THAOS®
Transthyretin Amyloidosis Outcomes Survey

PATIENT FACTSHEET

Disease background – TTR amyloidosis

TTR amyloidosis is an inherited disease that occurs due to an abnormality in a gene called, transthyretin (often abbreviated to TTR).[1] It is irreversible, progressive neurodegenerative disease, which can be fatal within 10 years of the first symptoms appearing.[2]

TTR amyloidosis is a rare disease thought to affect approximately 10,000 people around the world, although definitive worldwide epidemiology data are lacking. There are some countries where families of people with this disorder are more likely to be found and these areas are known as 'endemic' regions; examples include parts of Portugal, Sweden and Japan. The condition is also seen in other areas of the world in 'non-endemic' regions such as Europe, South America and the United States.[2]

Transthyretin

TTR amyloidosis develops when the transthyretin protein forms incorrectly due to a mutation (fault) in the *TTR* gene.[1]

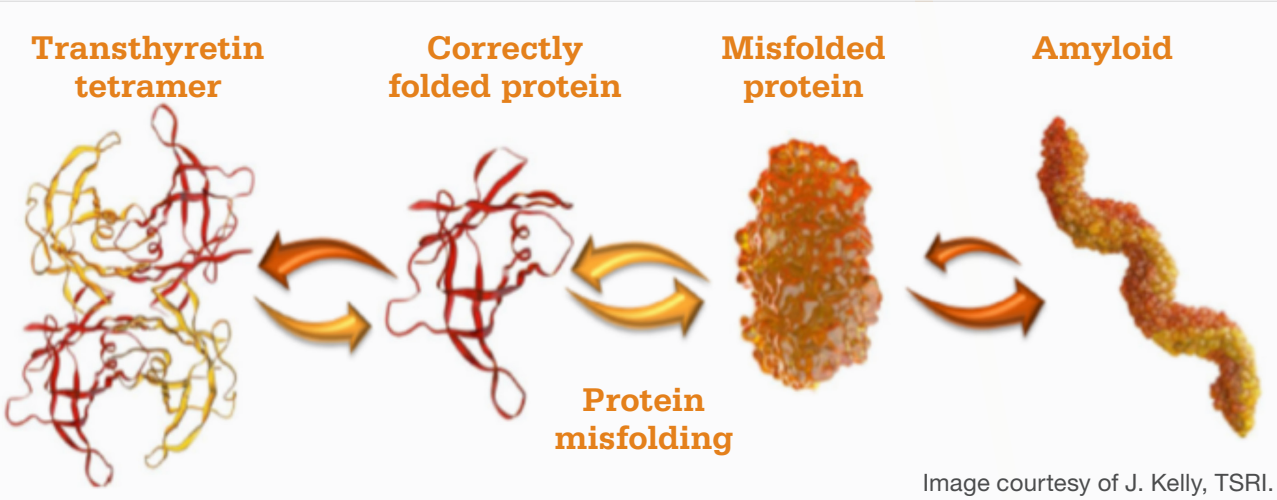

Image courtesy of J. Kelly, TSRI.

Transthyretin is a protein made by the liver that is used to carry thyroxin and retinol (vitamin A) around the body to where these molecules are needed.[1,3] The shape of the transthyretin protein (the tetramer shown in the figure) is critical to its ability to carry out the task it has been created to do. If the shape of the protein changes or forms incorrectly, it may not be able to perform its role as intended.

The incorrectly formed protein can then build up in the tissue and around the organs in the body. This build-up of protein is known as amyloid deposition and these amyloid deposits can interfere with the normal functioning of the body's nerves and organs.[4]

The location of these amyloid deposits determines the main symptoms that will develop over time. The deposits can form in the peripheral nerves, which carry information to and from the brain and spinal cord to other parts of the body, and also the kidneys, heart, digestive system, and in the eyes.[1,4]

The impact of genetics

In TTR amyloidosis, the TTR protein forms abnormally because of an inherited mutation in the gene for this protein.[2]

There are over 100 different mutations that may be present in the TTR gene.[2] Not everyone who carries a mutation in the *TTR* gene will develop this disease but the reason why these people don't develop the disease is not known.[4]

Amyloidosis

TTR amyloidosis will fall into one of two types, although a large number of patients will experience symptoms of both:[2]

- TTR familial amyloid polyneuropathy, which mainly affects the peripheral nerves
- TTR familial amyloid cardiomyopathy, which mainly affects the heart

TTR familial amyloid polyneuropathy[2]

In TTR familial amyloid polyneuropathy (TTR-FAP), amyloid is primarily deposited in the peripheral nerves resulting in a condition known as polyneuropathy. This amyloid deposition causes a malfunction in the peripheral nerves, which carry information to and from the brain and spinal cord to other parts of the body such as the feet/legs and hand/arms. As these nerves are responsible for a person's ability to sense pain and temperature, as well as the ability to move one's muscles, these are the sensations that are lost because of amyloid deposits.[1,4]

In early-onset TTR-FAP, age of symptom onset is typically in the 30s, while in late-onset TTR-FAP symptom onset usually occurs in the 50s. The main feature of this type of TTR amyloidosis is pain or lack of sensation in the feet and legs.[3,5]

Ultimately this pain and lack of sensation travels up the legs before affecting the arms. As the disease progresses, patients will also begin to lose muscle strength and function in their legs and arms. Other parts of the nervous system can also be affected resulting in changes in the gastrointestinal system leading to diarrhea and/or constipation, problems urinating, and sexual dysfunction in men.[2]

TTR familial amyloid cardiomyopathy[1]

In TTR familial amyloid cardiomyopathy (TTR-CM), amyloid is primarily deposited in and around the heart. As this deposition continues, the heart muscle weakens, and the ability of the heart to pump blood around the body is affected. This can ultimately lead to heart failure.[2]

Symptoms commonly seen with TTR-CM are similar to those of heart failure, such as shortness of breath, fainting, tiredness and swelling in the lower legs/ankles due to the accumulation of fluid and the heart's inability to pump this around the body. In addition, TTR-CM may present with the signs and symptoms commonly associated with TTR-FAP, such as lack of pain and temperature sensation in the feet and legs, and stomach disturbances such as constipation and diarrhea.[2]

Prognosis

TTR amyloidosis is a progressive illness and the symptoms will eventually worsen over time. It is important to remember that the prognosis and symptoms of amyloidosis are different in everyone and can vary depending of the type of mutation a patient has.[1,6]

Please talk to your physician about your prognosis and the best way of controlling your symptoms.

For more detailed information on TTR amyloidosis, please visit www.ttrfapconnection.com

References

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