Marfan Syndrome and Cardiac Complications

Webcast

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Introduction

Andrew Schorr:
Have you ever heard of a condition called Marfan syndrome? That's a genetic condition that causes problems with the heart, lungs, skin and vision. There are about 50,000 cases of that in the US, but there are many people who don't know it. If only they did, their life could be lengthened. Meet a leading expert in Marfan syndrome and hear the latest next on Patient Power.

Hello and welcome to Patient Power sponsored by Northwestern Memorial Hospital. There's a condition called Marfan syndrome, and it's a genetic condition that causes problems with the heart lungs, skin and vision, and in some people if untreated it can shorten their lives. They may live 30, 35, 40, 45 years, but not the much longer life that we would all want. But there is help if only they can be identified and connect with a leading specialist.

We'd like to connect you now with a leading specialist, and that is Dr. Chris Malaisrie. He is an assistant professor in the division of cardiothoracic surgery at Northwestern Memorial Hospital and the Feinberg School of Medicine of course at Northwestern. He's co-director of the Marfan syndrome and Related Disorders Clinic at Northwestern Memorial Hospital and the Bluhm Cardiovascular Institute. Dr. Malaisrie, thank you so much for joining us. Marfan syndrome, help us understand what it is. It's a genetic condition, so what's gone wrong if somebody has it?

What is Marfan Syndrome?

Dr. Malaisrie:
Marfan syndrome is a connective tissue disorder, and it's inherited. It's inherited as an autosomal dominant fashion. It affects approximately one in 5,000 people. There is no racial preference or gender preference, that is both males and females are affected equally, Asian, Black and Whites. It leads to about 50,000 affected cases in the United States and probably about 200,000 patients worldwide.

The genetic abnormalities have already been identified. The fibrillin-1 gene, which is on the 15th chromosome, has a mutation, and so far there's over 600 gene mutations associated with the fibrillin-1 gene. The gene mutation itself leads to an abnormality in proteins of the connective tissue. That's sort of the matrix that bonds the cells together, and that abnormality leads to, as you've already

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mentioned, the cardinal features of Marfan syndrome, which include the cardiovascular system, the skeletal system and the ocular system.

Complications

Andrew Schorr:
Now, let's talk about that a little bit. So I mentioned that people could have a shortened life. What goes wrong where they could die? And I want to just share a little story along the way. We don't know whether this was a confirmed case of Marfan, but my dearest cousin, Abbott, years ago, about 20 or so years ago at age 35, had what we believed to be a ruptured aorta, a major artery, and just bled to death internally and died within minutes, really. And it was thought that maybe from his body type that maybe what had been going on and had not been diagnosed was Marfan's. So tell us about the body type, clues to Marfan's, and inside, maybe, let's say with the aorta, what could be going wrong.

Dr. Malaisrie:
The outward symptoms of Marfan's are several actually. We've talked about the sunken chest. Physicians call that pectus excavatum, so severe sometimes that children will need to have surgery to correct the sunken chest. Or the opposite of that is the pigeon chest, what we call the pectus carinatum. Other signs of the skeletal system include a very long arm span. If you actually measure out tip to tip from finger to finger that arm span turns out to be greater than the height of the patient, which is an interesting finding and something we look for in the clinic. The fingers and thumbs are very long. Scoliosis is a problem with Marfan patients. That's the S curve spine that you sometimes see in children. The ability to completely extend the elbows to 180 degrees is another finding. Marfan patients also have very large shoe sizes with flat feet. Finally, some patients will have problems with their hips, which can be seen on x-rays.

Andrew Schorr:
All right. Now, so underneath the skin then let's say with the blood vessels, a major vessel like the aorta, because of this connective tissue disorder what's not right with the aorta?

Dr. Malaisrie:
Findings associated with the cardiovascular system is probably the most tricky because you just can't see them on a physical examination. And typically patients don't have any symptoms related to problems with their cardiovascular system, and one problem I'm talking about here is aortic aneurysm. Typically the aneurysm occurs at the aortic root, which is just on the very top of the heart. That's the first part of the aorta as it leaves the heart. The aneurysm is typically asymptomatic and grows very slowly over time so patients will typically have no symptoms until an aortic catastrophe occurs, which in Marfan's patients typically takes the form of either an aortic dissection or a frank aortic rupture. And probably the most famous person to have an aortic dissection is John Ritter, who was a famous actor from L. A. who starred in a hit show called *Three's Company*, if people remember that.

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Andrew Schorr:
Right. So like with my cousin, sudden death, maybe no warning signs other than could they possibly have the gene or were there some clues related to their anatomy, right?

Dr. Malaisrie:
Exactly. Unless there is reason to suspect a patient has Marfan syndrome a physician would otherwise not go looking for an aortic aneurysm.

Diagnosis

Andrew Schorr:
All right. Let's talk about this a little bit more now. You mention that it could run in families. So with all the testing that we do of babies would there be anything that might be seen on some test, or even let's say if a mom had amniocentesis and they're looking at all the chromosomes and all that, would anything show up there if you didn't know to look for it?

Dr. Malaisrie:
Unfortunately, no. We do not routinely test for the fibrillin-1 mutation for all pregnancies. Really, the only reason to test the child at this point is if the parents themselves have a history of Marfan syndrome or there's some sort of family history. Otherwise as a child you typically don't see the typical manifestations, typical findings of Marfan syndrome until they become teenagers.

Andrew Schorr:
All right. Now, again I'm thinking kind of personally, but with my cousin or for that matter if this was the case with John Ritter, if there was something observed, you know, physical or maybe some other kind of symptom if there could be any, what work-up could a physician do to see if in fact it was Marfan?

Dr. Malaisrie:
The typical work-up first is to suspect that Marfan syndrome is a possibility. And if that's the case an echocardiogram is of the utmost importance, not only for the diagnosis but also to evaluate whether or not the patient does indeed have an aortic aneurysm. Other tests that we perform for Marfan syndrome is the slit lamp test, which is a test for the eyes because a lot of these patients have a slipped lens which can be found fairly easily by the ophthalmologist.

Treatments and Preventative Measures

Andrew Schorr:
Let's take my cousin. I'm just thinking about that. If let's say he had an aortic aneurysm, this bulge in the aorta that was building and then possibly rupture leading to sudden death, what would you do? If it's observed then what happens? Is there immediate surgery? Are there different surgical approaches? Do you shore up or wrap up the aorta? What do you do?

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Dr. Malaisrie:
The strategy for patients with Marfan syndrome and aortic aneurysm is to repair the aneurysm before a catastrophe occurs. Clearly, sudden death is the catastrophe we want to prevent for these patients. And as you said before, the average life span of a patient with Marfan syndrome who is undiagnosed and untreated is approximately 45 years. Patients who have timely surgery and diagnosis can have a normal life span to as great as 70 years of age.

So the surgery that we propose for patients with aneurysms is called an aortic root replacement. And what that involves is up-and-down incision on the chest. We call that a sternotomy. It is open heart surgery, so a patient will go on cardiopulmonary bypass or the pump as we call it. The aortic valve is replaced along with aortic aneurysm, and typically because the patients are typically young, in the 20s or 30s, a mechanical valve is the valve choice that is usually recommended. Tissue valves are recommended for patients who are unable to tolerate life-long anticoagulation, meaning Coumadin or warfarin.

The aneurysm wall itself is replaced with a Dacron graft, which is essentially a polyester weave. A polyester graft has a limitless life span, meaning that it does not degrade over time. There is no rejection of the graft itself, and you don't need to be on Coumadin for the graft. However you do need to be on Coumadin if a mechanical valve is chosen. So the gold standard operation for a young patient 20 or 30 years old with Marfan syndrome would be an aortic root replacement using a mechanical valve attached to a graft conduit.

Now, an alternative surgery is a valve-sparing aortic root replacement. The reason there's interest in that is because the aortic valve for the Marfan patient is typically normal, so we try to replace just the aortic root but leave the aortic valve in place. At this point we have about 10- to 15-year endurability data, and this technique does look promising. The reason to have this operation, the valve-sparing aortic root replacement rather than the traditional aortic root replacement is that you don't need to be on Coumadin if you're able to spare your existing aortic valve. So I think the valve-sparing aortic root replacement which we do offer here at Northwestern is a very good alternative to the traditional mechanical valve conduit that we use for Marfan patients.

Andrew Schorr:
Dr. Malaisrie, now, I know not everybody has surgery. There's some drug therapy too. Where does that come in?

Dr. Malaisrie:
For patients that have small aneurysms that are not yet ready for surgery the typical medical regimen is a beta blocker, which is a very common drug that's used for hypertension, high blood pressure. The drug slows the heart rate and lowers the blood pressure. And we use it to help prevent continued expansion of the aortic aneurysm.

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The second part of the medical therapy is exercise restriction. All patients should have some sort of exercise restriction, and typically we recommend avoidance of competitive sports, meaning professional-level sports or even varsity-level sports. Avoidance of contact sports like skiing and horseback riding and that sort of thing where contact becomes an issue. And the third thing is avoidance of isometric exercises. And what are isometric exercises but anything that you have to strain to do such as heavy bench pressing or squatting. These sort of exercises have to be restricted.

Andrew Schorr:
We got a question about that actually, e-mailed in. Jerry from La Grange, Illinois said, "Why can't people with Marfan syndrome lift weights?" So why would that be a concern?

Dr. Malaisrie:
With isometric weight lifting patients are actually able to drive their blood pressure all the way up to the 200s. Normal blood pressure is about a 120 or less, so with the increase in, sudden increase in high blood pressure that becomes a risk for aortic dissection or continued pressure on the aortic aneurysm. So that sort of weight lifting is not recommended for that reason.

Andrew Schorr:
And even after people have the surgery would they still be on the same restrictions?

Dr. Malaisrie:
After the surgery the aortic root is replaced so patients are protected from dissection and ruptures. A lot of patients can resume normal activities. So this is dealt with on a case-to-case basis of course, but typically after surgery patients can resume a normal lifestyle.

Andrew Schorr:
Dr. Malaisrie, so let's talk about sports for a minute and recognizing that many people are maybe going around undiagnosed in earlier years. So here's a kid with big wing span, as they'd say in basketball, and some coach sees him and says, whoa, look at the reach of that kid. I want him on my basketball team. Now, it seems like as you were saying, with Marfan's that wouldn't be such a good idea.

Dr. Malaisrie:
Yes, and that's part of the tragedy with Marfan syndrome is a lot of the patient are very tall and become very good candidates for varsity basketball, and these patients should not participate in competitive sports, the risk being sudden death on the basketball court or the swimming pool or what have you. These are the cases that you read about of the sudden death of the young athlete. It becomes very important for people to recognize that a child or the teenager really isn't a good candidate for sports due to their unnatural height or wing span.

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Andrew Schorr:
Would there be any clues in the mobility of their joints, because you're talking about connective tissue, so I wonder would their joints operate differently that maybe could be a clue?

Dr. Malaisrie:
Sure. The joints are typically very lax, and there's a couple of cases that come to mind that are suspicious for Marfan syndrome. The first is obviously being from Illinois, Abraham Lincoln. There is some question whether or not Abraham Lincoln had Marfan syndrome based on his tall stature and long arms and long fingers. But as history has it he was also a very good wrestler. The fact that he was a good wrestler goes against the possibility that he did have Marfan syndrome because patients with Marfan syndrome have very lax joints, meaning they're prone to dislocation, so that goes against the ability for Abraham Lincoln to be a very good wrestler.

Another case that came to light a couple of years ago was obviously Michael Phelps, but Michael Phelps was born in Baltimore, and he was appropriately evaluated for Marfan syndrome when he was a young boy.

Andrew Schorr:
If someone then is diagnosed, so what happens next? So let's say if it's that child or teenager identified, you're going to do that work-up, do you simply watch if for a while, do the medical therapies, you have the restrictions, and at some point if you're observing progression you then say we need to do, as you described, pretty major but lifesaving surgery? How does that journey go, if you will?

Dr. Malaisrie:
Sure. So typically the patient will have the medical therapy and exercise restrictions. We recommend an imaging study, typically an echocardiogram, which is just sound waves with a probe, surface probe, which is a very noninvasive test, be performed every year to evaluate progression of their aortic aneurysm. Typically the number that comes to mind to most physicians is five centimeters for indication for repair of the aneurysm. However, this is not an absolute number. Patients with aneurysms as small as four and-a-half can be operated on based on their body size, meaning that a five centimeter aneurysm for a 200-pound man is a different aneurysm for a five-foot-two woman. So it's also based on the relative size of the aneurysm to the person.

When the aneurysm does become large enough to warrant surgery the surgery even though it is open heart surgery is a very safe operation, typically because the patients are very young. I know that patients don't like to think about the risk of death at such a young age, but that risk is typically only about one percent at major centers, so 99 percent chance the patient is just going to do just fine.

Andrew Schorr:
But the risk of not treating the Marfan's is high?

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Dr. Malaisrie:
Absolutely. Going untreated with a large aneurysm certainly runs the risk of sudden death, aortic rupture and aortic dissection. So leaving it alone runs a much larger risk.

Andrew Schorr:
Jennifer from Springfield, Missouri wrote in. She says, "My son has Marfan syndrome and it seems that he's tired all the time. Is this due to the Marfan's, or could it be something else?" That's probably a $64,000 question, right, because fatigue can go with so many things, but I'd love to hear your answer.

Dr. Malaisrie:
Sure. There's multiple reasons that a child could be having fatigue. Certainly the two systems that would have to be evaluated are the cardiac system and the pulmonary system. Patients sometimes also have mitral valve prolapse, meaning a floppy mitral valve, and this could be causing fatigue for the patients. This is different from the aortic valve and aortic root aneurysm that I was previously speaking about.

For the lungs, patients sometimes have a mild form of lung disease. Some patients also have spontaneous pneumothorax, which is a dropped lung, meaning that there's small blebs or pimples on the surface of the heart which can pop leading the lung to drop, and this could be an acute cause for shortness of breath.

Andrew Schorr:
Wow. That seems to be quite rare, but I imagine you're familiar with it at Northwestern in that you have a center for this. Now, let's go on. So people say, well, if I have Marfan am I because of maybe some genetic abnormality at risk of other things. And Candace from Wichita wanted to know, is there any connection between Marfan and increased risk for osteoporosis?

Dr. Malaisrie:
That association is not known at this point.

Andrew Schorr:
Anything else, though, where you say, well, if we diagnose somebody with Marfan's we need to look out for these other conditions? Are there any dots you need to connect, if you will?

Dr. Malaisrie:
Other things that we also have to look for are spine problems. Sometimes the patient will have what we call dural ectasia, and that could lead to symptoms such as leg pain, leg numbness and chronic pain of the lower extremities.

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Related Conditions

Andrew Schorr:
Dr. Malaisrie, now, I know your clinic also covers some related conditions even more rare than Marfan's. What are some of those conditions? How are they different?

Dr. Malaisrie:
Sure. Another system which is associated with Marfan syndrome which is also a connective tissue disorder is called Loeys-Dietz syndrome, LDS in short. These patients also have the same problems with the ascending aorta and aortic roots as Marfan's patients. There are several overlapping features of Marfan's patients, and that includes the long, spindly fingers, the chest abnormalities, the scoliosis, which is the S-shaped spine, the dural ectasia, meaning the spine problems I was speaking about earlier. But unique features for patients with Loeys-Dietz syndrome include a cleft palate and a bifid uvula, which can be easily identified, meaning that the uvula is split into two, and the arterial system for these patients tends to be very tortuous. If you look at angiograms for these patients they often take a corkscrew appearance typically of the carotids and intracranial arteries.

Andrew Schorr:
Going back to Marfan's. So I know that it's not all the time where other family members may have it, but there certainly is a genetic connection. So if you have before you a young man and you confirm the diagnosis of Marfan, does that mean necessarily then that other family members should be tested? And if they are tested how big a deal is it to have that test? Is it a blood test or how do you do it?

Dr. Malaisrie:
Yeah, sure. There is about a 50 percent chance that any other family, first-degree relative will be affected, so all first-degree relatives should be tested for Marfan syndrome. And the tests include an echocardiogram and an eye test. The genetic blood testing is reserved only for cases which aren't clinically diagnostic, meaning that the doctor is not able to make a diagnosis of Marfan syndrome based solely on clinical findings. So although a blood test is available for the genetic disorder it's not always required to make diagnosis of Marfan syndrome.

Andrew Schorr:
So it's a rare condition. We're talking about maybe 50,000 Americans with several thousand who don't know it and maybe many doctors who've never seen it. For people listening to this program, then, what would you recommend? It seems like connecting with a specialty clinic and a specialist, your whole team there at a major center like that, makes sense because that's where you could get I guess the most knowledgeable and specialized care.

Dr. Malaisrie:
As you were speaking earlier about connecting the dots, certainly if families can think of someone in their family who died suddenly at a young age, that should

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bring up some red flags. The typical body habitus of the Marfan patient should also bring up some red flags. So if you think of Michael Phelps who doesn't have Marfan syndrome or Abraham Lincoln, these sort of body habitus should bring up some red flags as to whether or not that family member has Marfan syndrome. If that does become suspicion I would recommend seeing your primary care physician, and from there the doctor should make a referral over to a center that is more familiar with the Marfan syndrome and has a Marfan clinic.

Andrew Schorr:
That said, though, this can be terrifying for somebody, and I think of family members that I may communicate all this to, they say, oh, my goodness. But to hear you tell it though, with the monitoring you have and the approaches someone who might otherwise be at risk of an early demise can lead a pretty normal life.

Dr. Malaisrie:
Yes, exactly. No one wants to face the possibility of open heart surgery at such a young age, but granted the high risk of aortic rupture and dissection for patients with aneurysms, heart surgery can become very much a lifesaving procedure for these patients.

Andrew Schorr:
Well, I'm glad you have a team there at Northwestern Memorial that can help people with this uncommon but life-shortening condition if left untreated. Dr. Chris Malaisrie, assistant professor in the division of cardiothoracic surgery and co-director of the Marfan syndrome and related disorders clinic at Northwestern Memorial Hospital, thanks so much for being with us on Patient Power.

Dr. Malaisrie:
Thank you very much.

Andrew Schorr:
I've learned a lot, and we will do this time and again. Our next program is going to be in a whole other area, on cochlear implants, bringing hearing to people who could otherwise not hear. Thank you so much for being with us on Patient Power. Remember, knowledge can be the best medicine of all. See you next time.

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