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Understanding This Rare Disease Called ATTR Amyloidosis

Thursday, January 28, 2021

You probably know someone with heart failure, gastrointestinal (GI) problems, or nerve pain. They are all common problems. But in rare cases, these could be caused by a life-threatening disease called *transthyretin amyloidosis* (or ATTR amyloidosis, for short).

Although ATTR amyloidosis is currently considered rare, there is growing evidence that it may be more common than once thought. Some experts believe that the disease is underdiagnosed due to a lack of awareness. ATTR amyloidosis is not easily diagnosed because its symptoms are similar to those of other, more common conditions.

What is ATTR amyloidosis?

Amyloidosis refers to a disease caused by a buildup of abnormal proteins, called *amyloid,* in the body's organs and peripheral nerves. These protein deposits can cause organs to not function properly and lead to nerve damage. Often, symptoms of amyloidosis are not specific or may seem similar to symptoms caused by other conditions.

ATTR amyloidosis is caused by a protein called transthyretin, or TTR, that changes its shape and forms into fibrous clumps. These clumps of misshapen protein are deposited into various organs and peripheral nerves, which can cause them to function abnormally.

ATTR amyloidosis can be caused in 2 different ways. It can be hereditary, meaning passed from a person's mother or father. In the hereditary form, mutations in the *TTR* gene are thought to cause the protein to destabilize and to change its shape. Or, it can be related to destabilization of TTR due to aging.

Effects on the heart and nerves

While there are various forms of amyloidosis, ATTR amyloidosis most commonly affects the heart and/or the nerves, though other organs may also be affected.

ATTR cardiomyopathy (ATTR-CM). ATTR-CM primarily affects the heart, as clumps of amyloid are deposited in the heart tissue. This affects the heart's ability to function properly. Symptoms are often similar to those of other heart conditions such as heart failure and enlarged heart. They also may include:

- Fatigue.
- Leg, ankle, or abdominal swelling.
- Shortness of breath with activity.
- Sudden drop in blood pressure upon standing.
- Trouble breathing when laying down.
- Irregular heart beat (arrhythmia).

This condition may be inherited from a parent but may also occur in people without a family history of the disease. People with the hereditary form typically experience symptoms in their 50s or 60s. Some people, however, may not have symptoms until their 70s, or even later. The non-inherited form is more common in Caucasian men over age 65.

ATTR amyloidosis polyneuropathy (ATTR-PN). ATTR-PN is a disease that primarily affects the peripheral nerves and is caused by mutations in the *TTR* gene passed from an affected mother or father. The buildup of amyloid happens primarily in the nerves that detect touch, pain, and heat. It can cause a loss of sensation, tingling, numbness, or pain in the hands and feet (also known as peripheral neuropathy). People with this disease also often have damage to the autonomic nervous system (nerves that affect how organs work), digestive tract, and other vital organs, sometimes including the heart. People with ATTR-PN may experience symptoms such as:

- Diarrhea, constipation, or both at different times.
- Nausea, vomiting.
- Loss of appetite.
- Sexual dysfunction.
- Muscle weakness.
- Various eye problems.
- Sudden drop in blood pressure upon standing.
- Carpal tunnel syndrome.

Symptoms of ATTR-PN generally occur in adulthood at widely varying ages, as early as in the 20s or as late as in the 70s or later. This condition affects both men and women.

What's new for people with ATTR amyloidosis, and what can you do if you think you or someone you know may have it?

It is a promising time for people with ATTR amyloidosis. Treatments for certain patients with ATTR amyloidosis have become available, and other treatments are being investigated in clinical trials. Ask your healthcare provider. For more information about available clinical trials for amyloidosis, go to clinicaltrials.gov.

It is important to get an accurate diagnosis as soon as possible, because treatments may be more successful if started early. If you suspect someone in your family may have had ATTR amyloidosis, or if you suspect you may suffer from symptoms of this disease, speak with your healthcare provider. A number of tests (such as a noninvasive imaging test or tissue biopsy and genetic testing) may need to be performed in order to determine a correct diagnosis. It's also important to work with a healthcare team who specializes in diagnosing amyloidosis.

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Originally published, Thursday, January 28, 2021