

**SPEAKER:** What is the pathophysiology of central nervous system involvement? Well, just as in the peripheral nerves, we see deposition of GL3 within the Schwann cells. We do see GL3 deposition within neurons. But we still think that there is the component of a deposition within the vascular endothelium that goes on to lead to a microvascular disease, resulting in these white matter changes.

The white matter changes or the white matter burden does not necessarily correlate with neurologic dysfunction. And in fact, it could be silent. Oftentimes, patients who present with white matter changes, they're incidentally found on an MRI during a neurologic workup for migraine or other symptoms. And in these patients, they might be misdiagnosed as multiple sclerosis, actually, when they see this white matter burden. So instead of calling it a multiple sclerosis, it might also be considered a leukodystrophy. But in fact, in this case, it's more of a vascular leukoencephalopathy.

In addition to this white matter burden, we might see cryptogenic strokes or hidden strokes, strokes that do not present with a specific symptom. And oftentimes, this is an earlier onset. This stroke occurs in an earlier age group independent of whether or not you have kidney or cardiac involvement.

We also see it in both male and female patients with Fabry disease, so it's often misdiagnosed or undiagnosed for years because the knowledge of our clinicians that stroke is-- cryptogenic stroke or early onset stroke can be a marker of a brain disease. And this is important because our patients need to have appropriate monitoring and secondary stroke prevention.

If we look at a registry of Fabry patients, up to 7% of men and 4% of women will have had stroke as part of their Fabry disease with a median age of onset between 39 and 46 years old. So this is should then add to the differential diagnosis of neurologists and stroke neurologists to include Fabry disease.

It is important for neurologists to understand that stroke could be the heralding symptom of Fabry disease. So if we look at a study of 721 patients who had cryptic stroke between ages 18 and 55, 5% of men and 3% of women were later confirmed to have Fabry. So this is an important point to add to your differential diagnosis in young stroke patients.