HEREDITARY AMYLOIDOSIS IN TWO ROMANIAN FAMILIES: A NEW TRANSTHYRETIN VARIANTA (GLU 54 GLN)

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Transthyretin (TTR) amyloidosis is the most prevalent type of hereditary systemic amyloidosis and results from a mutation in the TTR gene. Over 100 such alterations have been described and now we wish to report yet another variation detected in two unrelated Romanian individuals with TTR amyloidosis. The first patient is a 54-year-old man with a progressive peripheral sensory motor polyneuropathy, autonomic dysfunction, and a restrictive cardiomyopathy. At 45, he had the onset of orthostatic hypotension, paresthesias of the lower extremities, dysphagia, and chronic diarrhea. Subsequently, there was rapidly progressive cardiac dysfunction, heart failure and pulmonary hypertension. Notably, his father was diagnosed with idiopathic cardiomyopathy at age 50 and died few years latter.

The second patient is a 46- year- old woman who presented with restrictive cardiomyopathy and a bilateral carpal tunnel syndrome. At age 40 she developed symptoms of heart disease and also had a carpal tunnel syndrome treated surgically. Her father died at age 50 after a long standing history of cardiomyopathy and severe sensori-motor neuropathy.

In both cases, biopsies of abdominal subcutaneous fat and rectum showed after Congo red staining birefringent deposits. Direct genomic sequencing of the full TTR gene coding region indicated G- to - C transversion at the first base position in codon 54 (GAG -> CAG) which leads to the heterozygous mutation Glu54Gln in exon 3 of the gene. Mass spectrometric analysis of TTR immunoprecipitated from serum showed no molecular mass difference between wild type and TTR variant.

To the best of our knowledge these are the first reported cases of E54Q -associated TTR amyloidosis.

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