NOVEL SETX MUTATION CAUSING AOA2

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Introduction: Ataxia with oculomotor apraxia type 2 (AOA2) is the second most common autosomal recessive inherited ataxia in European population. This early onset, slowly progressive disease is characterized by cerebellar symptoms, oculomotor apraxia, axonal sensorimotor neuropathy, cognitive impairment and other neurological features including pyramidal symptoms, head tremor, dystonia and chorea. Typical laboratory finding is elevated serum alpha-fetoprotein (AFP). Brain MRI studies nearly all the time show cerebellar atrophy mainly in the vermis. The genetic cause of AOA2 is a mutated SETX gene on chromosome 9q34, which encodes senataxin, a nuclear protein has DNA/RNA helicase activity and possibly plays role in DNA repair and RNA processing.
Objective: In this paper, we document one case with a new SETX mutation (c.502:CT) combined with a large SETX deletion (including exon 11-15) causing ataxia with oculomotor apraxia type 2 (AOA2).
Methods: The patient had a detailed neurological history and examination performed. Head MRI, biochemical studies and genetic analysis was obtained.
Results: First symptoms appeared at age 25 with deteriorating dexterity, gait instability and dizziness. The diagnostic work-up found dysarthria, extraocular muscle dysfunction, smooth ataxia in all four limbs and trunk and mild pyramidal symptoms with elevated AFP levels and cerebellar atrophy on the MRI. Family history was unremarkable. The diagnosis of AOA2 was confirmed by genetic testing.
Conclusions: We delineate a new SETX gene missense mutation, which when combined with a heavy SETX deletion results in AOA2. The clinical, laboratory, radiographic and genetical testing are described.
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