Transthyretin Familial Amyloid Neuropathy: the issue of early diagnosis

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BACKGROUND: Familial amyloid polyneuropathy (FAP) is a rare autosomal dominant inherited disease due to mutations of the transthyretin (*TTR*) gene with more than 130 different mutations identified. In Italy, nonendemic area FAP is associated with an important variability of phenotype, late onset and low-penetrance. The clinical presentation is a sensory-motor polyneuropathy, with Autonomic System, heart and gastro-intestinal involvement.

METHODS: We evaluated about 400 patients with radiculopathy, neuropathy or muscle pathologies at the Neuromuscular Clinic of the Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DiNOGMI) of University of Genoa from October 2014 to March 2015.

We selected 30 patients affected by sensorimotor polyneuropathy predominantly axonal or mixed axonal-demyelinating where the medical history and the paraclinical investigations could not allow a definite etiologic diagnosis.

Twenty-five patients were subjected to the genetic test for mutations in the TTR gene. In particular, we found in a 74 years old patient the Phe64Leu point mutation, diagnostic for TTR-FAP.

TTR-FAP, in our small study, accounted for 3,3% of the cases of previously undiagnosed neuropathies

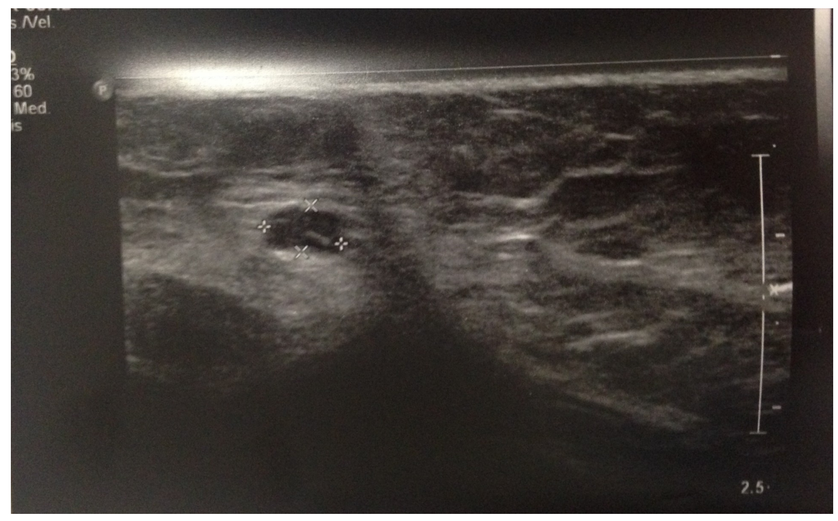
Unfortunately this patient has already severe neuropathy and the therapeutic options available do not allow a regression of the neuropathy, but only the stabilization of tetrameric protein in order to prevent further amyloid deposition.

CONCLUSION: In order to identify the early signs of TTR-FAP neuropathy, we decide to apply a follow-up protocol in the asymptomatic carriers of TTR mutation.

This protocol should be performed every year:

- ✓ neurological examination with NIS and Norfolk scales
  nerve echography
- ✓heart rate variability with deep breathing for the autonomic system and heart examination (ECG, proBNT, troponin T, cardiac echography)
- ✓renal impairment evaluation (proteinuria, creatinine clearance/cystatin c clearance)

and ocular analysis every two years.



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