SPEAKER: So Fabry Disease is one of multiple diseases called lysosomal storage disorders. And ultimately this means that some of the proteins or enzymes necessary to degrade some of the proteins in our body are missing. And this results in an accumulation or a deposition of this substrate.

And the important thing to remember about Fabry is that it is a progressive disease, so meaning we have in-utero studies that deposition occurs in patients that have a genetic trigger for the disease. And it only accumulates over time. So you're going to see an upward shift in how patients present from a symptomatic perspective.

And so in younger patients, you may seem derangements in sweating, so hyperhidrosis or anhidrosis. Typically, anhidrosis would be the manifestation. You can see abdominal pain, sort of non-specific GI complaints, generalized pain, fatigue. All of these may be some things that could be implicated in patients that may have Fabry Disease.

And you can imagine as a pediatrician, that's a pretty hard thing to ferret out. If someone tells you, well, I have fatigue, and I have non-well-described abdominal pain that occurs intermittently, it's going to be really hard to think about Fabry. But we hope that people can start thinking about that.

But as you accumulate substrate over time, more organs can become involved. And the two organ systems that have classically been focused on have been the kidneys and the heart. And up until a few years ago, kidney pathology was the leading cause of death in patients with Fabry.

And we typically do see kidney involvement before we would see cardiovascular involvement. And so it's an important thing if you had any suspicion, obviously you would want to do surveillance for kidney function, looking for proteinuria and these sorts of things. And ultimately some people move down a biopsy pathway, which can be diagnostic of Fabry based on that intervention.

But then other systems, as I said, such as the cardiovascular system, can become involved. And if you think about this, every cell that is involved in the circulatory system could be subject to becoming diseased because of Fabry, because this obviously is a genetically triggered disease. And so it really is one of those cumulative effects over time about how quickly the cardiovascular system can become involved and to what degree it can become involved.

And I think the opportunity for us to learn more about this in the cardiology community is high. And many people ask me, well, you do genetic testing, for example. Why? What difference does it make?

And there are a couple of reasons that I like to pursue genetic testing. One is that it informs me how to screen the rest of the family, so cascade screening, where we screen first-degree relatives. But there are certain diseases that have a therapy that would be atypical to any other type of cardiomyopathy in that realm, if you will.

So a patient with traditional hypertrophic cardiomyopathy because of a sarcomeric mutation, for example, we're going to have traditional therapies that we would apply. Most of those are to reduce symptoms to potentially impact dysrhythmia and maybe kind of change the trajectory or curve for potential sudden cardiac death.

However, if I found out the patient has Fabry, I can offer them therapies that I would not offer to a traditional hypertrophic cardiomyopathy, such as enzyme replacement therapy or potentially chaperone therapy, depending on their mutation. So it is important to know because you have additional therapies that can make a difference in the outcome of these patients.

It was thought that perhaps there weren't a lot of impacts made by enzyme replacement therapy, for example, once you had evidence of cardiovascular disease. It actually turns out that isn't quite true, that we may have the opportunity to reverse some of the pathology that we see, at least on testing, such as cardiac MRI, for example, or on echocardiography. So I think it's really important for the cardiology community to consider this disease.

And we've all gone through this. Many people, we learn about Fabry long enough to take your board exam. And then we forget about it, and that's something that we want to try and get away from.

We're starting to see this more and more, is that it's important as genetic testing becomes more widespread as far as use, and because it will become more cost effective to be able to do, you are going to find patients with these mutations. And it's going to be important to consider how does that impact the family? I think the other thing is that when you see patients in your clinic, we're all very busy and very much stretched for time.

But whenever possible, just taking a pedigree is very helpful. And you can have other people, aside from yourself, to do this. But if you can do a three-generation pedigree, sometimes that will give you some insights, specifically because this is an X-linked disorder. You may see some diseases that are moving through in that inheritance pattern, such as early cerebrovascular accidents, early MI, or early heart failure presentations.

And so I do think that it's very important to consider this as a potential cause of hypertrophy that you might see in your patients because, one, it does have implications for the patient. You can offer them therapies that otherwise you would not offer. And it's implications for the families as well.

And I think the other thing as cardiologists, we've-- some of the communities have applied what I would consider inappropriate statements or titles to certain patient populations. And this is specifically to the females that are involved in X-linked disorders. And so in the past, whether it would have been Fabry or Duchenne or anything else, we would have said, well, the mom is a "carrier," quote unquote. And that implies that they simply carry it. They don't have manifestations of the disease.

As a cardiologist, I am telling you that is not true in those X-linked diseases. And they can have cardiac disease on the female side just as serious, if not more serious or severe than the males. And some of my most advanced heart failure patients have been females.

So the other thing is to approach this disease in a way that's somewhat agnostic from a gender perspective. The diagnostics are going to be a little bit different. And you'll hear about that in other sections, about male versus female and enzymatic activity and those sorts of things.

But remember, just because a female is a "carrier," quote unquote, does not mean that she is simply moving that DNA from herself onto her offspring. It has implications for her as well. So please keep that in mind when you're looking at these patients, when you're looking at genetic testing. And remember to screen everyone because potentially everyone's at risk.