Transthyretin cardiac amyloidosis in the elderly patient: always a wild type?

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Background: Transthyretin amyloidosis (ATTR) exists in two forms: a genetic form transmitted by autosomal dominant inheritance (ATTRv) and a wild type form (ATTRwt). Clinically, the hereditary form tends to have an early onset in adulthood and it is characterized by a particular tropism for nervous as well as cardiac tissue. In contrast, the "wild type" form has a later onset with major cardiac involvement and neurological manifestations usually limited to carpal tunnel syndrome (1).

Methods and results: in our centre, from January to October 2022, 20 patients older than 75 years received a diagnosis of cardiac ATTR (73% male, 27% female, mean age 83±5). In all patients, blood tests showed a significant and stable increase in the values of troponin Ths (0.070±0.074 ng/mL) and NT-proBNP (1533±1204 pg/ml), with the absence of a monoclonal component in the blood and urine, and miocardial bisphosphonate scintigraphy positive grade 2/3. All patients showed absence of peripheral neuropathy with the presence of carpal tunnel syndrome in 9 cases. Before starting therapy with Tafamidis all patients underwent genetic testing by amplification of exons 2, 3 and 4 of the TTR gene with subsequent sequencing. Unexpectedly, in 3 elderly male patients (15%) the genetic test resulted positive with 3 different mutations of pathogenetic significance (Val50Met; Ile88Leu; Val142Ile). First-degree relatives (10 consanguineous, average age 49±12 years) agreed to be subjected to genetic screening; of these 4 (1 male and 3 females, age 47±8 years) were positive for the corresponding mutation and underwent echocardiogram, MRI and myocardial scintigraphy. All of these tests were normal and they were included in an annual follow-up protocol at the to identify an early manifestation of the disease.

Conclusions: our experience shows that 15% of patients older than 75 years and diagnosed with cardiac ATTR may be affected by a genetic form. Making genetic diagnosis in this context is particularly important for screening family members: current therapies are in fact much more effective if started early before organ damage can occur (2).