

SPEAKER: So one key concept we need to be aware of is the natural history of Fabry Disease when related to target organ injury-- when related to the kidney injury, heart disease, and certain nervous system diseases.

First concept, this depends on the severity of the mutation. So let's go, first, for classic Fabry Disease, severe mutations. The individuals who have these childhood symptoms of pain, neuropathic pain, loss of sweat, angiokeratoma. In these individuals, in classic individuals, the first target organ to be injured is the kidney. In childhood, you have pathological albuminuria. Again, others, you have overt proteinuria. Age 40, you have the need to dialysis.

The heart disease develops a little bit later. So left ventricular hypertrophy is usually absent below the age of 20. So left ventricular hypertrophy will develop along the development of overt proteinuria. However, heart events-- so arrhythmia that require intervention, heart failure-- so the fact that the patient has heart symptoms, has a heart event, has a cardiac event, that will occur after the first kidney event.

So the mean age at dialysis is around 40 for males and for females, but the mean age at the first cardiac event is 45 for classic males and 55 for classic females. So in the natural history, kidney comes first, and the heart comes after the kidney involvement.

What about central nervous system involvement? What about the stroke, transient ischemic attacks? Well, this may occur at any point in the disease. So they may occur before overt kidney or cardiac disease or after. They usually occur after, but they are much less common than kidney or cardiac involvement. So the natural history, the place of natural history is not so clearly established.

Can some patients have heart disease before kidney involvement? Well, there is a huge variability, a individual variability, as for any disease. But the time cost, the most frequent time cost, kidney comes first, heart comes second.

This is for classic males, for individuals with classic Fabry Disease. What about females? Females with classic disease frequently have milder kidney involvement. So around 5% to 10% will develop this severe kidney disease and get into dialysis as early as males, and dialysis preceding the cardiac event. But a larger proportion of females, they have mild kidney disease, and the first manifestation will be cardiac disease later in life.

What about later-onset mutations? What about less severe mutations? In less severe mutations, the main organ involvement relates to the heart. So there is usually no severe kidney involvement. They may develop proteinuria at age 50, 60. They usually do not need dialysis ever, but they die from heart disease at age 60 or 70-- arrhythmia, heart failure, et cetera. And they may have central nervous system involvement. They may have a stroke preceding or after their heart involvement.