BroadcastMed | Grand Rounds: Spontaneous Coronary Artery Dissection: New Insights and New Questions About This Not-So-Rare Condition

RAJIV GULATI: Hello. I'm Rajiv Gulati. I'm a cardiologist at Mayo Clinic. I spend most of my time in the cath lab. I'm here with Dr. Sharonne Hayes, who's a colleague from the Women's Heart Clinic, and we're going to talk today about spontaneous coronary artery dissection, new insights and new questions about this not so rare condition. I'm going to spend my time talking about a retrospective study we've done at Mayo Clinic, looking at our experience over many years and tell you what we've really learned more recently about this very interesting condition.

So here's a very brief case, a recent case, a real deal. 42-year-old female, a couple of months ago, who came into hospital with an out-of-hospital ventricular fibrillation arrest. She was resuscitated in the community, had anterior changes on her ECG and a positive troponin, so an acute coronary syndrome. And she came to the cath lab, and you'll see here that the LAD has a smooth, 70% narrowing in the mid-vessel. The guidelines will tell us exactly what to do here. We should treat with antiplatelets, put in a stent as quick as possible, and then treat with a statin to prevent recurrence.

Well, in this case, there was a little bit of an unusual twist to the story in that there were no discernible atherosclerotic risk factors. So here we did an intravascular imaging study, using OCT, or optical coherence tomography, and you'll see here on the right-hand panel that the central lumen there, that black structure, is completely free of plaque. There's no plaque at all. But surrounding that lumen, there's a large echolucent structure, which is a hematoma, an intramural hematoma between the media and the adventitia causing compression of the central lumen. So this is not a typical acute coronary syndrome. There is no cholesterol plaque. This is a hematoma compressing the lumen. This is part of the spectrum of spontaneous coronary artery dissection. And we really would not have known this if we hadn't done an OCT or intravascular imaging study.

Well, why does it matter? Well, it matters because of a number of reasons. And we can learn about that when we look at our retrospective study. Here, we did a series of-- we looked back over 20 or so years and identified 87 people who had suffered an acute coronary syndrome relating to spontaneous dissection. The mean age was relatively young, 42.6 years, and the vast majority, you'll see here, were female. And if you were a female, the highest risk factor was being in the postpartum period, the first three months after delivery.

You'll see that about half of the patients presented with a full blown STEMI, and there was multivessel spontaneous coronary dissection identified in almost a quarter of these angiograms. One particularly interesting facet is that when we followed these people over time that there was a recurrence rate, a recurrence of spontaneous dissection, in around about 20% of females over this 12-year period, none of them males. The few that there were, none of them experienced a recurrent event.

Another couple of interesting features were, there was a very low prevalence of atherosclerotic risk factors. In fact, when we compared the risk factor profile with matched controls who had typical acute coronary syndromes, there were markedly fewer responses in the spontaneous dissection group. We also found, somewhat unexpectedly, a high prevalence of non-coronary disease, and that is, in particular, non-coronary fibromuscular dysplasia. Somewhat serendipitously, we looked at the femoral sheath angiograms that had been performed prior to closure device placement, and you'll see here's an example of a beaded, irregular appearance in the iliac artery. This is typical for fibromuscular dysplasia.

And in the 16 femoral sheath angiograms that had been done, eight exhibited fibromuscular dysplasia. So clearly there is a signal for non-coronary FMD being in association with spontaneous coronary dissection.

Well, how about the treatment? Well, of course, this is a retrospective look back at how things were, how people were treated over this time. And we can't make any full blown conclusions, because it wasn't a randomized study. But you'll see here that 31 out of the 87 were treated conservatively, and 39 were treated with acute angioplasty, with a few people being treated either with bypass surgery or fibrinolytics as an in-depth treatment strategy.

Focusing particularly on the patients who are treated with percutaneous intervention, because that is the typical treatment for acute coronary syndrome with coronary disease, and we found when we compared the acute outcomes in patients with spontaneous dissection compared to patients with a typical acute coronary syndrome, the rate of technical success of PCI was markedly lower in the SCAD groups. Only 62% of patients with spontaneous dissection had immediate successful PCI, compared to a much higher proportion of patients with typical acute coronary syndromes.

Well, what does that mean? Does that mean we should be avoiding PCI in all patients with spontaneous dissection? Well, what about patients who come in with a STEMI or an occluded vessel? Should we seriously avoid PCI in these people?

Well, we tried to address that question by looking back at the baseline flow of patients who were treated with PCI. And we found that if the vessel was effectively occluded, so TIMI zero to one flow, then the chance of a successful percutaneous intervention procedure was pretty decent, here, you'll see at 71%. On the other hand, if the flow at baseline was OK, TIMI two to three, only 32% of those procedures were successful and uncomplicated. So the message here might be that if the flow at baseline is acceptable, TIMI two to three, then if you're going to undertake an angioplasty or PCI, you can expect a torrid time, either failure or a highly complex procedure. So maybe we should seriously question whether we pursue PCI in patients with normal flow and spontaneous dissection.

The reasons for technical failure in this group were split three ways. A third of the time, the coronary wire ended up in a false lumen. The majority of time, the reason for failure was because of propagation of dissection and loss of flow after stent placement. So when the stent is placed, that intramural hematoma will compress, go downstream, and cause more occlusion of the vessel downstream. Some of those patients could be rescued with multiple, more stents but loss of flow as a result of stent placement was a frequent phenomenon.

Just a couple of examples here. You'll see here, in the mid LAD, there's a focal stenosis related to a spontaneous coronary dissection a young female but normal flow. This looks like a focal lesion, and from an angioplasty perspective, it looks like a fairly straightforward lesion to treat with a stent. In fact, that's what was done, and multiple stents had to be placed because of propagation of dissection. And you'll now see there is no flow downstream of where the stents were placed. So complete loss of flow after stents were placed because of compression and displacement of the intramural hematoma and a large anterior infarct ensued, having initially noted to be normal flow at baseline.

This is another LAD. Different patient, but still a young female with a spontaneous dissection. And you'll see here a more impressive length of dissection in the LAD. Also going across the screen, you'll see a dissection in an obtuse marginal but normal flow in both vessels at baseline. This patient was managed conservatively, so no intervention was done and had a repeat study three months later. And you'll see here, in the LAD, there's been complete healing, so complete resolution of that spontaneous dissection. And also in the obtuse marginal, going across the top of the screen, near complete healing there, too. So conservative therapy here was the right thing to have done, near complete healing in two vessels.

And when we look back at our patients who have been treated conservatively, it was notable for no in-hospital complications, and repeat angiography, which had been performed in 13 patients, 17 vessels, the majority showed complete resolution or partial resolution. So this gives an idea of the natural history of spontaneous coronary dissection when left alone, favors healing. And this data is consistent with a recent publication from a Spanish group, who evaluated both spontaneous dissection and atherosclerotic dissection. Patients who are treated conservatively, again, indicate-- tended to demonstrate healing when left alone.

So the lessons that we've learned from this retrospective look back is SCAD is perhaps not as rare as has been previously thought, and we believe will be increasingly recognized in future, particularly in high-risk groups, young females with no atherosclerotic risk factors. And that's because of awareness and because of increased use of intravascular ultrasound and OCT, which can help identify the mechanism of acute coronary syndromes. It's a non-atherosclerotic condition. This is not related to risk factors or to plaque. Extracoronary abnormalities, as fibromuscular dysplasia and dissection in other vessels are common, and Dr. Hayes will be talking some more about that.

The reasons why-- there are many reasons why it's important to diagnose this condition, because the management is actually different to typical acute coronary syndromes. We've shown here with this data that conservative therapy may be superior to percutaneous intervention. We have to question what the role of antiplatelet therapy should be here. If the process is intramural hematoma, maybe blood thinners are not the right thing.

I raise the question of statins, because although the numbers were small, in our study, we looked back, statins were actually associated with a higher risk of recurrent dissection. Small numbers, but a signal, perhaps, that statins may not be the right drug in this situation either.

I'm going to hand over to my colleague Dr. Sharonne Hayes now, who's going to talk about other aspects of spontaneous coronary dissection and moving forward.

SHARONNE N. HAYES: Thank you, Rajiv. I'm Sharonne Hayes. I'm the founder of the Women's Heart Clinic, here at Mayo Clinic in Rochester, Minnesota. And I came about research and practice of spontaneous coronary artery dissection in a somewhat complementary and different way from my colleagues in the cath lab, who were looking at that vast experience that we've had over the past 20 years. Although I had cared for patients with this condition in the past, it was through patient-initiated research that we first started looking at this somewhat prospectively.

Another hat I wear is the medical director of, of course, for women who have heart disease, to train them as advocates in partnership with Women Heart, the National Coalition for Women with Heart Disease. And at one of these courses, one of the attendees came up and asked me what I knew about SCAD and challenged Mayo Clinic to research this condition. And I replied that, well, not a lot is known, and in part, because it's so uncommon, it would be hard to do something prospectively. And she then said that on Women Heart's online community, there were actually over 70 women who had found each other, who'd experienced this condition and were very eager to move research forward and in fact, had developed a rather sophisticated, once I looked at it, research agenda.

Now, the challenge in developing a research program around women who only knew each other online was that this was truly virtual. They were not Mayo Clinic patients, and they lived all over the world. So we set out to have a small pilot. We got IRB approval for 12 patients. Within a week of opening the study, we had over 18 volunteers and more came in after that. So that showed the interest in this highly-motivated group of patients.

We subsequently published this very small pilot, more of a proof of concept, but the story of these women bringing this research forward was published in the *Wall Street Journal,* and through that, allowed us to find many, many more patients and now currently have two studies going on, one which is a continuation of this registry, where we are looking, and enrolling women, after angiographic confirmation-- men and women, by the way-- where we're doing a detailed medical history and assessment of medical records and looking at all of the imaging and history and risk factors to try to better understand this.

A complementary study is a DNA biobank, and in this study, we are looking to get both the patients and their parents, and because these are a relatively young group, sometimes their parents are alive, and looking at probands and their family members to see if we can't, with exome sequencing, ultimately find some other genetic causes for spontaneous coronary artery dissection.

My colleague, Dr. Gulati, who you already heard from, is probably, I think I can confidently say, read more angiograms of SCAD patients than anyone in the world, and in fact, read 28 today for us for this study. We have enrolled over 135 patients and almost 200 individuals, we have blood samples for the DNA. So we are continuing to work, from a research standpoint, on some perspective looks, both at how our clinical practice can inform care and also to, perhaps, inform acute versus long-term care. And particularly, for these individuals who tend to be younger, they want to know what their future as well as, perhaps, what their family and relatives.

In terms of those causes, we do not know the single cause of SCAD. And I think based on what we know now, one way to sort of put them in buckets of general causality, we know that among women who have SCAD, about 30% are going to be in the peripartum time, and this is a period of, obviously, great hormone fluxes. We have not identified whether it is the flux or a specific trigger that might be responsible.

You've heard about fibromuscular dysplasia, and this has been confirmed by other investigators who have looked at this, that the risk for spontaneous coronary dissection in individuals who have already been diagnosed with fibromuscular dysplasia, that correlation has already been made.

Additionally, there are a few collagen vascular defects, such as Ehlers-Danios type IV or vascular EDS, and several others that have been associated with either aneurysmal disease or dissection in other vessels and SCAD. However, in the vast majority of these patients who we have screened, we have not found a specific single gene defect. And so all of those who have other conditions are really idiopathic or other.

In the retrospective study and anecdotally in our clinical practice, a number of these individuals have had extreme physical exertion just before their SCAD episode. And whether that was truly causal or was the trigger in a susceptible individual, we aren't sure yet.

So out of this research, both the retrospective and the ongoing prospective registries, this has really built our clinical practice to the point that, in this rare disease, where in the 20 years leading up to this, we had cared for 87 patients. We've cared for well over that in the past year. So it is-- and our treatment and our evaluation of these patients has really been evolving due to observations that we've made in this first two years of practice.

So for each of these patients, we really take a detailed history of their SCAD episodes, both the symptoms that brought them to medical care, as well as those that might have been leading up or other observations about their health. We've been performing a very extensive review of their past medical records, and what has been interesting is that several had had a myocardial infarction in the past that had been attributed either thrombus that lysed, atherosclerosis, or a coronary vasospasm. But in retrospect, when we've reviewed those angiograms, now with a second definite myocardial function due to SCAD, we are thinking some of these are presenting with a recurrent SCAD.

And so increasingly, we are looking very carefully at prior imaging, and some of them have a family history of other family members having a very early myocardial infarction with limited risk. We do some routine labs, and we look for inflammatory exam. And for the physical examination, most of these individuals have a normal physical examination, but we do focus on extracoronary findings, bruits, evidence of lax skin, findings of connective tissue disease. We check an echo if they've had a myocardial infarction. And then other testing as indicated for their symptoms. Many of them present with chest discomfort, some of which is pretty clearly, by history, non-cardiac and others, it is either typical angina or it is angina that is nitrate-responsive and that we suspect might be due to spasm.

All of these individuals who come to Mayo get a medical genetics consultation, which we feel is one of the real value adds that we can provide to them. Many have young children or even daughters of reproductive age, and they're very concerned about them. And they get a personalized assessment of risk and recommendations for genetic testing, if appropriate.

The other thing we did not do at the beginning of our clinical practice is looking at CT angiographic screen, and we have developed a screening protocol to minimize radiation and to, hopefully, maximize sensitivity for any extracoronary vascular disease. As indicated, we, in our retrospective study, found a disproportionate number of individuals with fibromuscular dysplasia, and pretty early in our practice, we noticed several individuals with carotid bruits, or who had had vascular symptoms.

Here's an example of a patient who had both carotid FMD as well as a dissection. And we have found these in several individuals, both who had either a clinical event, but most of them, it was asymptomatic and picked up incidentally.

We've developed a protocol with our radiologist in order to minimize radiation and the time and number of scans, recognizing that we cannot look at every blood vessel, and we have to balance the risk of radiation, number of scans, cost, and risk to the patient. But we actually do a scan, which is a single scan. We have them on the table. Their arms are down. We scan up the neck. And then they put their arms up, during the same contrast bolus, and we look at the chest, abdomen, and pelvis. They get a large dose of contrast, but these are typically young individuals with normal kidneys, and we instruct them to drink. And the study is interpreted by our vascular radiologist. We actually have two radiologists, one looking specifically at neuroradiology and body radiology. And we've seen aneurysms, tortuosity, fibromuscular dysplasia in a number of vascular beds, including carotids and the visceral vessels, and so we are continuing to recommend this screening.

So when we are counseling our patients, I think that it is a very challenging consultation because so much of what we are so used to being able to say with confidence to our patients who've had an atherosclerotic myocardial infarction, we really don't have the confidence, in terms of prognosis, recurrence, or how to prevent. So of course, we always fully address the chief complaint, and this is often chest pain. We do consider spasm, particularly if those symptoms fit. And we don't do specific provocative testing in these individuals who already have fragile vessels or at risk vessels, but often, we'll employ a course of empiric nitrates or calcium channel blockers, or both, and see if symptoms remit, and they often do.

Because of the age of these patients, particularly the women, pregnancy and contraception are top of mind. Some desire another pregnancy and our recommendation is they do not pursue pregnancy, even if they did not have a peripartum dissection. We also are recommending, not with a lot of data, that they use non-hormonal contraception. So looking at either sterilization of a partner or themselves or considering an IUD with locally hormonal looting, but something effective. Some of our patients have gotten pregnant, either as a planned pregnancy or unplanned, and I think the management of that requires a real team.

Many have questions about exogenous hormone use, such as post-menopausal hormone therapy. We don't have a lot to guide us and I think that that-- we do think that the pregnancy-related hormones may be more the flux. And so we would recommend, in a very individualized manner, any hormone therapy after menopause. We would recommend not oral contraceptives.

Many of these women have not participated in cardiac rehabilitation after their myocardial infarction, some because they look too healthy, and they said, well, you can rehab on your own. And in others, there was a real fear that because we know that physical activity may be a provocation, that they should not lift anything, should not do anything physically active. We think that's probably not justified, in light of the fact that these are young women and they may have more risk later from falls and deconditioning if we stop physical activity now. But moderate physical activity and definitely cardiac rehabilitation are highly recommended.

It has gotten out through the social media and patient groups that fibromuscular dysplasia is an important concern. It's become more important and more anxiety-provoking in the fact that these individuals who already have had a coronary dissection for which we do not know the cause, nor do we have a specific treatment or a preventive measure, now have a second condition for which we do not have a cause nor good ways to prevent or predict outcome.

And so we're having that discussion about what it means. We do have some anecdotal evidence that just knowing they have fibromuscular dysplasia, even if it is not to the degree with obstruction that we would need to do anything about, has been helpful in the care of these individuals. One, who only a couple of months after she was diagnosed with fibromuscular dysplasia, had some sort of atypical neurologic symptoms. And because she knew that she was at risk for dissections elsewhere, sought care early and was found to have a carotid dissection. This is, obviously, the kind of story that is not very reassuring to our patients.

Recurrence risk is a big question, and many of these individuals were told this is a fluke. You will never have one of these. Don't think about it again. And others were told there was a very high risk. I think our retrospective study shows that, and our clinical practice shows that recurrence risk is real. I think it will be very important for us to better identify which factors may influence that recurrence risk.

In terms of medical management, we are recommending aspirin for all of these individuals without a lot of good data. But many of them have had stents or are at risk for thrombosis. We individualize the other therapy. In terms of clopidogrel or other antiplatelet agents, beta blockers and ACE inhibitors, we would use the nondissection indicators, whether it's after PCI, whether left ventricular dysfunction or angina, as the guiding principle but not routinely. And again, because of caution, we do not recommend statins routinely in these individuals, although some have risk factors that warrant statin treatment. We do not recommend warfarin and strongly consider nitrates and calcium channel blockers as empiric therapy for possible spasm.

We've developed a list, because I've seen a lot of these patients have some of the common questions. Many will ask if they need to have genetic screening of family members, and we do not recommend that unless they have an identified genetic cause. A disproportionate-- this is anecdotal-- have migraine headaches. This may be a connection. We are recommending that they do not use vasoconstrictor or other types of migraine therapies, that they may have been using this may require a consultation with neurology. There is no specific treatment for fibromuscular dysplasia, although some, who have significant stenosis, we're recommending at least one follow-up CT scan.

Many of these are-- this is a large proportion of young women, who are mostly still menstruating and a number have-- a disproportionate number have menorrhagia. We don't really have a hormonal option to treat this and so uterine ablation has been a solution for many of these young women with good satisfaction. We alluded to the counseling on pregnancy and cardiac rehabilitation.

Because perhaps of the way many of these women have connected on social media, they are very interested in advancing the science so that other women don't have to ask the same questions. So many are asking to participate in research, and we are glad that we can offer this. Many also want support for themselves and family outside of the medical realm. And so we can refer these individuals, and in fact, any woman with heart disease to Women Heart, the National Coalition for Women with Heart Disease, their online community. There is a separate group for SCAD, but this is all women.

We, at Mayo Clinic, now have a Facebook page, an open Facebook page, where we've posted updates on our research progress, as well as other information. And there's actually a closed page for survivors. So we are hoping that we can provide to this group, who has given so much of themselves, the patients who have brought themselves forward and in fact, continue to help recruit and tell other women about the research and clinical care, to be able to have better answers for them in the next couple of years. Thank you very much.