

TTR-FAP: diagnosis of familial and sporadic cases

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Transthyretin-related familial amyloid polyneuropathy (TTR-FAP) is a rare, autosomal-dominant, adult-onset, systemic disease caused by mutations in the transthyretin (TTR) gene that lead the TTR protein to misfold and deposit as insoluble amyloid fibrils in peripheral and autonomic nerves, the heart, gastrointestinal tract, kidneys, eyes, and connective tissue of the transverse carpal ligament.

Initial clinical symptoms may appear between the second and ninth decade of life and, without treatment, TTR-FAP leads to death on average within 10 years of symptom onset.

The disease can be difficult to recognize due to extreme phenotypic heterogeneity and nonspecific clinical symptoms. Because of the late onset and low penetrance of TTR mutations in some areas, TTR FAP can present as sporadic cases leading to frequent misdiagnosis. As a result of such misdiagnoses, definitive diagnosis can be delayed for as much as 2–6 years, postponing adequate management and genetic counselling and leading to possible irreversible damage.