

SPEAKER: If Fabry disease is suspected, then you need to confirm the diagnosis. Even if a patient sounds like a slam dunk, you will sometimes get burned if you just assume that it's Fabry disease. For example, I've had two patients who presented with pain in their hands and feet, progressive kidney disease, and hypertrophic cardiomyopathy who had a family history of confirmed Fabry disease. But when I did the testing, they ended up having something else and not Fabry disease.

So you do absolutely want to make sure that you confirm the diagnosis even in those obvious cases, and clearly in a case where you have a less specific presentation. So for example, if somebody comes in with hypertrophic cardiomyopathy, one of the things that's important on the differential diagnosis is Fabry disease. You will want to do testing.

So one of the frequent questions we get is what's the best approach to testing? I think that if you are wanting to rule in or rule out Fabry disease that you should always do both enzyme activity testing and sequence--sequencing and molecular testing looking at the DNA. There are a couple of reasons for that. One is that the enzyme testing is not very reliable in women and can sometimes give both false negatives and false positives in men as well.

Another reason is that the molecular testing, while it is very good at detecting mutations, is not 100% sensitive. So you can occasionally miss that. Thus, looking at it from two different directions helps to confirm the diagnosis with greater certainty.

The other reason that it's important to look in both ways is to classify the type of mutation that you have. Now, we classify Fabry disease as classical or non-classical. Typically, classical is very low enzyme activity, but it doesn't have to be zero. And some patients with classical disease will still have some potential for residual activity, and that becomes important in selecting a therapy. But the patients with higher residual activity, it's also important in determining which therapies that would be most valuable for them.