-rate resistance training. But really any of strenuous isometric extreme endurance exercise, we ask patients to avoid.

The PTSD and the depression related to such a unexpected and traumatic event oftentimes will be something that we do continue to address and make sure that our patients are checking with themselves and addressing their mental health after such an event. And then we always advocate for a heart-healthy diet for certain. But we don't think there's any dietary association associated with SCAD, so there's no specific diet we recommend for patients. We just advocate for them eating healthy. Any--

KATIE BERLACHER: The only caveat there would just be the caffeine in coffee and teas and Monster drinks and whatnot. We have had a handful of patients ask us questions about that. And they should avoid those things.

AGNES KOZCO: Yes, good point-- no stimulants for sure. You know, in our experience, and we actually take care of a relatively large population of women who have suffered from SCAD, we spend a lot of time learning about it and talking to our colleagues throughout the country about SCAD. And so we feel like we have a lot of comprehensive information resources to give to these women. And so we would really recommend referral of patients to a women's heart specialist or center. I think that's the best place they're going to get up-to-date recommendation and care after this event.

KATIE BERLACHER: And just a side note on that, Agnes, we didn't talk about this in the beginning, but SCAD actually technically falls in the MINOCA category, or the MI and Non-obstructive Coronary Artery Disease, which is something that I think a lot of women's heart specialists are really focusing on because that's what a lot of women in general get diagnosed with. And so even if you have a patient who had a MINOCA event and you don't know what that was, whether it was vasospasm or microvascular disease and all these things that seem rather vague at the moment in the literature at times, it's really important that we get a diagnosis. Because we do treat people who have vasospasm versus who have SCAD versus microvascular disease differently.

And this is something that experts really should weigh in on. If you are not near a women's heart specialist, it may even be worse for your patient to go see them once. We co-manage with a lot of other cardiologists. We don't necessarily have to take care of them or see them all of the time. But a lot of times, our patients say that they feel better having seen us and getting some of the detailed questions answered before they go back to their standard cardiologist.

AGNES KOZCO: Perfect. Absolutely. And so we hope that you take home from this lecture that, again, it takes a high clinical suspicion. So remember your illness script for SCAD is a leading cause of ACS in women. And remember these two timelines, either postpartum or perimenopausal in that fourth or fifth decade of life, where if patients are presenting with classic ACS symptoms, but they don't have any atherosclerotic disease on initial imaging. Please keep these illness scripts in mind.

As of right now, coronary angiography is the gold standard for SCAD diagnosis. So try and get your patients to the cath lab early if you suspect this. But there is an evolving role for coronary CTA, perhaps in diagnosis and certainly in healing or resolution of SCAD.

Be certain to screen for associated conditions. Remember, we think there's some sort of underlying vascular vulnerability in many of these patients. The most commonly found is FMD, or Fibromuscular Dysplasia. And the screening is head-to-toe-- or, I'm sorry, head-to-pelvis imaging with CTA or MRA. And then acutely, from a medical management standpoint, we focus on beta blockers and treating hypertension, which is comorbid in about a third of patients to prevent recurrence of SCAD.

Invasively, we really only revascularization patients are unstable. And as far as antiplatelet therapy goes, we advocate for aspirin and then caution with antiplatelet therapy. But the data is evolving. In the long term, we talk to patients about avoiding triggers, which includes stimulants, hormones-- again, this encompassing pregnancy and future pregnancies as well-- and then any kind of extreme competition or lifting. And again, we encourage you to refer your patients to women's heart or SCAD center to get the best care.

All right. Thank you so much for listening to us today. We really appreciate the opportunity to talk to you about a topic we're really passionate about.

KATIE BERLACHER: Thanks, Agnes. This has been wonderful. You did a great job explaining this. I look forward to working with you in the future to better understand and care for these patients.

AGNES KOZCO: Thank you.