Characteristics of Patients With p.V50M and p.T80A Mutations Associated With Hereditary Transthyretin Amyloidosis

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Introduction: Hereditary transthyretin amyloidosis (hATTR or ATTRv [variant]) is a progressive, fatal disease caused by mutations in the transthyretin gene (TTR) that result in multisystem dysfunction, including polyneuropathy and cardiomyopathy. The p.V50M and p.T80A mutations are among the most common TTR mutations in European patients.

Methods: This analysis utilised data from patients enrolled in hATTR Compass, a genetic testing programme offered in the United States and Canada for patients suspected of having hATTR with polyneuropathy or a family history of hATTR. Next-generation sequencing was performed using gene panels for neuromuscular and cardiac disorders.

Results: Of 79 patients studied, 37 had the p.V50M mutation and 42 had the p.T80A mutation. The average age at testing for p.V50M and p.T80A patients was 56 and 52 years, respectively; white ethnicity was the most common (65% for p.V50M and 95% for p.T80A). Of the p.V50M and p.T80A patients in the genetic testing programme, cardiologists referred 27% and 33% and neurologists referred 38% and 26%, respectively. Common symptoms/manifestations for the p.V50M and p.T80A patients included heart disease (27% and 31%); bilateral carpal tunnel syndrome (8% and 17%); and sensory (35% and 29%), motor (19% and 12%), and autonomic dysfunction (22% and 14%).

Conclusion: Diagnosis of hATTR is challenging because it can present similarly to other diseases, but hATTR commonly presents with both polyneuropathy and cardiomyopathy. It is critical that clinicians recognise symptoms of hATTR and refer patients for genetic testing to facilitate diagnosis and initiate diseasemodifying therapy for this fatal disease.