

Dr. Melissa Lyle 02-19-2021

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SPEAKERS

Dr. Halena Gazelka, Dr. Melissa Lyle

Dr. Halena Gazelka

Welcome everyone to Mayo Clinic Q&A. I'm Dr Halena Gazelka. Cardiac amyloidosis occurs when a protein byproduct called amyloid builds up in the heart muscle. This inhibits the hearts ability to pump blood in is sometimes referred to as stiff heart syndrome. Well there is no cure, there are treatment options available to manage the symptoms, treat underlying conditions and slow the progression of the disease.

At the Mayo Clinic in Florida, a new multidisciplinary cardiac amyloidosis clinic has been launched to bring together multiple specialties to care for patients with amyloid. Joining us to discuss this today is Mayo Clinic cardiologist Dr. Melissa Lyle. Thanks for being here today. Dr. Lyle.

Dr. Melissa Lyle

Well, thank you so much for having me.

Dr. Gazelka

Well, I always like to say that I like to learn something every day when we do these. And I'm certainly expecting to learn something about amyloid today. So thank you so much for being here.

Dr. Lyle

Oh, of course, of course.

Dr. Gazelka

First, would you explain for our listeners in terms that we can understand what is cardiac amyloidosis?

Dr. Lyle

Sure, well, just like you mentioned Dr. Gazelka, amyloid, it's really an umbrella term, it just describes the misfolding of proteins. And when those misfolded proteins then aggregate together, they actually form long, amyloid fibrils. And then those can deposit in soft tissue, nerves or organs. And in the case of cardiac amyloidosis, they deposit in the heart muscle itself. And so cardiac amyloidosis actually results in a type of heart failure that we call a restrictive cardiomyopathy. That basically just means the heart is thicker and stiffer than a normal heart.

Dr. Gazelka

I understand that there are two main types of amyloidosis. Could you explain the difference between the two?

Dr. Lyle

Yes, so there are a variety of different proteins that actually can miss fold and form those amyloid fibrils that then infiltrate the myocardium or heart muscle. However, the two most common are immunoglobulins, which are things that fight infection, and it's specifically the light chain component of the immunoglobulin, as well as a protein called transthyretin. So in AL amyloidosis, it's actually a problem with the bone marrow. So the plasma cells in the bone marrow start to over produce these immunoglobulin light chains. And then they end up becoming misfolded and form the amyloid fibrils that affect the heart. And in ATTR amyloidosis, the liver actually produces a protein called transthyretin. And this is a carrier protein, so it transports thyroxine and retinol, which is just vitamin A. And it's a four-sided protein, when it becomes unstable, it can actually break apart and form smaller proteins. Those smaller proteins are the ones that can miss fold and form amyloid fibrils that again, can infiltrate and weave their way into the heart muscle.

Dr. Gazelka

That's fascinating. So, the disease either comes from one's bone marrow and their bones or from their liver?

Dr. Lyle

Exactly.

Dr. Gazelka 3:26

Dr. Lyle, you've been referring to light chains. Can you explain to us what is a light chain and what does it mean?

Dr. Lyle

Yes, so the bone marrow, those cells in the bone marrow that produced the immunoglobulin that is a protein that fights infection. The immunoglobulin is actually made up of two components, both a heavy and a light chain. So, the light chain is a component of the immunoglobulin, and that's actually what gets over produced in the setting of AL amyloidosis.

Dr. Gazelka

But would you normally have the immunoglobulin and it just is overproduced or it's made wrong?

Dr. Lyle

So, normally you would have the immunoglobulin, and you would have your light chains, both kappa and lambda. However, in the setting of AL amyloidosis, there's just way too many light chains. So with the overproduction of those light chains, then they're more likely to miss fold and form those amyloid fibrils.

Dr. Gazelka

Do we have any idea what causes someone to develop amyloid?

Dr. Lyle

So, in the case of AL amyloid, it really is the problem with the bone marrow for some reason those plasma cells go haywire and start over producing the light chains. In the case of ATTR amyloidosis, there's actually two types. The hereditary form called hereditary ATTR amyloidosis is related, actually, to an inherited mutation. And that genetic mutation makes that protein unstable, more likely to break apart and then be able to form the amyloid fibrils. And the other type of ATTR amyloidosis, wild type ATTR amyloid, there's no inherited or genetic mutation. For some reason, we don't really know why, the protein just becomes unstable and then forms those amyloid fibrils.

Dr. Gazelka

I'm going to imagine that a lot of our listeners have never heard of amyloidosis. How common is cardiac amyloidosis?.

Dr. Lyle

Yes, that's a great question. So, AL cardiac amyloidosis, and really AL amyloidosis in general is actually relatively rare. However, ATTR amyloidosis is really not that rare, it was just previously under diagnosed. And now because of greater awareness, and also increasing education about ATTR amyloidosis, we have recognized that it's actually a fairly common cause of heart failure in our patients, particularly our older population. And it's a very common cause of heart failure with someone who still has a normal pumping function of their heart.

Dr. Gazelka

You explain that sometimes this is hereditary, and sometimes it's not. Who would be at particular risk of developing the disease?

Dr. Lyle

Yes, so with AL amyloidosis, it seems as if men and women are equally affected, and the average age of diagnosis is after about the age of 50. Now, in wild type ATTR amyloidosis, which typically manifests as cardiac amyloidosis, there seems to be a predilection for the older population, particularly males, and the average age of diagnosis is after the age of 75. Now, for hereditary ATTR amyloidosis, we actually see this present in a younger patient population. It's interesting because the specific mutation that we see the valine 122 isoleucine mutation, that's actually the most common genetic mutation in the United States for ATTR amyloid, is present and about 3 to 4% of the African American population.

Dr. Gazelka

So how would someone know if they were at risk? Are there certain signs or symptoms that would develop?

Dr. Lyle

Yes, so cardiac amyloidosis typically will present as a form of heart failure. And, so, the signs and symptoms are those that are similar seen similarly seen with heart failure. So, patients can often come

in with shortness of breath when they exert themselves or shortness of breath at rest. And then also they can have lower leg swelling, abdominal swelling, and then even generalized fatigue. Those are all symptoms that we would look out for as possible, possibly related to cardiac amyloidosis. Abnormal heart rhythms can also be seen such as atrial fibrillation that can be associated with cardiac amyloidosis as well.

Dr. Gazelka

It's interesting, it sounds like there is a lot of overlap between those symptoms and symptoms that you can see in many other illnesses or disorders.

Dr. Lyle

Exactly right. So, it often can be sort of vague presentations, but that's why it's important to bring those symptoms up to your physician as soon as possible, so that we can look for other red flags. Sometimes amyloidosis is associated with other findings like bilateral carpal tunnel syndrome or lumbar stenosis, so then your physician can help tease out if you may be at risk for amyloidosis.

Dr. Gazelka

That's very interesting. How does the physician diagnose if a patient might have amyloidosis?

Dr. Melissa Lyle

So typically, we would look first at an echocardiogram or an ultrasound of your heart, and that will give us an idea if there is a suspicion of cardiac amyloidosis. Occasionally, we will use cardiac MRI to help get the pictures of the heart that are necessary. And then we work to focus on a diagnosis of whether it's AL versus ATTR amyloidosis using a combination of bloodwork and imaging techniques.

Dr. Gazelka 9:32

It's very interesting. Is there a way that this can be prevented either the hereditary or the spontaneous form?

Dr. Lyle

Unfortunately, we don't have any preventative strategies for cardiac amyloidosis. But the key is really early detection. We want to make sure that we can detect these patients earlier so that we can get them on the right treatments.

Dr. Gazelka

What are the right treatments if someone was diagnosed?

Dr. Melissa Lyle

Yes, so great question. So for AL amyloidosis, just as a reminder, it's that problem with the plasma cells in the bone marrow, and they start over producing those light chains. So, our hematologists really are going to gear their therapy towards controlling the plasma cells in the bone marrow. And then that's actually with chemotherapy. So, we use chemotherapy to control the plasma cells and an occasional situations, an autologous stem cell transplant might be needed as well. In the case of ATTR amyloidosis, however, there are a lot of new therapies now, so it's sort of an exciting time for cardiac

amyloidosis related to TTR amyloid. One category of therapy, actually at the liver, it stops the liver from producing that transthyretin protein in general. And so, by stopping the production of the transthyretin, it slows or halts the progression of the disease. Those medicines are referred to as the RNA silencers, and that's medications referred to as patisiran and Inotersen. And they've actually are currently FDA approved for the treatment of hereditary ATTR polyneuropathy. So related to nerve problems, but there's clinical investigations looking at the involvement in the treatment options for cardiac amyloid. Another category of therapy actually are the stabilizers and those keep that transthyretin from becoming unstable and breaking apart. And tafamidis is the medication that's FDA approved currently, for both hereditary and wild type ATTR cardiac amyloidosis.

Dr. Gazelka 11:55

It sounds very complex, and I can see why you have a whole clinic to manage this.

Dr. Lyle

Yes.

Dr. Gazelka

Melissa, when I wasn't an anesthesia resident beaucoup years ago, I remember doing transplants for patients who had amyloidosis, organ transplants. And is that just patient to a very advanced disease? Or do we do those anymore?

Dr. Lyle

That's a great question. So actually previously, for the hereditary form of ATTR amyloidosis. We were doing liver transplantation. However, now with the advancements in therapy with the RNA silencers, we're trending away from needing a liver transplant and just being able to offer the medication for the hereditary ATTR amyloidosis. Now, unfortunately, we still see some of our patients that present at a later time within stage heart failure. And at that time, they are still being evaluated and considered for heart transplantation.

Dr. Gazelka

It is fascinating. What an amazing and important discovery that must have been when those medications came out, because liver livers are few and far between and I can imagine patient's disease could advance while they were waiting for a liver.

Dr. Melissa Lyle

Yes, absolutely. So, we are very thankful to have these new therapies, and then clinical investigations continue. So hopefully we'll have even more advancements in the future.

Dr. Gazelka

That's amazing. Melissa, can you tell us a little bit about the cardiac amyloidosis multidisciplinary clinic?

Dr. Melissa Lyle

Yes, so we are working to build a multidisciplinary amyloid clinic here at Mayo Clinic, Florida. And what we are doing is basically having a collaborative effort amongst several different specialties, including

hematology, cardiology, transplant cardiology, as well as neurology and nephrology. And our goal is really to provide an efficient evaluation for our patients, so that we can quickly come to the correct diagnosis and offer the best treatment option. And we're engaging all of our different specialties, really for this comprehensive visit to provide the best overall care.

Dr. Gazelka

You know, you mentioned something that was interesting to me, and that was hematology and oncology, and I heard you say earlier that chemotherapeutic agents are used in management of some types of amyloid. Does that mean that this is cancer? Or the drugs used differently?

Dr. Lyle

So yes, we do consider AL amyloidosis a form of bone marrow cancer, we specifically call it a plasma cell dyscrasia because those plasma cells start over producing the light chains. And the hematologists really steer the treatment options, as cardiologists we help manage their signs and symptoms of heart failure. But the hematologists will make recommendations in regard to the specific chemotherapeutic regimen. There's been a lot of advancements in terms of the chemotherapy for amyloid as well, and then they will decide whether or not that autologous stem cell transplant is needed.

Dr. Gazelka

That is a really fascinating, Thank you for all that you shared with us today.

Dr. Lyle

Yes, of course.

Dr. Gazelka

Our thanks to Dr. Melissa Lyle, cardiologist at the Mayo Clinic in Florida, for coming today to speak with us about cardiac amyloidosis. I know that I learned something today, and I sure hope you did, too. We wish everyone a wonderful day.