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Very Late-onset Friedreich ataxia: later than life expectancy?

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- Dr. Pierre Arnold reports no disclosures.
- Dr. Vincent Alvarez reports no disclosures.

Conflict of Interest

None declared.

Friedreich ataxia (FA) is an autosomal-recessive hereditary ataxia with a prevalence of around 1 case per 30'000. It is a severely debilitating disease characterized by progressive gait and limb ataxia, dysarthria, lower-limb areflexia, muscular weakness and pyramidal signs, and is due to GAA triplet expansion in the frataxin (*FXN*) gene located on chromosome 9q13 [1]. Patients usually begin the disorder at puberty or before the age of 25 years in most studies, but rare cases of 'Late-Onset Friedreich ataxia' (LOFA) have been described. LOFA patients were recognized to have a median age of onset of 28.8 years (range of 25.5 to 48), have a milder phenotype and often retained lower limb reflexes [2,3]. Very Late-Onset Friedreich ataxia (VLOFA) has also been reported [4,5], with the first manifestations appearing in the seventies. Here we report an 82 year-old lady who presented with balance difficulties that led to some loss of independence. Symptoms began at about age 80 with subsequent mild dysarthria. She denied any similar familial history, rending autosomal dominant disease unlikely. On examination, cognition was normal, but she had hypometric ocular saccades, dysarthria, generally brisk deep tendon reflexes except for bilateral absent ankle jerks and a bilateral Babinski sign. There was also reduced ability for rapid, alternating motor tasks. There was no loss of sensations, including proprioception. The patient also showed important gait ataxia. The Scale for the Assessment and Rating of Ataxia (SARA) was rated 15 (gait: 3; stance: 1; sitting: 1; speech disturbance: 2; finger chase: 1; nose-finger test: 2; fast altering hand movements: 2; heel-sheen slide: 3). There was no pes cavus, scoliosis, deafness or diabetes. The nerve conduction study was normal, including amplitude of the sural nerve action potentials. Cardiac echography and EKG were normal.

FA was considered as a diagnosis based on ataxia with a bilateral Babinski sign and absent Achilles reflexes and normal blood vitamin E levels with undetectable serum antinuclear auto-antibodies (against Hu, Yo, Ma2, CV2/CRMP5, Ri, Tr, and GAD). The diagnosis was confirmed when an unstable GAA triplet expansion was demonstrated on both alleles of the *FXN* gene, with 170 and 1300 tri-nucleotides respectively. The small GAA expansion probably explains why the patient developed FA in her eighties, as other studies suggest a correlation between the size of the expanded tri-nucleotide repeats and severity of the disease and an inverse correlation with the age of onset [6,7].

To our knowledge (excluding one possible but not proven case) [8], this lady represents the highest age of onset for a diagnosed FA patient. Even though FA is typically encountered in young patients, this report confirms that it cannot be excluded based on the advanced age of the patient, and should remain a possible differential diagnosis of older patients with ataxia, along with other genetic causes, such as SCA6 [9].

Author's Roles:

1. Vincent Alvarez : Author of the first draft
2. Pierre Arnold : Performed investigation critical reviewing,
3. Thierry Kuntzer : Critical reviewing

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